THE EFFECTIVENESS OF STRUCTURED FOOD PATTERN ADVICE FOR ACHIEVEMENT OF MACRONUTRIENT TARGETS IN NUTRITION INTERVENTION

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DECLARATION

I hereby declare that this thesis, submitted in fulfilment of the requirements for the award of Doctor of Philosophy, in the Department of Biomedical Science, University of Wollongong, is my own work unless otherwise referenced or acknowledged. This document has not been submitted in whole, or in part, for qualifications at any other academic institution.

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Lynda Jacqueline Gillen

14th April 2005

DEDICATION

To my parents, Mavis (deceased) and Jack an inspiration still at 91 years of age,

to my second mum Joan,

my sisters Jeanette, Helen and Tracey,

and to my children David, Todd, Laraine, Brant, Jarryd and Adam,

and close friends Rose, Alan, Leonie, Paul, Barbara, Pat and Keely and Kay

for their continued support

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LIST OF ABBREVIATIONS

%E	Percentage of energy
ADA	American Diabetes Association
ADIPS	Australasian Diabetes in Pregnancy Society
AHA	American Heart Association
ALA	Alpha-linolenic acid
ANOVA	Analysis of variance
APD	Accredited Practicing Dietitian
AusNut	Australian nutrient tables
BMI	Body mass index
BMR	Basal metabolic rate
CHD	Coronary heart disease
CHO	Carbohydrate
CVD	Cardiovascular disease
DASH	Dietary Approaches to Stop Hypertension
DH	Diet history
DHA	Docosahexaenoic acid
EE	Energy expenditure
EE_{est}	Estimated energy expenditure
EI_{rep}	Reported energy intake
EPA	Eiocosahexaenoic acid

FAO	Food Authority Organization
FPG	Fasting plasma glucose
FR	Food record
GDM	Gestational diabetes mellitus
GI	Glycaemic Index
HDL-C	High density lipoprotein cholesterol
IGT	Impaired glucose tolerance
ISSFAL	International Society for the Study of Fatty Acids and Lipids
KANWU	Kuopio, Aahrus, Naples, Wollongong, Uppsala
kcal	Kilocalorie
kJ	Kilojoule
Kg	Kilogram
L	Litre
LDL-C	Low density lipoprotein cholesterol
LCn-3	Long chain omega-3 fatty acid
MNT	Medical Nutrition Therapy
mmol	Millimoles
MUFA	Monounsaturated fatty acid
n-3	Omega-3
n-6	Omega-6
OGTT	Oral glucose tolerance test
P	Confidence value

PAL	Physical activity level
P:S	Polyunsaturated: saturated fatty acid ratio
PUFA	Polyunsaturated fatty acid
R	Correlation coefficient
RBC	Red blood cell
SD	Standard deviation
SEM	Standard error of the mean
SFA	Saturated fatty acid
T2DM	Type 2 diabetes mellitus
Total-C	Total cholesterol
USDA	United States Department of Agriculture
VLDL-C	Very low density lipoprotein cholesterol
WHO	World Health Organization

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ABSTRACT

Dietary advice to individuals in Medical Nutrition Therapy for the prevention and treatment of disease should be based on the best available evidence. A review of the evidence identifies appropriate nutrients on which to base advice. However, evidence to support the application of advice for the achievement of nutrient targets in free-living individuals has not been adequately determined. In this doctoral program the hypothesis tested was that structured advice based on the pattern of intake from food group sources of required nutrients will result in better achievement of dietary targets and thereby clinical outcomes than advice based on existing core food guides.

In developing a more comprehensive food guidance system, nutritional therapy for diabetes treatment provides an appropriate example in which individual macronutrients and the type of fat are targets of advice. A cross-sectional survey of the food habits of a sample of women with Gestational Diabetes Mellitus was conducted to confirm the relevance of food patterns to specific clinical outcomes, in this case, glucose tolerance. Secondly, foods commonly consumed by these women enabled the identification of food groups likely to impact on macronutrient and fat profiles within the diet. Subsequent determination of a total diet model demonstrated that a structured approach to dietary advice relating to nine food groups (vegetables, starch, fruit, milk, soymilk, meat, oily fish/soybeans, monounsaturated and polyunsaturated fats) for the identification of sources of saturated and unsaturated fats would achieve nutritional adequacy and targets for

energy and individual macronutrients with minimal variation. This then formed the basis of individualised advice in dietary intervention trials.

Applying the newly developed advice system in an intervention trial demonstrated its feasibility in women with Gestational Diabetes Mellitus. Compared with a similar group receiving standardised low fat advice, 80% achieved saturated and polyunsaturated fat targets compared with nil in the standard intervention group, without detrimental changes to the overall macronutrient profile.

The clinical effectiveness of the advice system was again demonstrated in a second trial. In this study men and women with Type 2 Diabetes Mellitus followed two alternative patterns of advice based on the newly developed food guidance system for six months. In these two groups respectively, 79% and 100% of subjects, achieved targeted proportions of total polyunsaturated fat compared to 25% in a control group ($p<0.05$). In addition, greater improvements were achieved for HDL-cholesterol (+18% and +21% compared to +13% control, $p<0.05$) and triglyceride levels (-12% and -11% compared to -2% control).

In summary, this thesis has outlined the development and evaluation of an advice system to support nutrition intervention in people with diabetes. Individualised advice based on a structured food pattern identifying food group sources of target nutrients was both feasible to implement and effective in practice. The application of this knowledge will help support nutrition intervention research as well as provide an evidence-based approach to Medical Nutrition Therapy.

CHAPTER 1 INTRODUCTION

1.1 Evidence-based practice in nutrition intervention

This thesis, by detailing the development and evaluation of an advice system for nutrition intervention, supports current philosophical concepts relating to evidence-based medicine. Evidence-based medicine involves the specific use of the best evidence currently available to guide decision-making with regard to individual patient care [1]. In practice, this means integrating clinical expertise with evidence from clinically relevant and systematic research. It is generally accepted that the principles of evidence-based medicine apply to all areas of clinical practice, including the field of nutrition and dietetics [2]. Thus, the specific application of clinical and nutrition knowledge in the treatment of disease is known as Medical Nutrition Therapy (MNT) [3].

This knowledge refers to a hierarchy of research evidence in both animals and humans demonstrating direct causal relationships and indirect effects between specific nutrients and disease and/or disease factors [4]. The randomised controlled trial (RCT), the highest level of research evidence, confirms the specific application of this knowledge for achievement of nutrient targets and substantiation of benefit in terms of health-related clinical outcomes.

A systematic review of the research literature and other clinically relevant sources provides a set of evidence-based recommendations, defining a framework that

supports the quality of clinical judgments and facilitates individualised patient care rather than a single treatment for all[5].

Whilst individualised advice is fundamental to the principles of evidence-based practice, delivery in a scientific and effective manner with measured outcomes is also required[3]. The quality and specific blend of nutritional evidence from a mixture of scientific knowledge, clinical experience and expert consensus, however, has not always been certain. Consequently, the application of the principles of evidence-based nutrition has necessitated changes in clinical approaches and the need for RCTs to provide evidence to support practice.

Nutrition therapy for diabetes, for example, has long been considered the 'cornerstone' of treatment. However, the 'ideal' nutrition prescription that previously applied to all diabetes patients has been replaced with an emphasis on health care provider and individual patient goals[3]. The change is largely due to the position of diabetes in the research literature as one of a cluster of metabolic abnormalities collectively known as the Metabolic Syndrome[6, 7]. Hence, the traditional focus on glycaemic control has shifted to a broader focus on metabolic control[8], where improvements in overweight, blood pressure, blood glucose and lipid levels, and lipoprotein profile are all aimed at the prevention or reduction in risk of diabetes- and vascular disease-related complications.

For the prevention and management of diabetes and its complications, the American Diabetes Association (ADA) incorporates into its guidelines[8] dietary recommendations from relevant US organizations, such as US Department of

Agriculture (Dietary Guidelines for Americans), American Heart Association (AHA), and National Cholesterol Education Program, and suggests that advice based on food patterns provides a practical approach for the achievement of health benefits. A total diet approach is recommended, where all foods fit into a healthy diet [8, 9]. However, the bulk of research evidence on metabolic control supports attention to specific proportions of different types of dietary fat [10]. Where reduction in the amount of saturated fat (SFA) is required, replacement with dietary polyunsaturated fat (PUFA) is indicated, with the greatest benefits from increased omega-3 (n-3) and reduced omega-6 (n-6): n3 ratio. The guidelines reflect this evidence, recommending saturated and polyunsaturated fat in the diet as specific percentages of total energy intake [8] and specific PUFA: SFA (P:S) and n-6: n-3 ratios [11]. However, the application of advice for the achievement of recommended fat proportions has not been well documented in intervention trials to support this evolution in practice. Furthermore, few definitive RCTs have been conducted in people with diabetes to confirm the effects of specific dietary interventions [10].

To assist the specific application of nutrition advice under free-living conditions, food guidance systems enable the conversion of theoretical nutrient targets into practical advice on foods under free-living conditions. Current advice for diabetes treatment draws on a variety of advice systems, ranging from carbohydrate (CHO)-counting systems [12], which focus almost exclusively on CHO-rich foods, to core food guide classifications [13, 14] and exchange lists for meal planning [15], which emphasize CHO-rich foods and high CHO diets as the preferred pattern of intake [16]. Few, however, have reported their methodological basis [17] or evaluated their

effectiveness in producing desired outcomes [18]. Their adequacy for the achievement of individual fat proportions and subsequent clinical benefit, therefore, is presently unknown.

To substantiate the benefits of dietary intervention, structured methods and proven assessments apply. A systematic framework for advice would support the practical evaluation of nutrition interventions in terms of specific health outcomes and enable individual nutrients and foods to be tested as part of the overall diet, while changes in biomarkers of dietary intake would confirm the results.

For strategies to control/change dietary intakes, reference is made to previous research. Large-scale lifestyle intervention trials demonstrating the effectiveness of nutritional advice based on specific targets for total energy, fat and saturated fat intakes in order to reduce the incidence of diabetes and related complications [19-21]. In terms of existing low fat strategies, however, achievement of relative amounts of polyunsaturated fat appears to be problematic [22]. For example, where reductions in total fat intake in response to general low fat advice may unintentionally reduce all types of dietary fat [23]. Alternatively, adjunct advice for increasing unsaturated fat intakes mainly focuses on exchangeable edible fat portions [24], with limited impact on individual fat ratios within the overall diet, but may instead result in higher energy and n-6 PUFA intakes with subsequent loss of benefit [25]. Incorporation of all dietary fat sources has greater potential for achievement of overall fat proportions and is more consistent with guideline recommendations for a total diet food pattern approach to advice [8].

To effectively guide advice for the achievement of specific nutrient targets, food group development and construction of an overall pattern of intake to incorporate sources of the required nutrients provides a framework on which to base individualised advice. In the Dietary Approaches to Stop Hypertension (DASH) trial, foods from 13 individual food groups were provided as sources of specific nutrients to hypertensive patients to demonstrate the effectiveness of food pattern advice for the achievement of focused clinical outcomes [26]. In this case, targeting a broarder range of nutrients for specific clinical outcomes required reference to a greater number of food groups than currently available from core food groupings aimed at general nutritional adequacy. In the case of diabetes, individual fat types are the specific nutrients targeted. Food pattern analyses demonstrate the way in which specific proportions of individual fats are achieved in practice, through major shifts in intakes across several food groups [23]. The application of this knowledge to the development of an advice system and its implementation in free-living individuals in an intervention trial to test achievement of specific nutrient variables and subsequent clinical benefit would provide a methodology for nutrient intervention and evidence for practice.

The aim of this research, therefore, was to develop a set of macronutrient-based food groups and to evaluate the effectiveness of advice based on their specific pattern of intake for the achievement of theoretical nutrient targets and thereby health benefits. Specifically, the thesis considers the application of advice in RCTs to free-living individuals with diabetes mellitus, targeting specific relative proportions of different types of dietary fat and subsequent improvements in

overweight, blood glucose and blood lipid levels. This would support evidence-based practice for nutrition intervention in MNT for diabetes and related conditions.

CHAPTER 2 LITERATURE REVIEW

This chapter reviews current research evidence and practices supporting nutrition intervention in the treatment of diabetes. It is divided into seven sections. The first (Section 2.1) describes diabetes and clinical features related to the Metabolic Syndrome as indicators of altered metabolism. The second (Section 2.2) is a systematic review of the literature in the context of a hierarchy of research evidence that supports specific macronutrients, in particular the type of fat in the diet, as targets for nutrition intervention and subsequent improvements in metabolism. A critical review follows (Section 2.3) in which current applications to direct nutrition intervention are assessed in terms of their support for the evidence-base. This includes an assessment of nutritional guidelines and food guidance systems for diabetes treatment. A look at previous approaches to nutrition intervention research (Section 2.4) assesses the feasibility of advice approaches in practice and reveals specific inadequacies for the achievement of macronutrient targets, particularly for the type of fat, and the relevance to assessments in substantiation research. Finally (Section 2.5), the inadequacies or gaps in the research and requirements for the adequate achievement of specific nutrient intakes are summarized, resulting in an hypothesis (Section 2.6) and subsequent aims (Section 2.7) for the provision of evidence to support practice that anchors this thesis.

2.1 Diabetes and Related Complications

2.1.1 Type 2 diabetes mellitus

Type 2 diabetes mellitus (T2DM) is one of a cluster of metabolic abnormalities (abdominal obesity, atherogenic dyslipidemia, hypertension, and glucose intolerance) referred to as the Metabolic Syndrome [6, 7]. Although the etiology of the Metabolic Syndrome is largely unknown, insulin resistance involving reduced glucose uptake and increased glucose and lipid outputs, has been identified as a common underlying pathophysiological defect [27]. T2DM is characterized by glucose intolerance (fasting plasma glucose (FPG) $\geq$7.0 mmol/l or 2-h post glucose load (2-h) $\geq$11.1 mmol/l and confirmed on another day) [28] and appears to be indicative of the state of insulin resistance rather than an absolute deficiency in insulin. Consequently, usual treatment does not require insulin and the condition is most often managed with dietary and general lifestyle modification alone or in combination with oral therapy [8, 28]. If alternative therapies become ineffective at maintaining blood glucose levels within an acceptable range, insulin therapy may then be required [28].

In Australia, the total prevalence of known and newly diagnosed T2DM among adults 25 years and over is 7.4%, half of whom are unaware they have the condition [29, 30]. These findings represent a more than doubling of the incidence of diabetes in Australia since a previous survey conducted in 1981 [31]. Similar surveys undertaken in the US reflect the Australian findings [32, 33]. The dramatic increase in diabetes over the past 20 years, estimated to be up from 300 000 to almost 1

million Australians in 2001 [34] represents a massive increase in the total health burden on Australians. Parallel rises in overweight and obesity [29] indicate a serious public health problem and present a major challenge for health professionals. The annual total costs of diabetes in Australia have been calculated at $1 billion and rising [35]. Diagnosed diabetes was the 7th leading cause of burden of disease (5.4%) in Australia in 1996 [36]. Considering the high prevalence of undiagnosed diabetes and subsequent failure to recognize diabetes as the underlying cause in many cases of cardiovascular disease (CVD) mortality and morbidity, these figures are likely to be huge underestimations of the true situation. International studies estimate a similar health burden where 4% of the population with diabetes can account for 12% of total health care costs [37].

In keeping with known associations with the Metabolic Syndrome, T2DM is considered both a disease and a risk factor for other diseases [28]. Glucose intolerance (diagnosed and undiagnosed) is a major independent risk factor for CVD [38-41], regardless of blood lipid levels, while elevated blood lipid levels are associated with increased risk of coronary heart disease (CHD) beyond that conferred by diabetes [42]. Macro-vascular disease is, therefore, a major cause of premature death and morbidity among people with glucose intolerance due to myocardial infarction, stroke and large vessel occlusive disease [43-46]. Major, irreversible, long-term micro-vascular disease complications include retinopathy and blindness, neuropathy and renal failure (dialysis/transplantation), foot ulcers and lower limb amputation, and erectile dysfunction [28, 47].

Approximately one third of people with Impaired Glucose Tolerance (IGT) (FPG <7.0 mmol/l and 2-h <11.1 mmol/l) [28] will go on to develop T2DM in their lifetime [48]. People with Impaired Fasting Glucose (IFG) (FPG ≥6.1 and <7.0 mmol/l or 2-h <7.8 mmol/l) [28] are also at increased risk [49], as are women first diagnosed with any degree of glucose intolerance during pregnancy, that is, with Gestational Diabetes Mellitus (GDM) [50]. Genetic influences are strong [51-53]: Aboriginal and Torres Strait Islanders [54, 55]; people with non-English speaking backgrounds [56, 57]; and those with a first degree relative with T2DM [58] are also at increased risk. There are also close associations between obesity and insulin resistance [59-61]: obesity in adult life [62, 63]; weight gain [64, 65]; duration of obesity [66-68]; and other clinical features of the Metabolic Syndrome (elevated lipid levels, CVD and hypertension) [69, 70]feature prominently and suggest environmental (behavioural) influences play a major role [71, 72]. Long term diet [25, 73] and physical inactivity are heavily implicated[74]. While physical activity is known to have a strong influence on insulin sensitivity [75, 76], dietary influences are much more complex with individual nutrients possibly exerting combined and separate effects, directly and indirectly via obesity [77].

2.1.2 Gestational diabetes mellitus

GDM identifies a subgroup of the diabetes population with demonstrated glucose intolerance first identified during pregnancy [78]. Normal pregnancy is associated with a reduced insulin sensitivity and increased insulin secretion [79]. While the former redirects nutrients to the fetus, the latter is thought to be an homeostatic response for maintaining relatively good blood glucose control despite the rising

insulin resistance of pregnancy. Whether greater insulin resistance [80] or reduced insulin secretary capacity or both [81] is common in all or some of these women is unclear, however, multiple defects in insulin action and impaired compensation for insulin resistance have both been reported and may represent the early detection of both chronic insulin resistance and beta cell dysfunction in pregnant women [82].

In the Illawarra region of Australia, the incidence of GDM has been reported at 7.2% of pregnant women [83], and may range from 1%-14% throughout the world [84, 85 86], with the highest prevalence in ethnic groups [87], making GDM one of the most common medical complications of pregnancy and hence a major medical concern.

Adverse perinatal outcomes include intra uterine death, maternal hypertensive disorders, fetal macrosomia (large-for-gestational age baby), premature delivery, caesarian section, and special care of the newborn [86]. Pregnant women have a continuum of perinatal risk related to rising maternal blood glucose levels [88]. Hence, primary management strategies are the prevention of adverse perinatal outcomes based on maintaining glycaemic control and nutrition therapy is considered the cornerstone of treatment. While post-partum glucose metabolism generally returns to normal, women with GDM are at increased risk of recurring GDM in a future pregnancy (35%) [89], and of developing T2DM in the following 5-10 years (up to 70%) [90], as well as obesity and T2DM in the offspring [86]. CVD and CHD risks are high in these women [91, 92], with endothelial dysfunction (an early marker of macro-vascular disease) and lipid abnormalities observed as early as the index pregnancy [93-95]. Women who develop T2DM have a four to five-fold increase

in CHD mortality rate compared with non-diabetic women, canceling any hormonal advantage over men [96, 97]. Hence, the diagnosis of GDM identifies women with a disturbed metabolism and is therefore a risk factor for T2DM and related complications.

While those at risk of GDM are readily identifiable (older, shorter, obese, multi-parous, of specific ethnicity, with a family history of diabetes and/or history of previous GDM) [98, 99], pregnant women without conventional risk factors also develop GDM. Although GDM is a little studied area of diabetes research, close associations with features of the Metabolic Syndrome suggest diet and physical activity are important [99].

In summary, Diabetes Mellitus clinically defines glucose abnormalities associated with insulin resistance and the Metabolic Syndrome. Total prevalence of diabetes and related conditions is increasing worldwide, adding substantially to the overall health burden. Diagnosis of diabetes is a risk factor for CVD and micro-vascular disease complications. Close associations with weight gain and obesity as well as parallel increases over the past 20 years indicate strong environmental (behavioural) influences, implicating dietary factors and reduced physical activity.

2.2 Evidence supporting macronutrient targets in nutrition intervention

Evidence for a relationship between diet and diabetes and associated features of the Metabolic Syndrome draws on a hierarchy of nutrition research [4] involving both animals and humans. To begin, the mechanistic relationships between nutrition

factors and IR have been well documented in feeding trials using animal models (in vitro and in vivo). Human studies involving dietary macronutrient manipulations, although relying on less direct observations of insulin sensitivity, for example measures of glucose and lipid metabolism, nevertheless support the findings in animal studies. Epidemiological studies, while not able to show direct causal relationships, provide valuable support for animal and human feeding trials by demonstrating possible associations between nutrient intakes and the development of disease and risk factors for disease, such as overweight and body fatness and glucose and insulin levels in free-living populations. The strongest level of evidence, however, comes from the RCT, where manipulations of nutrients in humans confirm the conclusions drawn from mechanistic and observational studies. This systematic hierarchical approach enables discrimination between different forms of research and allows a broad assessment of the available evidence and the identification of gaps in the research [4]. Further, the methods used in RCTs involving free-living individuals provide evidence for the application of research knowledge.

2.2.1 Dietary fat

Mechanistic Studies

Storlien et al report that the strongest evidence for a relationship between diet and clinical markers of insulin action relates to dietary fat intake [100]. Early in vitro and in vivo studies, mainly in rodents, demonstrated that high fat feeding results in impaired insulin action in both fat and muscle tissue [101, 102], the latter being the

major site of insulin stimulated glucose uptake. Compared to tissue from rats fed an equi-caloric high CHO diet, insulin resistant rats also show major increases in muscle triglyceride stores [103] and impaired glucose transport systems [104, 105], suggesting impaired glucose utilization, a relative reduction in metabolic rate and subsequent accumulation of body fat [106]. In vivo studies, involving chronic high fat versus high CHO feeding, also report a rapid deterioration in whole body insulin action in rodents consuming the high fat diets [107, 108].

Although these studies suggest a clear relationship between high fat feeding and insulin resistance, more recent research manipulating fat sub-types has provided further evidence that distinctions in the pattern of fatty acid consumption may be just as important [109, 110]. SFA intakes are associated with detrimental effects. While substitution with PUFA appears to have a neutral or protective effect against the processes that lead to obesity and insulin resistance [111], these effects appear via multiple control points [74], where PUFAs are more readily mobilized from adipose tissue, preferentially incorporated into lipid membranes, and more readily oxidized [112] compared to SFAs. PUFAs also appear to inhibit insulin-stimulated hepatic triglyceride secretion [113, 114], a major determinant of skeletal muscle fatty acid uptake, and a regulatory effect on gene expression, suppressing both lipid synthesis [115] and adipocyte differentiation [116]. Increased n-3 PUFA consumption has been shown to prevent insulin resistance [110] through a reduction in lipid stores and a relative increase in the percentage of n-3 fatty acids in muscle membrane lipids [117], resulting in improved insulin stimulated glucose disposal in both liver and skeletal muscle. While the benefits of PUFA appear to be clear, in vitro studies

demonstrating increased susceptibility to oxidation suggest high PUFA diets may be more atherogenic [118]. A high n6:n-3 PUFA ratio in high fat diets also appears detrimental due to excess accumulation of adipose tissue and changes in skeletal muscle lipid stores and membrane lipid composition [117, 119]. Further, the effect of fat type may be mediated by glucose concentrations, where pancreatic beta-cell capacity to respond to increased glucose concentrations has been shown to be dramatically reduced in the presence of SFA [120, 121], possibly due to a number of mechanisms including inhibition of cell proliferation and insulin mRNA expression, increased apoptosis (cell death) and fatty acid synthesis resulting in fat accumulation and ultimately beta-cell dysfunction. Under euglycaemic conditions fatty acids switch from synthesis to oxidation, while the addition of MUFA promotes beta-cell proliferation, even at low glucose concentrations [120]. These mechanistic studies highlight the complexities of metabolic nutrient interactions and affirm the role of fatty acids in determining gene expression and cell function with the potential for impairments in both insulin sensitivity and insulin secretory capacity. Furthermore, saturated fats have been shown to increase neuronal activity in areas of brain hypothalamus associated with feeding, and suppressing activity in areas associated with satiety [122].

Indirect effects in humans

The association between dietary fat and insulin resistance in humans has been substantially reviewed [123]. Research in humans largely supports the evidence from animal studies but mainly through results from epidemiological studies. Few

studies have been conducted using in vivo techniques to assess insulin action in humans following high fat/low fat diets [124], and for those that have been conducted, results have not been clear [125-127]. Relying on less direct associations, high fat diets in humans again appear deleterious, independent of fatty acid profile [128]. In terms of blood lipid levels, saturated fats appear more detrimental than unsaturated fats. In a review, Grundy concluded that compared to oleic acid (MUFA), considered to have a neutral effect on blood lipids, dietary SFAs (palmitic, myristic, lauric) raises serum cholesterol concentrations, while stearic acid (SFA), does not [129]. These effects appear due to influences on gene regulation, the major effect likely due to suppression of LDL-C receptor expression, with little or no effect on high density lipoprotein cholesterol (HDL-C) or very low density lipoprotein cholesterol (VLDL-C) concentrations. In contrast, n-6 linoleic acid (the most predominant dietary PUFA) lowers total cholesterol (total-C) relative to oleic acid, and possibly lowers all lipoprotein fractions. Wardlaw et al demonstrated that the addition of either PUFA or MUFA to high SFA diets resulted in significantly lower serum total and low density lipoprotein cholesterol (LDL-C) levels and a dramatic lowering of serum triglyceride concentrations [130]. Furthermore, these changes were accompanied by an overall replacement of palmitic acid by unsaturated fatty acids in serum phospholipids with specific replacement matching those fatty acids present in the diet. By comparing human muscle samples from male patients undergoing coronary surgery with normal men, reduced concentrations of PUFAs in skeletal muscle phospholipids were associated with reduced insulin sensitivity [131]. A number of studies support this close relationship between the fatty acid

composition of the phospholipids of skeletal muscle cell membranes and insulin sensitivity [123]. Similar results have been observed for high MUFA compared to high CHO diets. Replacing MUFA with CHO in T2DM patients, however, has resulted in significant increases in plasma triglyceride, VLDL-C, glucose and insulin values [132]. Substitution of MUFA with PUFA (from 3-14% PUFA) may be more beneficial, resulting in greater reductions in total and LDL-C and triglyceride levels [133, 134]. However, compared with a high MUFA diet, T2DM subjects on a high PUFA diet reported higher plasma total and LDL-C, fasting glucose and insulin levels [135].

More specifically, increasing n-3 PUFA intakes in humans has been shown to reduce serum cholesterol [136] and plasma triglyceride levels [137], especially in those with elevated levels, improve thrombogenic properties such as platelet aggregation [138, 139], arrhythmias and heart disease risk [140], and competitive pathways for essential fatty acid production has been linked to alterations in eicosanoid production [141, 142]. In addition, changes in the food supply over evolutionary time periods have promoted a change in n-6:n-3 ratio from an original 1:1 to around 15:1 in Western diets [143]. While the benefits of lowering the ratio in humans are plausible, further research is required.

Epidemiological Research

Cross-sectional studies rely on associations with measured clinical outcomes. Marshall et al conducted a cross sectional study in which the diets of 1076 subjects living in the San Luis Valley in Colorado were assessed using 24-hr diet recalls [144]. Subjects diagnosed with IGT or diabetes reported greater total fat intakes as a

percentage of energy (%E) than subjects with normal glucose tolerance. When 134 of these subjects with IGT were followed for 1-3 years, increased fat consumption preceded the development of T2DM after controlling for obesity (Marshall et al 1994).

Twin studies are useful for standardizing genetic predispositions. Mayer et al looked at the usual dietary intake and insulin concentrations of 544 non-diabetic female twins [145]. A 20g/day increase in total dietary fat was associated with a higher fasting insulin level before and after adjustment for obesity (Mayer et al 1993), but was significantly attenuated by physical activity. Within identical twin pairs, total dietary fat was positively related to fasting insulin levels before, but not after adjustment for obesity.

The Seven Countries Study also followed a large cohort of non-diabetic men over 30 years and found that both total and saturated fat were associated with the development of diabetes.

In the Zutphen Study the diets of non-diabetic men were assessed using a diet history (DH) interview and found not only detrimental associations between total, SFA and monounsaturated fatty acids (MUFA) and glucose tolerance, but an inverse association between PUFA (vegetable fat) and insulin levels [146]. Colditz et al also observed an inverse association for vegetable fat (as well as calcium and magnesium) and the risk of diabetes amongst 84,360 US women over a six year period [147]. This association was again attenuated by obesity.

While higher fat intake is associated with increased body weight and fatness [148] and in particular central adiposity [149] (the major risk factor for the Metabolic Syndrome) [150], evidence from epidemiological studies are considered to be inconclusive with regard to total dietary fat intake and the promotion of obesity independent of total energy intake [151]. Hence, it is argued that energy density may be the crucial dietary factor. However, there is considerable evidence to suggest that the increase in obesity may depend more on fat profile than on total fat intake, where relationships between diabetes, central adiposity and total fat, SFA and even MUFA intakes have also been observed, but not for dietary PUFA, which may provide protection [74, 111, 149].

Observational studies have also identified links between the quantity and quality of dietary fat and the development of GDM. For example, Moses et al examined the diets of women with a recurrence of GDM using DH interviews and food records (FR), and found that more of their total energy intake was consumed as fat when compared with the dietary intakes of women with no recurrence [152]. Increased weight between pregnancies was also associated with a recurrence of the condition, again providing parallels for increasing dietary fat and overweight. However, there was also a proportionate reduction in CHO and fibre intakes, which need to be considered when interpreting such observations. More specifically, Bo et al reported an independent association between SFA and the development of gestational glucose abnormalities, especially in the absence of conventional risk factors [153]. In a study of maternal plasma phospholipids, SFA concentrations were significantly higher and PUFA (n-3 and n6) and MUFA concentrations significantly

lower in women with GDM than in healthy, pregnant women [154], indicating possible links between higher SFA consumption, cell membrane composition, and insulin resistance. Wang et al conducted a study on nulliparous pregnant Chinese women diagnosed with GDM and compared them with age-, gestational age-, height- and parity-matched women with normal glucose tolerance and IGT using a 24-hour recall dietary assessment method [155]. Increased PUFA intakes and an increased P:S ratio were associated with a reduced incidence of glucose intolerance in pregnancy (independent of body weight and body mass index (BMI)), hence linking inadequate PUFA intakes with the clinical expression of insulin resistance. While GDM is a relatively little studied area of nutrition research, studies indicate that women who develop GDM have prior metabolic abnormalities, possibly a reduced sensitivity to insulin and/or beta-cell dysfunction which need to be addressed [156]. Where diet composition may accentuate the hormonal influences that induce insulin resistance in late pregnancy, high PUFA intakes and a high P:S ratio may have a protective effect. There is currently a serious lack of randomised controlled dietary intervention trials in free-living GDM subjects to fully assess the role of dietary fat in the diet.

Foods as Sources of Unsaturated Fat Intake

Studies referring to foods as sources of PUFA support the benefits and demonstrate practical approaches for increasing PUFA in the diet. Most studies have favoured fish (whole fish and oils) and nuts. The benefits of fish oils have long been expounded, particularly as a source of n-3 PUFA. However, in terms of

insulin sensitivity, modest improvements have been reported [157, 158]. While their triglyceride lowering effects have been duly noted, their use in diabetes patients has been questioned due to possible impact on glycaemic control and detrimental effects on LDL-C concentrations [8]. More recent research, however, has allayed concerns of adverse effects on glucose metabolism [159, 160]. Accordingly, Friedberg et al conducted a review of the effects of fish oil on glycaemic control in diabetes [161]. All studies reviewed showed a reduction in mean triglyceride concentrations in association with fish oil and a slight but significant increase in serum LDL-C concentrations with no adverse effects on diabetic control. Durrington et al observed no adverse effects on glycaemic control or LDL-C levels, in diabetic patients treated with n-3 PUFA supplements [162]. The supplement was found to be an effective means for lowering serum triglycerides in patients with CHD and hyperlipidaemia, including those with diabetes whose triglycerides had previously remained elevated despite lipid lowering drug treatment. Evidence from the general population has indicated that food containing n-3 fatty acids (specifically eiocosahexenoic acid (EPA) and docosahexenoic acid (DHA) in fish) offers cardio-protection [163-165]. Further, researchers involved in the Oslo diet study [166] in which subjects were supplied with oily fish in addition to dietary advice, reported diabetic improvements independently from alterations in other dietary factors or cholesterol lowering. The Seven Countries Study also made a food-based observation for the possible protective effects of fish consumption in terms of diabetes risk [70]. Data from the Nurses' Health Study indicated women who consume fish regularly may

reduce their risk of CVD. This was the first long-term study (conducted since 1980) confirming the health benefits of fish oils in women [167].

Epidemiological studies consistently show an inverse relationship between nut consumption and CHD [168-170], predominantly through lipid lowering effects [171]. Although nuts are a rich source of unsaturated fat, they also contain significant amounts of vitamin E (antioxidant properties), fibre, magnesium, potassium and arginine [169]. Thus, the protective effects appear to be mediated through several mechanisms that may be specific to consumption of the whole nut. Unsaturated fatty acids and fibre may bring about improvements through reductions in triglyceride and cholesterol concentrations [133, 172] and improvements in anti-thrombogenic pathways, as previously noted. Magnesium and potassium may improve blood pressure [173], and arginine may lower blood pressure through vasodilatory mechanisms [174].

Epidemiological evidence also reveals a negative association between nut consumption and body weight [168, 170]. Again, several mechanisms appear to be involved. Nuts (legumes) are rich sources of fibre and protein, both of which enhance satiety [175, 176]. Whole nuts are inefficiently absorbed [177]. When subjects were fed whole peanuts, 17-18% of dietary fat was excreted in the stool. Although energy dense, nuts have a high satiety value and chronic ingestion of nuts evokes strong dietary compensation [176] and little change in energy balance [171]. Therefore, (pea)nuts may promote increased energy expenditure (EE) due to their highly

unsaturated fat composition [178], being preferentially oxidized [112], and their protein content [179].

One chronic feeding study reported significant weight loss in a group consuming nuts despite participants being asked to maintain body weight and activity levels and their energy intakes being comparable with a control group [180]. Where several experimental human feeding trials involving a variety of nuts have shown either no change or a reduction in body weight among nut consumers, poor absorption may be an explanation [133, 181, 182].

Unfortunately, epidemiological reviews do not differentiate between intakes of the various types of nut [169, 183], while their fat profiles vary considerably. For example, almonds, hazelnuts, macadamia nuts and peanuts are composed mostly of MUFA, while pine nuts, brazil nuts and walnuts are highest in PUFA [184]. Walnuts are unique in that they are a rich source of both n-6 and n-3 PUFA [185]. The n-3 PUFA is the form alpha-linolenic acid (ALA) (18:3n-3), which can be elongated and desaturated in the human body as the essential precursor of the n-3 PUFA in fish oils (EPA 20:5n-3 and DHA (22:6n-3) [186] with similar benefits [187]. Conceivably, therefore, the consumption of walnuts can lower both plasma triglyceride and cholesterol concentrations [188].

In a randomised cross-over intervention trial, Almario et al found that walnut supplementation did not increase body weight despite increased energy intake[188]. A low fat diet + walnuts caused weight loss (1.3+0.5kg) and a reduction in plasma total and LDL-C concentrations compared with habitual diet and a low fat diet

without walnuts. However, HDL-C was also reduced when walnuts were added to habitual diet but not on the low fat diet + walnuts.

Lifestyle Intervention Trials

Intervention trials in which dietary advice is provided to free-living individuals provide evidence for the benefits of the application of nutritional theory. A number of large-scale lifestyle intervention trials have demonstrated reductions in diabetes risk and related complications by targeting changes in dietary fat intake and physical activity levels. The Diabetes Prevention Program, a large multi-centre trial involving 3243 non-diabetic at-risk men and women (overweight with elevated blood glucose levels) showed that intensive treatment, including individualised advice for low caloric, low fat (<25%E), low SFA diets and increased physical activity significantly reduced the incidence of diabetes (58% reduction) compared with standardised general advice over 3.5-5 years. The result was also significant compared with a general advice group receiving oral therapy, which achieved a 31% reduction in risk compared with the control group.

Similarly, the Finnish Diabetes Prevention Study, involving 523 high risk individuals (first degree relatives with T2DM, overweight (BMI$\geq$25), or IGT) provided an intensive treatment group with specific advice aimed at achieving <10%E SFA and 20-25%E MUFA/PUFA [189-191]. Over five years, subjects from this group significantly lowered plasma glucose concentrations, blood pressure, serum lipids, and body weight and significantly increased HDL-C levels compared to standardised general advice.

The KANWU study went a step further to determine whether a change in dietary fat quality could alter insulin action in 162 free-living men and women with IGT [25]. Advice aimed at provide an iso-energetic diet, containing either a high proportion of SFA (17%E SFA, 14%E MUFA) or MUFA (8%E SFA, 23%E MUFA) plus a random assignment of fish oil supplement (containing 3.6g n-3, two taken three times/day) or placebo. After three months advice, insulin sensitivity was significantly impaired and LDL-C increased on the high SFA diet. In contrast, the high MUFA diet did not alter insulin sensitivity and LDL-C was reduced. The addition of a fish oil supplement had no influence on insulin sensitivity or insulin secretion. The favourable effects of substituting MUFA for SFA were, however, limited to low to moderate fat intakes (<37%E).

Hence, results from lifestyle intervention trials support the bank of current research evidence suggesting advice strategies aimed at total diet modification, in particular manipulation of the fat profile (low total and SFA and high MUFA) within the context of a low to moderate fat diet, improves clinical measures associated with increased risk of diabetes and related complications. Similar large-scale studies increasing PUFA intakes have not been undertaken.

In summary, high fat and high saturated fat diets promote clinical abnormalities associated with aspects of the Metabolic Syndrome and hence IR. Increasing PUFA, in particular n-3 fatty acids, demonstrates largely protective effects. However, due to the competitive nature of fatty acids an increased P: S ratio and reduced n-6: n-3 ratio offer the greatest benefits. Notwithstanding, energy cannot

be disregarded in terms of the promotion of obesity and related effects. Observations in GDM women offer similar but limited evidence for differential effects of relative amounts of SFA and PUFA in the diet. Evidence for specific individual foods as sources of PUFA/ n-3 PUFA largely involve fish oil supplementation with concerns for increased LDL-C concentrations. The consumption of whole food sources, such as fish and nuts, provide similar benefits to oils in the diet, as well as other synergistic components that may also provide benefit. Lifestyle intervention trials demonstrate that advice targeting the theory on dietary fat profile can be applied in practice to reduce the risk of T2DM and related complications in free-living at-risk groups. Clinical intervention trials demonstrating specific approaches to increasing relative proportions of dietary PUFA and subsequent effects in diabetes groups are required.

2.2.2 Dietary carbohydrate

Mechanistic Studies

Like fat, both the amount and type of CHO have been shown to have differential effects on insulin sensitivity in animals. These studies, again mainly in rats, have shown detrimental effects of diets very high in sucrose and fructose on insulin action [77] and insulin sensitivity [192]. These effects appear to be due to the fructose component of sucrose [193], probably via a stimulatory effect on hepatic lipogenesis [194] and subsequent hepatic triglyceride secretion [195], not seen with high glucose feeding. Raised serum triglyceride concentrations during high sucrose (fructose) feeding have been shown to have a direct correlation with insulin resistance [196, 197]

(via increased skeletal muscle uptake and storage). Furthermore, pregnant rats fed a high sucrose diet have been observed to have an enhanced ability to secrete triglycerides from the liver, to avoid triglyceride accumulation (fatty liver), and reached the threshold for adipose fat accumulation earlier relative to non-pregnant rats [198]. While replacing sugar in the diet with starch reduced plasma triglycerides in both pregnant and non-pregnant rats, chronic hyperinsulinemia (elevated basal insulin levels) has also been observed (in vitro) to promote insulin-stimulated triglyceride secretion in the liver. Normo-insulinemia (fasted or food deprived state), on the other hand, favours an inhibitory response to acute insulin stimulation [199]. Therefore, it is possible that any pattern of intake that raises basal insulin levels has the potential to stimulate chronic hepatic triglyceride secretion and subsequent insulin resistance.

Indirect Effects in Animals

While improvements to metabolic indices have been reported from the use of complex CHOs, or starchy foods, study results are by no means uniform. However, in vitro and animal studies have demonstrated that different metabolic responses can be accounted for by varying degrees of processing. Plasma glucose and insulin responses (in vivo) correlate closely to the rate of starch hydrolysis (in vitro) [200], which in turn is dependent upon the degree of processing of the starch prior to consumption [201], providing an explanation for the beneficial effects attributed to some starches but not others.

Some studies have attempted to manipulate both CHO and total fat in combination. Fernandez et al experimented with guinea pigs (physiologic ally more similar to humans than rats) and showed that both the type of CHO and the amount of fat affected plasma lipid concentrations [202]. Dietary composition was either high or low fat with the CHO component made up of either starch or sugar, providing four experimental diets in all. The combination of high fat and sugar was the most detrimental, resulting in elevated plasma LDL-C and high levels of plasma triglycerides compared with the other diets. Substitution of starch in the high fat group subsequently reduced LDL-C and triglyceride concentrations.

While high CHO/low fat diets have been shown to lower HDL-C and raise triglyceride levels and generally produce higher post-prandial glucose response [203], the type of CHO in combination with the type of fat may also be important[204]. Rats fed sucrose had higher plasma cholesterol concentrations than rats fed cornstarch. However, this difference disappeared after the rats were treated with fish oil [205]. Although reductions were reported for both diets, the fish oil treatment had the greatest impact on the highest cholesterol concentrations, that is, the sucrose diet. These studies demonstrate fuel partitioning under different metabolic conditions and the differential roles of fat sub types as well as a dietary fat: CHO ratio for possibly both insulin secretion and insulin sensitivity. However, mechanistic evidence is still at an early stage.

Indirect Effects in Humans

High CHO diets have been implicated in the development of obesity, which in turn has strong associations with insulin resistance [77]. Aarsland et al reported a marked net whole body fat synthesis during acute (1-4 days) CHO overfeeding (2.5 times energy requirement) in humans, confirming the body's ability to convert excess CHO to fat [206]. While hepatic secretion of de-novo fat increased 35 times, the investigators concluded this was not the major site of fat synthesis during CHO overfeeding, proposing that the most likely site is adipose tissue.

The effect of sucrose intake at the liver, however, is similar to rats, resulting in elevated plasma triglycerides and fasting insulin concentrations, again mainly due to the fructose component [207-209]. Previous hyperinsulinemia and/or hypertriglyceridemia magnified this effect, in some cases dramatically, suggesting an increased sensitivity to sucrose (fructose) in some people [210] and may be insulinogenic in humans (but not glucogenic) [211]. These studies lend support for Zammit's hypothesis that dietary patterns that elevate basal insulin levels determine acute effects of diet on hepatic triglyceride secretion and subsequent insulin insensitivity [195].

Epidemiological Research

Observational studies have generally found no correlation between total CHO intakes and the incidence or risk of IGT or T2DM [147, 212-214]. However, the total CHO content of the diet does not take into account fibre content and/or the

glycaemic or insulinaemic effect of the food consumed. In human clinical trials it has been found that foods that are more slowly digested stimulate reduced glucose and insulin responses [215]. Factors known to reduce the rate of digestion include dietary fibre (soluble and insoluble), the nature of the starch (amylose versus amylopectin), food form (degree of processing) and increased frequency. For example, controlled feeding studies have shown benefits of whole grains on glucose and insulin responses compared with refined gains [216, 217]. In addition, whole grains (along with fruits and vegetables) have been consistently associated with reduced risk of CHD [218]. Data from the Health Professionals Follow-up Study (a national longitudinal survey of 51,529 male US health professionals) found no differences for total CHO intakes, but diets with low cereal fibre content and high glycaemic load increased the risk of T2DM in men [214]. A large survey of women (Nurses Health Study - 121,700 women aged 30-55 years) found similar results [219]. The Framingham Offspring Study, involving a cohort of 2834 subjects, found an inverse association between whole-grain intake and insulin resistance and a lower prevalence of the Metabolic Syndrome, largely due to cereal fibre content. While glycaemic load and glycaemic index (GI) were positively associated with insulin resistance, only GI was associated with prevalence of the Metabolic Syndrome [220].

Feeding Trials in Humans

The glycaemic response to foods has been noted to reflect many differences in food form and hence the GI, a ranking of foods according to post-prandial glucose response compared to 50g glucose or white bread, is an attempt to quantify these

effects [221]. Low GI foods extend the absorption time and slow the rate of nutrient delivery, thus lowering the postprandial response and have been used in clinical feeding trials in diabetic and non-diabetic subjects to successfully predict acute postprandial glycaemia following the consumption of individual foods and mixed meals [222, 223]. Chronic feeding studies focusing on the GI, however, have produced some inconsistent results. In a review by Miller it was reported that lowering the GI of the average diabetic diet (by exchanging ≥50% of the CHO from high to low GI foods) resulted in improvements in CHO or lipid metabolism or both [224]. Dietary interventions however have found difficulties controlling for fat and fibre levels because many low GI foods tend to be fibre-rich and low in fat. For example, Jenkins et al reported that in a low versus high GI dietary intervention trial, the highest fibre intakes resulted in the greatest fall in total-C and the higher the P:S ratio the greater the fall in LDL-C [223]. Low GI interventions that controlled for fibre (moderate intake) and fat (moderate intake with no specific attention given to fatty acid ratios) may have enhanced the possible benefits of low GI diets by manipulating these other dietary factors. However, increasing meal frequency and reducing the size of each feed seems to provide the same metabolic advantages [225]. This leads to the concept of GI load, which captures both quality and quantity of CHO in the diet, and has been positively associated with obesity [226], insulin resistance, especially in overweight individuals [218]. The GI concept itself, however, is controversial. While many low GI foods are minimally processed and high in fibre others are high in fat and sugar, both of which effectively lower the GI [221]. This seeming anomaly has prompted criticism of the GI for its exclusive focus on

postprandial glucose whilst ignoring the macronutrient mix and the insulinemic effect of foods [8]. Proponents of the GI, for example, suggest there are no detrimental effects of sugar intake based on its effect on postprandial glycemia [224]. However, other metabolic consequences of sugar ingestion such as effects at the liver may be more clinically significant in the etiology of insulin resistance [227]. While the GI is a useful tool for predicting the postprandial glycaemic response to a particular food, background insulin insensitivity may modify this response, which cannot be predicted using the GI.

In GDM women, where the influence of energy and macronutrient intake has been assessed, a relationship has been found between higher CHO (55-60%) intakes and lower incidence of macrosomia (large-for-gestational-age infants) [228]. Indeed, no women consuming diets containing more than 210g CHO/day had large-for-age infants, suggesting the imprudence of very low CHO or high fat diets.

In summary, while optimal types and amounts of CHO in the diet remain the subject of future research, there is evidence from animal, human and epidemiological studies to suggest fibre, cereal fibre and GI load may be protective dietary components. Although the GI concept is controversial, the weight of current evidence indicates it to be a useful tool for characterizing the quality of CHO beyond dietary fibre content. Therefore, total diet approaches aimed at lowering the glycaemic load through the redistribution of wholegrain cereals and fibre-rich, low glycaemic-effect foods may provide dietary protection against risk.

2.2.3 Dietary protein

Mechanistic Studies

The mechanistic action of protein on insulin resistance is little known. However, different types of proteins may also induce different metabolic effects. A review by Anderson et al concluded that consumption of soy protein rather than animal protein significantly reduced serum concentrations of total-C, LDL-C and triglycerides [229]. Although few studies have directly assessed the role of dietary proteins in the regulation of insulin sensitivity and glucose homeostasis, rats fed soy protein were shown to have lower plasma insulin concentrations than those fed casein [230]. While cod protein feeding fully prevented the development of obesity-induced insulin resistance in high-fat fed rats through a direct action of amino acids on insulin-stimulated glucose uptake in skeletal muscle cells [231].

The CHO:protein ratio may also be of importance. Lavigne et al again demonstrated that in rats fed a high-sucrose diet, cod and soy proteins reduced FPG concentrations compared with casein [232]. Dietary cod and soy proteins were found to improve glucose tolerance and whole body insulin action on glucose disposal. Similarly, rats consuming low fat diets were given either casein or soybean protein isolate in combination with sucrose or starch [233]. Plasma cholesterol concentrations and rates of VLDL-C and triglyceride secretion were higher on the casein diet, but only in combination with sucrose. These protein-induced differences were not seen with the starch diets. Such studies once again

highlight the metabolic effects of nutrients in combination and underscore the need to address all dietary components in studies of diet and disease.

Indirect Effects in Humans

Human feeding studies of protein intake are very few. It is understood that this is due to technical difficulties in isolating proteins in the laboratory context. However, Hubbard and Sanchez have reported that a soy protein meal induced lower post-prandial blood insulin concentrations in human subjects than a casein meal [234]. In untreated T2DM subjects, the insulin response curve was lower after ingestion of a meal containing fish or soy proteins compared with casein [235]. Furthermore, studies of insulin responses to a variety of foods have found that protein is an important predictor of postprandial insulin response and can induce as much insulin secretion as some CHO-rich foods [236]. These results are somewhat out of proportion with the relatively small blood glucose responses to these foods, with beef protein found to be the most discrepant and suggest the insulinemic effect of foods, independent of glycemia, may have considerable clinical significance.

In summary, there is currently less evidence for the optimal amount of protein in the diet or its effects on insulin sensitivity and blood glucose levels than for other macronutrient variables. Nevertheless, in terms of dietary induced metabolic effects, there is some evidence to indicate that the type of protein may also be important. Therefore, advice for the inclusion of whole foods such as fish and nuts

for the type of fat they contain may provide added benefits due to their specific protein content.

2.2.4 Summary of evidence on macronutrient targets

Our current understanding of the diet-disease relationship, drawn from mechanistic studies, is that high fat feeding and the pattern of consumption of individual fat types affects insulin action at multiple control points. PUFAs, in many cases, have opposite or beneficial effects compared with the detrimental effects observed for SFAs (on the metabolic events leading to obesity and insulin resistance). Additionally, the type of fat, in company with hyperglycaemia, may have detrimental effects on cell function. High sucrose feeding also reduces insulin sensitivity, probably due to the stimulatory effect of the fructose component of sucrose on hepatic triglyceride secretion. Interestingly, minimally processed starchy foods, soy and fish proteins may have a protective effect on insulin sensitivity.

Human studies, drawing on less direct measures of insulin sensitivity offer support for these findings, with high fat diets resulting in reduced insulin sensitivity in humans. Compared with high SFA or high CHO diets, diets high in MUFA and PUFA lower most lipid sub-fractions, with the greatest reductions occurring on high PUFA diets. Earlier concerns for detrimental effects on glucose homeostasis in diabetes subjects have been allayed by more recent studies. Serum and skeletal muscle phospholipid fatty acid contents reflect dietary fatty acid ratios, with reduced phospholipid PUFA concentrations associated with reduced insulin

sensitivity. Increasing n-3 intakes demonstrates cardio-protective effects mainly through fish oil (whole fish and supplements) and nuts. Increased sucrose (fructose) in the diet raises triglyceride concentrations in humans. While background hyperinsulinemia enhances this effect, substitution with dietary starch reverses it. Research on dietary starch suggests the inclusion of whole grains, increased fibre intakes, reductions in the GI and increased meal frequency all contribute to reductions in post prandial glycaemic response to CHO-rich foods. The effects of protein on insulin resistance in humans are not clear at this time, but studies of insulin response suggest differential influences between soy, fish and animal proteins.

Epidemiological research adds another layer of support to these findings, where both total and saturated fat consumption are positively associated with increased fasting insulin levels, IGT and development of T2DM. In contrast, vegetable fat has a negative association with insulinemia and risk of diabetes. Obesity, however, appears to be a potent modifier of these effects, with energy density an independent risk factor in the development of obesity and related changes in metabolism, requiring additional attention. In terms of dietary CHO, the effects are less clear. Where epidemiological data has failed to demonstrate a relationship between total CHO and T2DM, low cereal fibre content together with increased glycaemic load is associated with increased risk.

Hence, the hierarchy of research evidence provides support for macronutrient targets in nutrition intervention in terms of diabetes and related conditions. At each

level of the hierarchy there is strongest support for a reduction in total fat intake and discrimination between types of fat in the diet. A reduction in saturated fat and replacement with PUFA, particularly n-3 PUFA, might provide benefit at multiple stages of metabolism and, therefore, may impact on disease risk. While the evidence-base is strong, the actual achievement of these dietary targets and subsequent benefit in free-living diabetes groups is still to be confirmed in RCTs. Associations with other macronutrient variables also require further research, but indicate that the amount and type of CHO (due to effects on glycaemia and risk of diabetes) are also important.

2.3 Applications of the Evidence Base in Nutrition Intervention

The previous section outlined current research evidence in order to determine appropriate targets for nutrition intervention in the treatment of diabetes. This next section reviews the clinical applications that support the theory on nutrition. Translation of the evidence-base requires a number of systems formulated to direct advice to free-living individuals to enable a change in dietary intake in order to gain a benefit in terms of related clinical markers of health and disease. In order to comprehensively assess the appropriateness of existing nutrition applications, the following is a review conducted in three parts. First, current nutrition guidelines for diabetes, including those for GDM management and CVD risk, are assessed in terms of how closely they correspond to the macronutrient targets established in the previous section. Second, current food guidance systems are examined to assess how well they correspond to the guidelines and/or macronutrient targets in

order to estimate their capacity for the achievement of theoretical dietary intakes. Finally, the relevance of these systems for assessments in substantiation research to provide evidence for specific health-related outcomes in terms of specific dietary intakes is also discussed. Thus, this section provides an evaluation of the capacity of current nutrition applications for the conversion of theoretical macronutrient targets into practical advice on foods for people with diabetes.

2.3.1 Nutritional guidelines

Based on the extensive body of research, current guidelines in nutrition for the prevention and treatment of diabetes and related complications largely reflect the evidence-base with the emphasis on limiting intakes of both energy and fat intakes. ADA guidelines for diabetes provide recommendations in terms of macronutrients as proportions of total energy intake [8]. Where the recommendation for protein is based on a lack of research evidence to support a change in usual intakes (15-20%), the most specific recommendations relate to the area of most substantial research evidence, the fat fraction of the diet. Even so, due to a lack of trials conducted specifically in diabetes populations, the recommendations on fat are largely borrowed from general population guidelines, that is, less than 10% of energy from SFA (for persons with elevated LDL-C levels it is less than 7% of energy)(A-Level evidence). Approximately 10% of energy should be from PUFA (C-Level evidence). The latter recommendation has a lower level of support due to a lack of studies in persons with diabetes to allay concerns for a possible accompanying rise in plasma LDL-C levels, mostly in response to n-3 (fish oil)

supplementation. Research supporting the cardio-protective effects of foods containing n-3 fatty acids has prompted the recommendation for “Two to three servings of fish per week” (B-Level evidence). However, neither a target amount for n-3 PUFA nor the amount consumed from the two servings of fish is provided by ADA. For this, this review refers to the International Society for the Study of Fatty Acids and Lipids (ISSFAL) recommendations, which list specific intakes from within the fat profile [11] by considering both the beneficial effects of n-3 fatty acids and the detrimental effects of SFA and n-6 PUFA in the overall diet. In the case of the latter, adverse effects are considered to result from competition with n-3 fatty acids for eicosanoid pathways. Hence, for a healthy diet, two interdependent dietary changes are recommended, that is, increasing n-3 PUFA intakes and simultaneously reducing the proportion of SFA and n-6 fatty acids in the diet. For a 2000kcal diet, recommended minimum daily intakes for n-3 fatty acids (0.65g EPA+DHA and 2.22g ALA) are accompanied by upper limits for saturated fats (<8%E) and n-6 PUFA (3%E). Hence, providing a P:S ratio of at least one and an n-6:n-3 ratio under 10 is recommended.

While the total proportion of fat in the diet is not specified by ADA, the remaining 60-70% of energy intake from CHO and MUFA must account for individual metabolic profile and weight management goals. Where moderate caloric restriction is recommended, due to the high energy density of fat, similar restriction is expected to result in low to moderate fat diets.

With reference to CHO intake, food-based recommendations are provided in terms of the type (whole grains, fruits, vegetables, and low-fat milk) and total amount to be included in the diet (A-level evidence). While the latter is considered more important, the high level of support for specific CHO-rich foods suggests that the type of CHO is indeed important. Further, while there is insufficient evidence of long-term benefit of low-glycaemic-index diets (B-Level evidence), epidemiological evidence for reducing glycaemic load and knowledge of the food factors that extend absorption time and slow the rate of nutrient delivery (fibre, degree of processing, fat and protein content) suggests those foods recommended in the first instance (whole grains, fruits, vegetables and low-fat milk) can readily be classified as low-GI and fibre-rich. The consumption of dietary fibre is recommended to a level equivalent to, but not greater than, 'other Americans' (B-Level evidence). In order to achieve recommended levels for fibre intake, specific types of CHO-rich foods may need to be targeted. Attention to the spacing of meals is also recommended.

Despite concerns that fructose may adversely affect plasma lipid levels (added fructose is not recommended as a sweetening agent) sucrose (50% fructose) and sucrose-containing foods are given no restriction (A-Level evidence). This appears to be based on an assumption that the resultant level of glycemia in response to 'sugar' is moderate compared to isocaloric amounts of starch and that this is the most relevant consequence of sugar consumption (albeit a measurement previously questioned in terms of low GI diets and a lack of evidence for long-term effect). Studies looking at the influences of sucrose support detrimental effects of

the fructose component on triglyceride synthesis at the liver with consequent IR and glucose intolerance [193, 211, 227, 237, 238].

ADA guidelines are relatively non-specific for GDM women [8]. An appropriate individualised nutrition prescription and meal plan is recommended based on nutritional assessment, glycaemic control, energy balance and appetite, without ketosis, making appropriate adjustments throughout pregnancy. For overweight pregnant women, primary treatment is moderate caloric restriction (30% of estimated energy needs) in an attempt to lower glycemia and reduce macrosomia. Caloric restriction in pregnant women, however, must be viewed with caution. Although effects on the fetus are still unclear [239], controlling maternal blood glucose levels in obese and/or severely insulin resistant women may impede fetal growth [240]. Therefore, to improve pregnancy outcomes, nutritional therapy for GDM is as it often is in practice for T2DM, the combination of dietary restriction, CHO counting and intensive monitoring of blood glucose levels. While these approaches directly address post prandial glycemia the research literature suggests this may not be the most important factor in the etiology of GDM and future risk. Where screening for GDM was initially developed to identify women at risk of T2DM, current approaches to risk management in these women need to look beyond birth outcomes [156]. Dietary management that addresses metabolic control may be more beneficial for both short- and long-term risks as well as avoid the risks associated with low CHO diets. However, the influence of dietary modification on metabolic abnormalities and perinatal outcomes has not been adequately assessed with few controlled dietary intervention trials to suggest optimal nutritional therapy for

women with GDM and provide evidence-based statements regarding specific dietary approaches to GDM management [241].

Where ADA suggest a total diet food pattern approach [242] may provide the greatest benefit, the provision of advice that takes into account the overall diet requires reference to a variety of foods. With the exception of fish as a source of n-3 PUFA, food-based recommendations are limited to CHO-containing foods.

In contrast, AHA guidelines [243] emphasize healthy eating habits and behaviours, acknowledging the various metabolic contributions made to CVD by the growing rates of obesity, hypertension and diabetes for the general population. Consumption of a varied diet of foods from each of the major core food groups is recommended, with specific advice to eat at least two servings of fish/week; five or more servings of vegetables and fruits/day; and six or more servings of grain products/day, preferably whole grain. For controlling energy, monitoring portions (size and number) is also suggested, as well as limiting foods with a high sugar content/caloric density and foods high in saturated fat, trans-fats and dietary cholesterol. Sodium and alcohol intakes are also limited. More specific recommendations are provided for those with or at increased risk of established dislipidemia, diabetes and insulin resistance for whom it is suggested unsaturated fats replace saturated fats, with CHO intake, especially sugars and refined foods, should be limited and replaced with high-fibre CHO foods instead.

Thus, dietary guidelines for diabetes and other clinical abnormalities related to the Metabolic Syndrome provide specific recommendations for individual fat types.

Provided as relative proportions of total energy intake, advice for the achievement of the recommendations in free-living individuals need to be set in the context of the total diet and personal and preferences incorporated. While this is acknowledged in the guidelines, how this is achieved in practice requires further evidence-based support. Whilst a broad theory base supports the recommendations, the specific application of individual fat targets and subsequent effectiveness has not been adequately assessed in free-living diabetes groups.

2.3.2 Food guidance systems

The specific application of nutrition intervention is supported by food guidance systems, which aid the conversion of nutrient targets into food-based advice. In order to develop appropriate intakes, a suitable database of estimates for the nutrient composition of all foods normally consumed is required. The general concept is that foods are categorised by lists or groupings, and mean estimates of the nutrient and energy content for each list are similar to individual food compositions. In general, food guidance systems provide a selection of food choices or food groups in a recommended or suggested daily intake pattern that delivers nutrients for the optimal health of the general population [16]. In this way using common food groups and standard serving sizes, a total diet approach to nutrition communication can be achieved [242].

It is generally recognized that for individual countries different systems are needed to account for differences in culture, overall nutrition, and the food supply [244, 245]. However, each applies to the general population and not to those with specific

dietary needs. As such, most food guides are primarily concerned with the maintenance of general physical health and account for the usual daily consumption patterns of that country. It is considered, therefore, that specific groups with distinct and/or varying dietary needs [246], for example vegetarians, or a dietary pattern determined to have a specific health benefit, such as the Mediterranean diet [247], require tailored food guidance systems.

However, to be effective, food guides for a specific purpose must incorporate the unique dietary components for the specific population and/or pattern of intake [247]. For this, prior research is required regarding food availability, food consumption patterns, and nutritional needs and standards [16]. Dietary targets for a specific health benefit or outcome are also required, as well as an understanding of food consumption patterns and how they can impact on results. For example, current trends in food sources of fat have identified shifts in intakes away from dairy foods, red meat and edible fats to grain based mixed dishes, high fat snack foods and fat enriched potatoes [248]. Hence, specific food groups and individual foods and their pattern of intake may need to be targeted for achievement of specific dietary and clinical outcomes. The criteria used for food group classification will, therefore ,differ between systems depending on the specific purpose. For most, however, the focus is on foods as sources of energy, protein and essential minerals, vitamins and fibre for general health maintenance.

A comparison of 12 official international food guide pictorial representations found that the fundamental classifications for foods into basic food groups are

surprisingly similar between countries [16], many having been adapted from the USDA food guide pyramid [14], and included grains, vegetables, fruits, milk and dairy products, meat, fats and sugar. For individual foods, the categorization of potatoes and root vegetables (either with other vegetables or with grain foods), beans and legumes (mostly valued for their protein content and/or placed with vegetables for their high vitamin, mineral and dietary fibre content), and nuts (mainly grouped for protein content but also with fats and oils) were found to be the most varied. Most guides were inconsistent in terms of the CHO content of foods, making it difficult to evenly distribute CHO over a day. Any observable differences in categories were for vegetable and fruit groups (some guides categorized them as a single group), the milk and dairy product group (either listed separately for mineral content or with protein foods) and, despite widely varying nutritional differences, fat and sugar groups (mostly grouped together, but some guides omitted them altogether). This was due to perceptions that they were 'ingredients' rather than 'foods' and hence, of no nutritional value (Australia [13] and Canada [249]), and/or the belief that their inclusion as part of a healthy diet would be perceived as advocating increased energy intakes. Hence, intakes of fat and high fat foods (when included) were generally limited in a blanket approach, with sources of different types of fat not well defined, even in the simplest terms such as saturated and unsaturated fat sources. Furthermore, no country identified fish, legumes, soy foods, or nuts as rich sources of unsaturated fats, with only one country, Korea, placing nuts in the fats and oils group. These findings are not in keeping with current research knowledge of the roles of 'essential' fats in the diet and are not supportive of the

need to increase intakes of unsaturated fat. In order to meet intakes of different types of fat in the proportions recommended, the identification of food sources of unsaturated fats may be of importance.

In addition, portion size appeared particularly problematic in that consumers likely have their own personal perceptions of size [250]. In the review of international food guides [16], some countries were found to avoid quantitative recommendations altogether, but most recommended specific quantities or emphasized suggested portion size. This appears to be important in order to alleviate confusion for the consumer [251].

With regard to the overall pattern of dietary intake, most countries reviewed consistently recommended a greater consumption of grains, vegetables, and fruit groups with lower intakes of meat, milk and dairy groups [16]. In terms of macronutrient delivery, the emphasis placed on CHO-rich foods translated to a high CHO diet as the preferred pattern of intake for health by all countries [16]. This is largely without a clear distinction between whole and refined grains. Again, these findings appear to be out of step with current research evidence and existing recommendations that refined CHO and sugar should be replaced with either minimally processed whole grain products and/or healthy sources of fats and protein. This begs the question of whether general population guides can adequately meet the needs of alternative dietary patterns, such as those high in protein or modified fat, and whether they should form the basis of advice to high risk groups, for example overweight individuals with a history of diabetes and/or

heart disease, which accounts for a large cross-section of the general population. Most importantly in substantiation research (considered in more detail in the next section of this thesis), food guidance systems need to be flexible to support new aspects of the diet that need to be tested. Therefore, whether a food guide established 50 years ago [14], which now forms the basis of most food guidance systems, can support current research evidence and changes in perceptions of what constitutes a healthy diet is a significant research question.

The ADA Exchange Lists, established for the treatment of diabetes and weight management, differ from core food guides in that sources of dietary starch (breads, cereals, starchy vegetables, and legumes) are listed together, enabling their distribution throughout the day to assist blood glucose control, and not with low CHO vegetables and other foods, such as modified 'fats', sugar-free sweets and 'sweeteners' and fat-free/sugar free drinks, condiments and seasonings, that have little impact on blood glucose levels. Similarly, to assist achievement of a healthy fat profile, a 'fat list' is provided into three sub-lists based on the main type of fat they contain: SFA, MUFA and PUFA. The SFA list contains butter, cream and lard, as well as high fat foods highest in saturated fat such as bacon, chitterlings, salt pork and coconut milk. The MUFA list includes avocado, oils, olives, nuts, peanut butter and sesame seeds, while the PUFA list includes margarine, mayonnaise, walnuts, oils, dressings and seeds. Therefore, ADA exchange lists are more supportive of overall metabolic control than core food groups. However, they stop short of a total diet approach inclusive of all foods in the diet. For example, individual foods in which fat is the secondary nutrient, such as soy products

(soymilk, soy yoghurt, tofu, etc) and fish, are not readily distinguished (categorized) from similar foods rich in dietary SFA (dairy products and meat). Whether advice that refers only to the edible fat portion of the diet can adequately address overall fat modification is questionable and such applications used in RCTs are reviewed in detail later in Section 2.4.2 Trial applications to dietary fat modification.

Whilst food guidance systems are commonly used for education and meal planning, their application in intervention trials for the adequate achievement of dietary change and subsequent outcomes has not yet been sufficiently tested [17]. First, the methodology behind individual food guidance systems needs to be considered. Unfortunately, the methodological basis of food guidance systems has not been well documented and little research has been conducted in terms of how closely the macronutrient composition of individual foods matches mean estimates for energy and macronutrients [17, 252]. A rationale for the 1995 ADA exchange lists has been provided as verification of published estimates for mean energy and macronutrients [17]. However, calculations of the variation and range for each exchange list were found to be relatively large and agree with assessments of earlier versions of the exchange lists that indicated actual energy intakes might be higher than estimated.

Hence, from this review of food guidance systems it can be concluded that, at least in theory, no existing food guidance system groups foods in a way that is conducive to the adequate achievement of overall changes in the proportions of different types of fat in the diet. Therefore, no system is considered suitable to

guide advice for the treatment of diabetes and associated aspects of the Metabolic Syndrome.

2.3.3 Summary of applications of the evidence base

Current nutritional guidelines for the treatment of diabetes are the result of a shift in focus that largely supports the research evidence for macronutrient targets and proportional intakes of individual fat types to address the clinical features of the Metabolic Syndrome. Recommendations for the type of fat are provided as percentages of total energy to acknowledge the relationship between total energy intake and overweight and obesity as risk factors for disease. Current clinical practice strategies for both T2DM and GDM, however, often focus on glycaemic control and the direct effects of CHO intake on post prandial blood glucose levels. Whilst the evidence for this approach is not clear, it can result in a narrow focus on a single nutrient (CHO intake). Where the guidelines emphasise controlling the total amount of CHO in the diet, in practice food-based advice refers to both amount and type with preferences that correspond to whole grains, high fibre and lower glycaemic responses (milk, fruit). More research, however, is required if recommendations are to adequately define the total diet and measurable clinical outcomes.

To support the guidelines, food guidance systems enable a total diet approach to advice to assure nutritional adequacy. Whilst existing food guides may also be useful for reducing the total amount of fat in the diet, again the common focus is on CHO-rich foods and high-CHO diets as the preferred pattern of intake, but mainly

without distinguishing the type of CHO, such as wholegrain and high fibre choices. Unique dietary components need to be incorporated into the advice system to ensure adequate achievement of specific dietary targets [16]. Therefore, current systems may be inadequate for the achievement of specific proportions of different types of fat and CHO. Although ADA exchange lists group starchy CHO foods together and edible fat portions by fat profile, there is no system currently that distinguishes all foods by fat profile and positions them in a manner that supports advice for proportional shifts in the type of fat in the diet.

2.4 Approaches to Nutrition Intervention Research

While the apparent inadequacies of existing applications to nutrition intervention have been described, practical approaches to nutrition intervention in RCTs also need to be reviewed. In this way, the capacity of existing applications for the achievement of specific nutrient modifications and expected clinical outcomes can be more adequately assessed.

2.4.1 Lifestyle approaches to nutrition intervention

Results from lifestyle intervention trials, reported earlier in Section 2.2.1, demonstrate the significance of intensive individualised advice targeting macronutrient variables as risk factors for the prevention and treatment of disease [20, 21, 191]. The Diabetes Prevention Program [20] and the Finnish Diabetes Prevention Study [19, 189] each assessed the efficacy of intensive lifestyle intervention strategies in preventing or delaying T2DM in free-living 'at-risk' overweight individuals. Both

studies referred to established food guidance systems and specific individualised lifestyle goals targeting changes in diet (<30% of energy as fat and <25% of energy as SFA) and physical activity levels to demonstrate the effects of lifestyle modification on weight loss and consequent diabetes risk. In the Diabetes Prevention Program the intensive treatment was significantly more effective in preventing the development of T2DM in high-risk individuals over an average 2.8 years than a control group receiving standardised general dietary advice with limited follow-up. Similarly, subjects in the intensive treatment group in the Finnish Diabetes Prevention Study were more likely to attain lifestyle goals and hence achieved a significantly greater reduction in risk compared with a general advice group.

In China, the Da Qing IGT and Diabetes Study [21] randomised high risk individuals into four parallel treatment groups, control (standardised advice) versus three active treatments: diet only, exercise only or diet and exercise combined. Those in the exercise groups were given individualised advice for the type and rate of increase in leisure activity, while the diet groups were provided with individualised advice referring to total calories and exchange lists for common food groups, including a separate 'fats' group. Overweight subjects were encouraged to reduce energy to lose 0.5-1kg/month. After six years of bi-annual follow-up, all diet and exercise groups achieved significant reductions in the incidence of diabetes compared with the control group. Nutrient analyses found no significant differences between groups for macronutrient intakes. However, differences in diet quality and/or proportions of the different types of fat in the diet were not assessed, and it

may be reasonable to suggest that differences in diet quality may have resulted from specific food-based advice without impacting on the macronutrient profile.

While the benefits from lifestyle interventions are clear, strategies for the achievement of dietary targets and the effects of individual nutrient manipulations in these trials are not necessarily transparent enough for transfer to practice. Methods used in intervention trials need to be adequately reported to enable the generalisation of results to similar groups under similar conditions. These studies targeted weight loss as a modifiable risk factor for diabetes and related complications. Whilst the appropriateness of reductions in total energy, fat and SFA for the achievement of weight loss and subsequent risk reduction have been confirmed, evidence for a reduction in risk independent of weight loss is not as clear. The methods from these trials do not provide transparent processes for the achievement of dietary targets nor do they provide unequivocal evidence for specific intakes of individual nutrients or foods. Furthermore, increases in PUFA intakes and subsequent benefit in free living diabetes subjects has not been adequately assessed.

2.4.2 Trial applications to dietary fat modification

This section reviews clinical intervention trials that provide more specific detail of the practical application of existing food guidance systems and strategies for manipulating dietary fat. These studies highlight the difficulties faced by researchers and clinicians alike in achieving specific proportions of the different

types of fat in the diet and appear particularly problematic for adequate increases in the proportion of dietary PUFA.

For example, a weight loss intervention trial conducted over 32 weeks demonstrated the practical application of the ADA Food Exchange System and USDA Food Guide Pyramid for maintaining adequate intakes of most vitamins and minerals in energy-restricted diets of 219 healthy, overweight and obese pre-menopausal women [22]. In terms of the fat content of the diet, mean total fat intake was reduced by about 6% of energy intake (from 33.2% of energy pre-study to 26.9% of energy at 32 weeks). This change, however, resulted largely from reductions in both SFA (11.3% to 8.3% of energy) and MUFA (10.1% to 8.3% of energy), with little change to PUFA intakes (5.2% to 4.8% of energy). The latter were low compared to the levels recommended for dietary PUFA and resulted in a mean P:S ratio of 0.57, which was also well below the ratio of $\geq$1 recommended for the general population.

Nydahl et al reported on an experimental study design and the problems associated with manipulation of fat type [24]. Conducted among healthy college students, the study consisted of three experimental diets: a reference diet (high SFA) and two fat modified diets (moderate and high MUFA). The study endeavoured to achieve these differences in dietary fat proportions via exchangeable edible fat portions (margarine and other fats used in cooking and spreading) in week day meals without changes to the total fat content. However, it was determined that these dietary sources accounted for <30% of total daily fat

intake reported by the student population. Therefore, target fatty acid compositions were unable to be achieved through exchangeable fat portions in week day meals alone. At least one weekend meal and snack foods had to be included in order to enable desired increases in unsaturated fat proportions. Additionally, margarines especially manufactured for this purpose were more similar in SFA and MUFA content than anticipated due to issues with taste and mouth-feel acceptability. This resulted in intakes that were also more similar than intended for the test diets, with higher than expected n6:n-3 ratios in both modified fat dietary intakes.

The KANWU study demonstrated under relative free living conditions how changes in fat profile (high MUFA versus high SFA) can be achieved to improve insulin action in humans[25]. Again, advice targeted the edible fat portion of the diet (supplied) to achieve the required fatty acid proportions over three months. While substituting MUFA for SFA resulted in favourable alterations in clinical markers of insulin action, increases in total fat consumption were also reported, with a number of individuals reporting high fat intakes (>37% of energy), at which level favourable effects were no longer seen.

The Nydahl et al and KANWU studies demonstrate the underlying difficulties related to manipulations within the dietary fat profile. Both studies approached the challenge of fatty acid manipulation using exchangeable edible fat portions as delivery agents for increasing the proportion of unsaturated fat in the diet. The problem with this strategy was the assumption that most fat intake is derived from this fraction of the diet. As Nydahl et al found, exchanging saturated for

unsaturated edible fat portions alone may have inadequate impact on overall proportional intakes of dietary fat. This may be particularly so for intervention groups already following a low fat diet, such as those previously exposed to dietary advice, for example patients with established diabetes. The temptation here is to simply increase the amount of exchangeable edible fat, predominantly as unsaturated fat. As demonstrated in the KANWU study, this strategy runs the risk of increasing overall dietary fat intakes. An additional consideration is that those groups already indoctrinated into a 'low fat' regime may be resistant to increasing the amount of edible fat in the diet. While the KANWU study was successful in substituting MUFA for SFA in the diets of free-living subjects using exchangeable fats alone, some individuals increased their fat intake to a level where the clinical benefits of improving the fat profile were not observed, suggesting the impact of improvements in fat quality is limited to low to moderate fat intakes.

Hence, results from clinical intervention trials demonstrating applications to modify the fat profile confirm the need for a total diet approach for controlling total energy intake and the amount and type of fat in the overall diet and suggest that attention to all fractions of the fat profile provides benefits beyond those relating to total fat reduction. Considering secondary sources of fat intake and individual food sources to ensure desirable P:S and n6: n-3 ratios might be a better approach to advice for improvements in health/disease outcomes.

2.4.3 Food pattern applications to nutrition intervention

In the formulation of advice, food patterns offer information on how a 'healthy diet' can be achieved. This section outlines specific information on foods as sources of nutrients and required shifts in intakes for particular dietary outcomes. Such information forms the basis of advice in terms of intakes from specific foods and/or food groups within the overall diet. In terms of fat intake, the benefit of food pattern advice stems from its inclusiveness of all foods in the diet and, therefore, the ability of advice to address all sources of dietary fat, not just added fat. Where the literature indicates controlling energy intake should underpin all dietary intervention strategies, the high energy density of high fat foods also requires attention. The development of advice based on food patterns offers the opportunity to adequately meet these challenges in a truly total diet approach to nutrition intervention.

Firstly, in order to determine how to bring about changes to the dietary fat profile, analyses of population consumption patterns offer direct information on food sources of fat intake and resultant clinical outcome measures. For example, over the period of dramatic parallel increases in the prevalence of obesity and T2DM (1981-2000) [30], fat consumption as a percentage of overall calories has been falling [248]. Observations of the food patterns of the general population over similar time periods describe shifts in both the quality and quantity of dietary fat. In the US, trends in energy and macronutrient consumption, monitored over the past 40 years, show reductions in reported mean energy intakes for all age groups [253]. These reductions in energy have paralleled reductions in reported total fat intake

(9-10% of energy), but not all from saturated fat (2% of energy). In general, the average adult consuming a low fat diet consumed less energy than high fat consumers and fewer grams of total fat [253]. Foods with modified-fat content also contributed a greater percentage of total calories in low fat diets. Fruit and grain consumption was also higher, with low fat milk contributing a greater portion of total milk intake, which in terms of absolute amounts, was similar or greater than in high fat diets [253]. Popkin et al showed that between 1965 and 1996 there has been a population shift from animal-based sources of fat toward fast foods, fried foods and grain based mixed dishes [248]. More specifically, sources of fat in the diet have shifted from dairy, red meat and edible fats, to grains (mixed dishes), high fat snacks and potatoes (with added fat) [248], suggesting that the ratio of visible to invisible fats has been reduced, and that beneficial visible fats, such as unsaturated oils, have been the preferred target of 'low fat' messages rather than invisible fats such as those used in processed and fast foods.

The effectiveness of dietary change is considered contingent on the transfer from high total/saturated fat diets to low fat, nutrient dense diets [253]. For this, explicit rather than broad behaviour changes are required targeting key food sources in the diet, for example, switching food choices from full-fat to low-fat milk and from high fat snacks to fruit [253]. This strategy introduces the idea of incorporating individual foods as sources of specific nutrients in order to achieve nutrient targets. For example, where PUFA intakes need to be increased, sources of PUFA and in particular n-3 PUFA are quite specific. Walnuts and fish have been used successfully in previous studies (outlined in Section 2.2.1 in a review of food

sources of PUFA) to deliver this type of fat for the achievement of health benefits, How this information can be incorporated into advice for free-living individuals without increasing fat and energy intakes requires reference again to RCTs. The following studies report on food intake patterns for specific manipulations to the dietary fat profile.

During a 12 month intervention trial aimed at alterations to individual fat intakes under free living conditions, 63 adults with existing T2DM reported specific patterns of dietary change [23]. At baseline, subjects already reporting low fat intakes (<30%) did not report low SFA intakes as might be expected compared to existing guidelines. This suggests total fat reduction had likely resulted in reductions to all fat types and mainly to the unsaturated fat content of the diet. In order to achieve differential proportions for individual fat types in low fat (27% of energy) and modified fat (37% of energy) diets, this study reported that changes in food patterns and particular cuisine choices were required. The dietary change process reported by Tapsell et al involved complex shifts in both the quality and quantity of fat intake using a systematic approach to individual dietary modeling. This involved shifts in the intake of fat from SFA-rich foods (meat, dairy products, fast foods and cakes) to unsaturated fat-rich food sources (spreads, oils and nuts) regardless of the amount of fat consumed. More specifically, those achieving the target fat proportions changed their intakes to low fat dairy products and leaner cuts of meat, more oils, spreads and nuts, and consumed fast foods less than twice a week. In terms of cuisine choices, the low fat and modified fat groups consumed South East Asian and Mediterranean cuisines, respectively. This study further demonstrates

the complexities of the dietary change process and implicates the lack of guidance that may be experienced by people receiving general dietary advice. Analyses of this type, however, help explain how dietary change can be achieved and therefore are important to inform both intervention trials and clinical dietary management. From this analysis it is apparent that categories of foods and individual food sources from across the overall diet are important for the achievement of dietary change for the achievement of specific nutrient intakes. The concept of an appropriate food group intake pattern for the achievement of dietary goals and consequent clinical benefit has been tested in the DASH dietary intervention trial.

The DASH trial was a randomised multi-centre feeding trial that compared clinical responses to parallel patterns of food intake [254]. Subjects were 459 adults with untreated systolic blood pressure less than 160mm Hg and diastolic blood pressure 80-95mm Hg. All foods were provided over three eight week feeding periods – a control diet (typical American diet), a diet rich in fruits and vegetables, or the DASH diet (a combination diet rich in fruits vegetables, low-fat dairy foods, reduced in total fat, saturated fat, and cholesterol. The primary clinical outcome was systolic blood pressure response. The DASH diet, without sodium reduction or weight loss, significantly lowered blood pressure in virtually all sub groups examined (race, sex, age, BMI, years of education, income, physical activity, alcohol intake and hypertension status), and was particularly effective in African Americans and those with established hypertension [255]. The fruits-and-vegetables diet also reduced blood pressure in the same subgroups, but to a lesser extent. As a result, it was concluded that the DASH dietary pattern may be an effective

strategy for preventing and treating hypertension in a broad cross section of the US population, including those at highest risk of blood pressure-related CVD. It is acknowledged, however, that additional research is required to confirm these results in free-living individuals [255].

Unlike nutrient focused dietary intervention trials, the DASH trial was designed to test eating patterns rather than individual nutrients in an effort to identify practical, palatable dietary approaches that might impact on blood pressure related morbidity and mortality in the general population [254]. DASH diets were compared to control diets by analysing dietary sources of nutrients using 13 food groups in total [26]. Major energy sources were refined and whole grains (23% DASH and 35% control). Whole grains also contributed markedly to protein, fibre, calcium, magnesium, potassium, zinc, and folate intakes (11-46%). Vegetables made major contributions to fibre, vitamins A, C, E and folate as well as an average 15% of magnesium, potassium and calcium intakes. These results highlight the importance of staple foods as sources of multiple nutrients, the balance of which need to be considered when providing advice for changes in a single nutrient. Improvements in the nutrient content of the DASH dietary pattern compared with the control or 'western' diet were accomplished by varying the selection of food items (for example, from refined to wholegrain) and quantities of certain food groups (red meat intake was reduced to increase fruit and vegetable intakes). The DASH diet provides a model for a food based pattern of intake to deliver an equivalent of 2000kcal/day: 4-5 fruits, 4-5 vegetables, 2-3 low fat dairy products, 7-8 grain products (preferably wholegrain), $\leq$2 meats, poultry, fish, 4-5 nuts, seeds and

legumes/week with emphasis given to all food groups[256]. The greater number of food groups (compared with core food groups), acknowledges the importance of individual foods as sources of nutrients enabling advice to meet specific nutrient targets. For example, a separate food group for nuts, seeds and legumes as sources of unsaturated fatty acids enabled their inclusion in the DASH food pattern, effectively contributing to the overall reduction in the proportion of saturated fat in the diet. This also suggests that a representative food from this category could be incorporated into the overall pattern of intake to test its ability to ensure adequate amounts of unsaturated fat and associated health outcomes. More specifically, walnuts and fish as individual food sources of PUFA could be tested in diabetes groups for substantiation of the effectiveness of recommended nutrient intakes and related health outcomes.

2.4.4 Relevance to substantiation research

To support health-related claims on individual foods nutrients and bio-active ingredients, substantiation research is aimed at the establishment of evidence, requiring measurable dietary differences [257]. This requires an appropriate study design and proven approaches to advice, validated in practice, in order to achieve specific effects on clinical outcomes in intervention trials.

Measurement of the diet, however, is difficult especially under free-living conditions [258]. Evidence confirming dietary intakes and achievement of subsequent health benefits require similar valid methods for the collection and assessment of data. For example, data from a validated Diet History (DH) can be confirmed by

comparison with Food Records (FR), described in detail in Section 3.4 as sources of bias in intervention trials.

The identification of relevant and valid clinical markers of disease can provide measurable clinical outcomes for the substantiation of health-related claims on individual food and nutrient variables [257]. In terms of diet-related CVD risk, accepted clinical reference points are LDL-C and HDL-C, fasting triglycerides, and blood pressure levels [259-262]. Since accumulation of body fat represents the most important risk factor for T2DM, and its distribution predicts the development of IR and related clinical abnormalities, markers of overweight and body fat accumulation are considered relevant markers of nutrient effects [119, 123, 257]. Hence, potential claims for health effects of dietary intakes can be made either directly in relation to body weight, body fat and abdominal fat, or indirectly based on energy/food intake and associated measures of appetite and satiety [257].

Finally, valid biomarkers are required to confirm dietary intakes [257]. The fatty acid composition of lipids in body tissues can correspond to dietary fat intakes [263]. This is particularly marked in plasma or serum (or erythrocyte membranes) and is a convenient and reliable biomarker to confirm assessments of diet and dietary change and, hence, support health-related claims [25].

Thus, the guidelines for assessments in substantiation research have been established. However, in terms of the application of advice, structured systems need also to be developed and validated in practice for the establishment of advice methodologies to ensure dietary change and consistent outcomes in free-living

groups. In this way, a structured approach to advice would provide a framework into which single food/nutrient variables to be tested can be identified and incorporated within the overall diet without change to confounding dietary variables.

2.4.5 Summary of approaches to nutrition intervention

A number of approaches to nutrition intervention have been reviewed. Lifestyle intervention trials have demonstrated that regular advice based on specific goals for controlling energy and fat in the diet reduces the incidence of clinical markers of disease in those at risk of diabetes. Nutritional adequacy and reductions in the total amount of dietary fat, and to a limited extent the amount of saturated fat, have also been demonstrated in these trials. However, in clinical trials demonstrating more specific modifications to the dietary fat profile, the impact of existing advice systems on the proportions of different types of fat, in particular P: S and n6: n-3 ratios, appears limited. Indeed, general low fat diet advice strategies may unintentionally result in reductions in all fractions of total fat intake. Adjunct advice strategies aimed at concomitantly increasing unsaturated fat intakes have focused on exchangeable edible fat portions. A limiting factor in this approach may be the small contribution of edible fats to the total fat content of the diet, particularly in low fat diets.

An examination of food patterns exposes that a major portion of dietary fat is from SFA-rich staple foods such as meat and dairy. Advice to increase the edible fat fraction, therefore, may have little impact on overall fat ratios, but instead may

increase total fat and energy intake with subsequent loss of benefit. Alternatively, reference to secondary fat sources and, therefore, all foods in the diet has greater potential to impact on overall individual fat proportions. Food pattern analyses demonstrate the way in which specific individual fat proportions are achieved, largely through shifts in fat intakes from SFA-rich staple foods to unsaturated fat-rich sources across several food groups (fish, oils, nuts) within the total diet. Hence, advice referring to a food group pattern of intake might be effective for the achievement of target nutrients. For example, the DASH dietary trial demonstrated how incorporation of appropriate food groups supported advice for a beneficial pattern of intake with focused clinical outcomes. In this way, a greater number of food groups enabled advice to target a wider range of nutrients, suggesting individual food sources of nutrients are appropriate for the achievement of specific nutrient intakes. In substantiation research, where changes in specific nutrient variables need to be identified, a structured approach would enable manipulation of some nutrients whilst controlling others. In terms of identifying the benefits of individual food sources of nutrients a standardised methodology is required in which individual foods and nutrients to be tested can be incorporated into the overall diet for consistent outcomes within the free-living context.

2.5 Requirements for Further Nutrition Intervention Research

The application of the principles of evidence-based practice in MNT requires knowledge of the best available evidence for the relationship between risk factors of disease and possible dietary exposures. In the case of diabetes, traditional

practices focus on blood glucose control and CHO-rich foods. Therefore, strategies to redistribute CHO, increase fibre intakes and reduce the glycaemic effect of the dietary pattern are fairly well established. However, targets for differential proportions of fat within a total diet framework are also recommended [8]. Therefore, dietary advice that focuses almost entirely on CHO content, for example CHO counting systems, are inappropriate on their own. While measures of glycaemia may be useful in diagnosis, a narrow focus on this clinical marker alone may have limited value in the dietary treatment of patients with diabetes [204]. In view of research evidence in relation to underlying IR and CVD risk, current diabetes guidelines advocate a shift in focus to individualised advice for improvements in overall metabolic control as distinct from a singular focus on glycaemic control. Therefore, targeting overweight, blood pressure, blood glucose and blood lipid levels is required to satisfy this broader interpretation of the evidence-base and evolution in practice. Translating the guidelines into advice practices for consistent clinical outcomes, however, requires further research in order to explore the content, feasibility and impact of a dietary treatment based on current research knowledge.

In a review of the evidence to support macronutrient targets in nutrition intervention (Section 2.2), both animal and human studies are reasonably consistent in implicating the role of high fat and high saturated fat intakes in the development of IR and related clinical features such as overweight and obesity, hypertension, and dyslipidaemia, as well as overall diabetes and CVD risk. There is also support for consumption of unsaturated fats from natural sources, such as vegetable oils, fish

and nuts, particularly as sources of n-3 PUFA in the treatment of IR-related conditions rather than a reduction in total fat intake alone. Furthermore, the combination of high amounts of fat (SFA), sucrose (or refined CHO), and excess animal protein, all common components of a Western dietary pattern, may have the most detrimental effects of all on insulin sensitivity and associated clinical markers of disease [253]. Hence, the long-term benefits of advice based on specific dietary targets, in particular those for reducing total and saturated fat intakes have been confirmed worthy in lifestyle intervention trials.

Implementation of the evidence-base requires referent to existing applications to nutrition intervention (Section 2.3). Current dietary guidelines largely support the research evidence. The most specific recommendation is for individual fat types (<10% E SFA and approximately 10% E PUFA), and fish as an individual food source of n-3 PUFA. A total diet approach, however, is recommended in which CHO-rich foods (whole grains, fruits, vegetables, and low-fat milk) and their distribution over a day is emphasized as part of a healthy dietary pattern. Food guidance systems are then used in dietary counseling to guide advice. However, existing systems may be inadequate for addressing specific proportions of individual fat types in the overall diet. In order to effectively guide advice, food guidance systems need to incorporate the unique dietary components targeted. To date there is no system that distinguishes all food sources by the type of fat they contain and none that provides a pattern of intake that targets different proportions of fat in the diet.

Approaches used in intervention trials (Section 2.4) confirm the appropriateness of advice in terms of achievement of a dietary targets and consequent clinical benefit. Existing approaches seeking to modify the dietary fat profile have been shown to achieve nutritional adequacy and appropriate reductions in total fat, and to a lesser extent the proportion of SFA in the diet. However, inadequate amounts of unsaturated fat in the diet, especially PUFA content, have also been observed. A reliance on exchangeable edible fat portions to reach unsaturated fat targets is problematic, particularly in low fat diets, and may result in higher fat and energy intakes, compromising potential benefits.

Studies reporting food pattern applications to nutrition intervention demonstrate the way in which the overall fat profile reflects intakes across several food groups within the total diet and how changes in individual fat proportions require shifts in intakes from specific food sources delivering significant amounts of SFA and PUFA to overall intakes. Therefore, effective strategies for achievement of specific nutrient intakes may include targeted advice on key food sources. A structured food pattern approach to advice would support the incorporation of individual food sources of unsaturated fat into the total diet whilst controlling other dietary variables for consistent outcomes and the substantiation of benefit.

2.5.1 In conclusion

The philosophy underscoring MNT demands evidence-based practices to support it. For the treatment of diabetes, the shift in focus from CHO intake and glycaemic control alone to individual advice addressing a range of clinical outcomes aimed at

overall metabolic control demonstrates that research evidence is a dynamic process. Nutrition applications need to support the evolution in practice. Dietary guidelines draw on the evidence base and recommend specific macronutrient targets for the treatment of diabetes. Where existing food guidance systems are not adequately structured to support these targets, development of an advice system based on research evidence and tested in RCTs provides evidence-based support for the application of advice and a methodology for subsequent research and its transfer to practice.

The evidence provided in the conduct of this thesis reveals that a structured total diet approach to advice in which individual foods are identified by the types of macronutrients they contain supports advice for the achievement of macronutrient targets. This in turn has provided a framework in which key foods can be identified as sources of required nutrients and linked to related health outcomes for the substantiation of benefit in RCTs. Where diabetes treatment has provided the basis for this research, the identification of key sources of PUFA and the development of a pattern of intake for controlling total fat and energy were determined and tested in diabetes groups under free-living conditions. The methods described, however, would apply to other nutrition therapies and intervention groups and serves to provide an outline for nutrition intervention and the gathering of evidence for practice.

The studies conducted as part of this thesis describe the theoretical development of a structured food guidance system for the achievement of target macronutrient

proportions and controlled energy intakes and its implementation and practical assessment in RCTs. In this way, the following hypotheses have been adequately tested.

2.6 Hypothesis

Structured advice referring to a food pattern linking macronutrients to individual food sources will result in better achievement of dietary targets and improvements in clinical outcomes than general dietary advice.

2.6.1 Sub hypotheses

1. In the context of clinical practice, total diet advice based on food group sources of macronutrients and individual fat types will result in better achievement of target energy, macronutrients and individual fat proportions than general dietary advice under free-living conditions.

2. Advice based on the food group intake pattern being tested in (1) will result in greater improvements in health-related clinical outcomes than general dietary advice, thus substantiating a benefit under free-living conditions.

2.7 Aims

The four studies described in subsequent chapters outline the theoretical development of an advice system (Studies 1 and 2) and its practical application in the clinical setting for free-living individuals (Studies 3 and 4). The following aims relate to each of these studies in turn.

1. To establish a link between specific food patterns and the clinical expression of disease.

2. To develop an advice system that links theoretical nutrient targets to common food sources of macronutrients and individual fat types.

3. To test that the advice system developed in (2) is feasible to implement in clinical practice and will result in better achievement of target energy and macronutrient proportions by free living subjects than general dietary advice.

4. To test that the advice system tested in (3) is effective in practice and will result in greater improvements in relevant clinical outcomes in free-living subjects than general dietary advice.

CHAPTER 3 METHODOLOGY

This chapter details the methodological principles underpinning the studies undertaken as part of this thesis in support of nutrition intervention practices, and described in subsequent chapters. It is divided into four sections. The first (Section 3.1) gives a brief outline of the studies conducted and the role of each in the establishment of evidence for practice. Different types of evidence are defined and the RCT described within the research evidence hierarchy. The second (Section 3.2) provides the rationale for study design and the development of methods for nutrition application in RCTs. The third (Section 3.3) outlines background research undertaken to support the development of methods for nutrition intervention, and the fourth (Section 3.4) provides a summary of the sources of bias, inherent in intervention trials, that need to be addressed if evidence for practice is to be established.

3.1 Establishment of Evidence for practice

The four studies conducted as part of this thesis are in effect layers of evidence for nutritional and research intervention. First, typical food patterns conducive to better glucose tolerance were extracted from observations within an appropriate study sample. These were then developed into a food guidance system to direct intervention for diabetes treatment. Finally, the feasibility and effectiveness of these methodologies and underlying evidence-based nutrition principles were tested by application in two RCTs. Each layer involved the collection of evidence to

put into research practice and can be mapped to Studies 1 to 4, described in detail in Chapters 4-7, respectively. In this way, gathering the best evidence is in essence the endpoint of this thesis, where it provides the rationale for developing the methodologies outlined in the sections following.

3.1.1 Hierarchy of research evidence

As stated at the beginning of this thesis, evidence-based practice is the specific application of knowledge on nutrition and clinical data in the treatment and prevention of disease [3]. To this end, dietary studies are defined according to a hierarchy of research evidence on which to base conclusions regarding diet-disease relationships and the establishment of evidence for practice [4]. Two broad categories of nutrition research exist: feeding trials (animal and human), where intakes of one or more dietary components are manipulated and responses compared; and epidemiological studies where diet and disease components in free living individuals are linked in both an observational (cross sectional and cohort) and experimental sense (RCT). The former provide mechanistic evidence for direct relationships between a particular nutrient or proportions of nutrients and clinical abnormalities. The latter, while not able to demonstrate direct causal relationships, provide valuable support for mechanistic studies by demonstrating possible associations between nutrient intakes and clinical markers of disease.

3.1.2 Randomised controlled trials

The RCT represents the highest level of research evidence within the research evidence hierarchy for diet-disease relationships and, therefore, is the most appropriate study design for the establishment of evidence-based practices for nutrition intervention [3] and the substantiation of benefit [258]. The RCT differs from the observational or cohort study in that it allows the investigator to allocate random treatments and, therefore, has the potential to produce high quality results similar to a controlled experiment. In this way, comparisons between treatments provide measurable outcomes in terms of both the achievement of the nutrients targeted and consequent clinical benefit. To support the application of research knowledge, studies need to be conducted in a sample of the treatment population in the clinical practice context under free conditions in order that results may be transferred to the broader context. The RCT was chosen as the best design for the intervention studies conducted as part of this thesis. In this way, different advice approaches were able to be compared in free-living diabetes groups. Evidence for practice was attained by assessing achievement of dietary targets and changes in clinical outcomes in response to each approach.

3.2 Methods development

3.2.1 Rationale

In this thesis, Section 2.1 provided an overview of diabetes and its associations with the Metabolic Syndrome. Section 2.2 provided a review of the literature on IR-

related nutrition research to establish evidence to support relationships between macronutrient variables and variations in clinical markers of IR such as overweight, blood glucose levels and blood lipid profile. The weight of research evidence supports changes in the proportions of individual fat types for the dietary treatment of IR-related abnormalities such as diabetes. The amount, type and frequency of CHO in the diet are also important. Importantly, these findings are supported by guidelines for the MNT of diabetes and related complications, reviewed in Section 2.3.1, which recommend individual types of fat as specific percentages of total energy intake as part of total diet advice based on food patterns. Attention to the CHO fraction is also recommended in terms of amount, type and distribution throughout the diet. Reviews of current food guidance systems, Section 2.3.2, and nutrition applications, Section 2.4, outline the inadequacies of existing approaches to advice and indicate that to adequately address the research evidence and guidelines required the development of an appropriate food guidance system and its application in RCTs to substantiate dietary and clinical outcomes that, in turn, validate the intervention framework. The guidelines, therefore, provide reference points on which to base study design and methods. Specific proportions of macronutrients thus become dietary targets for the development of advice.

3.2.2 Methods from previous dietary intervention trials

Lifestyle RCTs demonstrate nutrition interventions conducted under free-living conditions and provide methods and guidance for the practical application of strategies for dietary change [19-21, 264]. Previously reviewed for providing evidence to

support dietary fat targets in nutrition intervention (Section 2.2.1) and again looking at the methodologies used in lifestyle approaches to nutrition intervention (Section 2.4.1) these trials focused on modifiable risk factors in the prevention of diabetes and its related complications. They have demonstrated that structured individualised programs improve compliance to advice, resulting in better adherence to dietary targets and, therefore, greater likelihood of achieving improvements in clinical outcomes than control groups receiving standardised general advice with flexible follow-up. Features of the intensive approaches were structured programs with regular contact, programmed follow-up and individualised goals for specific changes in dietary intakes and physical activity levels. The Finnish DPS also found that individuals achieving a greater number of lifestyle goals achieved a greater reduction in risk, regardless of the treatment approach.

Clinical trials demonstrating modification of the fat profile, outlined in Section 2.4.2, have identified the difficulties for achieving adequate PUFA/n-3 PUFA whilst reducing SFA and controlling energy intakes using existing advice systems. Targeting amounts from the 'added fat' portion of the diet was also ineffective particularly within low fat/modified fat diets. Therefore, the development of a total dietary approach in which all foods are targeted is indicated.

Food pattern analyses, reviewed in Section 2.4.3, exposed traditional sources of fat in the diet as staple sources of SFA. Sources of PUFA were from a broader range of food groups, but more likely to be the target of fat restriction in low fat advice, for example oils and nuts. Targeting these foods as sources of fat to

include in the diet, whilst applying traditional low fat advice strategies to staple foods, might improve the ratio of fat types in the diet.

In keeping with the DASH study, which demonstrated the way in which a greater number of food groups (than core food groups) addressed a broader range of nutrients, reference to a greater number of food groups might also be required to address different types of fat in the diet. Hence, a food pattern inclusive of all foods in the diet but grouped to identify key sources of different types of fat would enhance advice to modify the fat profile and allow the control of overall fat and energy intakes. Therefore, with reference to previous research, an outline for an appropriate advice system and protocols for dietary intervention have been established.

3.2.3 Construction of a model food pattern

While the structure and context in which advice is given is important, the subject of this thesis is ensuring dietary advice matches the theoretical aims of the intervention, in this case macronutrient recommendations. This requires knowledge of the macronutrient content of individual foods and an understanding of consumption patterns and the variability that might be encountered due to individual food choices. Such knowledge and understanding supports the conversion of macronutrient targets into practical advice on individual foods and food groups in order to provide understandable and achievable information to free-living individuals. In this way, the exercise of developing an overall dietary intake from component foods/food groups supports advice for intervention by enabling

transparent processes and an appreciation of the impact of food groups and individual foods on nutrient variables. Accuracy of the process is critical for both adherence and outcomes and is dependent upon development/selection of an appropriate nutrient database, relevance of foods/food groups to dietary targets, and the ease with which resultant dietary patterns can be implemented as simplified advice. Large, computerized nutrient databases are, on the whole, inappropriate for this exercise [252]. They are cumbersome, time consuming and not useful for assessing nutrient intakes in terms of food groups and varying portion sizes. Exchange list systems offer a convenient alternative method for constructing individual diets [17]. Many current systems, however, are based on a compilation of (referenced and unreferenced) food databases, with few analyses for accuracy and variance [17]. Assessment of the ADA exchange lists for meal planning reported large within-group variations and application of the system to an overall dietary pattern was not reported [17]. To date, an assessment of Australian food guidance systems has not been reported.

The need for a simplified format for the calculation of overall nutritional intake is met through development of a 'ready reckoner' system to expedite the dietary modeling process [265]. The ready reckoner is a convenient and simplified reference for food composition data and provides a framework for assessing and modeling food consumption patterns for the achievement of dietary change. In conjunction with exchange lists of foods of similar nutrient compositions, the ready reckoner is an important facilitator for individualizing advice and assuring it matches both nutrient and food-based targets. Based on food groups appropriate to nutritional

goals, the number of food groupings is minimized to enable speed and convenience for the clinical situation. While simplification may reduce the accuracy of the instrument, its relevance to dietary goals should not be compromised. Therefore, theoretical assessment of the accuracy and degree of variability within a dietary modeling system is required. Practical application in RCTs can then be carried out to assess the utility of the advice system in clinical practice and to confirm the theory in terms of achievement of dietary goals and related clinical outcomes.

3.3 Background Research

In order to develop an advice framework for application in a RCT for diabetes treatment, background research was conducted. Although nutrient recommendations for diabetes are specific in terms of proportional individual fat intakes, nutrition interventions require an understanding of the eating habits, food preferences and patterns of intake demonstrated by the study population to ensure advice is appropriate for changes in clinical outcomes. Where advice based on food patterns is recommended[8], the impact of food factors and food patterns on clinical outcomes is not as well studied as that for nutrient intakes. Similarly, as reviewed in Section 2.2, evidence to support advice on the pattern of CHO intake is not as strong as that for dietary fat intake. Therefore, in order to develop appropriate food-based advice for the overall pattern of intake, the examination of food patterns of a sample diabetes group was necessary to further elucidate the diet-disease relationship. This was done by establishing a link between specific

food patterns and clinical outcomes, in this case between CHO intake and glucose abnormalities (Study 1 CHAPTER 4).

Such relationships do not exist in isolation, however, and development of an advice framework for the total diet needed to account for multiple dietary factors and their metabolic effects. Hence, foods and food patterns needed to incorporate the findings from Study 1 and to be theoretically linked to guideline variables (macronutrient recommendations [8]) for the construction of a model food pattern to meet predetermined targets for energy, macronutrients and individual fat types for the treatment of diabetes (Study 2 CHAPTER 5). The following outlines the methods used in Studies 1 and 2, respectively, conducted as part of background research for the development of an advice framework targeting specific nutritional and clinical outcomes in intervention trials.

3.3.1 Food pattern analyses

Study 1: To establish the link between food patterns and blood glucose abnormalities

This study was conducted to establish a link between specific food patterns and glucose intolerance as the clinical expression of insulin resistance and clinical marker for diabetes treatment. The DASH feeding trial demonstrated the clinical benefits of food patterns designed to effect a change in blood pressure levels as the clinical expression of CVD [266]. In order to further elucidate relationships between food patterns and blood glucose tolerance, a cross sectional survey of the

food habits of a sample of women with demonstrated glucose intolerance (presenting with GDM at the beginning of the third trimester of pregnancy) was compared with that taken from a sample of glucose tolerant pregnant women. Food pattern analyses were used as an alternative to traditional nutrient analyses to enable a better understanding of the relationship between diet and clinically diagnosed glucose intolerance by providing specific information on foods for inclusion in an advice system for the treatment of diabetes.

The analysis of food patterns involves the study of individual food factors rather than broader aspects of the total diet in order to examine diet-disease relationships and related concepts [267]. Analyses of food choice patterns are less dependent upon the inadequacies of nutrient databases and allow the diet of a study population to be described in a manner that is useful in the clinical setting, both for the researcher/practitioner and the consumer [268]. To perform food pattern analyses, individual foods and food ingredients reported by individual members of the study population are first combined into groups. Criteria for the formation of food groups may vary dependent upon the objectives of the particular analysis, for example food components, culinary use, metabolic responses, and so on [269]. Analysis of food groups may, in turn, be conducted based on various criteria such as absolute weight in grams, number of servings, or %E intake [267]. This type of analysis can establish links between specific food factors and clinical markers of disease, either cross-sectionally [270] or prospectively [267], determine whether current nutrient guidelines can actually be met; provide guidance for healthy eating

patterns and information on how dietary change might be achieved in practice for a specific health benefit [271].

Limitations of food pattern analyses

Limitations of food pattern analyses stem from three main sources of bias: differences between populations, method/s of data collection, and criteria for interpretation.

Firstly, the outcomes of food pattern analyses can be directly affected by potential differences between populations according to age, sex, religion, and ethnicity [269]. Therefore, in terms of application, it is important that the data-set is taken from an appropriate study sample clinically similar to the target group [270]. Thus, in order to ensure the relevance of information drawn from the analyses conducted in this first study, the study sample was chosen to match the sample targeted for the subsequent intervention trial (Study 3 CHAPTER 6). That is, a convenience sample of well defined glucose intolerant patients (women diagnosed with GDM using an OGTT [272] drawn from a local clinic). GDM women also represent individuals who have a demonstrated increased risk of T2DM [273-275] and CVD [276, 277] compared with other members of the general population, making current eating habits relevant to primary prevention strategies for future risk management. The representativeness of the study sample is an important aspect of intervention research, and is discussed in detail later in Section 3.4 as a source of bias in intervention trials.

Secondly, the type of method used to collect dietary data can also impact on results from food pattern analyses [267, 268]. Therefore, it is again important that the chosen data collection method has unique requirements for this type of analysis. For example, rather than provide total intakes alone, the method should be representative of habitual intakes and sensitive to significant individual foods, cuisine choices and patterns of food intake over an average day. The DH captures a detailed history of recent past dietary intake [278] and performs well in clinical trials [279], and so was the data collection method of choice for all studies conducted as part of this thesis. The FR is commonly used to cross-validate dietary data collected via another method [279, 280], and was used for this purpose here. Both methods are discussed in detail in Section 3.4 as sources of bias in intervention trials.

Finally, the greatest limitation for food pattern analyses stems from several application specific decisions that investigators must make. Based on prior knowledge, interpretive assessments are made according to predetermined objectives and/or anticipated outcomes. The investigator determines the factors used for the aggregation of foods into groups, the number and type of food factors to be analysed as well as how to treat food group variables, for example as absolute weight, %E intake, or number of servings [267]. The decisions made shape the outcomes of the analyses according to study-specific objectives.

To address the limitations of the food categorization process for this study, several criteria were developed to define food groups and to identify specific patterns of

intake that may impact on the glucose tolerance of GDM women. Previous research points to the impact of the total amount of CHO on blood glucose levels [8], whilst evidence for the effect of source or type of CHO in the diet is less clear. In order to clarify the effect of source or type of CHO in the diabetes diet, this study focused on CHO-rich food sources categorised in two ways: according to food groups (cereals, fruit, milk, etc) and diet GI scores (low, intermediate and high, GI load and meal GI).

These criteria were chosen to identify foods of similar components and metabolic effect and represent classifications used in previous dietary analyses [214, 281]. Diet GI scores obtained from free-living subjects demonstrate a normal distribution, and are considered valid for use in common statistical procedures [281]. However, GI scores expressed as percent energy may be biased by the possibility of underreporting by the study group. Furthermore, in terms of variations in individual responses and the impact of other meal components, GI scores of individual foods have been found to have limited use in evaluations of glycaemic response. Consequently, individual foods organized into groups related to a more rounded estimate of the body's response (high, intermediate and low GI) may eliminate some of the error related to assigning individual foods exact GI values, discussed elsewhere [282, 283].

Such analyses may add insight to the limited research in this area, particularly from a clinical practice perspective, where findings may be applied directly to practice. The information from this study, while particularly relevant to GDM where there is

scant research on which to base clinical practice/research methods, is also relevant to other diabetes groups for whom information on foods and food patterns is of similar value.

3.3.2 Food Guidance Systems

Study 2: To model an advice framework based on food patterns for the achievement of macronutrient targets

This study was conducted to link food patterns to specific proportions of macronutrient variables including different types of fat in order to guide advice for the achievement of dietary targets for the treatment of diabetes in an intervention trial.

Where nutrient guidelines need to be converted into advice on foods, food guidance systems provide a set of food values for estimating the nutrient and energy content of the diet, as well as lists of foods of similar values to enable an outline of flexible food choices to meet estimated intakes [17], discussed in detail in Section 2.3.2. Food guidance systems, therefore, represent a useful dietary tool for the application of advice to match theoretical aims in a range of clinical and research settings. However, to be effective a food guidance system must incorporate unique dietary factors/components and targeted information on specific foods [16, 246]. Therefore, the particular purpose of the intervention and its specific dietary targets need to be addressed. Where the purpose of this thesis is to provide evidence for the application of nutritional guidelines for diabetes

management and thus establish an appropriate advice system, the focus therefore is on weight management and control of blood glucose and lipid levels. Dietary targets are drawn from research evidence, outlined in Section 2.2, and treatment guidelines, outlined in Section 2.3.1, and refer to specific proportions of macronutrients and individual fat types as well as controlling energy intake and the amount and type of CHO in the diet. A further layer that might be added would be to target an individual food source as delivery agent for increasing a specific nutrient, such as PUFA, and to model intakes into the overall diet as part of substantiation research.

In order to assess the appropriateness of an advice system for a specific purpose, an awareness of the assumptions and limitations inherent in food guidance systems is essential. First of all, the target population is an important consideration. Current systems have been developed largely for the maintenance of physical health and well-being of the general population [16]. There is an assumption here that one system based on criteria for nutritional adequacy is appropriate for the specific nutritional requirements of all populations. Achievement of adequate nutrition, however, may not address the particular need of a sub-population, and has been discussed in Section 2.3.2. Therefore, the development of advice and subsequent testing should be based on study samples with similar characteristics to those for whom advice is required.

Secondly, an appropriate advice framework is dependent upon the database of specific foods used in its development and the criteria used to aggregate individual

foods into food groups of similar values. Different criteria are required for different systems depending upon the purpose and specific dietary targets [16]. The links between specific food factors/components and clinical markers of disease established by food pattern analysis need to be confirmed in the application of advice developed from them. Nutrient values within each food group need to be similar. However, increased variation may occur for nutrient values not used as criteria in food group development. For example, where food groups are based on the particular goals for nutritional adequacy, as discussed in Section 2.3.2, the system becomes very specific for that purpose and not for others [16]. In the case of adequate nutrition, the emphasis is on foods as sources of energy, protein and vitamins and minerals [13]. While it is important to acknowledge these dietary variables in any food guidance system, the limitations imposed by these criteria on food group development need to be addressed in a system with additional goals in mind. This is particularly so for energy intakes if all foods are not grouped according to estimates of macronutrient and/or energy content. Where CHO distribution is required [8], portion size for CHO-rich foods needs to be standardised and differences in quality (wholegrain, fibre-rich, low GI) identified. Likewise, where specific changes in fat proportions are required, individual food sources need to be identified [23, 24, 284]. For example, foods grouped to enable similar values for total dietary fat content alone may limit the achievement of targets within the fat fraction, discussed in detail in Section 2.4.4. Indeed, there are a number of assumptions that limit the achievement of specific proportions of different dietary fat types using existing systems. Foods are often grouped according to total fat content with the

assumption that a reduction in overall fat intake will result in a reduction in the proportion of saturated fat in the diet and, therefore, will improve the ratios of other fat types. However, while current systems appear conducive to reducing total fat intake by sub-categorizing low fat options and limiting the amount of edible fat in the diet, they do not adequately define foods as sources of different types of fat and, therefore, are unable to support specific manipulations, discussed in Section 2.3.3. For diabetes treatment, the need to discriminate individual fat types has been recognized, but is largely confined to exchangeable edible fat portions. The assumption being that edible fat is the main source of dietary fat and that targeting this fraction of the diet will impact on overall intakes without changes to other dietary variables. However, edible fat sources may contribute only 30% of total fat intake, and staple food sources, such as meat, milk and cheese, largely define total and saturated fat intakes. Therefore, secondary sources of individual fats need to be adequately defined to enable an effective exchange of saturated for unsaturated fat-rich foods. Hence, as concluded in 2.3.2 no current advice system identifies sources of individual fat types in this way and, therefore, none are considered suitable to address nutrient targets in the treatment of diabetes and ultimately benefits in free-living diabetes subjects, discussed in Section 2.3.3.

With the limitations of current systems in mind, development of a food advice framework for the application of specific treatment advice for diabetes required not just a working knowledge of the nutrient composition of foods, but an understanding of food intake patterns and how they may impact on results. In this way, background research was conducted to identify foods and patterns of intake

for inclusion in the system. To this end, the following steps were taken: i) to identify common food sources of the nutrients under study; ii) to apply appropriate criteria for the development of food groups as sources of the nutrients under study, as well as unique sources of specific nutrients; iii) to model a sample food group intake pattern that would provide targeted proportions of the nutrients under study; and iv) to conduct statistical analyses of the resultant food groups and sample food group intake pattern to confirm the appropriateness of advice in terms of potential variation in intakes compared with nutrient targets.

The identification of foods and food patterns drawn from a local sample of glucose intolerant women from Study 1, resulted in an appropriate food data base providing a reference for common food sources of macronutrients, culturally appropriate and locally available. Subsequent food group development based on criteria drawn from the treatment guidelines (macronutrients and fat types) enabled identification of a set of food groups and individual foods for inclusion in an appropriate intake pattern modeled to achieve guideline targets.

Accuracy of the modeling process is critical for achievement of dietary goals. While accuracy of the food database also has an impact, so too does simplification of the database into food groups and average rounded nutrient values to expedite the process of dietary modeling. Therefore, in this study assessment of the accuracy of the system was undertaken, where the application of statistical analyses estimated potential variation in intakes due to individual food choices to meet the equivalent intake pattern.

Hence, constructing a total food intake pattern to match dietary targets supports the theory for their application in dietary intervention, but required a different set of constructs to those used in food group development. Here nutrient goals and food group sources were merged for the development of a model food intake pattern to ensure the nutrient proportions under study in the intervention trials. Reference to the model would provide advice in terms of the amount and frequency of major food groups as sources of macronutrients and different types of fat for the achievement of macronutrient targets, estimated energy requirements, and overall nutritional adequacy.

3.3.3 Dietary Intervention trials

In terms of effective practice, the methods used in dietary intervention trials to bring about changes in diet and clinical markers of disease in free living populations provide information for the clinical application of research evidence. The implementation of an advice system under free-living conditions provides evidence for its transfer to clinical practice and its use in future trials for the substantiation of benefit. For the purposes of providing evidence for nutrition intervention, a dietary advice framework was applied in the clinical practice context in RCTs, conducted as part of this thesis, in women with GDM Study 3 CHAPTER 6 and in men and women with T2DM Study 4 CHAPTER 7.

Study 3: To test the feasibility and applicability of an advice framework based on food patterns for achievement of the fat profile recommended for diabetes

This study was a RCT conducted to test the clinical feasibility and applicability of a dietary advice framework that identifies food sources of macronutrients and individual fat types for nutrition intervention in a free-living sample of women with GDM.

Study 4: To substantiate the clinical effectiveness of an advice framework based on food patterns and the incorporation of an individual food source for increasing the proportion of PUFA in the diet

The second trial was a longer term randomised controlled dietary intervention trial in free living adult men and women with T2DM conducted in the clinical practice setting, to test the transfer of the advice framework to other diabetes groups, to assess the incorporation of a single food source, walnuts, of a specific nutrient, PUFA/n-3 PUFA, into the advice framework, and to confirm the clinical effectiveness of advice based on food patterns to ensure specific intakes for macronutrients and individual fat types.

It is rare however for a RCT in free-living samples to provide data for a pure nutrient-disease relationship due to the greater likelihood for confounding variables and bias. Unless these limitations are adequately addressed it may be difficult to extrapolate to fee-living populations [258, 285]. The following outlines confounding factors and sources of bias in dietary intervention trials and the methods used to address them.

3.4 Sources of bias in intervention trials

Representativeness of the study sample

For the purposes of developing evidence-based methods and practices, dietary intervention trials need to be conducted under the conditions for which results are to be generalized. For this thesis, two intervention trials were conducted in samples of local free-living glucose intolerant individuals (women with GDM, and men and women with T2DM, respectively) identified clinically by their level of glucose intolerance as determined by oral glucose tolerance test (OGTT) [28, 78], and seen under clinical conditions. As outlined previously, study design was developed from information gained in background research in a representative sample (Study 1 CHAPTER 4).

Sample size

Estimation of an appropriate sample size for an intervention trial uses data already available form other trials. For example, the standard deviation of the mean of a similar population can be used to calculate the expected standard error of the mean of a new population [285]. The ability to detect significant differences between comparison groups is heavily dependent on the power of significance tests. The power relates to the proposed difference and the standard error of the difference, which is dependent on sample size, and the significance level set for the probability of detecting a difference, usually set at P=0.05.

Published data for estimates of sample size and standard deviation to determine an effect in humans, however, are limited. In a previous dietary intervention trial with a similar sample size to the T2DM study sample outlined in this thesis, changes in proportions of individual dietary fat intakes were determined but did not demonstrate a difference in clinical outcomes between low fat and modified fat diet groups [23]. Although there are some differences in dietary strategies (for example, significant reductions in dietary SFAs were not anticipated in the control group), attention to study design will demonstrate achievement of dietary targets and feasibility of the specific intervention approach. This is likely to represent conservative estimates because specific aspects of study design would be expected to substantially increase the power of achieving a significant difference between groups [286], that is, repeated measures at baseline and over specified time points and structured dietary advice are likely to reduce the between-subject variance and strengthen results. A high level of dietary compliance in the study groups (pregnancy and diabetes diagnosis are motivations for adherence to dietary advice to achieve good clinical outcomes) has a similar effect. Adjusting for sex is also likely to reduce the variation and increase the power [285]. Nutrition trials that recruit high-risk individuals, however, require relatively small numbers because the spread (variance) of end points is minimized [286]. In this thesis, trial groups were highly defined with homogenous characteristics between individuals. Therefore, large numbers were not required and results could still be readily extrapolated to the wider diabetes community.

Duration of the intervention

An insufficient trial period to adequately accumulate quality end points can reduce statistical power [286]. For this thesis, studies were conducted with standard clinical practice conventions in mind. Because Study 3 involved GDM women, the period of intervention was limited to the third trimester of pregnancy (from diagnosis at around 28-30 weeks to delivery at 36-40 weeks gestation). For this reason, this intervention was conducted as a pilot study to assess feasibility of the dietary strategy in free-living subjects under clinical conditions. Study 4, involving T2DM patients, however, was conducted over a six-month period to enable the assessment of long-term compliance and changes in clinical outcomes. This was considered sufficient time to test adherence to dietary advice and chronic nut consumption over the longer term, and for incorporation of biological biomarkers and changes in relevant clinical outcomes in order to substantiate a benefit [257].

Dietary adherence and compliance

Compliance to dietary advice and adherence to specific intakes and targets for nutrients and energy is essential in dietary intervention trials for two reasons: firstly, to allow confidence in conclusions drawn from relationships between dietary change and changes in relevant clinical outcomes; and secondly, to confirm feasibility for extrapolation to the clinical setting and free-living individuals. Factors that impact on dietary compliance include study design, length of the intervention period and the utility of advice and palatability of the diet being tested. Compliance was enhanced through attention to study design where individualised advice, specific dietary targets, and regular support played a role. Study lengths were

consistent with clinical practice timeframes and were considered reasonable. In Study 4, long-term adherence was assessed over six months, a period that may be expected in clinical practice following diagnosis of diabetes and/or when seeking a change/s in clinical outcomes, such as blood lipids, and/or blood glucose control. Dietary intervention involving free-living populations need to be structured and supportive of dietary change so that the quality of dietary data in terms of over/under reporting and unintended changes to background dietary variables are minimally affected. The studies outlined in this thesis offered support for the achievement of dietary change by referring to foods commonly consumed and locally available, and exchange lists to support individual food choices.

Dietary monitoring

Dietary monitoring is an important aspect of dietary intervention trials as it confirms compliance to the foods/nutrients under study and ensures reliability and repeatability of results and transfer to the treatment population for whom conclusions are made [258]. For interventions seeking to estimate clinical practice methodologies, some of the methods used to monitor dietary compliance should be feasible to implement in the clinical practice setting. In the interventions reported in this thesis, monitoring dietary compliance was undertaken in two ways, as part of normal clinical practice with regular visits between subject and dietitian. On these occasions the dietitian, in checklist fashion, readily assessed adherence to dietary advice by referring to the individualised food group intake pattern provided initially to each subject. In addition, a dietitian telephoned subjects in Study 4 on one

occasion between each clinic visit. At specific time points at the beginning and end of each study more formal dietary assessments were undertaken in the form of DH interviews and weighed FR, described later in this Section.

Dietary variables

The cooperative, synergistic, additive and confounding effects of various food components need to be acknowledged [258]. The ability to control non-intervention dietary intake (reference diet) in accordance with nutrition intervention goals assists dietary adherence and allows a more accurate assessment of the intervention. In this thesis, changes in dietary fat proportions were required without alterations to intakes of energy and other nutrients. Therefore, advice needed to address the total diet with the required changes incorporated. Therefore, each group was provided with similar advice except for that relating to specific fat intakes/individual food source (walnuts). The complexities inherent in dietary change to effect intakes of specific fat types have been discussed previously in Section 2.4. As demonstrated by Tapsell et al shifts in food group sources of fat intake encompass several food groups [23]. Appropriate food group classifications, therefore, are important in order to retrieve food based data relevant to the manipulation if dietary fat under study. In this case, food groups needed to reflect individual fats in order to inform practice on specific food intakes for the adequate achievement of fat targets.

Capturing food habits

Dietary intake is highly complex, where there are thousands of distinct food items available for consumption and most people eat a variety of food items every day. Collecting complete and accurate data on the varied diets consumed by free-living study participants poses several challenges. The appropriateness of the methodology to the research question and an understanding of the limitations that exist can reduce the degree of error and provide a realistic estimate (Margetts). Although the error inherent in dietary data collection is acknowledged, any data tested statistically should be recorded as precisely as possible [286]. This is dependent, to a great extent upon matching the method of data collection to the purpose for which the data will be used. For the purposes of individualising dietary advice in the clinical context, an accurate assessment of background or 'reference' diet is also important [258], taking into consideration usual intake patterns, variations and personal preferences. Hence, a tool that is sensitive to the distribution of foods, cuisine type, food and meal patterns would be a good fit for a dietary intervention trial seeking to provide food pattern advice. An outline of the appropriateness and limitations of the two methods used in this thesis for the collection of dietary data follows.

Diet History

The DH is a retrospective meal-based dietary measurement that enables a reasonable level of reproducibility and validity for intake of individual foods and food groups as well as meal patterns [287]. An interviewer administered questionnaire, the DH aims to cover a lengthy time period in order to capture

habitual diet. Its strength lies in being able to assess frequency of intake of individual foods and content and frequency of meals, resulting in a detailed assessment of usual meal patterns and overall consumption patterns. Heavy reliance on memory and inaccuracies in estimating the frequency of consumption and portion size can be overcome to a large extent through the ability of the interviewer and adequacy of interview design. Including adequate instruction, open-ended questions and other various tactics, such as visual aids and recording information on food preparation methods, food types, recipe ingredients, as well as including a 'food frequency checklist' of common/relevant foods can reduce participant burden whilst building a reasonable picture of overall intake. A questionnaire of this type has been developed in the Illawarra region and validated within local diabetes populations [278, 279, 288]. This format was adapted and provided the primary data from studies reported as part of this thesis.

Food records

The weighed FR is an alternative data collection method, usually providing a few days worth of intake. In contrast to the DH, this is a prospective method in which the subject is required to record all foods and drink and the amount consumed daily. Its strength is in its ability to capture quantitative data. For this reason, the weighed FR is often used as the standard for comparison with another method [289], and was used for this purpose in the studies presented as part of this thesis. Although based on weighed portions and household measures, this may not be the most precise estimate of the person's 'usual' dietary intake. Foods that were eaten

infrequently may be missed, portion size may be inaccurately measured. A further limitation is the 'training effect' [280], where participants are aware of study aims or at least well aware of the aims of the dietary advice provided and consume foods accordingly but only for the recording period. The 'instrument effect' also has an impact, where the effort required to weigh and record foods disrupts normal eating patterns [290].

Comparison between two data sets

A second data set provided from an alternative data collection method can be used to create a standard for statistical comparison [286]. To assess the relative validity of data from the DH used in this thesis, a comparison was made with data from the FR to estimate the degree of error and acceptability of the data obtained. Where data collection methods are either retrospective or prospective in their evaluation of dietary intake, the DH and FR are as examples of each, respectively, and therefore, as they display different sources of error, are useful in comparison [291]. As previously discussed, the DH is subject to random error due to poor memory and systematic error due to underreporting. In contrast, the FR is subject to reporting bias, where recording intake influences food choices and results in altered intakes during the recording period [292].

In the intervention studies reported in this thesis, the DH and FR were compared using Bland Altman plots [286] in which the difference between the two methods is plotted against the sum or average. The two methods agree if the difference between the data (measuring the same intakes) is small enough to use either

method interchangeably. Plotting the differences provides visual evidence of a relationship between the difference and the mean, but this can also be assessed for significance using the correlation coefficient. A mean difference close to zero, however, shows little overall bias. Whether the difference (distance of the mean from zero and the width of the 95% limits of agreement) is acceptable, however, depends on subjective judgment based on the size of the measurement and its purpose for which a difference is considered acceptable. For the purposes of the studies conducted as part of this thesis, the decision needed to be clinically relevant and related to what was considered reasonable variation from expected nutrient targets.

Nutrient analysis

Computerised nutrient databases assist the process of nutrient analysis. Accuracy of the selected nutrient database/s, therefore, is an important consideration. Databases have been shown to vary significantly in their mean deviations from chemical analyses values for some nutrients. While differences between individual foods are known to vary by up to 45%, food databases demonstrating relatively good accuracy report mean macronutrient values within 15% of reference values [252]. Further, the nutrient content of the whole diet, based on random variations across food items (which tend to cancel each other out) has been estimated to vary by as little as 5% [293].

Accuracy of the database is dependent on the quality of available food composition data and therefore the technology used to obtain it. It is also dependent on the

range of foods included in the database. In reality, specific food values in the primary database are also based on means. Inadequacies stem from missing foods or recipes and food combinations for which individual components have to be used to assemble the consumed food. The computer software used for the primary nutrient analyses reported in this thesis was the latest version of a program providing updated national food composition data from 11 databases and approximately 4500 foods. Individual foods, commercial brand name items, generic foods items and whole meals were included as well as variations in nutrient content according to cooking methods. Where a food or meal was not found, substitutions were made with similar foods and equivalent recipes entered. Due to the extensiveness of the database this occurred in a minority of cases. Estimates for long-chain fatty acid intakes, however, were not possible using the same database. For this, fat containing foods were re-entered into a separate database for analysis of individual fatty acids. The limitation here was that this database contained fewer food choices so that substitutions with foods of similar fat proportions (total fat content was matched first) occurred more often and therefore had a greater impact on results.

Dietary validation

Procedures that validate dietary data are an important aspect of dietary studies to provide confidence in conclusions drawn from relationships between dietary intake data and clinical outcome measures. Having acknowledged measurement error, the principal behind the validity of dietary data requires a set of replicate readings

from each member of a sample [286]. However, the measurement of dietary data is indirect and represents an unknown quantity from the truth. Further, comparison can usually only be made with another similarly indirect method. Hence, there is no gold standard reference methodology against which dietary data can be compared. Therefore, validation of reported dietary data in this thesis has been provided using several methods: comparison with another data collection method (FR), how well reported energy intake relates to basal metabolic rate (BMR), biochemical markers of fatty acid consumption (the lipid composition of RBCs), repeated measures, as well as assessment of changes in associated clinical markers of metabolic abnormality (weight, glucose control) [257].

Underreporting

Since there is no gold standard for the comparison undertaken above, it is important to attempt to confirm validity, if any, using a further assessment method. Biomarker measures of EE such as urinary Nitrogen excretion and doubly labeled water have confirmed the frequent under-estimation of food intake [294]. Individuals reporting low energy intake can alter results and subsequent conclusions depending on whether their data has been included or excluded [295]. Therefore, methods of validation most often refer to energy intakes. Because primary outcome variables for this thesis were energy and macronutrients as a %E intake, the potential bias in reported energy intake needed to be estimated. One method employed to identify underreporting and/or to examine effects under-reporters may have on the data, is the Goldberg cut off [294], based on the assumption that energy

(EI) intake=energy expenditure (EE) under stable weight conditions [296]. However, EI:BMR=physical activity level (PAL) is used [294] in the absence of a measure of actual EE,, where the energy requirements of individuals are dependent on variations in basil metabolic rate (BMR) according to age, sex and body size and, therefore, can be expressed as PAL to represent daily metabolic rate and, in turn, can be compared to mean reported energy intake (EI_{rep}: BMR) for the study population. Assuming a sedentary lifestyle, agreement is dependent on a calculation of the confidence limit below which energy intake is unlikely to be valid. If mean activity level for the population is known, an upper limit can also be determined. In Study 4, a lower limit only was used based on estimated activity levels defined by the World Health Organisation [297]. Alternatively, a direct comparison between reported EI_{rep} and estimated EE (EE_{est}) can be made for each individual. In Study 4 these were calculated using the Schofield Equation [298] and again WHO defined activity levels [297].

Repeated measures

By obtaining data from each member in a sample more than once, the data can be evaluated in terms of replicate readings at each time point and/or over time to investigate the differences between groups at each time point [286]. For assessment of these differences, the use of the t-test has its limitations. Firstly, the more tests there are, the more likely it is that two sets of data at any given time point will produce a significant difference. This is especially relvant when there is more than two groups and more than two time points. Secondly, small groups make it difficult

to estimate the variance, or measurement error, on which such analyses depend (Bland). Alternatively, the analysis of variance (ANOVA) compares the variation between groups to the variation within the groups and uses all the data to estimate the variance, and thereby provides a more powerful comparison between groups and over time and was used for statistical assessments in this thesis.

Biomarkers

Due to a relationship between dietary fat composition and the fatty acid composition of body tissues, individual fatty acids in body tissues can potentially be used as markers for intakes of different types of dietary fat and dietary change [257]. However, the relationship can vary between individual fatty acids and for different tissues [117]. The fatty acid composition of tissues such as serum lipids and phospholipids in erythrocyte membranes reflect changes in dietary fat composition during the preceding weeks [117 299-302] and is the most reliable and only readily accessible lipid fraction available for biomarker analysis [257]. The relationship between long-chain essential fatty acids (EPA and DHA) in the diet and in tissues is strong, whereas the relationship between SFA in the habitual diet and in tissues is much weaker. As changes in intakes of individual fat types were the primary outcome for studies conducted as part of this thesis, changes in PUFA concentrations in blood samples were biomarkers of PUFA intake [257].

Clinical markers

While clinical outcome variables are considered secondary for this research, they are standard reference points for practice and in substantiation research, and this type of data from the studies conducted as part of this thesis will contribute considerable information for future studies focusing on these variables. Hence, an important clinical outcome measure for T2DM patients is the effect of nutrition intervention on relevant clinical indices. Due to associations between IR, body fat accumulation, and blood glucose and lipid levels, changes in weight, body fat and glucose tolerance were assessed as relevant markers of dietary change. For example, the HbA1c tested a change in long-term blood glucose control while, BMI due to its strong correlation with total body fat [257] was a useful assessment of weight management. Blood lipid levels identified changes to dietary fat intake related to the Metabolic Syndrome.

Ethical issues

Unique ethical issues arise relating to working with humans, including the individual's right to be fed, disruption of food/cultural traditions, and the impact of the intervention on disease prevention [258]. Volunteers must be fully informed of all requirements of the research and of their rights to ask questions, complain or discontinue at any time. Separate avenues of complaint must be provided. The researcher and all members of the research team have a duty to protect the privacy of all participants involved in their research. Every endeavour must be taken to ensure that all participant information is treated with confidentiality.

Specific permission must be sought from each participant for subsequent use of this information. Results should be reported as group data or anonymously without revealing the personal details of any individual. Confidentiality and privacy issues relating to the publication of research findings or reporting in a public forum should be adhered to and participants informed of the intent. Ensuring the research meets specific regulations and standards is met by a system of ethical approval from appropriate legal bodies/committees. The research reported in this thesis obtained prior approval and followed all ethical guidelines and requirements by the Human Research Ethics Committee of the University of Wollongong and Illawarra Area Health Service of New South Wales.

CHAPTER 4 PILOT STUDY LINKING FOOD PATTERNS WITH CLINICAL OUTCOMES

A significant portion of this chapter has been published in the peer-reviewed article:

Gillen L, Tapsell LC, Martin GS, Daniels S, Knight S, Moses RG. The type and frequency of consumption of carbohydrate-rich foods may play a role in the clinical expression of insulin resistance during pregnancy. Nutr Diet 2002;59(2):135-143

LG was responsible for study design, data collection and assessment, preparation of the manuscript and involved in critical discussions of study design and outcomes. LT was responsible for critical discussions of study design, analyses and preparation of the manuscript. GM and SD were involved in dietary assessment design and data collection. SK and RM were involved in coordination of the study.

4.1 Introduction

For the purposes of this thesis, a pilot study was conducted in order to assess the significance of food patterns and relevance to known clinical outcomes in a clinic sample of the treatment population. A cross sectional observational study examined the food habits of a convenience sample of women with GDM, a group with demonstrated glucose intolerance and at-risk of pregnancy complications and T2DM and CVD in the longer term. While dietary studies have traditionally focused on the impact of macronutrient variables on clinical outcomes, this study aimed to examine habitual food patterns likely to influence glucose intolerance and hence related outcomes. Based on clinical and research knowledge, data obtained from this type of analysis would likely be informative and relevant to the practical application of research knowledge for improvements in blood glucose-related clinical outcomes.

GDM, or glucose intolerance during pregnancy, has an incidence of 7.2% in the Illawarra region of New South Wales [83]. Associated adverse outcomes of GDM can include assisted delivery, caesarian section and admission of the newborn to special care [303, 304]. The risk of subsequent development of T2DM, in both mother and child, is also greatly enhanced [305-307]. Those most at risk tend to be older, overweight, multiparous, have specific ethnic origins, a family history of diabetes [99, 308] and/or history of GDM [98]. However, even women with no identifiable risk factors can display clinical symptoms of insulin resistance at an appreciable rate (3%) [99], suggesting other factors may play a role.

An increased insulin resistance is characteristic of pregnancy and women become glucose intolerant if they are unable to increase endogenous insulin secretion to overcome this physiological resistance [80, 309, 310]. Controlling blood glucose levels may help preserve both optimal beta-cell function and maximise insulin sensitivity. Hence, a diet that assists glycaemic control [311, 312] might be beneficial in ameliorating the features of insulin resistance for all women during pregnancy. While clinical trials have shown that managing the consumption of the type and frequency of CHO-rich foods can benefit glycaemic control and reduce insulin demand [225, 313, 314], few studies have assessed patterns of intake in the diets of free-living pregnant women and those who develop GDM. We have previously reported that women who develop a recurrence of GDM report higher fat intakes than those who do not [152], but were unable to detect a significant difference in total CHO intake. Large prospective studies have also been unable to detect a relationship between total CHO intake and diabetes risk [147, 212, 315]. This type of

assessment however does not account for the glycaemic effect of CHO-rich foods or the ability of foods to increase demands for insulin. Consequently, a qualitative assessment of the consumption of both the type and frequency of CHO-rich foods may uncover patterns of intake during pregnancy likely to play a role in the clinical expression of insulin resistance.

In this study, we compared the patterns of consumption of CHO-rich foods reported by a group of free-living women newly diagnosed with GDM and a group of healthy glucose tolerant pregnant controls.

4.2 Methods

4.2.1 Participants and Study Design

All pregnant women attending the Prenatal Clinic at The Wollongong Hospital are offered an oral glucose tolerance test (OGTT) at the beginning of the third trimester of pregnancy to determine GDM status. Diagnosis is based on the recommendations of the Australasian Diabetes In Pregnancy Society (ADIPS) [272]. It is conventional practice for any women diagnosed with GDM to be referred to the Illawarra Area Health Service, Diabetes Centre for medical management. These women are usually seen within two working days. Between August 1999 and January 2000 a convenience sample of 16 pregnant women newly diagnosed with GDM and 24 healthy pregnant controls (as determined by OGTT), and matched for age and pre-pregnancy weight, were recruited on request on first attendance at the

Diabetes Centre (prior to any dietary intervention) and at the Prenatal Clinic, respectively.

All women were of similar gestational age (28-33 weeks). Data on age, pre-pregnancy weight, parity, and incidence of GDM in a previous pregnancy and family history of diabetes (yes/no), were collected by self-report. Height and current weight were measured at the time of interview. BMI (weight (kg)/ height (m^2) was calculated for both pre-pregnancy and current weight, while weight gain during pregnancy was assessed as the difference between the two weights. The Human Research Ethics Committee of the University of Wollongong and the Illawarra Area Health Service provided ethical approval for this research.

Four dietitians administered an open-ended DH questionnaire developed specifically for the study of diet in pregnant women screened for GDM in the Wollongong area of the Illawarra region, Australia [279, 316]. The women were asked to describe their 'usual' intake ('usual' meaning for the previous two- to three-month period). All women were asked if they had changed their 'usual' diet (yes/no) on first becoming pregnant and/or over the period of the pregnancy and, for those with GDM, since being diagnosed. Dietary data were entered into FoodWorks Nutrition Software, (Version 2.03, 1999, Xyris Software, Qld, Australia) for nutrient analysis. This software used the NUTTAB 95 Australian food composition database [317].

Food intake data were analysed for energy and macronutrient composition, expressed as kilojoules (kJ) and grams (g) respectively, and reported as means ±

standard deviation (SD). CHO-rich foods were classified according to five broad food groups: cereal/grains, fruits, vegetables, milk and sugar-rich foods, then divided into 15 sub-groups in order to identify, more specifically, the food sources of CHO intake (Table 4-1). For each subject, the total energy (kJ) and CHO (g) provided by each food group and sub-group were calculated, and a mean intake value was established. In addition, the frequency of consumption of CHO-rich food groups (defined as the number of times the food group was reported in a meal or mid-meal regardless of serving size) was assessed.

Table 4-1 Carbohydrate-rich food groups and subgroups used for analysis of food intake patterns

Cereals/grains	Fruits	Vegetables	Milk	Sugar-rich[a]
Bakery goods	Whole (fresh/frozen/canned)	Total (fresh/frozen/canned)	Milk/Yoghurt	Foods
Biscuits	Juice	High carbohydrate[b]	Other milk products	Beverages
Breads		Low carbohydrate[c]		
Breakfast cereals				
Pasta				
Rice				

[a] Where carbohydrate content is > 50g/100g and sugar contributes > 50% of total carbohydrate content, [b] Where carbohydrate content is ≥ 10g/100g, [c] Where carbohydrate content is <10g/100g

A GI value was assigned to each food within the broad food groups, according to published values[221]. If the GI of a food was unknown and a suitably similar food could not be substituted, the food was excluded from the analysis. ***Appendices A and B*** outline food substitutions and exclusions, respectively.

The assignment of GI values enabled foods to be classified into sub-groups according to GI (high, intermediate or low), which were similarly assessed for amount and frequency of consumption. An 'average' diet GI score for each subject's overall diet was also calculated, as follows:

$$\textit{Diet GI} = \frac{\text{Sum of GI value of individual foods X CHO content (g)}}{\text{Total CHO content for the day} - \text{excluded CHO}}$$ [318]

Individual meal GI scores were obtained using the method described for mixed meals [319]. A glycaemic load score was obtained for overall diet and individual meals from the sum of the [GI value of the individual foods X the CHO content] (g) [214]. To control for total energy intake, all nutrients as well as the scores for diet GI and glycaemic load, were expressed as percent energy (32) using the calculation [mean nutrient intake (diet score) / energy intake] X 100.

Differences between the two study groups were assessed using independent two-tailed t-tests and results expressed as means ± standard deviation (SD), with the level of significance reported at $P<0.05$. Such comparisons were made for: demographic data defining age, gestation, weight and weight gain; dietary data comparing total intakes for energy (kJ), macronutrients and fatty acid sub-fractions (percent energy), total intakes from CHO and CHO sub-fractions (g); energy (kJ) and CHO (g) from the CHO-rich food groups and sub-groups, as well as the frequency of consumption of these foods (a simple count of the number of times a

food was reported); average diet GI and meal GI scores and GI load scores, respectively.

4.3 Results

Characteristics of the GDM and control groups are presented in Table 4-2. No significant differences were found between groups for matched variables (age and pre-pregnancy weight), or for other measures of weight and weight gain during pregnancy, or stage of gestation at the time of the survey. The GDM women, however, were shorter and had a greater parity compared to women in the control group ($P<0.05$). Data on incidence of previous GDM and family history of diabetes were compared and not found to be different. Four of 16 women with GDM and one of 24 control women had a previous pregnancy in which GDM was diagnosed, while six women with GDM and three from the control group reported a family history of diabetes. Fourteen of 16 women with GDM were born in Australia or the UK, hence, ethnicity was not considered to influence the results of this dietary study.

Table 4-2 Maternal characteristics of women with GDM and healthy pregnant controls[a]

	GDM	Control
Characteristics	n=16	n=24
Age (yrs)	31.4±4.8	29.2±5.6
Gestation (wks)	29.4±1.7	29.4±1.2
Parity	1.9±1.5	0.6±0.7*
Pre pregnancy weight (kg)	63.1±14.7	67.0±18.5
Pre pregnancy BMI (kg/m^2)	24.3±5.6	24.2±5.5
Weight (kg)	73.4±14.8	76.6±9.9
BMI (kg/m^2)	28.3±5.5	27.4±2.5
Pregnancy weight gain (kg)	11.5±4.4	10.6±5.2
Height (cm)	161.2±4.3	167.8±6.0*

[a] Mean ± standard deviation.

* P<0.05 by two tailed t-tests.

Similarly, no differences were found between groups for reported dietary change during the current pregnancy. Eight of 16 women with GDM and 16 of 24 control women reported a dietary change on first becoming pregnant, while 7 GDM women and 16 controls reported a dietary change over the period of the pregnancy. For the GDM group, seven of 16 women reported a dietary change since diagnosis (in most cases 2-3 days prior to the survey). Only three GDM and two control women reported no dietary change at all during the current pregnancy. The dietary intakes of energy and CHO were not significantly different between the two groups (Table 4-3).

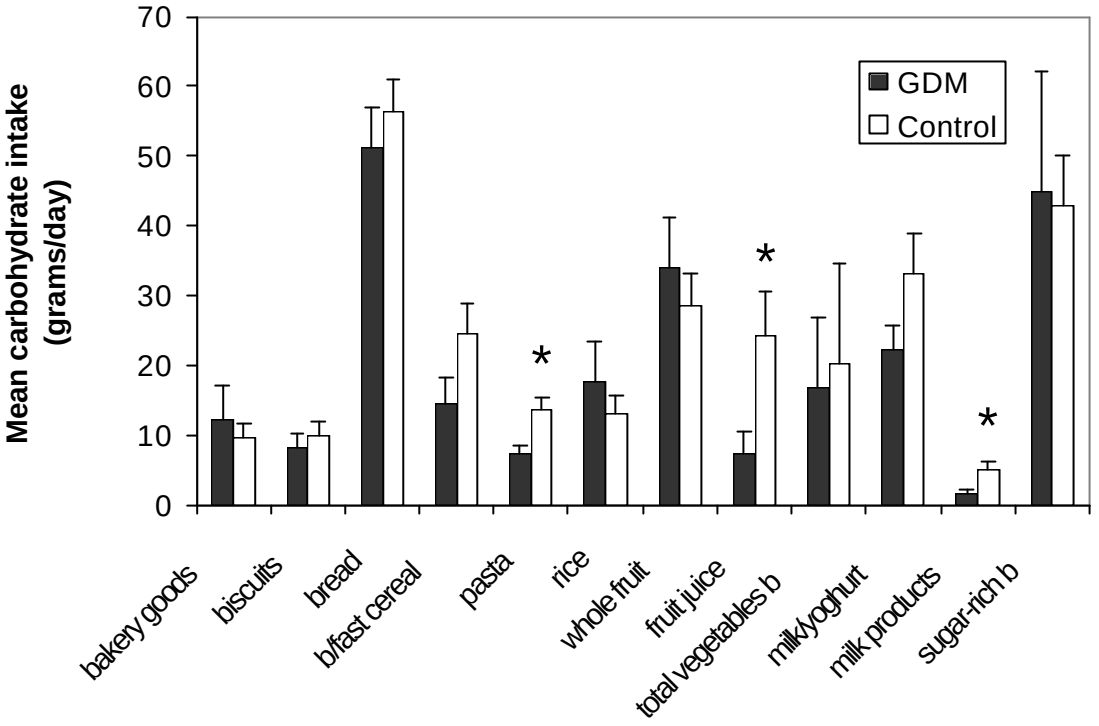
Table 4-3 Mean total dietary intakes for GDM and control groups

	GDM[a] (n=16)	Control[a] (n=24)	P-value[b]
Total Energy (kJ)	8814.0±2888.7	10384.1±2344.2	0.07
Carbohydrate (g)	263.1±96.2	309.0±71.3	0.09
Carbohydrate (% E)	48.0±7.3	48.0±6.8	1.00
Protein (% E)	18.4±4.7	17.4±2.2	0.39
Fat (% E)	31.0±8.9	32.5±7.2	0.55
MUFA (% E)	10.6±3.0	10.7±2.3	0.86
PUFA (% E)	6.6±5.1	5.1±2.2	0.17
SFA (% E)	12.6±4.4	14.4±4.8	0.24
Fibre (g)	25.1±7.9	25.2±8.2	0.97
Sugar (g)	128.2±78.8	162.1±53.6	0.11
Starch (g)	128.6±37.9	141.5±34.9	0.28

[a] Mean ± standard deviation.
[b] determined by t-tests for differences between groups.
% E = percent energy.

The GDM group consumed smaller amounts of CHO (g) from pasta, fruit juice, and milk products ($P<0.05$) (Fig 4-1). There was also a non-significant trend by the GDM group to consume less (g) milk/yoghurt ($P=0.09$).

Fig 1 Mean carbohydrate intakes from carbohydrate-rich foods by GDM and control groups[a]



[a] Values are mean ± SD
[b] no differences were observed from further sub-divisions of these food groups.
* P<0.05 two-tailed t-test.

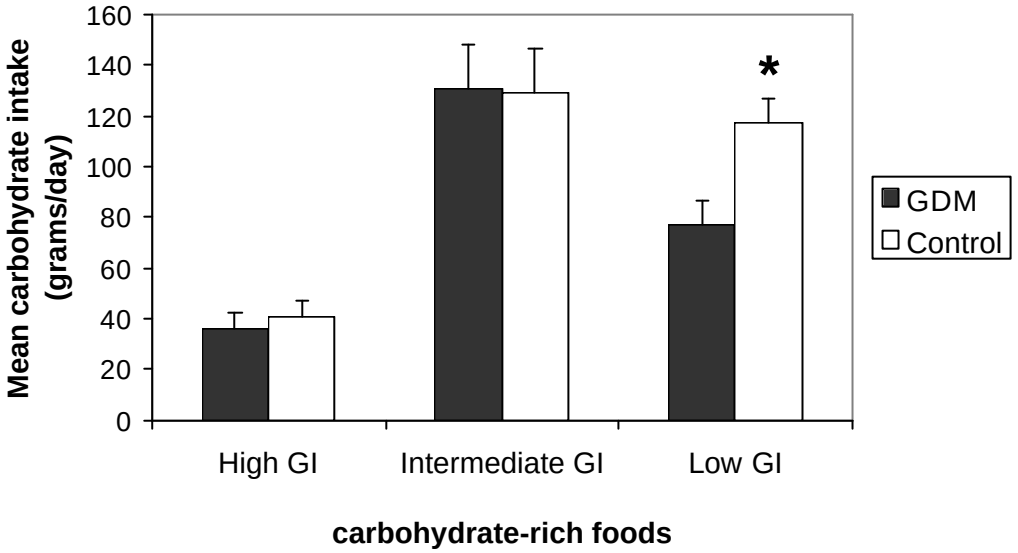
Figure 4-1 Mean carbohydrate intakes from carbohydrate-rich foods by GDM and control groups

The GDM group reported a lower frequency of consumption from high CHO vegetables or foods and beverages from the sugar-rich group (P<0.05), despite similar intakes in terms of total kJ and CHO (g) from these foods. A trend for less frequent intakes was also demonstrated for the cereal/grains group (P=0.06).

The GDM group of women consumed significantly less total energy and CHO from low GI foods, expressed in terms of kilojoules (2450.8±1255.9 kJ GDM vs 3592.0±1645.3 kJ control) (P=0.02) and CHO grams (P=0.01) (Fig 4-2). This

observation was made also for dinner meals, (530.0±501.7 kJ GDM vs 920.0±564.6 kJ control) (P<0.05) and (15.9±14.8 g GDM vs 28.8±18.5 g control) (P<0.05). The GDM women also reported consuming less low GI cereal/grains, again, both in terms of kilojoules (2413.4±1322.8kJ GDM vs 3625.0±1717.0kJ control) (P<0.05) and CHO grams (79.1±39.5g GDM vs 117.1±55.2g control) (P<0.05).

Fig 2 Mean carbohydrate intake from foods of known GI values by GDM and control groups[a]



[a] Values are mean ± standard deviation. * P<0.05 two-tailed t-test.

Figure 4-2 Mean carbohydrate intakes from foods of known GI values by GDM and control groups

No differences were found for energy or CHO intakes from high or intermediate GI foods, however, these foods were reported less frequently by the GDM women over an average day (high GI foods: 5.9±2.4 GDM vs 8.3±4.1 control) (P<0.05);

(intermediate GI foods: 15.6±6.2 GDM vs 19.5±5.3 control) (P<0.05). In particular, high GI vegetables were reported less often by the GDM group (2.9±1.5 GDM vs 4.7±2.9 control) (P<0.05).

The mean diet GI for each group was not significantly different (58.3±4.4 GDM vs 56.7±4.3 control). However, when adjusted for total energy intake the GDM group had a significantly higher diet GI score than the control group (74.8±31.8 GDM vs 57.6±16.3 control) (P<0.05). No differences were found when comparing mean glycaemic load scores (14130.5±6018.8 GDM vs 16234.8.1±4027.2 control) nor when expressed as %E (159.5±24.0 GDM vs 157.9±26.1 control). The mean dinner meals GI score for the GDM group was significantly higher than for the control group (65.6±6.6 GDM vs 59.2±8.0 control) (P=0.01). Furthermore, the average standard deviation across all meal GI scores was higher for the GDM group (14.3 GDM vs 9.3 control), indicating greater variation in GI scores for meals across the day, although no further differences for meal comparisons of GI were found. Similar comparisons for meal glycaemic load scores were not significantly different between the two groups.

Foods of unknown GI, excluded from the analyses, made up ≤ 10% of the CHO intake for 15 of 16 women with GDM and 23 of 24 control women, with no significant differences between the two groups for the amount of food excluded as a percentage of either total energy (kJ) or total CHO (g).

CONCLUSION

4.4 Summary

The limited evidence-base for dietary intervention in the management of GDM comes from clinical trials using individual foods and set meals to modify blood glucose levels [223, 320, 321]. Far fewer studies have reported on the food choice patterns of pregnant women under 'free living' conditions. In particular, the diets of women with GDM are very much underreported [310]. Those who have examined populations at risk of diabetes have focused mainly on macronutrient intakes and 'suspect' foods and have failed to identify dietary differences that warrant specific recommendations [152, 213, 322].

In this study differences were found in the pattern of CHO intake reported by women diagnosed with GDM compared with glucose tolerant pregnant controls. By controlling for other risk factors related to GDM (age and pre pregnancy weight), and recruiting at similar stages of gestation, few significant non-dietary differences were found between the two groups, except the GDM women were shorter and had greater parity ($P<0.05$), two aspects found previously for GDM women [323]. While significant differences in energy and macronutrient intakes were not found in this sample, the trend by the GDM group to consume less energy and CHO is a phenomenon observed for other diabetic populations [152, 213]. Whether lower intakes reflect actual dietary changes or recall bias in response to diagnosis is uncertain

and may represent a limitation of the study. The types of foods restricted by the GDM group however were not those normally associated with underreporting [268].

In this study, the GDM group reported consuming less CHO from low GI cereal/grain foods, in particular pasta, and from fruit juice and milk groups. While none of these foods have a high GI value, it could be speculated that these women perceived these foods as worthy of restriction. Although we did not assess this, all but three of the women in this group reported some type of dietary change during the current pregnancy and, while the GDM women had not yet received any specific dietary advice for diabetes management of the current pregnancy, four of the 16 had a prior GDM pregnancy and may have been exposed to previous dietary advice. Similarly, high CHO (starchy) vegetables were consumed less frequently throughout the day by the GDM group, suggesting these women were trying to limit their intakes of these foods. Hence, the food choice patterns described diverge from those recommended for pregnant women, a nutritionally at-risk group with additional requirements for the nutrients contained in these food groups, for example vitamin C and calcium from juice and milk, respectively. Additionally, although the total amount consumed from foods with higher GI values were similar for both groups, the GDM group reported selecting them on fewer occasions during the day ($P<0.05$). Again, these behaviours are contrary to current diabetes management strategies that focus on smaller portions and more frequent intakes over the day.

The patterns reported by the GDM women contributed to a significantly higher average diet GI score, expressed as a percentage of total energy intakes, when compared to the control group ($P<0.05$). The GDM group also reported significantly lower intakes of low GI foods at dinner and subsequently higher GI meal scores for that meal ($P<0.05$).

Even modest reductions in GI scores, within the range of values found in a free-living diabetes population, have been shown to improve blood glucose control [281, 324]. Similarly, foods with comparatively higher GI values, consumed more regularly over the day, have been shown to modify blood glucose levels by spreading the GI load [212, 315]. The lack of any significant difference in our study between the two groups for total GI load scores further suggests partitioning the load may be more important for controlling blood glucose levels than the load *per se*, although this was not apparent from differences in meal glycaemic load scores. It should be noted however that unless fluctuations in meal GI and load scores for each person in the group coincide for different meal-times, mean representations may be unable to detect any significant differences between groups. Arranging individual meal scores from lowest to highest regardless of time frame may prove more informative. Despite this, the evening meal, possibly the main meal of the day, was significantly different for meal GI scores between the two study groups, and may have been the only meal with consistent enough intakes between individuals to detect a significant difference. How these meal scores impact on other meals such as breakfast the next day is uncertain, but clinical evidence suggests an effect for glucose and insulin responses to later meals [325, 326].

4.5 Theoretical significance

Women who develop GDM fail to overcome insulin resistance in pregnancy due to a variety of factors, the most alterable of which may be diet. Clinical trials using low GI CHO-rich foods and increased frequency of intake to modify blood glucose levels have shown the greatest potential benefit [223, 225, 313]. This small cross-sectional survey of the food habits of free-living pregnant women has identified patterns of intake from CHO-rich foods that support this view. Compared to glucose tolerant pregnant controls, women with GDM reported less CHO-rich foods with low GI values, in particular, pasta, fruit juice and milk products, and a reduced spread of consumption of foods with higher GI values. While both groups reported dietary changes in response to pregnancy, reference to previous research suggests the patterns of intake reported by the GDM group are likely to impact on glucose tolerance.

4.6 Limitations and areas for further research

This study has focused on food patterns as a means for understanding dietary relationships in GDM. Analyses of food choice patterns are less dependent on the inadequacies of nutrient databases and allow the diet to be described in a manner that is useful outside the research setting [327]. A limitation is that it is sensitive to the way food consumption data are categorized [269]. Accordingly, several criteria were used to define food groups and identify patterns of intake. Food source and GI identify foods of similar components and metabolic effect [214, 281], and are considered valid criteria for statistical assessment [281].Possible bias due to

underreporting, however, has been overcome by organizing foods into groups based on a more rounded estimate (high, intermediate and low GI), eliminating some of the error between individual responses and exact GI values [282, 283].

Appropriateness of the methodology too can reduce the degree of error for estimating dietary intakes [328, 329]. The pattern of intake is dependent on the way consumption is reported and, a meal-based DH that requires a sequential re-telling of regular intakes, is sensitive to the daily spread of individual foods and food groups [287]. The modified version used for this study was validated in a local diabetes population and is considered sufficiently valid and reliable for use in studies of pregnant women in the Wollongong area [279]. While a DH taken prior to diagnosis and the exclusion of women with risk factors for diabetes during the current pregnancy may have avoided the possible introduction of dietary and other forms of bias, the omission of data obtained from women with a previous GDM pregnancy did not significantly alter our results. Nonetheless, the results do indicate that a qualitative assessment of the patterns of CHO intakes of a convenience sample of women with and without GDM can uncover dietary differences not readily identifiable using traditional macronutrient comparisons.

A larger prospective dietary intervention study is required to confirm the role of food patterns in the dietary management of GDM and to further assess the impact of food patterns on the clinical expression of insulin resistance during pregnancy.

4.7 Relevance to thesis and implications for practice

The results from this study of the food habits of glucose intolerant and normal glucose tolerant pregnant women suggest qualitative differences in food choice patterns that have the potential to provide physiological benefits during pregnancy. While both groups reported dietary change during the course of the current pregnancy, different perceptions about the relationship between diet, health and disease, as well as previous exposure to dietary advice may account for dietary differences between the two groups. While one might expect previous exposure to dietary advice to result in beneficial patterns of intake, traditional 'negative' nutrition messages can translate into food restrictions that impact on food variety and frequency of consumption. Nutritional and metabolic susceptibility to disease has been previously noted [327, 330], and may therefore be an important consequence of dietary change and has implications for the dietary management of pregnant women who have an increased susceptibility to glucose intolerance at this time.

For this thesis, the pilot study results demonstrated the importance of food pattern analyses for assessing aspects of the diet-disease relationship by providing dietary information not obtainable using a nutrient-based approach. In this way, the relevance of food patterns to the dietetic process, to inform practice and on which to base advice was confirmed. In terms of advice for diabetes, this study recognized the role of CHO in the diet and justified attention to this nutrient in advice approaches using frequency of intake and different aspects of the food form to influence glycaemic control.

CHAPTER 5 DEVELOPING FOOD PATTERNS TO GUIDE ADVICE TO ACHIEVE MACRONUTRIENT TARGETS

A significant portion of this chapter has been reviewed for publication in the Journal of Nutrition and Dietetics and revisions have been resubmitted to the Editorial Board:

Gillen LJ, Tapsell LC. The development of food groupings to guide dietary advice for people with diabetes. Nutr Diet: In review

LG was responsible for the implementation of study design, data collection and analyses, involved in critical discussions of study design, analyses and study outcomes as well as preparation of the manuscript. LT was responsible for critical discussions relating to study design, analyses and preparation of the manuscript.

5.1 Introduction

A theoretical study was conducted to develop and statistically test a food advice framework for the achievement of nutrient targets in an intervention trial. With diabetes as the example, nutrient targets were macronutrients and fat types as proportions of total energy intake. Developing a set of food groups and specific intake pattern provided an outline and a methodology of the processes involved in dietetic practice for the conversion of the theory on nutrients into practical advice on foods.

Diet is often quoted as the cornerstone of treatment for diabetes, and there is considerable evidence that advice targeting specific dietary change offers substantial benefit [20, 21, 190, 331, 332]. Current guidelines for the treatment of diabetes and related complications provide nutrient intake recommendations, the most specific of which target the proportions of different types of fat in the diet [8]. Where

dietary advice necessarily refers to foods, the system of advice generation, however, needs to assure that nutrient targets can be met.

A number of food guidance systems are available with varying purposes. For example, the carbohydrate counting system in diabetes management [333] focuses on the distribution of carbohydrate-rich foods throughout meals to support glycaemic control. General food guidance systems, such as the Australian Guide to Healthy Eating (AGHE) [13] and the Food Guide Pyramid [14], outline the number of servings from core food groups required to meet nutritional requirements for the general population. Exchange lists published by the American Dietetic Association (ADA) [15] take a total diet approach, where 'all foods can fit into a healthful eating style' [334], and provide some information on the type of fat contained in foods [335]. While certain food groups are generally recognised for contributing a particular type of fat, for example meat and dairy for providing saturated fat, none of the current guidance systems provide adequate reference to food sources high in monounsaturated or polyunsaturated fats. Hence, general low-fat advice strategies based on these systems do not necessarily address specific relative amounts of the different types of dietary fat [22]. While it is acknowledged that individualising advice is fundamental to the treatment of diabetes, a structured food-based advice strategy to guide the achievement of appropriate targets for each type of fat is also required. This must satisfy both recommended and practical evaluations in order to determine whether the resultant intake pattern does indeed achieve the nutrients targeted.

The aim of this paper, therefore, is to describe the development and characteristics of a food categorisation system for the treatment of diabetes, resulting in a set of food groups inclusive of the type of fat (vegetables, starch, fruits, milk/soymilk, meat/oily fish/soybeans, and fat-MUFA/PUFA) and its application in terms of a reference intake pattern to guide advice to meet energy and nutrient targets with minimal potential variation.

5.2 Methods

5.2.1 Study design and theoretical evaluation

The process for the systematic development and evaluation of a specific food group intake pattern to guide advice for the achievement of overall energy and nutrient targets is summarised in Fig. 5-1 and outlined in detail below:

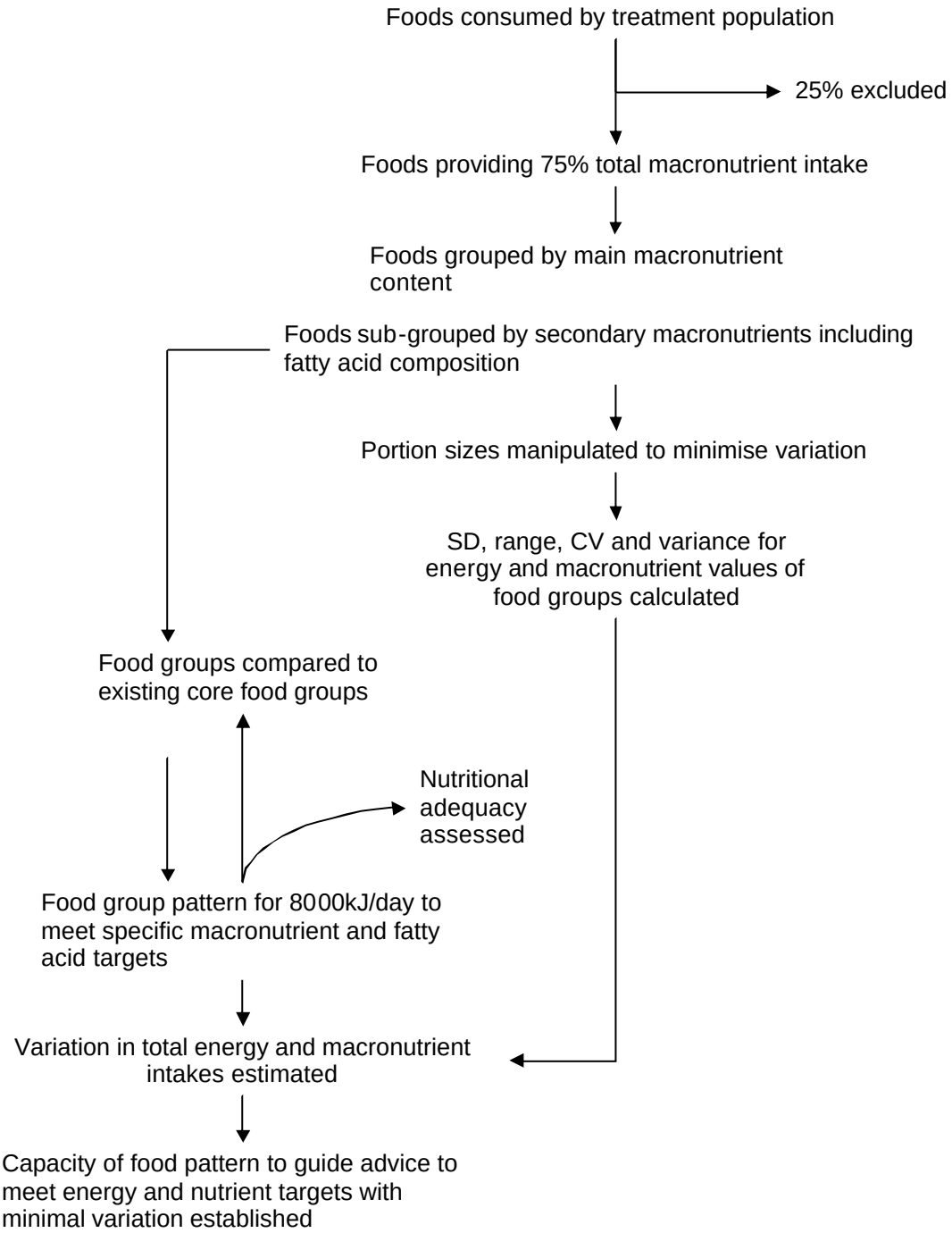


Figure 5-1 The systematic development and evaluation of a good group pattern to guide advice to ensure energy and nutrient targets

Development of food groups as sources of macronutrients and fat types

Identification of foods to include in the food groups

Foods to be included in a set of food groups for the achievement of specific nutrient targets were identified from foods commonly consumed by 16 women with gestational diabetes mellitus (GDM) from Wollongong, Australia. Characteristics of the study sample have been previously described [336]. Individual foods reported in a diet history [337] by each woman were analysed for energy and macronutrient content using the nutrient analysis software program FoodWorks (Version 2.1, 2000, Xyris software, Brisbane, Australia) incorporating nutrient tables for use in Australia (AUSNUT, Canberra, 2000). Mixed dishes and prepared foods were analysed using individual ingredients where possible. Using pooled data, the percentage contribution of common food groupings, such as cereal, meat, and cheese, to total macronutrient consumption for carbohydrate, protein and fat was determined. The groupings were then rank ordered under these macronutrient variables to determine major food sources of each (Table 5-1). Food groupings contributing to approximately 75% of total intake for each macronutrient were taken as representative of foods commonly consumed by the study sample.

Table 5-1 Rank order of the percentage (%) contribution of common food groupings to approximately 75% of macronutrient content of the diets of 16 women with GDM

Food Groupings	**Protein** % total intake	**Food Groupings**	**Carbohydrate** % total intake	**Food Groupings**	**Fat** % total intake
Meat	23.8	Cereals/bread	42.1	Oil/margarine	18.0
Cereals/bread	21.1	Fruit	16.9	Meat	11.7
Milk/yogurt	14.9	Sugar-rich	12.7	Cereals/bread	11.3
Fish	7.4			Milk/yogurt	11.1
Vege/legumes	6.6			Cheese	9.9
				Fast food	7.8
				Nuts	4.5
Total intake:	*73.8*		*71.7*		*74.3*

Categorisation of the included foods base on macronutrient composition

Individual foods belonging to the common food groupings were then categorised by the relative proportions of all macronutrients contained in a single serving. Thus, with reference to existing standards [13, 14], mean energy (kJ) and macronutrient content (grams) per serving were derived. Each macronutrient was considered in turn, commencing with the main macronutrient (carbohydrate, protein or fat). A fourth category accommodated foods which did not have the levels of macronutrients identified in the other three lists, mainly vegetables, but never-the-less needed to be included in terms of total energy and micronutrient intakes. Sub-categories were developed based on secondary macronutrient compositions. For example, in the case of fat content, the need to identify the type of fat required SFA-rich versus PUFA-rich sub-categories in the milk and meat groups, but not MUFA-rich as this type of fat largely mirrored SFA content. Fast foods, such as ham/cheese burgers and fried chicken, had similar fat profiles to that of SFA-rich high-fat meat and cheese and, therefore, were included in that group. Similarly, fat-

rich foods (oils, spreads and nuts) were categorised as PUFA-rich or MUFA-rich, according to the main type of fat they contained. This process would also have necessitated a SFA-rich sub-category within the fat-rich group except the study sample was already limiting fat-rich food sources of this type of fat, for example butter.

To minimise variation between individual foods within each food group, the following steps were followed:

i) A reference food was identified within each main macronutrient category. For example, bread was taken as the staple food for carbohydrate.

ii) Portion sizes for individual foods in each list were modified to produce a gram amount for the main macronutrient close to that of a standard serving of the staple food. Thus, portion sizes for foods listed under carbohydrate were modified to more closely match the 15 grams of carbohydrate taken for one slice of bread.

iii) Sub-categories were based on secondary macronutrients and also on other nutritive components such as the presence of starch and sugar.

Thus, a set of reference food groups representing the mean macronutrient content of common foods was determined (Fig 5-2).

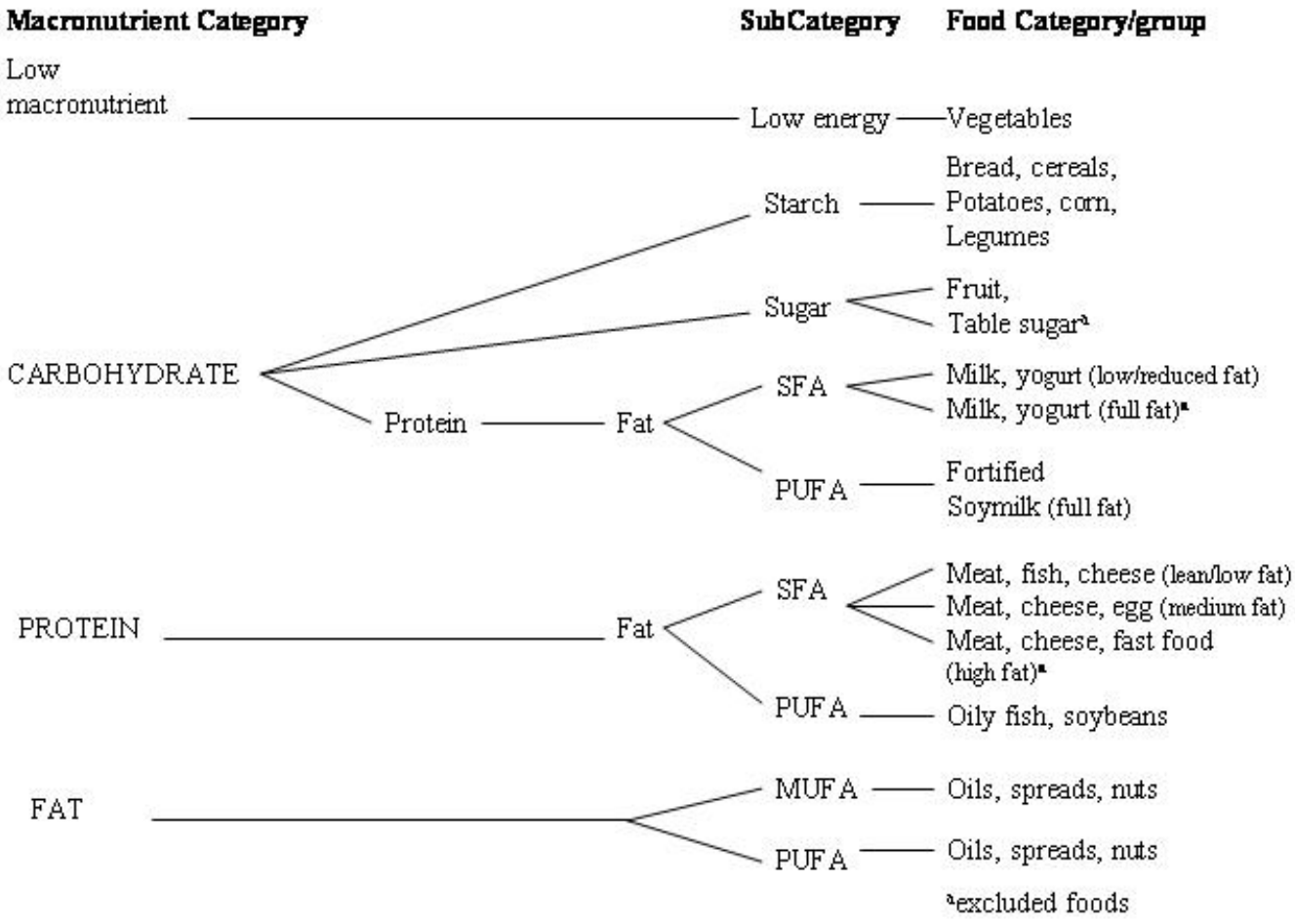


Figure 5-2 Categorisation of individual food portions based on equivalent macronutrient and fat compositions

Estimation of food group variation

All foods contributing to a single food group were analysed to determine mean nutrient content, range, and coefficient of variation (CV = SD/mean x 100) set at ≤15% for the main macronutrient. Reference to existing methodologies was required in order to assess the acceptability of expected variation. Thus, the SD and range results were compared to those reported for the 1995 ADA Exchange Lists for Meal Planning, the only other set of exchange lists to provide specific data on within-list variations from mean nutrient estimates [17].

Comparison with core food groups

In order to establish whether general nutritional adequacy might be achieved from an intake pattern based on the reference food groups, they were compared with core food guide classifications outlined in AGHE and Food Guide Pyramid [13, 14]. Additionally, food groups that did not meet nutrient density criteria consistent with ADA guidelines, that is, foods with high (saturated) fat or sugar (sucrose) content, were identified as 'foods to limit' and excluded from the final set of food groups for which intake levels were set.

Determination of a recommended food group intake pattern

Construction of a food group intake pattern to meet nutrient targets

Mean amounts for the energy and macronutrient content from each of the food groups were rounded-off to the nearest whole number, with the following

exceptions: the protein content of one serving of milk was rounded down to 10g instead of up to 11g due to a greater number of individual food items containing nearer to that amount; the fat content of medium-fat meat was rounded down to 5g rather than up to 6g in order to be consistent with the sum of available data for individual fat types; finally, the small CHO content of soybeans and nuts was ignored to enable a better representation of more common foods listed in these groups, such as fish, and oils/spreads, respectively.

In this way, a simplified nutrient composition table in a 'ready reckoner' format was produced. A total diet pattern was constructed from a defined number of servings from selected reference food groups using corresponding ready reckoner estimates to produce specific targets for total energy and macronutrient intakes. Based on the average requirement for moderately active, weight stable adults, the target for energy was around 8,000 kJ/day [338, 339]. Core food recommendations were adhered to by aligning the number of servings from the reference food groups with minimum daily requirements from core food guide classifications [13, 14]. Nutrition principles for diabetes management [8] were also considered in order to enable advice on portion control, CHO-counting, and identification of the type of CHO (wholegrain, high fibre, low GI). Macronutrient goals corresponded to low fat intakes and current diabetes recommendations [8]: approximately 30% energy as total fat (<10% saturated (SFA) and ~10% total polyunsaturated (PUFA) fat) and around 20% protein, leaving 50% energy as carbohydrate. Atwater Factors were used to convert percentage of energy to grams of macronutrients [340]. Steps in the determination of the recommended food group pattern are outlined below:

(i) Foods from the carbohydrate group were included in the diet first, where 50% of energy translated to around 250g carbohydrate, or 15 exchanges of foods delivering 15g carbohydrate per exchange [allowing for some carbohydrate from vegetables]. Ready reckoner estimates for the protein and fat content of these foods were also calculated at this stage.

Protein targets were next addressed by referring to the recommended amount from cooked meat or meat equivalent [13], with an average amount from all sources achieving, 5oz [150g]. Protein means were added to those obtained from carbohydrate-rich foods, established in (i).

(iii) Targets for different types of fat were lastly addressed, mainly through the inclusion of foods that deliver PUFA, since SFA from carbohydrate and protein foods was already found to be adequate from the inclusion of lean and low fat groups in steps (i) and (ii).

Total kJ and grams of macronutrients from the overall intake pattern were calculated and compared to targets.

Matching dietary advice to the recommended food group intake pattern

Using this framework, dietary advice would refer to a specific number of servings per day from each of the reference food groups defining the recommended food pattern. The advice would be appropriate for diabetes, allowing individualised food choices and the type and distribution of carbohydrate-rich foods and meals throughout the day.

Nutritional adequacy of the food group intake pattern

Overall nutritional adequacy was assessed qualitatively by comparing the number of servings from across the food group intake pattern with core food requirements for adults [13, 14]. A random selection of food items to represent each of the food groups in the recommended pattern and in the amounts specified was compared with ≥75% of intakes recommended [339, 341] for energy, protein and vitamins A, C, E, folate, and minerals, iron, calcium, magnesium and zinc. Selection of a 'random' food item was achieved when an individual blinded to the food database chose a number between zero and the number of foods contained in the corresponding food list, inclusively. When foods from that list were arranged in reverse order, the food corresponding to the number chosen became the representative food. This process was repeated independently for each food group.

Comparison with unrounded estimates of dietary intake

The effect of using rounded estimates for calculations of total dietary intakes needed to be assessed. Based on the food group intake pattern developed for 8,000kJ, total estimates for energy, CHO, protein, fat, and each fat type were calculated from 'rounded' ready reckoner estimates and from the original unrounded means, and the differences compared.

Variation due to individual food choices

The variation in intakes for total energy and macronutrients that might be expected from food choices within the restraints of the food group intake pattern was also

assessed. This was achieved by taking the sum of variances from each food group for CHO, protein, fat and each fat type, respectively. The square root of the sum of variances provided a total standard deviation (SD) for each macronutrient variable and, in turn, a SD for total energy intake. In this way, energy and macronutrient distributions from all possible food combinations to meet the prescribed pattern of intake were determined.

The steps undertaken to achieve the assessments of the effects of rounding and variation due to individual food choices are outlined below:

(i) A total mean estimate in grams for each macronutrient and fat type in the overall food pattern was determined from the sum of the original means for each of the included food groups

(ii) The SD of each estimate determined in (i) was calculated using the formula:

$$SD_{[\text{total grams}]} = \sqrt{(x_1\, SD^2_1 + x_2\, SD^2_2 + x_3\, SD^2_3 + \ldots + x_n\, SD^2_n)}$$

Where, SD = standard deviation

x_1 = number of serves from food group 1

SD^2_1 = variance for the total mean (grams) from food group 1

(iii) The total grams ±SD determined in (i) and (ii), respectively, for each macronutrient variable were converted to energy (kJ) using Atwater Factors.

(iv) The resultant energy±SD for total carbohydrate, protein and fat determined in (iii) were summed to give total energy and SD for the overall diet.

The co-efficient of variation (CV) for each macronutrient variable and total energy were calculated from mean total energy±SD determined in (iv). CV<15% was the arbitrary estimate set for reasonable variation for intakes of total energy and each macronutrient and fat type from the food group intake pattern..

5.3 Results

Development of food groups as sources of macronutrients and fat types

Identification of foods to include in the food groups

Major food groups commonly consumed by the study sample were rank ordered to reveal 24% of protein intake came from meat, 42% of carbohydrate came from cereal-based foods, and 18% of fat from oils and margarines. Cereal-based foods also made major contributions to the protein (21%) and fat (11%) fractions of the diet, while milk and yoghurt made secondary contributions to both protein (15%) and fat (11%). Combining milk, yoghurt, meat and cheese provided most of the fat intake - predominantly saturated fat.

Categorisation of the included foods based on macronutrient composition

Three hundred and forty eight common food items composing approximately 75% of the total macronutrient content of the diets of the study sample were categorised according to macronutrient composition to form nine sub-categories and 13 final

food groups outlined in Fig.5-1. Corresponding mean estimates for energy and macronutrient content of individual food portions are provided in Table 5-2.

Table 5-2 Mean±SD and range for estimates of the main macronutrient content of food groups based on macronutrient composition

Macronutrient		**Carbohydrate (g)**			**Protein (g)**			**Fat (g)**		
Food List	No.	Mean	SD[a]	Range	Mean	SD[a]	Range	Mean	SD[a]	Range
Vegetables ½ cup cooked/1 cup raw	33	2.3	±1.1	0-4[b]	1.9	±0.9	1-4	0.0	±0.0	0-0
Starchy foods 1 slice/ ½ cup	89	14.9	±1.8	11-19[c]	3.1	±1.5	1-10	0.8	±0.7	0-2
Fruit 1 piece	38	15.2	±1.4	13-18[d]	1.2	±0.8	0-3	0.1	±0.3	0-1
Table sugar 1 tspn/5g	1	5.0	±0.0	0-0	0.0	±0.0	0-0	0.0	±0.0	0-0
Milk (low/reduced fat) 1 cup	12	14.6	±1.6	12-17[e]	10.8	±0.9	10-12	1.9	±1.9	0-4
Milk (full fat) 1 cup	5	15.2	±0.8	14-16	11.8	±1.9	10-15	11.4	±0.6	11-12
Soymilk (full fat) 1 ¼ cup	1	15.0	±0.0	15-15	11.0	±0.0	11-11	12.0	±0.0	12-12
Meat(lean/low fat) 30g/1 oz	68	0.1	±0.4	0-2	7.2	±0.7	6-8[f]	1.8	±1.1	0-4
Meat (medium fat) 30g/1oz	30	0.4	±0.8	0-3	7.2	±0.8	6-9[g]	5.7	±0.8	5-7
Meat (high fat) 30g/1oz	24	0.5	±1.0	0-3	7.0	±0.8	6-8	9.3	±1.3	8-12
Oily fish, soybeans 30g/1oz	6	0.5	±0.8	0-2	7.2	±0.4	7-8	3.5	±0.6	3-4
MUFA-rich 1 tspn/5g	24	0.5	±0.6	0-2	0.4	±0.9	0-2	5.2	±0.5	5-6[h]
PUFA-rich 1 tspn/5 grams	17	0.2	±0.5	0-2	0.2	±0.4	0-1	5.1	±0.3	5-6[i]

ADA published values [17]: [a] 0-4.7; [b] 1-14; [c] 11-23; [d] 11-20; [e] 11-17; [f] 5-9; [g] 5-11; [h] 3-5; [i] 3-6

Estimation of food group variation

For each of the 13 food groups, within-list variation was low: CV<15% for primary macronutrients (data not shown); and SD <2g, although the number of foods listed varied from 1 to 89 (Table 5-2). The vegetables group was the exception to this with greater variation, but with very low macronutrient content. Therefore, serving size modification aimed at reducing the variation for energy (CV<15%) (data not shown) as the main dietary variable for this food group rather than macronutrient content. Standard deviation and range for individual foods within each list compared well with those reported in the literature [17], the results demonstrating in most cases a narrower data set. Therefore, mean estimates for each of the reference food groups were considered representative of the energy and macronutrient content of individual food items listed within each group.

Comparison with core food groups

Food guides [13, 14] generally refer to five core food classifications (bread/cereals, vegetables, fruit, milk, meat and equivalents) outlined in Table 5-3. In addition, the AGHE refers to a broad variety of extra 'foods to limit'. In contrast, our categorisation process derived 13 food groups, 10 of which were determined to be appropriate for the nutritional management of diabetes. Hence, foods listed in the reference food groups identifying table sugar/sugar-rich foods, full-fat milk and high-fat meat/fast foods represent more specific 'foods to limit'. Further, differences between our food groups and the guides were: the inclusion of CHO-rich starchy vegetables with cereal-based starches such as bread rather than with other

vegetables with low CHO content; cheese listed as a protein-rich food with meat rather than with milk and these groups sub-categorised to address differences in the amount and type of fat they contain; and finally, the inclusion of high-fat foods such as oils, spreads and nuts; again with sub-groups for proportional differences in the type of fat. Although more discriminating between foods, our final set of food groups were consistent with core food guide classifications in that a minimum number of servings across the overall pattern of food group intake would ensure adequate nutrition.

Table 5-3 Comparison of existing food guidance systems and macronutrient-based reference food groups used to construct a pattern of intake to guide advice for diabetes treatment

Core Food Guide[a,b] Classification	Average Serve size	USDA[a] Serves/day	AGHE[b] Serves/day	Reference Diet Model[c] Serves/day	Macronutrient-based Reference Food Groups
All vegetables, legumes	½ cup cooked	3-5	4-8	5	**VEGETABLES** Excludes potatoes, corn, legumes
Bread, cereals, rice, pasta, noodles	1 slice ½ cup	6-11	8-14	9	**STARCH** Plus potatoes, corn, legumes (not soybeans)
All fruit	1 medium	2-4	2-4	4	**FRUIT**
Milk, yogurt, cheese	1 cup	2-3	2-4	2	**MILK** (low/reduced fat) Excludes cheese **SOY MILK** (full-fat)[d]
Meat, fish, poultry, eggs, nuts, legumes/ dry beans	Cooked meat equivalent 2-3oz[a] 65-100g[b] 30g(1oz)[c]	2-3	1-1.5	5	**MEAT** (lean/low fat) Excludes oily fish, nuts, legumes Includes cheese (medium fat) Includes eggs and cheese **OILY FISH/SOY BEANS**[d]
'extra foods' including margarine, oils, sweets, biscuits, snack foods & alcohol	Limited[a] 145kcal[b] 1tsp fat[c] 10g nuts[c]	Limit	0-3	3 5 Limit	**MUFA** Includes oils, spreads, nuts[e] **PUFA** Includes oils, spreads, nuts[d] - sugar-rich foods - milk/yogurt(full fat) - meat/fast food (high fat)

[a] Food Guide Pyramid [14]
[b] Australian Guide to Healthy Eating [13]
[c] Pattern of intake developed from Reference Food Groups to provide approximately 8000kJ
[d] High in PUFA
[e] High in MUFA

Determination of a recommended food group intake pattern

Construction of a food group intake pattern to meet nutrient targets

Rounded mean estimates corresponding to each list of foods provided a “ready reckoner” of energy and macronutrient compositions for the final set of food groups (Table 5-4). Subsequent food group assemblage using ‘rounded’ ready reckoner estimates achieved an intake pattern corresponding to that defined in Table 5-3. Therefore, in theory the prescribed food group pattern achieved the nutrient proportions targeted (provided in brackets): 8290kJ (8000kJ), 67g total fat 30%E (30%E), 15g SFA 7%E (<10%E), 22g PUFA 10%E (10%E), 106g protein 22%E (20%E) and 235g carbohydrate 46%E (50%E).

Table 5-4 'Ready Reckoner' format for energy and macronutrient content of food groups

FOOD CATEGORIES	Serving Size	CHO *Gram*	PTN *Gram*	FAT *gram*	Energy *kJ*	Energy *(kcal)*	SFA *gram*	MUFA *gram*	PUFA *gram*
VEGETABLES	½ cup	2	2	0	80	(20)	0	0	0
Carbohydrate									
STARCH Bread, Cereals, Vegetables, Legumes	1 slice/ ½ cup	15	3	1	335	(80)	0	0	0
FRUIT	1 piece	15	1	0	285	(70)	0	0	0
MILK Low/reduced fat Milk, yogurt	1 cup	15	10	2	500	(120)	1	1	0
SOY MILK (full-fat)	1 ¼ cup	15	10	12	845	(200)	1	3	7
Protein									
MEAT Lean/low fat Meat, Fish, Cheese	30g (1oz)	0	7	2	195	(45)	1	1	0
Medium fat Meat, Cheese, Egg	30g (1oz)	0	7	5	335	(80)	3	2	0
OILY FISH/SOYBEANS	30g (1oz)	0	7	4	260	(60)	1	1	2
Fat									
MUFA Oils/Spreads/Nuts	5g (1tsp)	0	0	5	200	(50)	1	3	1
PUFA Oils/Spreads/Nuts	5g (1tsp)	0	0	5	200	(50)	1	1	3

Matching dietary advice to the recommended food group intake pattern

Food-based advice was constructed in terms of the required number of daily servings from each of the reference food groups included in the recommended intake pattern (Table 5-3). Foods of low glycaemic effect corresponded well to

existing food groups such as fruit and milk, with more discriminating advice largely confined to the starch group, which could be sub-categorized to identify wholegrain, high fibre and/or low GI individual food choices. In terms of CHO distribution, advice would refer to equivalent serving sizes from within the starch, fruit and milk groups.

Nutritional adequacy of the food group intake pattern

The recommended intake pattern was at least equivalent to the minimum number of servings outlined in core food guides [13, 14](Table 5-3). A random selection of food items to represent the food groups in the recommended intake pattern provided at least 75% of amounts recommended [339, 341] for other major nutrients outlined in the Methods section (data not shown).

Comparison with unrounded estimates of dietary intake

Calculation of the same 8,000kJ food pattern using original mean estimates (provided in Table 5-2) for each of the included food groups resulted in small differences in total energy and macronutrient intakes compared to those achieved using ready reckoner estimates (presented in 2.1 and in brackets here): 7980.9$\pm$365.5kJ (8290kJ), 65.0$\pm$4.1g (67g) total fat, (13.4$\pm$2.9g (15g) SFA, 21.6$\pm$2.6g (22g) PUFA), 102.5$\pm$5.8g (106g) protein and 239.6$\pm$7.2 (235g) carbohydrate. The effect of rounding, therefore, was considered minimal and justified the use of simplified estimates for ease in the development of a prescribed dietary intake.

Variation due to individual food choices

Estimates of variation from all possible food combinations suggest individual choices to match the model would be reasonably close to dietary targets, particularly for total energy intake (SD±365.5kJ/87.4kcal). The coefficient of variation for each macronutrient variable (CHO=3.0%, protein=5.7%, fat=6.3%, and for individual fat fat types was MUFA=10.7%, PUFA=12.0%, and total energy=5%) was considered clinically acceptable. Greater variation was determined for SFA (CV=21.7%).

CONCLUSION

5.4 Summary

There are many contexts in which dietary advice needs to be formulated. In both the clinical context and in nutrition research methods need to be clearly defined so there is some assurance of nutritional goals. Food groups based on exchange lists of foods support this process by enabling selections from a range of foods to meet both energy and nutrient requirements. Published exchange lists, however, have demonstrated some large within-list variations [17] and may not address all the requirements for macronutrient manipulation. For the purposes of achieving low-fat, energy-controlled diets and recommended proportions of each type of fat in the diet, this study tested an advice strategy based on the development of a set of macronutrient-based reference food groups and a recommended intake pattern. The advice was subsequently shown to adequately address targets for the type of fat consumed within a nutritionally adequate, energy-controlled diet. Further, being a reference framework, the general principles would apply to all, but when it came to specific foods a number of food combinations could be used, allowing increased flexibility for individual food preferences and health and lifestyle objectives. The structured advice approach, however, ensures consistent and accurate targeting of nutrients regardless of these individual differences.

As the focus of dietary advice is on foods and concerns relative amounts of macronutrient intakes, a recommended intake pattern was developed from food

categories using one criterion at a time and reference standards to ensure total energy requirements, macronutrient proportions and overall nutritional adequacy.

Working from foods commonly consumed by a local sample of women with GDM, major food sources of macronutrients were determined. In this way, the significance of secondary sources of macronutrient intake were uncovered and the importance of attending to multiple food components underscored. This resulted in a greater final number of food groups compared with existing core food guide classifications outlined in current food guidance systems [13, 14]. Corresponding food lists differentiated well between foods with substantially different relative proportions of macronutrients and the type of fat, for example, cows milk versus soymilk and meat versus oily fish, where the distinction between SFA-rich and PUFA-rich foods was apparent. In contrast, existing food guides do not differentiate well between foods in which fat is the secondary macronutrient contribution, mainly high protein foods, such as milk, meat, and nuts (in lists where nuts are included as a high protein food even though the main macronutrient they contain is fat).

ADA exchange lists [15] now sub-categorise exchangeable edible fat sources based on the major fat type. However, bearing in mind edible fat alone can account for just 30% of total daily fat intake [24], the application of ADA Exchange Lists is less likely to have an impact on individual fat proportions. For example, a weight loss intervention based on the USDA Food Guide Pyramid and ADA exchange lists showed reductions in total and SFA intakes, but little change to the proportion of PUFA in the diet [22]. Our greater number of food groups assured targets for the type

of fat, meeting the challenge for achieving both nutritional adequacy and appropriate dietary fat profile. Where not all food groups were included in the sample pattern, a substantial number of servings from PUFA-rich food sources were necessary, highlighting the importance of advice for the regular consumption of some foods and not others. While goals for the relative proportions of different types of dietary fat may also be met through judicious food choices, the present guidance systems are too blunt to make this assumption.

5.5 Theoretical significance

One of the biggest challenges in addressing macronutrient-referenced dietary goals is to provide valid and feasible advice on foods to consume. By confirming the theoretical achievement of nutritional goals, this paper has outlined a systematic approach to dietary advice referring to food groups that differentiate between foods based on primary and secondary macronutrient content. Having done so, the approach has demonstrated a methodology that can be used for other plans according to requirement. Whilst all foods may not fall clearly into any one group, the structured nature of the approach facilitates a level of capability for the achievement of macronutrient targets. The advice system, therefore, is appropriate not only in the diabetes context, but for the treatment of other clinical indices associated with the Metabolic Syndrome, including CVD and overweight, as well as general healthy eating strategies, and research to substantiate health-related claims on nutrient/food effects.

5.6 Limitations and areas for further research

While the categorization process has inherent limitations [268, 270], these mainly stem from the criteria used to categorise foods. In this case, the criteria for food group development were taken from the macronutrient parameters to be used in the development of the overall diet. Thus, the resultant food groups were used as building blocks for the construction of an intake pattern to meet predetermined dietary targets, and therefore were considered appropriate.

Specificity of the study sample, the relatively small number of foods listed and the fact that dietary estimates were based on a single food pattern may limit the generalisation of results. However, a single dietary pattern was important to demonstrate an 'ideal' template on which advice can be based for consistent dietary outcomes. This lends itself to substantiation research in which a single nutrient or food can tested within the overall diet plan [257]. Although the number of foods was limited, mean estimates for macronutrient content corresponded to those reported for exchange lists using a greater number of foods [17]. Further, variation due to any combination of individual food choices from within the recommended food pattern was low and likely narrower than existing advice systems that demonstrate wider variation within individual food categories [13, 17]. The advice system was therefore judged as adequate for consumption of different types of fat in the proportions defined by current recommendations, and particularly supportive of total diet advice for controlling energy intake (SD±365.5kJ/87.4kcal). Greater variation for saturated fat (likely due to the increased number of staple

foods containing this type of fat) was readily overcome in the construction process by ensuring the upper estimate for SFA variation (+2SD) was below the target level (<10% of energy). For any system, however, encouraging consumption of a wide variety of foods from within and across food groups reduces the risk of consumption patterns that lie at the extreme ranges of energy and macronutrient intakes as well as ensures nutritional adequacy [338, 339]. Acceptance of the advice system by practitioners and its utility in clinical practice and in diverse ethnic groups or for dietary interventions other than for diabetes would be of interest and may provide the basis for future research. The impact on weight, glycaemic control, and blood lipid levels compared with a control group receiving general advice would provide health-related outcomes to substantiate the benefits. Most importantly, its application in RCTs is required to confirm the theoretical evaluations and to assess its feasibility in diabetes groups under free-living conditions.

5.7 Relevance to thesis and Implications for practice

A structured methodology to guide advice for the achievement of specific nutrient targets has been developed and the importance of differentiating between foods of varying macronutrient content, particularly the type of fat, has been theoretically confirmed. PUFA-rich foods have been identified as those requiring identification and specific attention for regular intakes within the overall diet. A template for the application of advice has been developed and appears conducive to simplified advice in intervention trials.

Where the developed system has successfully combined specific macronutrient recommendations with existing guidelines and practices, advice would refer to daily servings from each of the reference food groups in a recommended pattern. The quality of CHO intake would be improved by differentiating wholegrain, high fibre, and/or low GI choices within the starch group and including at least one of these in each meal distributed throughout the day. Individual modifications would be achieved in consideration of usual eating patterns, with relative amounts of significant foods, for example, oily fish, soy foods and/or nuts for increasing PUFA intakes, developed in proportion with individual energy needs.

In recognition of the need for evidence-based practices for the provision of advice, this study outlines the development of a structured approach to advice for the treatment of diabetes and overall nutritional adequacy. Application of the advice system in RCTs would confirm the theoretical evaluations conducted here and provide evidence for the feasibility and effectiveness of the advice system in diabetes groups under free-living conditions. The method could also be used to test the delivery of adequate amounts of required nutrients within the total diet framework to substantiate the benefits.

CHAPTER 6 TESTING THE FEASIBILITY OF FOOD PATTERN ADVICE IN AN INTERVENTION TRIAL

A significant portion of this chapter has been published in the peer-reviewed article:

Gillen LJ, Tapsell LC. Advice that includes food sources of unsaturated fat supports future risk management of Gestational Diabetes Mellitus. J Am Diet Assoc 2004;104(12):1863-1867

LG was responsible for the implementation of the study, organization and conduct of data collection, dietary interventions and dietary assessment and analyses, preparation of the manuscript and involved in critical discussions of study design and outcomes. LT was responsible for critical discussions of study design and outcomes and preparation of the manuscript.

6.1 Introduction

The RCT is considered the gold standard by which evidence supports practice. For this thesis, having developed an advice framework for the theoretical achievement of nutrient targets, successful implementation in an intervention trial involving free-living individuals would confirm its feasibility in practice and appropriateness for substantiation research. Where food lists were representative of consumption patterns of a local sample of GDM women, application in a similar group would appear to be a natural extension of the research. Furthermore, diagnosis in the third trimester of pregnancy necessitates relatively brief and intensive treatment (over the remainder of the pregnancy) with short term clinical (delivery) outcomes. Hence, women with GDM represent an ideal study group for dietary intervention research and provide the study sample for the intervention described here.

GDM, or an impaired glucose tolerance first diagnosed during pregnancy [78], affects up to 14% of the pregnant population [83, 99, 342, 343]. The primary focus of GDM management is the prevention of adverse perinatal outcomes [8, 78]. Although the

obstetric benefits of this strategy have yet to be demonstrated [241, 344], there may be longer term advantages for a positive diagnosis [345, 346]. Women with GDM are at high risk of the recurrence of GDM in a subsequent pregnancy [89, 347, 348] and of T2DM in later life [90, 273-275, 306, 307]. CVD and CHD risks are also high [276, 277], with endothelial dysfunction (an early marker of macrovascular disease) and lipid abnormalities observed as early as the index pregnancy [93-95]. Women who develop T2DM have a four to five-fold increase in CHD mortality rate compared with non-diabetic women [349]. [30, 92, 96]. Hence, the diagnosis of GDM identifies a population 'at risk' and provides an important opportunity for the development of intervention strategies aimed at delaying or preventing onset of diabetes and its long term consequences [241, 346]. Lifestyle modifications have been shown to lessen the risk of diabetes and its complications [20, 21, 190, 350], providing good argument for the early establishment of dietary patterns aimed at reducing risk in the GDM population. Current GDM management practices focuses on glycaemic control [8, 78], targeting the CHO fraction of the diet [351]. Food guidance systems support advice for controlling the type, amount and distribution of CHO-rich foods as well as ensuring nutritional adequacy for pregnancy [15]. On the other hand, dietary fat has been linked with the etiology of insulin resistance [74, 100], and hence with diabetes and CVD risk. Cross-sectional observations also implicate the amount [152] and type of dietary fat [153] in the development of GDM, in particular a lower P:S ratio, compared to healthy pregnant women [155]. Therefore, controlling both the amount and type of dietary fat may be an important primary prevention strategy for these women. While guidelines for the prevention and treatment of diabetes and CVD [8 352] largely

support this strategy, targeted advice on fat-rich foods is necessary for the achievement of fatty acid goals. The aim of the study reported here was to compare the usual fat intakes of women with GDM given additional advice on food sources of unsaturated fatty acids to those advised on a general low fat dietary approach.

6.2 Methods

6.2.1 Participants and Study Design

From May through December 2002, 32 women newly diagnosed with GDM were recruited on request at their first attendance at the Illawarra Health, Diabetes Service, Wollongong, New South Wales, Australia. Routine screening for GDM is conducted in the Illawarra Region at the beginning of the third trimester of pregnancy. Diagnosis, using an oral glucose tolerance test (OGTT), is determined based on the recommendations of ADIPS (50). Women diagnosed with GDM are referred to the Diabetes Service for medical management. Participants were required to have a reasonable understanding of written and spoken English.

The study comprised a RCT conducted during GDM management from about 30 weeks gestation to delivery. The control group received general advice that focused on low fat strategies and the amount, type and distribution of CHO-rich foods. The intervention group received the same advice plus specific advice on the amount and frequency of food sources of unsaturated fatty acids. At an initial group education session all participants received education on home blood glucose

monitoring from a Registered Nurse Diabetes Educator, and general dietary advice from an Accredited Practicing Dietitian (APD) (standard management practices). Participants were then randomly assigned to one of two parallel dietary advice groups. The overall diet plan was calculated to meet specific targets for levels of protein, fat (and fat subtype) and CHO within individual energy needs. Each participant was required to follow the respective dietary advice for the remainder of the pregnancy, with the number of clinic visits based on need, provided at the discretion of the dietitian. Dietary and clinical data were collected at the time of randomization (baseline) and prior to delivery (intervention), at least four weeks after randomization.

All participants completed an interviewer-administered open-ended DH questionnaire validated within a GDM population in the Illawarra region [337] and presented in ***Appendix C***. The same dietitian conducted each DH questionnaire at baseline and intervention time points, asking participants to describe their 'usual' daily eating pattern with variations. Usual was defined as foods consumed regularly over the previous one-month period. A short food frequency questionnaire on common food groups was included in the interview to act as a cross-check. Participants were also required to complete three-day weighed FR at the same two time points, presented in ***Appendix D***. Each participant was individually instructed on how to measure and record all foods consumed over two typical weekdays and one weekend day. Standard metric household measures and standardised forms were provided for this process. Data on age, stage of gestation, gravida (number of pregnancies), parity (number of live births), incidence of GDM in a previous

pregnancy and family history of diabetes (known diabetes in a parent, grandparent or sibling), country of birth and ethnic origin (Australia/UK or other country) usual daily activity and pre-pregnancy weight were collected by self-report. Height and baseline and intervention weights were measured and recorded. BMI was calculated for self-reported pre-pregnancy weight, while weight gain was assessed as the difference between the pre-pregnancy weight and the measured intervention weight. The initiation of insulin was based on ADIPS recommendations and recorded for individual cases where appropriate. Individual insulin requirements during pregnancy were recorded. Pregnancy outcomes were also recorded in terms of newborn characteristics: weight, length and head circumference; and the nature of delivery: premature delivery (<38 weeks gestation), induced delivery and any other intervention beyond a normal vaginal delivery.

In order to establish energy requirements and to account for the impact of physical activity on pregnancy outcomes, reported daily activity was categorized as sedentary or light based on subjective judgment. Due to advanced stages of pregnancy no other activity category was required for this sample.

Control Group

Each participant was provided with an individualised portion-controlled CHO meal plan based on the redistribution of habitual CHO intake, reported informally at the initial group education session (standard practice at the Diabetes Service). To support the meal plan, exchange lists of CHO-rich foods were also provided. In addition, participants received ongoing general dietary advice based on core food

guide recommendations for pregnancy [13], and strategies for reducing total and saturated fat in the diet. Advice considered individual food preferences and incorporated the GI for CHO-rich food choices [221].

Intervention Group

Each participant received information similar to the control group in all respects plus information on additional food groups of fat-rich foods (Table6-1). Energy requirements were established individually, based on reported (DH) baseline intakes. Each diet was calculated to provide <10% of energy from SFA and approximately 10% of energy from PUFA as recommended by ADA for the treatment and prevention of diabetes and related complications [8]. To support the meal plan, exchange lists of fat-rich foods were provided (Table 6-2).

Table 6-1 Example of individualised advice provided to each subject in the intervention group (8000kJ (2000kcal) per day)

	Bread/Cereal Rice/Potato/ Pasta	Vegetables	Fruit	Milk	Lean meat	Oily Fish	Spreads/ Oils/Nuts MUFA	Spreads/ Oils/Nuts PUFA
Daily servings	8	5	4	600ml	600g (20oz)/ week	450g (15oz)/ week	2tsp	5tsp
Breakfast	2		1	330ml				
Morning Tea			1	30ml				
Lunch	3	2		30ml				
Afternoon Tea			1	30ml				
Dinner	3	3		30ml				
Supper			1	150ml				

Table 6-2 Exchange lists of foods with different fat profiles provided to the intervention group to support individualised dietary advice

Saturated fat*	Monounsaturated fat**	Polyunsaturated fat**
Amounts in brackets = 1 serve		
Milk (1 cup)	Oils (1tsp)	Oils (1tsp)
Skim, low or reduced fat	Olive	Sunflower
Trim custard	Canola	Safflower
	Sunola	Sesame
Yoghurt (7oz)	Peanut	Soybean
No fat, Low fat, Lite	Macadamia nut	Grapeseed
Diet lite	Almond nut	Cottonseed
Ice Cream (2 scoops)	Spreads (1½tsp)	Spreads (1½tsp)
Diet, Low fat, Lite	Canola margarine	Polyunsaturated margarine
	Olive margarine	Soy margarine
Deli Meats (1 slice = 1oz)	Sterol margarine (canola-based)	Sterol margarine (poly-based)
Light ham,	Peanut Butter	
Turkey, chicken breast	Avocado (1tb)	
97% fat free meats		
	Dressings (1tb)	Dressings (1tb)
Other Meats	French (with olive oil)	French (regular)
Trim all visible fat	Italian (with olive oil)	Italian (regular)
Cheese (2 slices)	Nuts (1tb)	
Free, extra lite, lite	Almond	Nuts (1tb)
Cottage, low fat ricotta	Cashew	Brazil
	Macadamia	Pine nuts
Egg (1 medium = 1oz meat)	Peanut	Walnut
Omega-3 enriched	Pecan	
	Pistachio	
	Other (15 each)	
	Olives	
	Potato snacks (in sunola oil)	
	French fries (in canola oil)	

* Advice was to prefer these low fat food choices to meet the prescribed number of serves from Milk and Meat groups

** Advice was to choose these foods to meet the prescribed number of serves from this fat type

Dietary data were entered into FoodWorks (Xyris software, Brisbane, Version 2.1, 2000, Xyris software, Brisbane, Australia) for nutrient analysis. This software

incorporated the Commonwealth Department of Community Services and Health nutrient tables for use in Australia: AUSNUT, Canberra, 2000.

Food intake data were converted to energy and macronutrient values, expressed as kilocalories (kcal) and %E, respectively. Bland Altman plots were used to determine the level of agreement between data taken from the DH and FR (55). DH data were used for all group comparisons. Achievement of dietary goals was defined as mean fatty acid intakes of <10% of energy as SFA, ≥7% of energy as PUFA, and P:S ratio ≥1 [8 352]. The number of individuals in each group achieving fatty acid goals was assessed.

To assess the quality of data, dietary data obtained from DH interviews and FR were compared using the Bland-Altman approach for comparison, where the 95% limits of agreement are set as two standard deviations from the mean of the difference [286]. Evidence of overall bias, indicated by observations of the mean difference away from zero and a relationship between difference and mean, was confirmed using the correlation coefficient ($P<0.05$). For each dietary variable, limits of agreement within target ranges of consumption were considered clinically acceptable.

In order to assess the relative contribution of different foods to total dietary fat intakes, foods were categorized based on predominant fatty acid content. The amount of fat provided by a single food was expressed as a percentage of the total fat consumed from all foods.

All statistical analyses were conducted using SPSS for Windows, Version 11.0, 2001 (SPSS Inc, Chicago, Ill.). Comparisons between control and intervention groups for data defining previous GDM (yes/no), family history of diabetes (yes/no), birth and ethnic origins, activity, nature of delivery, and numbers of individuals achieving fatty acid targets were performed using Pearson's chi-square tests. Comparisons for data defining age, height, weight, gestation, gravida and parity, and characteristics of the newborn were assessed using independent samples t-tests. Independent samples t-tests were also used to compare energy and macronutrient intakes at baseline, and for changes in intake as a percentage of baseline (% change) following dietary advice. Repeated measures ANOVA was used to assess differences in energy and macronutrient intakes over time (time points were baseline and intervention) with dietary advice group as the between-subjects factor. Results are expressed as mean$\pm$SD with the level of significance reported at $P<0.05$ for all comparisons.

The Human Research Ethics Committee of the University of Wollongong and Illawarra Area Health Service provided ethical approval for this research. Information provided to participants and consent forms for this study are provided in ***Appendices E and F***, respectively.

6.3 Results

Of the 96 women referred to the Diabetes Service during the recruitment period, 32 (16 control and 16 intervention) agreed to participate in the study. Exclusions were confined to one woman with poor English language skills. Baseline DH data were obtained from all participants. Two women, one from each group, did not complete an intervention DH due to early delivery of the newborn. FR data were obtained from twenty-seven participants (n=15 control, n=12 intervention) at the intervention time point. Gestation data indicate that women were first seen at around 30 weeks gestation for the collection of baseline data and that intervention data were collected at around 36 weeks gestation. Delivery of the newborn occurred at around 39 week's gestation. BMI data based on self-reported pre-pregnancy weight indicate that the average subject was overweight prior to the current pregnancy. No significant differences were found between the two groups of women in terms of age, height, self-reported or recorded weights, or corresponding BMI, weight gain, stage of gestation, gravida or parity. The two groups were also similar for numbers of participants reporting previous GDM, family history of diabetes, birth and ethnic origins, and categories of activity (data not shown). One control and two intervention participants required insulin treatment during the pregnancy. There were also no significant differences between groups for pregnancy outcomes defined by newborn characteristics, or nature of delivery (data not shown). (Table 6-3)

Table 6-3 Maternal characteristics of the control group, intervention group and the two groups combined (mean±SD)

	Control Group	Intervention Group	Combined Groups
Characteristics	n=16	n=16	n=32
Age (baseline) (yrs)	31.9±4.5	30.6±4.7	31.2±4.6
Height (cm)	162.4±6.4	161.9±5.8	162.1±0.1
Weight (pre pregnancy) (kg)	69.2±13.1	67.0±11.5	68.1±12.1
BMI (pre pregnancy) (kg/m^2)	26.0±3.4	25.6±4.5	25.8±3.9
Weight gain (kg)	13.7±6.6	12.7±6.5	13.2±6.5
Gestation (baseline) (wks)	30.7±0.9	29.0±6.0	29.8±4.3
Gestation (intervention) (wks)	36.2±0.9	35.6±2.1	35.9±1.6
Gestation (delivery) (wks)	38.9±1.2	38.4±2.0	38.7±0.3
Gravida (no. of pregnancies)	2.4±1.7	2.3±2.1	2.4±1.9
Parity (no. of live births)	0.9±1.1	0.8±1.2	0.8±1.1
Baby's birth weight (g)	3414.1±98.8	3452.4±184.7	3431.9±99.2
Baby's length (cm)	50.4±0.6	49.3±1.2	49.9±0.6
Baby's head circumference (cm)	34.8±0.9	35.1±1.6	35.0±0.3

No significant differences were found for energy and macronutrient intakes reported by the two study groups at baseline (Table 6-4). In terms of dietary recommendations, both groups reported mean SFA and PUFA intakes at baseline above and below recommended values, respectively, with all women reporting PUFA intakes well below the recommended level. As a result, calculated P:S ratio for both groups, and for all individuals, was well below target range at the commencement of the study.

Table 6-4 Target versus macronutrient intakes reported at baseline by the control and intervention groups and the two groups combined (mean+SD)

	Target	Baseline Intakes Control Group (n=16)	Intervention Group (n=16)	Combined Groups (n=32)
Energy (kJ)		10257.2±3526.2	9140.7±2620.6	9698.9±3073.4
Carbohydrate (%E)	50	48.0±7.2	47.5±6.3	47.8±6.7
Protein (%E)	20	18.1±3.8	20.3±3.3	19.2±3.7
Total fat (%E)	30	30.9±6.9	30.0±5.5	30.5±6.1
Saturated fat (%E)	<10	13.3±3.6	12.8±3.4	13.1±3.4
Monounsaturated fat (%E)	>10	11.0±2.4	10.3±1.7	10.6±2.1
Polyunsaturated (%E)	10	3.8±1.4	3.9±1.4	3.9±1.4
P:S ratio	>1	0.3±0.1	0.3±0.1	0.3±0.1

E=energy

Changes in macronutrient intakes in response to dietary advice are presented in Fig 6-1. Significant differences between the two dietary advice groups were limited to changes in fatty acid intakes. The control group reduced mean SFA (% energy) consumption to 14% below that reported at baseline, compared with a 39% reduction for the intervention group (P=0.008). The control group also reported a 30% increase from baseline for mean PUFA (% energy) intakes compared with a 134% increase for the intervention group (P=0.001).

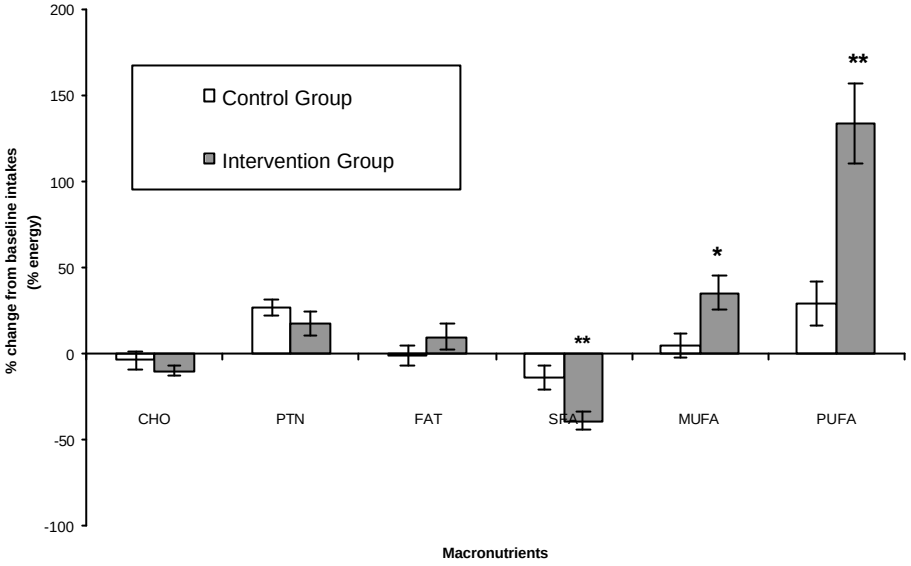


Figure 6-1 Changes in macronutrient intakes following treatment advice, control and intervention

Dietary intakes reported at 36 weeks gestation are presented in Table 6-5. Although both groups reported a reduction in energy, mean energy intake for the control group was significantly lower than that reported by the intervention group following treatment advice. While this difference failed to reach significance as a treatment group effect over time, the reduction in energy compared to baseline was significant for the control group only ($P<0.01$). Significant effects due to dietary treatment over time were again confined to mean fatty acid intakes. Differences in group profiles for mean PUFA intakes and P:S ratio over time were highly significant. The control group increased mean P:S ratio 31% above the ratio reported at baseline compared with a 310% increase for the intervention group.

Table 6-5 Target versus macronutrient intakes reported following dietary advice (36 weeks gestation) by the control group and intervention groups (mean+SD)

		Dietary intake at 36 weeks gestation	
	Target	Control Group (n=15)	Intervention Group (n=15)
Energy (kJ)		7488.0±987.2	8701.3±1829.8
Carbohydrate (%E)	50	45.5±5.7	42.8±4.7
Protein (%E)	20	22.7±2.6	23.3±3.7
Total fat (%E)	30	29.4±6.4	31.8±6.3
Saturated fat (%E)	<10	11.0±4.0	7.5±1.7*
Monounsaturated fat (%E)	>10	11.0±2.3	3.6±3.0**
Polyunsaturated fat (%E)	10	4.4±1.4	8.2±2.4***
P:S ratio	>1	0.4±0.2	1.1±0.2***

E=energy

Significant effect due to treatment over time using repeated measures ANOVA, * P<0.05, ** P<0.01, *** P<0.001, control group versus intervention group

In terms of dietary targets, these differences were reflected in the achievement of SFA and PUFA targets. Only the intervention group achieved mean SFA, PUFA and P:S ratio within the respective recommended ranges.

No individual participant from either group achieved PUFA intakes or P:S ratio within the target range prior to treatment (Table 6-6). Following dietary advice, the majority of individuals from the intervention group reported values consistent with both SFA and PUFA recommendations, with 12 out of 15 from this group achieving a P:S ratio within the target range. In contrast, only one participant from the control group reported adequate PUFA intake, with no individual from this group achieving the target P:S ratio. Hence, differences between groups for numbers reporting adequate PUFA (P=0.001) and optimal P:S ratio (P<0.001) following dietary advice were highly significant.

Table 6-6 Numbers of individuals achieving dietary goals at baseline and following dietary advice (36 weeks gestation), control and intervention groups

	Baseline (n=16)		36 weeks gestation (n=15)	
Dietary targets[a]	Control Group	Intervention Group	Control Group	Intervention Group
SFA (<10%E)	4	3	8	13
PUFA (≥7%E)	0	0	1	10**
P:S ratio (≥1)	0	0	0	12***

Data are numbers of individual study participants
** P<0.01, *** P<0.001 by Pearsons Chi-square, control group versus intervention group

Patterns of consumption of food sources of dietary fat were very similar between the control and intervention groups prior to dietary advice. SFA-rich foods such as milk, cheese and meat groups contributed around 50% of mean total fat intakes (41g fat per day vs. 35g fat per day) while PUFA-rich oils/spreads, fish, soymilk and nuts contributed less than 15% (12g fat per day vs. 10g fat per day).

Following advice, the control group increased their fat intake from PUFA-rich foods to 28% of total fat intake (17g fat per day), mainly through the increased use of oils and spreads. And, although fat from SFA-rich food groups was reduced (27g fat per day) the proportion of total fat consumption from these foods was still high (45% of total fat intake). In contrast, the intervention group almost reversed the proportions of SFA (22% of total fat intake) and unsaturated dietary fat (57% of total fat intake) reported at baseline by substantially reducing (17g fat per day) and

increasing (43g fat per day) consumption of fat from all food groups classified as SFA- and PUFA-rich, respectively.

The quality of the dietary data was viewed as favourable. Using Bland Altman plots, good agreement was demonstrated between DH and FR data for energy (kJ) and macronutrient (g) variables (55). There was no evidence of overall bias for data collected using either the DH or FR for any of the dietary variables tested. Agreement between data from the two methods was considered clinically acceptable, that is, the 95% limits of agreement were, for energy (E) 715.4-–864.6Kcal, protein 6.5-–3.1%E, CHO10.5-–10.7%E, total fat 8.8-–11.6%E, SFA 5.0—6.2%E, MUFA 5.0-–5.4%E, and PUFA 2.7-–3.7%E. DH data were therefore considered valid estimates of usual dietary intakes for statistical comparisons.

CONCLUSION

6.4 Summary

Several large studies have shown that lifestyle modifications are important primary prevention strategies for those at-risk of T2DM and CVD complications [19-21]. The diagnosis of GDM identifies 'at risk' women at an early stage in the possible development of these metabolic disorders, and thus these women represent an ideal study group for primary prevention strategies [346]. Where dietary fat has been implicated in the development of diabetes and CVD risk, the current focus on CHO intake may limit long-term benefit from dietary intervention. The study reported here aimed to demonstrate how a broader focus and targeted advice that modifies fat profile is an approapriate primary prevention strategy during GDM management. Importantly, nutritional adequacy, glycaemic control, weight control and perinatal outcomes were not compromised by this shift in focus.

Within the limits of the recruitment period, 32 out of 95 eligible women volunteered for the study with only one potential participant excluded based on the limited selection criteria. The data indicate that the average participant was 31 years of age, had a family history of diabetes, and was overweight prior to the current pregnancy, demonstrating multiple risk factors for future diabetes within this study sample [275].

Dietary data were considered a valid reflection of usual intakes. At the commencement of the study mean SFA and PUFA intakes reported by the study

sample were consistent with data reported for the general population in Australia [353, 354]. These intakes, however, are not consistent with current recommendations outlined by ADA and AHA [8, 352]. Interestingly, all individuals reported baseline PUFA intakes below the recommended range, indicating dietary risk and further suggesting the need to include advice on fats, in particular PUFA, as part of GDM management. While all women reduced SFA intakes in response to advice (general low fat versus targeted for individual fatty acids), only the intervention group achieved the PUFA target and, hence, optimal P:S ratio. General low fat advice strategies, on the other hand, did little to improve the fatty acid profile of the control group and brought about a significant reduction in mean energy intake (more than 2700kJ) compared to the intervention group (less than 500kJ reduction). While weight management is important for these women a reduction in kilojoules in response to dietary advice is a phenomenon previously observed in GDM women [303], which in the former can result in small for gestational age babies [240], an outcome no less concerning than large for gestational age babies.

In terms of individual participants, 12 out of 15 women in the intervention group achieved a P:S ratio $\geq$1 following dietary advice, whereas no individual from the control group achieved this target. This may be explained by considering the position of habitual fatty acid intakes in relation to their corresponding targets, and the need for opposing advice strategies. General dietary advice favors total fat reduction, relying heavily on core food guide classifications and recommendations that do not differentiate between foods on the basis of fat type [16]. Furthermore, Western staples such as SFA-rich milk and meat groups attract advice for daily

intakes to ensure nutritional adequacy particularly during pregnancy. Therefore, the frequency of consumption of these foods can define total SFA intakes, even when low fat products are used and may account for the increased consumption of fat from cheese products observed for our control group following advice. Conversely, PUFA-rich foods such as oils, spreads and nuts, by virtue of their high fat content and, in some cases, their position outside core food groups, are considered more worthy of restriction [13]. Thus, a focus on total fat consumption may have unfortunate consequences, resulting in low fat intakes highest in SFA, as observed for the control group. Australian population surveys conducted between 1983 and 1995 support this argument, revealing a decline in average total fat and PUFA intakes along with increased average saturated fat consumption [355]. While judicious food choices from existing core food exchange lists may achieve the desired fat profile, we consider the guidance systems too blunt to make this assumption. Consequently, for the intervention group in this study a wider range of food groups were used to enable fatty acids to be targeted. For example, soymilk was listed as an alternative to milk, oily fish types were listed separately from other protein-rich food sources, and nuts were listed with oils and spreads within well-defined MUFA-rich and PUFA-rich food groups. Hence, unsaturated fat-rich foods were readily distinguishable from SFA-rich foods, while individual food preferences determined actual food choices.

After advice, the control group largely limited intakes of unsaturated fatty acids to exchangeable edible fats, mainly oils and spreads, but amounts were inadequate for the achievement of fatty acid goals. In contrast, the intervention group reported

multiple shifts from SFA- to PUFA-rich food sources in order to achieve the appropriate P:S ratio, indicating targeted advice on specific foods is more likely to deliver the amount of unsaturated fat required.

At commencement of the study, meat and dairy staples provided over half of dietary fat intake reported by the total study sample. After advice, the intervention group reported over half of dietary fat intake from PUFA-rich foods. Major changes in food choice by the intervention group were increased consumption of oils and spreads (mainly margarines low in trans fatty acids), oily fish and nuts to approximately 1oz each per day, lean fish to 1 ½ oz per day, and legumes (mainly soymilk) to almost 3oz per day. Importantly, concomitant reductions in fat from meat and dairy from 5 oz to 3 ½ oz per day and 15 oz to 13 oz per day, respectively, were also reported, inclusive of lean and low fat choices. In contrast, the control group reported little change to the pattern of intake from fat-rich food sources.

6.5 Theoretical significance

In terms of dietary risk profile, this sample of women with GDM reported undesirable habitual fatty acid intakes. The inclusion of advice on food sources of unsaturated fatty acids demonstrated how optimal fatty acid profiles can be achieved, not possible when advice is limited to a focus on CHO-rich foods and/or general low fat strategies. The large increases required for foods rich in unsaturated fat reflect the low levels of consumption at baseline and demonstrate the need for a more dichotomous approach to dietary advice to adequately shift

intakes from saturated to unsaturated fat sources. Interestingly, the perception of advice for the consumption of ‘foods’ (soy, fish, nuts) rather than ‘fats’ (oils and margarines) overcame an apparent reluctance by some participants to preferentially consume fat. Even when oils and margarines were consumed, participants were sparing in their use, indicating that a reliance on exchangeable edible fats for increasing unsaturated fat in the diet may be difficult for consumers already indoctrinated into a low fat regime.

6.6 Limitations and areas for further research

Incomplete data collection was limited to one person from each group and therefore unlikely to affect results. While sample size was not large, the high degree of homogeny in terms of baseline demographic and dietary profile data supports representation of the wider population. The sample was likely to be biased toward women who were willing to keep FR and motivated to follow dietary instructions, however, there was no discernable difference between groups. Randomization of participants into two dietary advice groups then ensured similar group profiles prior to the implementation of different dietary advice strategies, thereby improving the chances of detecting differences between groups over time. With no differences between groups for insulin therapy or pregnancy outcomes, there were no apparent reasons why external factors might have impinged on achievement of dietary targets other than the intervention.

A larger prospective dietary intervention study in men and women with T2DM is required to confirm the transfer of this dietary strategy to other diabetes groups and

to substantiate the impact of food patterns in terms of clinical markers of diabetes and CVD risk.

6.7 Relevance to thesis and implications for practice

It would seem from the clinical outcomes demonstrated in this study that the total diet approach encompassed in standard practice was universally effective. The opportunity to provide dietary advice for women with GDM, however, should be addressed with a long-term view to their health status, particularly as they bear known risks for T2DM and CVD. Improving the dietary fat profile of the diet warrants consideration and this means targeting information on foods that deliver unsaturated fatty acids at the expense of saturated fats. Dietitians should provide a balanced emphasis on foods such as oils, margarines, nuts, legumes and fish along with the traditional core foods such as meat, milk and cheese to ensure optimal fatty acid intakes are actually consumed.

For this thesis, this study confirmed the feasibility of an advice system based on a model food pattern using all foods in the diet. The theoretical achievement of nutrient targets was confirmed by practical implementation in a clinic sample of the treatment group. In particular, specific advice on fat sources enabled differences in individual fatty acid proportions without impacting on other dietary variables within the total diet. This was important in order to confirm the appropriateness of advice for the achievement of specific nutrient changes to enable further research to establish a clinical benefit from the intake of a specific nutrient or food.

CHAPTER 7 CONFIRMING THE EFFECTIVENESS OF FOOD PATTERN ADVICE IN SUBSTANTIATION RESEARCH

A significant portion of this chapter has been published in the peer-reviewed article:

Gillen LJ, Tapsell LC, Patch CS, Owen A, Batterham M. Structured dietary advice incorporating walnuts achieves optimal fat and energy balance in patients with type 2 diabetes mellitus. J Am Diet Assoc 2005:In press (July)

Clinical results referred to in this chapter have been published in the peer –review article:

Tapsell L, Gillen L, Patch C, Batterham M, Owen A, Bare M, Kennedy M. Including walnuts in a low-fat/modified-fat diet improves HDL cholesterol-to-total cholesterol ratios in patients with type 2 diabetes. Diabetes Care 2004;27:2777-2783

LG was responsible for dietary intervention, dietary advice protocols, dietary assessment and analysis, involved in critical discussions of study design and outcomes as well as preparation of the manuscripts. LT was responsible for study design, organization and conduct of data collection and critical discussions of study design, analyses and outcomes and preparation of results manuscript. CP was involved in data collection and critical discussions of study design and outcomes. AO was involved in critical discussions of study design and outcomes. MB was responsible for statistical analyses and involved in critical discussions of study design and outcomes.

7.1 Introduction

Having confirmed the clinical feasibility of food pattern advice under free-living conditions, a second intervention trial was conducted to confirm the effectiveness of the advice system in terms of health-related outcomes as a result of changes to the macronutrient profile. If results are to be generalized to the diabetes population, it was also important to demonstrate the clinical transfer of food pattern advice from GDM women to the wider diabetes community, and to provide evidence for long-term adherence to advice (six months). Additionally, the incorporation into the overall diet of a single food source (walnuts) of a specific nutrient (PUFA) informs substantiation research, providing a framework for nutrition intervention to confirm health claims on individual nutrients/foods.

Evidence-based guidelines for the management of T2DM and related CVD refer to cardio-protective proportions of individual fat types [8]. Conversion of macronutrient targets into practical advice on foods, however, is one of the most challenging aspects of nutrition management. A total diet approach, 'where all foods can fit into a healthful eating style', is recommended [242], and an exchange system of food lists supports this process [15, 335]. However, general low fat advice strategies based on current exchange list systems do not necessarily lower the proportion of SFA [22]. Adequacy of the PUFA fraction, concomitantly lowered during low fat advice, may also require attention [23]. Conversely, advice to increase unsaturated fat intake may result in unintended increases in total fat and energy [25]. Even when food-based advice matches nutrient targets, achieving long-term adherence to dietary advice is problematic in free living populations [356].

Further research is required to establish evidence-based practices that ensure recommended fatty acid proportions within low fat energy-controlled diets. For this, new dietary advice approaches need to be tested in free living subjects. An exchange system based on the fat composition of foods, however, has not been established, nor has the position in the diet of individual high fat foods as significant delivery sources of essential fatty acids. While fish is recommended for its n-3 PUFA content based on evidence from the general population [8], fish and other individual food sources of n-3 fatty acids require further investigation in diabetes populations. The cardio-protective benefits of nuts and their unsaturated fat content have been reviewed [357]. Despite being energy dense, strong dietary compensation and little change in energy balance have been reported during

chronic consumption of nuts [171]. Hence, the incorporation of nuts into low fat energy-controlled diets may be an appropriate strategy for the adequate achievement of unsaturated fatty acid targets. Walnuts in particular, with high n-3 PUFA content, may provide an additional source of these fatty acids [184]. The feasibility of advice for the regular consumption of a high fat food has not been previously assessed in free living diabetes subjects. The study reported here aimed to assess the achievement of dietary fat targets in a sample of patients with T2DM randomly assigned to one of three dietary advice interventions over six months: a control group given general low-fat advice and two intervention groups given total diet advice using a recommended food intake pattern for the achievement of the recommended fat profile, with one group incorporating walnuts into the PUFA fraction of the diet.

7.2 Methods

7.2.1 Participants and Study Design

The study was conducted in Wollongong, Australia. Subjects with established T2DM were recruited by advertising through local media, at the Illawarra Health Diabetes Centre in Wollongong and among University of Wollongong (UOW) staff. The content of the recruitment advertisement is provided as ***Appendix G***. Inclusion criteria were assessed during a telephone screening survey (***Appendix H***): aged 35-75 years, diagnosed with T2DM for at least one year and generally well. Exclusion criteria were: on insulin therapy (or with HbA1c >9%), BMI>35kg/m^2, with

major debilitating illness, known food allergies or food habits inhibiting the study, illiteracy and inadequate conversational English.

The study was conducted under controlled trial conditions where subjects were randomly assigned to one of three parallel dietary advice groups each targeting 30% energy from total fat: low fat (LF) (control), modified low fat (MF) and modified low fat with specific advice to include 30g walnuts per day (Walnut). To avoid contact between participants receiving and not receiving walnuts, the LF and MF groups were seen at the Wollongong Diabetes Centre, while those in the Walnut group were seen in clinic rooms at the UOW. An experienced Accredited Practising Dietitian counseled all individuals. Each participant was required to follow the respective dietary advice for six months following randomization.

Dietary advice provided to each group is outlined in Figure 7-1. All participants were provided with an individualised portion-controlled CHO meal plan based on the redistribution of habitual CHO intake [333]. To support the meal plan, exchange lists of CHO-rich foods incorporating the GI [221] were also provided. In each group, participants were referred to core food guide recommendations outlined in the Australian Guide to Healthy Eating (AGHE) [13], and individual food preferences were considered.

Figure 7-1 Outline of dietary advice provided to each group

Food category	LF (control)	MF	Walnut
Carbohydrate-rich	No. portions Distribution CHO type	No. portions Distribution CHO type	No. portions Distribution CHO type
Protein-rich	Serving size	No. portions Fish portions	No. portions Fish portions
Milk allowance	Type of milk	Total (ml) Type milk (LF/PUFA)	Total (ml) Type milk (LF/PUFA)
Spreads/oils/nuts	Type of spread/oil	Total (g) Type fat (MUFA/PUFA)	Total (g) Type fat (MUFA/PUFA)
Walnuts	-	-	30g/day

In addition to the above, the LF group received standardised general dietary advice that corresponded to usual practice methods used at the Wollongong Diabetes Centre for reducing total and saturated fat in the diet. Distinctions between staple foods containing mainly saturated or unsaturated fat were emphasized in a 'good fat' versus 'bad fat' approach. The number of clinic visits was based on individual need provided at the discretion of the dietitian, as per usual clinical practice at the Centre.

Participants in the MF group received more structured advice in the form of a meal plan based on energy requirements, established individually from reported baseline intakes (Table 7-1). Development of the meal plan has been described in CHAPTER 5, and was based on a reference model calculated from mean estimates representing the macronutrient and fat composition of exchange lists of

staple foods to provide 50% of energy from CHO, 20% of energy from protein and 30% of energy from total dietary fat in the proportions of <10% of energy from SFA and approximately 10% of energy from PUFA. In order to differentiate fat type, each meal plan referred to nine categories of foods that corresponded to the macronutrient exchange lists, a greater number than core food groups [13]. The extra groups provided specific advice for the amount and frequency of individual PUFA-rich foods such as soymilk and oily fish, and for high-fat foods highest in unsaturated fat, such as oils, margarines and nuts. Exchange lists of 'MUFA-rich and PUFA-rich' foods were also provided, presented in Chapter 4 Methods 4.2. Monthly clinic visits were supported by one telephone contact between each visit to check compliance, assessed by 'cross-checking' reported daily intakes from all food groups against the meal plan provided.

Table 7-1 Example of individualised advice provided to each subject in the Walnut group (8000kJ (2000kcal) per day)

	Bread/Cereal Rice/Potato/ Pasta	Vegetables	Fruit	Milk	Lean meat	Oily Fish	Spreads/ Oils	Walnuts
Daily servings	9	5	4	600ml	600g (20oz)/ week	450g (15oz)/ week	2tsp	30g
Breakfast	3		1	330ml				
Morning Tea			1	30ml				
Lunch	3	2		30ml				
Afternoon Tea			1	30ml				
Dinner	3	3		30ml				
Supper			1	150ml				

Individuals in the Walnut group received a meal plan as described for the MF group but with the inclusion of 1oz (30g) walnuts per day as part of the PUFA content of the diet. To facilitate intake, one month's supply of individually wrapped daily portion packs of walnuts were provided to each person at each clinic visit. Contact and assessment of compliance was consistent with those methods outlined for the MF group.

At baseline, three, and six months all participants completed an interviewer-administered open-ended DH questionnaire, previously validated within a diabetes population in the Illawarra region [279, 337] and modified for this study, and three-day weighed FR as outlined in ***Appendices I and J***, respectively. Two experienced dietitians, not involved in dietary counseling, conducted DH questionnaires, asking each participant to describe his/her 'usual' daily eating pattern with variations. Usual was defined as foods consumed regularly over the previous three months. A short food frequency questionnaire on common food groups was included in the interview to act as a cross-check. Each participant was individually instructed on how to measure and record all foods consumed over two typical weekdays and one weekend day. Standard metric household measures and standardised forms were provided for this process.

Data on age, family history of diabetes, country of birth, and usual daily activity were collected by self-report. Height was measured at baseline. Weight and percentage body fat were measured at 0, 3, and 6 months using scales and a bioelectrical impedance component (Tanita TBF-622 foot to foot analysers). These

scales are applicable to standard clinical practice and in this context compare reasonably well with dual x-ray absorptiometry as a reference technique [358]. BMI was calculated for each measured weight. Reported daily activity was categorized as sedentary, light, moderate, or active based on subjective judgment using Food Authority Organization (FAO) definitions [359]. Clinical data on blood glucose and lipid levels were also obtained.

Dietary data were entered into FoodWorks nutrient analysis software program (Xyris, Version 3.2, Brisbane, Australia, 2002) using the Australian nutrient database AusNut Rev.14 [360] and the fatty acid database of Australian fatty acids (Rev.6 RMIT, Melbourne, 2002).

Food intake data were converted to energy and macronutrient values, expressed as kilojoules (kJ) and %E, respectively. Primary outcomes were the proportions of individuals from each group achieving fatty acid targets, defined as mean intakes of <10% of energy as SFA (1), $\geq$7% of energy as PUFA (PUFA:SFA (P:S) ratio $\geq$1) [8], minimum intakes for n-3 fatty acids [11]: 2.22g ALA, and 0.65g EPA+DHA and n-6:n-3 ratio <10 [361].

To assess the quality of the DH data, comparisons were made with FR data collected at the corresponding time point. An estimation of the potential bias in reported energy intakes was undertaken, where reported estimated intakes (EI_{rep}) were compared with EE_{est}, calculated using the Schofield Equation [298] with reference to estimated activity levels (16). Finally, erythrocyte fatty acid composition was assessed as a biomarker for reported intakes [362].

Trained professionals drew blood samples that were sent to a quality assured pathology laboratory (Southern IML Pathology) for analysis of HbA1c, total-C, LDL-C, HDL-C and triglyceride levels in keeping with standard clinical practice. Biomarkers were assessed in the UOW laboratory using standard techniques. Erythrocyte fatty acid composition was determined by gas chromatography. Erythrocyte membrane lipids were isolated by ultracentrifugation [363] and the fatty acids derivatized using a direct trans-esterification method [364]. The resulting fatty acid methyl esters were analysed by gas chromatography using a Shimadzu GC-17A equipped with a 30m x 0.25mm capillary column (FAMEWAX, Restek GMbH) with hydrogen as a carrier gas. Fatty acid identification was based on the retention time of authentic fatty acid methyl ester standards (Sigma-Aldrich, Australia).

Foods were categorized based on the predominant content of each fat type: SFA-, MUFA- or PUFA-rich. The contribution of these foods to total dietary fat intake by each intervention group at 0, 3 and 6 months was calculated as a percentage of the total fat consumed from all foods by that group. Similarly, major sources of n-3 PUFA were determined by calculating the n-3 fatty acid intakes from individual foods as a percentage of total n-3 consumed. Mean amounts (grams) of significant foods were also reported.

All statistical analyses were conducted using SPSS for Windows (Version 11.0, 2001, SPSS Inc., Chicago, IL. USA and STAT (Version 7.0, 2002, STATA Corp, College Station, TX. USA). For baseline subject characteristics non-Gaussion data were log transformed prior to analysis. Data were presented as mean±SD prior to

transformation to assist interpretation. The level of significance was reported at $p<0.05$. A one-way ANOVA was used for comparisons between groups, with post hoc analysis performed using Tukey's test. Non-parametric analysis was conducted using the Kruskall-Wallis test.

For comparison of dietary data assumptions of normality were made. A one-way ANOVA was used for comparisons of dietary data at 0, 3 and 6 months. Repeated measures ANOVA on data from those completing the trial assessed differences in macronutrient intakes over time (0, 3 and 6 months) with treatment group as the between-subjects factor. Results were expressed as mean $\pm$ SD with the level of significance reported at $p<0.05$. Differences in proportions achieving targets were assessed by chi square analysis. Changes in clinical outcomes were analysed with an intention to treat model using repeated measures ANOVA.

Data from the DH and the FR were compared using Bland-Altman plots, where the 95% limits of agreement are set as two standard deviations from the mean of the difference between the two data sets [286]. A mean difference close to zero indicates minimum bias. A significant correlation between the difference (DH-FR) and mean (DH-FR/2) provides evidence of systematic bias. For each dietary variable, the range of consumption reported for the two data sets were considered clinically acceptable when limits of agreement were no greater than 200kcal for energy, 2% of energy for macronutrients and 1g for n-3 PUFA. Differences in the extent of under-reporting (EE_{est}-EI_{rep}) between and within the method (DH and FR) over time were investigated using repeated measures ANOVA. Spearman's correlation co-

efficient was determined to assess the relationship between reported changes in dietary PUFA and erythrocyte levels in subjects.

The Human Research Ethics Committee of the University of Wollongong and Illawarra Area Health Service provided ethical approval for this research. Information provided to participants and consent forms for this study are provided in ***Appendices K and L***, respectively.

7.3 Results

Of 101 volunteers, 58 men and women (21 LF group, 20 MF group and 17 Walnut group) met the selection criteria. With 34 males and 24 females, there was no significant difference in the proportion of males and females randomised to each group. One participant from each group withdrew during the six-month intervention period. Thus, 55 subjects (20 LF, 19 MF, 16 Walnut) provided complete data sets for all three time points (0, 3 and 6 months) assessed during the trial.

There were no significant differences between groups for age, height, weight, or BMI, with the average participant bordering on obese at commencement of the study (Table 7-2). The three groups were also similar for numbers of participants reporting a family history of diabetes, ethnic origins, and categories of reported activity (data not shown). There was no significant difference in the proportion of males and females randomised to each group. Mean HbA1c results for the total study sample at baseline indicated good glycaemic control for a diabetes

population. There were no significant differences between groups for clinical characteristics except for total cholesterol.

Table 7-2 Baseline characteristics of subjects from each group and for the total sample

Parameter	Total sample	Control (n=21)	Mod Fat (n=20)	Walnut (n=17)	P#
Age (yrs)	59.3±8.1	60.1±8.2	59.8±7.4	57.7±9.0	0.634
BMI (kg/m^2)	30.0±3.7	29.2±2.6	30.2±4.6	30.7±3.9	0.453
Weight (kg)	84.5±12.8	81.9±11.2	84.6±14.3	87.6±12.8	0.397
Body fat (%)	33.6±9.1	31.2±8.1	35.1±10.2	34.5±9.1	0.352
HbA1c (%)	6.75±1.0	6.56±0.8	6.82±0.9	6.94±1.2	0.475
Cholesterol (mmol/l)*#	4.52±0.9	4.79±0.8	4.58±0.9	4.11±0.8	0.041
LDL (mmol/l)*	2.53±0.8	2.70±0.8	2.66±1.0	2.17±0.7	0.118
HDL (mmol/l)*	1.10±0.2	1.11±0.2	1.11±0.2	1.08±0.3	0.860
TG (mmol/l)*	1.95±0.81	2.18±0.82	1.76±0.84	1.90±0.74	0.255

*data were $\log_e$ transformed prior to analysis
#P value presented is for one-way ANOVA, control and walnut groups were significantly different using Tukey's test. Transformation did not correct non-normality, using Kruskal-Wallis P=0.035.

At baseline, there were no significant differences between groups for total energy, macronutrient and proportional fat intakes (mean±SD) (Table 7-3). In terms of dietary recommendations, mean SFA intake for each group was within the recommended range (<10% of energy), with over half of all individuals already achieving this target for this fat type. Mean PUFA intakes, however, were below target with only six out of 58 individuals from the total study sample consuming adequate dietary PUFA (≥7%E). Hence, P:S ratio and n-3 PUFA intakes were below target for all groups at commencement of the study.

Table 7-3 Energy and macronutrient intakes of all groups at 0,3,6 months intervention: amount consumed (mean±SD) and number (percent) of subjects achievi ng dietary targets

Variable	Target[a]	Control			Modified fat			Walnut		
Time		0 (n=21)	3 (n=20)	6 (n=20)	0 (n=20)	3 (n=19)	6 (n=19)	0 (n=17)	3 (n=17)	6 (n=16)
Energy (kcal)	2000	2053.8+568.1	2128.2+604.8	2146.0+431.8	2090.5+504.1	2015.6+541.7	1977.8+500.1	2024.7+664.6	2139.9+574.5	2006.6+376.2
CHO (% E)	50	46.4+6.6	45.2+7.2	43.1+8.1	44.1+7.7	42.2+6.4	41.4+6.0	46.9+6.5	43.9+5.7	43.5+3.8
PTN (%E)	20	20.8+2.8	21.0+2.0	20.7+2.7	20.6+4.5	22.5+3.1	22.6+3.6	21.9+3.4	20.9+3.3	21.5+2.5
Fat (%E)	30	28.5+6.4	29.4+6.9	32.6+8.5	31.2+7.1	31.7+5.9	32.7+6.1	27.7+7.2	32.2+5.2	31.8+4.1
SFA (%E)	<10%	8.9+2.5	8.6+2.8	10.2+4.1[b]	9.7+3.1	7.8+2.1	7.7+2.3[b]	9.0+2.8	7.8+ 2.4	6.9+1.6[b, f]
[n (%)]		14(67)	15(75)	11(55)[h]	10(50)	17(90)	15(79)[h]	8(47)	15(88)	16(100)[h]
PUFA(%E)	=7	5.3+1.3	5.9+1.3[c]	5.8+1.8[c]	6.3+2.8	8.0+2.0[c]	9.4+2.8[c]	5.4+1.5	11.7+1.6[c,e]	11.7+1.8[c,e]
[n (%)]		1(5)	4(20)[g]	5(25)[g]	4(20)	12(63)[g]	15(79)[g]	1(6)	17(100)[g]	16(100)[g]
P:S ratio	1	0.6+0.2	0.7+0.3	0.6+0.3	0.8+0.6	1.1+0.5	1.3+0.5	0.7+0.4	1.7+0.8[e]	1.8+0.5[e]
ALA (g)	2.22	1.3+0.7	1.5+1.1[c]	1.4+0.7[c]	1.4+1.0	2.0+1.1[c]	1.7+1.4[c]	1.4+1.0	3.7+1.7[c]	3.4+1.9[c]
[n (%)]		2(10)	5(25)[g]	3(15)[g]	4(20)	7(37)[g]	5(26)[g]	2(12)	16(94)[g]	15(94)[g]
EPA+DHA(g)	0.65	0.5+0.3	0.4+0.2[c]	0.4+0.2[b]	0.6+0.5	1.2+0.8[c]	1.2+1.1[b]	0.4+0.4	0.7+0.4[c]	0.8+0.6[b]
[n (%)]		5(24)	3(15)[h]	1(5)[g]	5(25)	14(74)[h]	14(74)[g]	3(18)	8(47)[h]	9(56)[g]
N6:n-3 Ratio	<10	6.6+2.9	8.2+5.7[d]	7.5+3.6	8.2+8.3	5.3+2.4[d]	8.3+5.0	8.6+8.4	5.7+1.4[d]	5.7+1.4
[n (%)]		19(91)	15(75)[n]	15(75)[i]	17(85)	19(100)[n]	12(63)[i]	12(71)	17(100)[n]	16(100)[i]

[a] Recommendations from ADA, AHA, ISSFAL and the literature (Hu, 2001).
[b] Significantly different between groups at the given time point (one way ANOVA, p<0.01)
[c] Significantly different between groups at the given time point (one way ANOVA, p<0.001)
[d] Significantly different between groups at the given time point (one way ANOVA, p<0.05)
[e] Significant effect due to treatment over time (repeated measures ANOVA, control versus walnut group, p<0.001)
[f] Significant effect due to treatment over time (repeated measures ANOVA, control versus walnut group, p<0.01)
[g] Significant difference between groups in proportions achieving target at the given time point (chi square, p<0.001)
[h] Significant difference between groups in proportions achieving target at the given time point (chi square, p<0.01)
[i] Significant difference between groups in proportions achieving target at the given time point (chi square, p<0.05)

After six months, energy intakes remained similar between groups with no significant changes from baseline. Significant differences between groups were confined to the fat profile, emerging as early as the 3-month time point and maintained at six months. The Walnut group was the only group to achieve all fat targets by the 3-month time point. These values were maintained at six months, with 100% of individuals achieving desired intakes for total SFA ($P<0.01$), total PUFA ($P<0.001$), and n6:n-3 ratio ($P<0.05$), with the majority of subjects achieving minimum n-3 fatty acid intakes. The MF group achieved all fat targets but the minimum intake for ALA fatty acids, with only 26% of subjects achieving this target at six months. Additionally, this group was unable to maintain the reduction in n-6: n-3 ratio seen at three months, whilst the Walnut group achieved the lowest n-6:n-3 ratio. In contrast, the LF group reported little change to mean PUFA intakes, with few individuals achieving target proportions for individual fat types.

After adjustments for sex, there were no significant changes in body weight throughout the trial for all study groups (Table 7-4). BMI also remained constant. There was a trend toward a significant interaction in body fat percentage ($p=0.057$). Post hoc follow-up indicated a significant increase in body fat in the control group only, but there were no other significant changes over time. At the three month measurement point, there was no significant overall change in body fat over time, but the change in body fat in the walnut group was significantly different compared to the control group ($p<0.04$).

Table 7-4 Change in weight, body fat, HbA1c and lipids over time

Variable	Control			Modified fat			Walnut			P value		
	0	3	6	0	3	6	0	3	6	time	group	T x g
N(F/M)	(8/13)			(10/10)			(6/11)					
Age	60.48 ±8.16			59.30 ±7.11			57.71 ±8.97					
Weight*	81.87 ±11.19	82.07 ±11.46	82.27 ±11.67	84.55 ±14.31	84.70 ±14.00	84.36 ±14.07	87.61 ±12.83	87.05 ±13.06	86.33 ±13.07	0.570	0.493	0.248
BMI	29.22 ±2.60	29.34 ±2.72	29.42 ±2.80	30.16 ±4.51	30.12 ±4.33	30.05 ±4.23	30.72 ±3.85	30.51 ±4.33	30.26 ±3.84	0.264	0.599	0.229
% body fat*	31.23 ±8.05	32.11 ±8.41	32.39 ±8.21	35.13 ±10.16	35.54 ±10.09	35.51 ±9.95	34.48 .±9.12	33.72 ±8.56	34.00 ±8.97	0.374	0.379	0.057
HbA1c	6.56 ±0.80	6.40 ±0.85	6.75 ±0.88	6.82 ±0.88	6.77 ±0.86	7.03 ±0.95	6.94 ±1.22	6.58 ±0.92	6.89 ±0.82	0.000	0.489	0.380
TC	4.79 ±0.82†	4.71 ±1.06	4.90 ±1.08	4.58 ±0.88	4.58 ±0.81	4.83 ±0.99	4.11 ±0.81†	3.94 ±0.70	4.02 ±0.77	0.037	0.021	0.434
LDL	2.70 (1.56)	2.68 (1.76)	2.69 (1.49)	2.58 (1.30)	2.59 (1.29)	2.73 (1.20)	2.17 (1.31)	2.01 (1.06)	1.95 (0.75)	0.634	0.032	0.316
HDL	1.11 ±0.22	1.19 ±0.24	1.25 ±0.27	1.11 ±0.24	1.24 ±0.20	1.34 ±0.21	1.10 ±0.24	1.16 ±0.24	1.30 ±0.62	0.000	0.766	0.046
TG	2.18 ±0.82	1.85 ±0.80	2.13 ±0.71	1.76 ±0.82	1.65 ±0.80	1.55 ±0.73	1.90 ±0.74	1.72 ±0.60	1.70 ±0.68	0.006	0.208	0.174

*Baseline and repeated measures analysis adjusted for sex.
†significantly different at baseline

HbA1c levels decreased at three months then increased, leaving a time effect for overall increase in HbA1c ($p<0.001$). The level, however, remained at or below 7% for each group. The total cholesterol levels of the Walnut group remained lower than the other two groups at each time point ($p=0.021$). There was also a significant time effect for changes in this variable ($p=0.037$), but univariate analysis failed to show a significant increase in any individual group. In contrast, while LDL-C levels of the walnut group were not significantly lower than the other two groups at baseline (Table 7-2), the continued lower levels produced a significant group effect in the trial ($p=0.032$), and in univariate analysis the Walnut group LDL-C levels decreased significantly over time ($p=0.036$) with no change observed in the other two groups (Table 7-4).

HDL cholesterol levels increased significantly in all three groups, producing a time effect ($p<0.001$). Post hoc analysis indicated a significant increase in each arm ($p<0.001$ for all groups), but the walnut group appeared to increase at a greater rate in the second six months, noting the significant time by group effect ($p=0.046$).

Mean triglyceride levels dropped in the first three months, a trend which continued for all but the control group where they rose again in the second three months. This produced a significant time effect ($p=0.006$), but the degree of variation in the data meant that no significant differences were found between groups in these changes. Again, the levels were not high, with mean values ranging from 1.55 to 2.18mmol/L.

DH data compared well with FR data. The mean difference was close to zero for each dietary variable, and the range for the limits of agreement lay within defined and clinically acceptable values (data not shown). Significant correlations were found between mean and difference values for reported protein intakes at six months ($r=-0.311$, $P<0.05$), SFA at three months ($r=-0.319$,$P<0.05$), EPA+DHA at baseline ($r=0.353$, $P<0.05$) and ALA at baseline ($r=-0.295$, $P<0.05$) and three months ($r=0.379$, $P<0.01$). On observation of the plots for reported protein, one extreme value at lower and higher intakes, respectively, appeared to create the regression line. An outlier in the SFA plot appeared to have a similar effect. The plots for ALA and EPA+DHA, however, appeared to show a general trend for greater differences at higher intakes.

Reported energy intakes from the DH were within approximately 10% of estimated requirements at all time points but the value was substantially higher for FR and this increased in magnitude with time (Table 7-5).

Table 7-5 Group mean differences between reported energy intakes (EI_{rep}) and estimated energy (EE_{est}) as an indicator of under or over reporting in the DH and FR

	DH	FR	DH	FR	DH	FR
Group mean difference (±SD)	-12.7(±33.2)	-17.6(±28.2)	-9.3(±25.2)*	-20.2(±30.9)*	-10.8(±24.0)*	-22.5(±31.0)*

* significantly different at $P<0.05$ between the groups at each time point; using repeated measures ANOVA

Dietary intake of very long chain n-3 PUFA (EPA+DHA) was strongly related to the levels seen in erythrocyte membranes at baseline, three months and six months ($P<0.01$) (data not shown). At six months, significant correlations were also seen

for the n-6:n-3 ratio ($P<0.05$) and total n-3 fatty acids ($P<0.02$) (data not shown). A significant change in the n-6 PUFA content of erythrocyte membranes over the duration of the study was determined due to treatment over time ($P<0.01$), with the greatest increases occurring in the Walnut group (Table 7-6).

Table 7-6 Erythrocyte fatty acid composition for all groups at 0,3,6 months intervention

Variable	Control			Modified fat			Walnut			RMANOVA (P value)		
Time	0	3	6	0	3	6	0	3	6	time	treatment	interaction
	(n = 21)	(n = 20)	(n = 20)	(n = 20)	(n = 19)	(n = 19)	(n =17)	(n = 17)	(n = 16)			
16:0	20.43±0.77	20.36±0.91	20.70±0.99	19.92±1.43	20.03±0.93	20.34±0.83	19.80±1.07	19.56±1.42	20.49±1.14	0.000	0.134	0.328
18:0	14.79±0.75	14.70±0.69	15.32±0.50	14.98±0.83	14.96±0.93	15.41±0.49	15.45±0.94	15.07±1.18	15.58±0.88	0.000	0.348	0.986
18:1n-9	11.70±1.11	11.60±1.00	12.45±1.17	11.42±0.64	11.32±0.66	12.00±0.70	11.93±0.85	11.47±0.97	12.36±0.89	0.000	0.301	0.488
18:2n-6	8.20±1.11	8.39±1.27	8.60±1.21	8.48±1.42	8.60±1.43	8.68±1.35	7.79±1.21	8.84±1.60	8.92±0.96	0.000	0.878	0.006*
20:3n-6	1.82±0.48	1.72±0.48	1.86±0.53	1.80±0.31	1.75±0.32	1.72±0.34	1.60±0.31	1.58±0.39	1.75±0.38	0.038	0.437	0.168
20:4n-6	13.91±1.59	13.66±1.43	14.19±1.34	13.53±0.89	13.14±1.02	13.47±1.66	13.38±1.36	13.06±1.32	13.86±1.41	0.000	0.344	0.652
20:5n-3	1.35±0.44	1.21±0.35	1.32±0.44	1.23±0.25	1.36±0.40	1.75±1.14	1.24±0.55	1.32±0.70	1.84±0.68	0.155	0.415	0.289
22:6n-3	5.67±0.88	5.74 ±1.00	5.28±0.90	5.87±1.20	6.19±1.04	6.10±1.24	5.60±1.37	5.61±1.30	5.31±1.38	0.060	0.232	0.255

Erythrocyte membrane fatty acid composition is expressed as % of total fatty acids.
Values are Mean ± SD.
*interaction term significant 0-3 months P=0.003 for contrast

Analysis of food patterns revealed some interesting data, with specific shifts in intakes by intervention groups between three and six months, but not the control group. At baseline, foods rich in SFA contributed the greatest proportion of fat intake for all groups (38% of mean daily fat intake), with meat providing the main source of dietary fat (about 22%), and nuts rich in PUFA providing about 10% of total fat consumption. After six months, this profile remained much the same for the control group, with SFA-rich staple foods (meat, cheese, milk and butter) the main source of dietary fat intake (39%). If anything, a small shift in fat sources from PUFA-rich to MUFA-rich foods was observed for this group. In contrast, the MF group reported a shift from SFA-rich to both MUFA-rich and PUFA-rich foods (29% and 32% of total fat intake, respectively). For the Walnut group, however, there was a big shift to PUFA-rich foods (45% of total fat), substantively walnuts (individuals reporting 100% compliance for consuming 30g walnuts/day throughout the length of the study). PUFA-rich nuts (almost exclusively walnuts) now contributed 31% of total fat intake for this group, with oily fish providing a further 6%.

The major sources of n-3 PUFA for the walnut group were walnuts, where 30g/day provided 50% of the total daily intake, and oily fish (350g/week) provided a further 17%. The major sources of n-3 fatty acids for the MF group were oily fish, where 500g/week oily fish provided 42% n-3 intake, and a combination of soy products, legumes and ‘n-3 enriched’ products provided another 22%.

CONCLUSION

7.4 Summary

Several large studies have demonstrated lifestyle modifications as important intervention strategies for the prevention and treatment of T2DM and CVD complications [19-21, 365]. The approaches used in these studies provide evidence for nutrition intervention practices. The RCT, represents the highest level of research evidence [258] and was the model used for this study to assess the efficacy of three dietary advice approaches. Structured advice referring to two alternative intake patterns based on a set of food groups identifying sources of unsaturated fats were more likely to achieve essential fatty acid targets than general low fat advice approaches. Importantly, none of the approaches adversely affected energy balance or blood glucose control in these T2DM patients.

Men and women with established T2DM were randomised into three dietary intervention groups. There were no significant differences between groups for dietary intakes at baseline. Mean total fat and SFA intakes were considered reasonable and low. PUFA intakes, however, were also low across all groups and below the levels recommended. Taking into account previous exposure to advice, these results suggest that current dietary advice practices for diabetes, whilst supportive of total fat reduction, do not enable adequate intakes of dietary PUFA. These practices appear fairly universal in Western cultures, so the findings would have reasonable relevance to those outside Australia.

In an attempt to increase the amount of PUFA, subjects in the MF and Walnut groups received structured advice for all food groups in the diet including specific advice on food sources of PUFA, with those in the Walnut group given advice for the regular consumption of walnuts. After six months, with no significant changes to mean energy or major macronutrient intakes, dietary fat profiles diverged significantly from the control group. The MF and Walnut groups achieved desirable increases in the proportion of total PUFA as well as further reductions in mean SFA, while the LF group reported little change to individual fat proportions.

Shifts in the fat profile could be explained by changes in food choice patterns, where fat from SFA-rich staple foods (milk, cheese, meat and butter) was substituted with regular intakes from significant food sources of PUFA. For the walnut group these foods were walnuts and oily fish, whereas the MF group reported oily fish, legumes (mainly calcium enriched soymilk), nuts and n-3 enriched foods. In contrast, the lack of change in sources of fat for the LF group concur with data from previous intervention trials[22, 23] and from Australian population surveys[353, 354] that suggest saturated fat remains the main type of dietary fat in the diet despite lowered total fat intakes.

7.5 Theoretical significance

At commencement of the study, subjects reported sub-optimal habitual PUFA intakes. A total diet approach incorporating walnuts and oily fish successfully modified the fat profile in line with current recommendations, without increasing energy intake in patients with T2DM. The greater success for individuals in the

Walnut group demonstrated the utility of incorporating a 'functional food' source into the total diet pattern for the achievement of adequate intakes of a required nutrient [366]. Furthermore, greater success by both intervention groups compared with the control group suggests the need for more structured advice practices in the clinical context. Judicious food choices from existing core food groups could also achieve desired fat proportions, but the guidance systems are too blunt to make this assumption.

While this study has demonstrated the impact of targeted advice on individual foods, it was important that this knowledge be set in the context of the whole diet. In order to address the relatively high n-6: n-3 ratio of walnuts advice for the concomitant inclusion of n-3-rich fish was also required. Thus, 30g walnuts/day and 350g oily fish/week provided 50% (mostly ALA) and 17%, respectively, of total n-3 fatty acid intake. This enabled achievement of the most desirable (lowest) n6: n-3 ratio by the walnut group. The MF group relied more heavily on fish, 500g oily fish/week providing 42% of n-3 PUFA, with the remaining n-3 intakes coming largely from a range of food choices including soymilk. This latter pattern of intake did not enable adequate achievement of the ALA fatty acid target by the MF group, with a lower n-6: n-3 ratio not maintained at six months. Moreover, the earlier achievement (at three months) of target PUFA and SFA proportions by 100% of individuals in the Walnut group indicate that the combination of walnuts and oily fish were more effective and more sustainable than the larger intake of fish alone.

Thus, the feasibility of total diet advice incorporating significant individual food sources of PUFA to individuals with T2DM under free-living conditions has been demonstrated. The effectiveness of the advice system being tested was confirmed by relevant health-related clinical outcomes. For example, changes in blood lipid levels confirmed the benefits of changes to the dietary fat profile for improvements in metabolic control [262]. The Walnut group in this study started and continued with lower total-C than the other two groups and lowered compared to raised levels at six months, but the changes were not statistically significant over time. However, LDL-C levels decreased significantly in the Walnut group with no change in the other two groups, providing a significant group effect. These results may be explained by the concomitant significant rise in HDL levels, by all groups, with the Walnut group increasing at a greater rate in the second six months. There were no detectable differences between groups for changes in triglycerides with the lowered levels seen in all groups significant over time. Previous evidence of decreased total-C and LDL-C in the diets of at-risk subjects has been from two-three servings of walnuts per day [367]. The significance of this study, therefore, is that improvements in blood lipids were achieved from a practical single serving per day.

7.6 Limitations and areas for further research

Of the 101 men and women who volunteered, only about half 50% were eligible for the study due to the strict selection criteria used. While this may limit generalisation of results, it ensured an homogenous intervention group, thereby strengthening the

ability to detect differences over time. The number of participants who did not complete the study (one from each group) was considered small and unlikely to affect results.

When explaining the results, differences in dietary advice protocols needed also to be considered. While the control group reflected general dietary advice and 'flexible' counseling practices, the two intervention groups were matched for the 'programmed' delivery of structured advice for all food groups in the overall diet, including exchange lists of MUFA-rich and PUFA-rich foods highlighting the significance of identifying these food sources for achievement of fat targets. Hence, results from alternative patterns of food intake could emerge.

Where primary outcomes were dietary variables and achievement of dietary goals, dietary compliance was an important aspect of study design. Regular contact and monthly provision of portion-controlled packs of walnut supplies enabled regular monitoring. The previous exposure to dietary advice would indicate the potential for high compliance by all groups. However, the Walnut group was the only group to achieve all fatty acid targets, reflecting the high adherence to the consumption of walnuts. Notably, after six months, the LF group had fewer individuals achieving the SFA target than at the beginning of the study (from 67% to 55%), with mean SFA intake increasing to a level above the recommended range.

The lack of change in body weight and BMI across all groups also confirmed the effectiveness of each intervention protocol with no reduction in energy intake, often seen in controlled dietary studies, and no weight gain effect often seen in

supplemental food studies. This suggests optimal dietary compliance and consistency across treatments. While differences in physical activity were not noted, and weight remained constant, the trend toward a difference in changes in body fat between the control and Walnut group was novel. Differences in fatty acid metabolism may have had a role, where diets lower in saturated fats and higher in unsaturated fat can impact on body fat distribution and fat mass [368-371]. Anecdotal evidence from subjects in the Walnut group suggests increased satiety from the consumption of walnuts, also reported in other nut studies [171, 372], but requiring further investigation. Regulatory mechanisms at the level of the hypothalamus [373] may be involved and is another area requiring further research.

Energy balance is an important aspect of T2DM and needed to be controlled. The impact of the regular consumption of high-fat foods on energy intake, therefore, required further assessment. At commencement of the study, reported energy intakes for the study sample were reasonable, within around 10% of estimated requirements. The lack of change in energy intakes, despite marked increases in oily fish and nut consumption by the two intervention groups, demonstrated the utility of structured total diet advice for the incorporation of high-fat foods.

Another important aspect of T2DM management is measures of blood glucose control. Results for the study sample were considered representative of good diabetic control at the beginning of the study. While some deterioration in glycaemic control might be expected over six months, mean HbA1c remained at or below 7% for each study group with no significant differences between groups,

indicating reasonable control of the diabetic state. Such results demonstrate the worthiness of all intervention protocols and help allay concerns that increased PUFA consumption (more than doubled in the Walnut group) might have adverse effects on glycaemic control.

The quality of dietary data was also assessed and found to be favorable for this type of analysis. The DH provided more accurate estimates of energy intake, while FR showed negative signs of subject burden [279, 288]. Bias was unlikely or explainable for most variables. For example, while differences between the two methods for ALA and EPA+DHA intakes at baseline were plausible, this was likely due to infrequent intakes of foods such as fish and not consumed during the three days of FR. In contrast, the DH covers all variation in intake and is more likely to capture irregular consumption patterns. More regular intakes of foods high in ALA and EPA+DHA at six months resulted in greater agreement and justified the use of the DH as the reference method for studying dietary change. In particular, changes in reported n-6 and n-3 fatty acids were confirmed over time through biomarker analyses, including the regular consumption of walnuts and fish, respectively. The strongest correlation with dietary intake was for reported EPA+DHA at all time points ($P<0.01$), although significant correlations for n-6: n-3 ratio and for total n-3 PUFA at the completion of the study also confirmed reported intakes.

7.7 Relevance to thesis and implications for practice

This trial has confirmed the feasibility of a structured advice system to bring about pre-determined changes in nutrient intakes and improvements in clinical outcomes

under free living conditions. For the treatment of diabetes, the theory on nutrients was successfully implemented through the identification of significant food sources of unsaturated fatty acids for recommended changes to the dietary fat profile. For the purposes of this thesis, RCT conditions substantiated the effectiveness of the advice system in terms of improvements in health outcomes such as blood lipid levels and percent body fat, clinical associations for diabetes and the Metabolic Syndrome. Furthermore, the successful inclusion of walnuts for the delivery of adequate PUFA and by extension n-3 fatty acid intakes without changes to other dietary variables demonstrated the utility of the system for assessments of individual food/nutrient effects.

Dietary assessment for individuals with diabetes should, therefore, consider the type of fat in the overall diet. Advice will require attention to both lowering SFA and ensuring adequate amounts of unsaturated fat, particularly challenging in terms of PUFA intakes. This study has demonstrated the value of using a food group approach to total diet advice in which separating out foods based on their fat composition is useful for achieving proportional intakes of different types of fat. In addition, incorporating walnuts within this framework is likely to assure adequate intakes of PUFAs, including substantial amounts of n-3 fatty acids.

CHAPTER 8 THE EFFECTIVENESS OF STRUCTURED FOOD PATTERN ADVICE FOR NUTRITION INTERVENTION

8.1 Summary

The effectiveness of MNT is dependent on the conversion of theoretical positions on nutrient intakes to practical advice on foods. This thesis has demonstrated that structured advice linking theoretical macronutrient targets to food sources will result in better achievement of nutritional guidelines and subsequent clinical benefit than general dietary advice. Using diabetes treatment as the example, an advice system based on specific food sources of macronutrients and individual types of fat was developed and applied in the clinical context. Achievement of targets for energy and individual fat proportions by subjects under free-living conditions confirmed the feasibility of the advice system, whilst improvements in clinical outcomes substantiated the benefit. In this way, evidence has been provided for MNT and the methodology for establishing this evidence has been exposed.

Diabetes is one of a cluster of clinical abnormalities known as the Metabolic Syndrome, linked to insulin resistance and CVD risk [6, 374]. The traditional focus for dietary management has been on CHO intake for direct effects on blood glucose control[3]. However, the weight of current research evidence supports consumption of specific proportions of different types of fat to benefit the broader concept of metabolic control and, hence, a range of related outcomes [10]. Nutrition guidelines for diabetes and related complications largely reflect the research evidence by

providing recommendations for specific proportions of saturated and unsaturated fats in the diet [8]. Current food guidance systems are not specific enough to ensure individual fat targets[16]. In fact, adjunct dietary advice that refers to exchangeable edible fat portions has the potential to increase total fat and energy [25] and the proportion of n-6 rather than n-3 fatty acids [24], which may compromise potential benefits. Consequently, this thesis considered that, in the case of diabetes treatment, the challenge was to develop a food-based system to concurrently guide advice for the provision of adequate nutrition as well as controlling energy intake, and the amount and type of CHO and fat in the diet.

In order to develop a food-based advice framework, the research focus was on food patterns for delivery of the required nutrient mix. Examination of the usual food intakes of a sample of glucose intolerant women in Study 1 of this thesis provided insight into the possible link between dietary change, food factors and patterns of intake, and abnormal glucose metabolism. In turn, data from this first study sample contributed to the identification of food groups as sources of macronutrient variables and the development of a model intake pattern to address the macronutrient content of the total diet, outlined in Study 2 of the thesis. In this way, a food guidance system for the achievement of individual fat targets and adequate nutrition was established using all foods in the diet. The theoretical basis of the system was confirmed via the practical application in women with GDM in Study 3, and also demonstrated in men and women with T2DM in Study 4. The latter study also confirmed the clinical effectiveness of the food group approach

and demonstrated the incorporation of an individual food source of a specific nutrient and subsequent improvements in health-related outcomes.

8.2 Limitations in study design

Generalisations that could be made from the combined studies are outlined in the following discussion. As acknowledged throughout this research, study design was important in order to effectively assess the relationship between specific food patterns and differences in nutrient intakes and subsequent clinical values [258]. In each of the trials conducted, differences in fat profile alone were achieved using parallel treatment groups in which advice was similar for all aspects of the diet except for specific information on certain foods as sources of individual fat types. Thus, it could be argued that the changes observed in clinical outcomes, for example significant differences for improvements in blood lipid profiles, were due to differences in the proportions of individual fat types, in particular increases in the amount of dietary PUFA, with shifts in food patterns guiding their achievement.

While the RCT is at the pinnacle of research evidence for diet-disease relationships, limitations applicable to all intervention trials apply [258]. In reality, proving 'cause and effect' relationships between a dietary treatment and clinical outcomes such as insulin resistance is inherently difficult. First of all, evidence from dietary studies in humans relies on less direct affects using known clinical markers of disease. Secondly, multiple food components and variation between individuals make it hard to identify a single dietary variable that impacts on these outcomes. Where the aim of research is to provide evidence to inform practice, this is largely

dependent on the careful and successful transfer of the theory on nutrient effects into appropriate advice on foods. Constructing a food pattern that identifies specific sources of required nutrients is a useful approach for aligning nutrient intakes with individual foods. While food pattern analyses may be biased due to prior knowledge on nutrient/food factor effects [267], the descriptive nature of results informs practice and enhances dietary advice in a way that nutrient analyses cannot.

Greater numbers of individuals in the intervention groups achieved dietary targets, clearly indicating a better transfer of nutrient intake theory to clinical practice. Advice to each individual, however, exposed the variation inherent in exchange list systems based on representative nutrient estimates, and highlights the need to emphasize variety in the delivery of advice to free-living individuals [17]. This thesis demonstrated that reference to a structured food intake pattern encompassing the macronutrient content of the total diet supports variety in food intake as well as low variation in nutrient intake. While additional food groups and sub-categories of foods reduced the variation between individual foods and allowed an emphasis on foods as secondary nutrient sources, too many lists, however, may prove cumbersome and impractical for the delivery of simplified food-based advice.

If nutrition research is to provide evidence for practice via reliable and valid results, compliance to dietary advice is an important issue that requires substantial support. The structured nature of clinic support and of the advice system itself was effective for the achievement of dietary targets in two trials involving individuals

with GDM and T2DM, respectively. The supply of walnuts in Study 4 to individuals with T2DM in standard portion amounts assured minimum PUFA targets and took the guesswork out of advice and subsequent measures of compliance. The lack of significant differences in weight between groups in both trials supported dietary compliance across treatments, while differences in lipid profile in T2DM subjects reflected differences in adherence to nutrient targets. Lower cholesterol levels for the Walnut group throughout this study were the result of a randomization phenomenon. This bias meant that a significant improvement in that group was more difficult to achieve, and only served to strengthen the particular outcome for a further reduction by this group.

Having achieved dietary differences, it was also important to provide evidence for the acceptability and practicability of the dietary protocol by individuals in the study samples. Up to six months adherence to advice by free-living T2DM individuals was a good indication of the feasibility of the developed system. However, advice to intervention groups was individualised and followed an intensive treatment format. These aspects of dietary counseling have previously been found to be effective [19, 20, 189, 191], but not always provided as standard clinical practice. The provision to subjects of a convenient daily portion amount of walnuts may have aided the 100% dietary adherence reported. However, the consumption of walnuts in a realistic amount also had an impact, suggesting ready transfer to the free-living context. This was confirmed in the form of positive feedback from subjects in this group.

The transfer of results to other groups is contingent on similar qualities between those in the study sample and those to whom results are to be generalized [258]. Results from any one cohort may demonstrate bias related to the characteristics of the group as well as the known bias association with greater motivation to comply in study volunteers. However, high motivation and exposure to previous advice are qualities associated with people with diabetes, and therefore may be characteristic of the wider diabetes community. In the trials reported as part of this thesis, a narrow range of selection criteria limited the numbers recruited but resulted in similar dietary and clinical characteristics at baseline, strengthening the ability to detect a difference due to treatment over time. Similarly, differences in the experience and skills of the practitioner must not unduly bias results. For this, the structured nature of the model food intake pattern evaluated in this thesis provided a template for practitioner and patient alike, allowing more standardised tailoring of individualised advice and systematic monitoring of dietary compliance.

The ‘validity’ of dietary data as primary outcome variables has implications for the interpretation of results and acceptance as evidence for nutrition intervention practices [294]. The lack of a reference measure or ‘gold standard’ against which to assess dietary intake data is considered problematic [285].Therefore, comparisons between methods is dependent on estimates of potential bias to provide an understanding of the relationship between the test measure and the truth. Compared with FR data, the quality of data from the DH method was considered favorable. Bias was either unlikely or explainable, with the FR showing negative signs of subject burden over time. The DH was useful in these analyses in that it

covered all variations in meal and intake patterns and therefore was a more accurate measure of habitual intake than the FR. In particular the DH captured irregular consumption patterns of individual foods such as fish. Where 'under-reporting' of energy intake is possibly the greatest source of bias in dietary studies [294], again the DH was assessed as less susceptible and confirmed as the most appropriate method for dietary analyses in this research. Biomarker analyses confirmed reported n-6 and n-3 intakes and changes in intakes over time, substantiating intakes of walnuts and fish as major sources, and adding support to the relationships between nutrients, foods and changes in clinical values, in this case, consistent with existing knowledge on dietary fat and its influence on metabolic markers of insulin resistance [74, 77].

8.3 Significance of the research to this thesis

Where this thesis sought to provide evidence for nutrition and dietetics practice, the establishment of a dietary advice system required an understanding of the relationships between food patterns and clinical outcomes. Although the focus was on changes in fat intake, established clinical practices needed to be taken into account. In the case of diabetes treatment, these target the CHO fraction of the diet. In support of this, the findings from observations of the dietary intakes of GDM women in Study 1 illustrated the complex nature of dietary change and its impact on food patterns within the overall diet. Whilst the results justified attention to CHO intakes, they demonstrated the variation in food factors relating to this nutrient and possible implications for blood glucose control. The results suggest that both the

type and distribution of CHO intake are important and that reference should be made to specific food groups, portion sizes and the overall pattern of foods within the total diet.

The process for developing an appropriate set of food groups and construction of a model dietary intake pattern demonstrated how individual food sources of required nutrients could be incorporated into the total diet to achieve targeted nutrient proportions. Whilst applicable to all nutrients, achievement of individual fat targets highlighted the inadequacies of core food groups for this purpose and the need to identify a greater number of food groups to address a broader range of nutrients and specific nutritional requirements beyond those required to provide adequate nutrition [266]. The substantial contribution of fat from secondary food sources, such as milk and meat as sources of SFA, and fish and soy as sources of PUFA, demonstrated the need to effectively identify these foods in advice seeking to enable an effective exchange of nutrient intakes and thus modify dietary fat profile. Whilst core food groups within the model readily achieved the saturated fat limit, achievement of optimal overall fat profile was dependent on the adequate inclusion of PUFA-rich food groups.

Using the RCT as the gold standard to confirm the feasibility and relevance of structured advice to diabetes groups, its practical application was tested in the free-living context. Importantly, the shift in focus from CHO intake and glycaemic control to the application of the theory on fat for overall metabolic control had no negative effects for controlling energy intakes, weight and glucose homeostasis

compared with control groups receiving conventional advice. Thus, the effectiveness of each of the dietary protocols for short-term clinical benefit was confirmed. Longer-term risk management in terms of clinical markers of IR and CVD risk, however, was only addressed in the intervention groups in which recommendations for different fat types were achieved.

Assessment of habitual intakes at baseline determined the consumption of dietary PUFA as inadequate across all groups in which habitual intakes were assessed. This was the case regardless of previous exposure to dietary advice as part of diabetes management in both GDM and T2DM and/or already lowered SFA intakes, as was the case in T2DM individuals. Thus, the focus of advice was largely on the adequate achievement of recommended PUFA intakes. In GDM women, the better achievement of the recommended fat profile in the intervention group, in terms of group and individual data, reflected increased intakes of PUFA-rich foods, mainly through shifts in fat intake from meat and dairy (using leaner cuts and low fat products) to oily fish, soy and nuts.

The successful transfer of advice from GDM women to the wider T2DM community was an important step in the validation process. Further, incorporation of an individual food (walnuts) as delivery agent for increasing PUFA intakes was simultaneously assessed and the benefits substantiated through relevant clinical outcomes. Hence, two intervention groups in this study demonstrated alternative food choices from within the same framework for achievement at six months of specific targets for individual fat proportions, including those set for n-3 PUFA

intake. On the one hand, an average 500g oily fish per week provided the main source of PUFA/n-3 PUFA in the diet. Alternatively, the incorporation of walnuts into the overall diet resulted in an even better achievement of PUFA targets (the recommendation for alpha-linolenic acid (n-3 PUFA) was only achieved by the Walnut group). Providing the substantial portion of PUFA intakes and 50% of n-3 PUFA intakes, 30g (1oz) walnuts per day reduced the dependence on fish to 350g per week. Importantly, the high n-6:n-3 ratio of walnuts was not reflected in the overall ratio for the total diet, verifying the value of total diet advice and underscoring the significance of complementary food combinations such as walnuts and fish. Furthermore, the early achievement of dietary targets by the Walnut group (in three months rather than six) indicated an important role for key food sources of essential nutrients in getting results, and by extension benefits, faster.

In contrast, the lack of impact on fat proportions in control groups (both GDM and T2DM) highlighted the inadequacies of existing advice systems to address targets for fat types. In GDM this may be attributed to the low priority given to advice on fat for these women. However, in T2DM general advice on fat and fat type, including the recommended 'two servings of fish per week' [8, 375], was provided to the control group in that study. Of concern was that SFA intakes for the control group actually deteriorated over the study period. This supports the argument that general low fat advice focuses attention on excluding visible edible fats, mainly unsaturated fats, whilst a large proportion of SFA intake is from core food staples.

For those incorporating walnuts into the total diet over six months, the weight gain often reported in 'supplemental' food studies did not occur [357]. Further, in view of the lack of differences between groups for weight change and physical activity levels, the trend toward body fat loss in the Walnut group was an interesting phenomenon and may reflect suggestions that diets lower in saturated fat and higher in unsaturated fats have a beneficial effect on body fat distribution and fat mass [368, 370, 371, 376]. Whether this was due to differences in fat metabolism and/or regulatory mechanisms at the level of the hypothalamus [377], however, requires further research. Anecdotal evidence suggests increased satiety may have been a factor.

Beneficial changes to the blood lipid profile provided further evidence of the effectiveness of the advice system for exchanging saturated for unsaturated fat in the diet, a phenomenon reported by previous studies in which the balance of fat intake has been shifted rather than reductions in total fat intake alone [262]. While improvements in blood lipid levels have been previously shown in response to walnuts, these studies used much larger 'supplemental' amounts [357], where long-term adherence may be an issue. This research has demonstrated the way in which a realistic amount of an individual food can be incorporated into the total diet to increase consumption of a required nutrient to adequate levels to obtain health benefits.

8.4 Applications to research methodology and clinical practice

In this thesis, the development of an appropriate advice framework for the treatment of diabetes required reference to the theory on nutrients and previous research on food patterns as well as evidence from previous dietary intervention trials. In this way, a set of reference food groups and overall pattern of intake was established in which all foods are addressed and the recommended diet is described in a way that supports advice. Theoretical evaluation and successful transfer to practice in RCTs provided a methodology for nutrition intervention.

RCTs provide the highest level of research evidence to support the theory on nutrients, demonstrating the practical application of advice methodologies and substantiating benefits in free-living individuals and. The results provide evidence for nutrition intervention and a methodological framework in which manipulation of specific nutrients and foods within the overall diet can be achieved and consistent health-related outcomes attained. The studies conducted as part of this thesis have shown how researchers/clinicians may use knowledge on food group composition to tailor advice to individuals for achievement of dietary targets (nutrients under study) and consistent clinical outcomes. Prior development of food groups and the construction of a dietary model with specific targets in mind ensured an appropriate food intake pattern on which to base advice for individuals. Whilst theoretical evaluations acknowledged the variation inherent in free-living intakes, the lack of differences between intervention groups for major macronutrient variables, including total fat intake, was an important result. Thus, the practical application of

the advice system demonstrated how total diet advice could effect a change in target variables without impacting on other dietary variables. More specifically, it confirmed the successful manipulation of individual fat types without unwanted increases in total fat and energy intakes that may dilute diet-disease associations and/or counter anticipated benefits [25]. This is an important premise in substantiation research methodology so that individual food/nutrient contributions to the diet can be identified in relation to specific health outcomes. In this way, the inclusion of walnuts to increase intakes of n-3 PUFA demonstrated the effectiveness of a structured advice framework for testing a single food as the only change to the diets of free-living individuals and the way in which assessments in substantiation research apply. While the treatment was for diabetes and individual fats were the nutrients targeted, in theory the principles would apply to other nutrients and food sources. Future research application would involve the substantiation of health claims on individual nutrients/foods. In terms of evidence for practice, future research might involve the application of the advice system in other treatment groups. Of particular interest would be adaptations for specific ethnic groups using culturally appropriate foods. Alternatively, the novel finding relating to body fat loss in response to the food pattern inclusive of walnuts (Study 4) suggests application of the system in overweight/obese subjects for the establishment of evidence on the correct macronutrient balance for the management of overweight [378].

MNT requires evidence-based support for the specific application of research knowledge. In the case of evidence-based practices for diabetes and related

complications, dietary approaches for long- and short-term risk management need to be confirmed. In terms of direct effects on glycaemic control, established practices attending to the amount and type of CHO in the diet appears justified, with equivalent amounts of CHO per serve to allow portion control. Where the glycaemic effect of individual foods largely match established core food groups, for example milk and fruit as low GI foods, an emphasis on these foods is considered reasonable. Further discrimination within the starch group (bread and cereals plus starchy vegetables) based on whole grains, high fibre and/or gycaemic index can be readily implemented. In the RCTs conducted as part of this thesis, this attention to the CHO fraction was incorporated into the advice system and was consistent across advice groups resulting in good glycaemic control for all groups. However, in terms of longer-term risk management for people with diabetes, the establishment of proven methods for addressing the fat profile was required to support the change in focus to overall metabolic control and recommendations for proportional intakes within the fat fraction of the diet.

Appropriate advice referred to a greater number of food groups than used to assure nutritional adequacy. The additional food groups distinguished between SFA-rich (meat and dairy) and PUFA-rich foods (soy, fish, oils and nuts) and enabled a model food intake pattern for the achievement of targets for individual fat types whilst controlling energy and other nutrients. Significantly, while differences in food choices were achieved, food groups developed to identify specific sources of PUFA were essential to the achievement of targets within the fat profile. Furthermore, overall nutrition was not compromised by modifications to core food

groups and staple foods. The incorporation of walnuts demonstrated the way in which an individual food can be included in a ‘healthy diet’ pattern for the convenient and swift delivery of adequate or substantial amounts of a required nutrient.

In summary, in MNT the application of advice requires evidence to support practice. This thesis has provided evidence from theoretical and practical research perspectives for a structured approach to advice. Hence, an advice system linking nutrients to food patterns and individual foods was developed to assure targets in nutrition intervention. Using the advice system for diabetes treatment, current recommendations on macronutrients and the type of fat in the diet were theoretically established in a model food pattern. Implementation of the advice system in diabetes groups under free living conditions was shown to be feasible and effective in practice affording evidence to support nutrition intervention research and MNT in the treatment of diabetes.

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APPENDIX A: FOOD SUBSTITUTIONS USED FOR GI ANALYSIS IN STUDY 1

Food Item	Substitution	GI
Cereal/grains		
Bread		
Breadcrumbs, commercial	Bread, white (wheat flour), mean	70
Bread, lebanese, white	Pita bread	57
Bread, mixed grain	Multi-grain, Tip Top	43
Raisin toast, commercial	Bread, white+sultanas+sucrose, mean	46
Breakfast Cereal		
Muesli slice, home prep	Muesli, b/fast cereal, toasted	43
Muesli bar, choc-coated	Muesli bar + chocolate, milk, mean	55
Muesli, swiss-style	Muesli, b/fast cereal, non-toasted	56
Bakery Goods		
Cake, carrot/chocolate/plain	Cake, pound	54
Cake, fruit	Cake, pound + sultanas, mean	55
Cake, rock	Cake, pound	54
McMuffin, bacon & egg	English Muffin bread	77
Meat pie/pasty	Pastry, flaky	59
Muffin, banana/bran/chocolate	Mean of all muffins	60
Pie, apple, high, family	Pastry + apple, mean	49
Pie, cottage	Pastry, flaky + potato, mashed	75
Pudding, sponge, steamed	Cake, sponge	46
Sausage roll	Pastry, flaky + sausage, mean	44
Scone, plain, commercial	Bread, white (wheat flour), mean	70
Vol au vent	Pastry, flaky	59
Biscuits		
Biscuit, plain sweet, unspecified	Arrowroot + Morning Coffee, mean	70
Cruskits, crispbread	Mean of all crackers	71
Tiny Teddy biscuits	Arrowroot + Morning Coffee, mean	70
Pasta		
Lasagna/cannelloni	Ravioli, meat-filled, cooked	39
Rice		
Rice, creamed, canned	Rice, Calrose, white+milk, whole, fluid + sucrose, mean	60
Rice, fried, Chinese restaurant	Mean of all white rice	83
Rice, white, boiled, unspecified	Rice, Calrose, white, cooked	87

Food Item	Substitution	GI
Fruit		
Salad, fruit, fresh	Fruit cocktail, canned in natural juice	55
Apple, canned, sweetened	Apple + sucrose, mean	52
Apple, stewed	Apple	38
Fruit drink, apple	Apple juice + sucrose, mean	53
Fruit drink, orange	Orange juice + sucrose, mean	55
Jam, 100% fruit or unspecified	Mean of all jam	53
Jam, stone fruit	Jam, Glen Ewin, apricot spread	55
Mandarin	Orange	44
Nectarine	Peach	42
Vegetables		
Nachos, home prep	Corn chips, Doritos	42
Potato, chips, commercial	French fries, fine cut	75
Potato, mashed, dried	Instant potato, prepared	83
Potato, new, peeled, boiled	Potato, new, canned, drained	65
Potato, pale skin, baked	Potato, Pontiac, baked in oven, mean	93
Potato, pale skin, mashed	Potato, Pontiac, mashed, mean	91
Potato, pale, skin, peeled, boiled	Potato, Sebago, peeled, boiled, mean	87
Taco shell, El Paso	Corn chips, Doritos	42
Milk Products		
Flavoured milk	Milk, whole, fluid + sucrose, mean	46
Frozen Yoghurt	Mean of all yoghurt	25
Smoothie, banana	Milk, whole, fluid + banana	41
Sundae, McDonalds	Ice cream, full fat + sucrose, mean	63
Thickshake, McDonalds	Milk, whole, fluid + ice cream + sucrose, mean	51
Sugar-rich products		
Sugar-rich beverages		
Mineral water, flavoured	Soft drink, Fanta	68
Soft drink, all flavours	Soft drink, Fanta	68
Sugar-rich foods		
Chocolate, candy -coated	Chocolate, milk + sucrose, mean	57
Chocolate, dark/milk	Chocolate, milk	49
Chocolate, milk, with nuts	Chocolate, milk + peanuts, mean	32
Golden syrup	Sucrose, mean	65
Gums	Sucrose, mean	65
Ice confection	Sucrose, mean	65
Licorice	Sucrose, mean	65
Picnic Bar	Snickers Bar	41
Sugar confectionary, jelly type	Jelly beans	80
Miscellaneous foods		
Beer nut, salted		
Beans, mixed, canned		
Dumpling		
Falafel/hummus	Peanuts, roasted, salted, mean	14
Soup, bean, home prep	Mean of all beans	37
Sauce, black bean	Bread, white (wheat flour), mean	70
Soup, chicken noodle, dry mix	Chick peas, boiled, mean	33
	Mean of all beans	37
	Black beans, boiled	30
	Noodles, 2-minute	46

APPENDIX B: CARBOHYDRATE-RICH FOODS OF UNKNOWN GI EXCLUDED FROM GI ANALYSIS IN STUDY 1

Cereal/grains

Biscuit, choc-coated
Biscuit, chocolate chip
Biscuit, cream-filled
Biscuit, cream-filled, choc
Bun, fruit, iced
Cake, iced
Chocolate Bavarian
Cornflour
Ice cream cone
Lamington
Mint slice, biscuit
Nut Feast, Uncle Toby's
Pancake
Pastry, shortcrust
Rice cracker, plain, Sakata
Rice pudding
Spring roll, deep fried
Spring roll, Thai, restaurant
Tabbouleh
Tim Tam, Arnotts

Fruit

Apricot nectar
Fruit bar
Prune

Vegetables

Coleslaw
Potato gems
Potato salad
Potato scallop, deep fried
Rhubarb, stewed, sugar added

Milk products

Beverage, chocolate, Cadbury
Buttermilk, cultured
Fruche
Malted milk powder
Paddle pop

Sugar-rich products

Cherry Ripe
Chocolate topping
Crunch, chocolate
Kit Kat
Violet crumble

Miscellaneous foods

Cheesecake
Devon/fritz
Ice cream cone
Moussaka
Pie, fruit
Pie, lemon
Pudding, self-saucing
Quiche
Slice, vanilla
Soup, minestrone
Soup, pea & ham
Tart, custard
Twisties, chips

APPENDIX C: INTERVIEWER-ADMINISTERED DIET HISTORY QUESTIONNAIRE IN STUDY 3

Illawarra Health & Smart Foods Centre

Interviewer-administered Diet History

Client code: _____ Interviewer: _____ Interview number: _____ Date: _____

Age: _____ DOB: _____ Height: _____ cm Pre pregnancy Weight: _____

Current Weight: _____ BMI: _____ Parity: _____ Est. Date of Delivery: _____

Previous GDM pregnancies: _____ Family History of Diabetes: _____

Country of birth: _____ Ethnicity: _____

Medications: _____

History of health conditions: _____

Supplements: _____

Physical activity:_____

Part 1: Breakfast How many days in the week do you eat breakfast? _____

Prompts	Type	Serving Size	Frequency
CARBOHYDRATE			
Bread/toast/fruit loaf Muffin/crumpet Cereal–cold/hot Potato/corn			
Baked beans Fruit/juice			
Milk/Soymilk Yoghurt			
PROTEIN			
Meat/bacon/sausages Cheese Eggs (regular/n-3)			
Fish/fresh/canned/paste			
VEGETABLES			
Tomato Mushroom Canned			
FAT			
Margarine/oil/dressing Peanut butter/nuts Avocado/olives			
Butter/cream			
Other Foods			
Tea/coffee			
Sugar/milo honey/jam/vegemite/sauce Cordial/soft drink			

Part 2: Morning Tea How many days in the week do you eat morning tea/snacks? _____

Prompts	Type	Serving Size	Frequency
CARBOHYDRATE			
Bread/toast/fruit loaf Muffin/crumpet Biscuit/crackers/cake Cereal bar Baked beans Fruit/juice			
Milk/Soymilk Yoghurt			
PROTEIN			
Cold meat/chicken Cheese Eggs (regular/n-3) Salmon/tuna/sardines			
VEGETABLES			
Salad Cooked Canned			
FAT			
Margarine/oil/dressing Peanut butter/nuts Avocado/olives Butter/cream			
Other Foods			
Tea/coffee Sugar/milo			
jam/honey/vegemite/sauce			
Cordial/soft drink			

Part 3: Light Meal How many days in the week do you eat a light meal at home? _____ Away from home?_____

Prompts	Type	Serving Size	Frequency
CARBOHYDRATE			
Bread/toast/roll/flat bread Muffin/crumpet/croissant Biscuit/crackers/cake Potato/corn Baked beans			
Fruit/juice Milk/Soymilk Yoghurt			
PROTEIN			
Cold meat/chicken Cheese Eggs (regular/n-3)			
Salmon/tuna/sardines			
VEGETABLES			
Salad Cooked Canned			
FAT			
Margarine/oil/dressing Peanut butter/nuts Avocado/olives			
Butter/cream			
Other Foods			
Tea/coffee Sugar/milo			
jam/honey/vegemite/sauce Cordial/soft drink			

Part 4: Afternoon Tea How many days in the week do you eat afternoon tea/snacks? _____

Prompts	Type	Serving Size	Frequency
CARBOHYDRATE			
Bread/toast/fruit loaf			
Muffin/crumpet			
Biscuit/crackers/cake			
Cereal bar			
Baked beans			
Fruit/juice			
Milk/Soymilk			
Yoghurt			
PROTEIN			
Cold meat/chicken			
Cheese			
Eggs (regular/n-3)			
Salmon/tuna			
VEGETABLES			
Salad			
Cooked			
Canned			
FAT			
Margarine/oil/dressing			
Peanut butter/nuts			
Avocado/olives			
Butter/cream			
Other Foods			
Tea/coffee			
Sugar/milo			
jam/honey/vegemite/sauce			
Cordial/soft drink			

Part 5: Main Meal How many days in the week do you eat the main meal at home? _____ Away from home?_____

Prompts	Type	Cooking method	Serving size	Frequency
CARBOHYDRATE				
Potato/pumpkin/mashed Sweet potato/corn Pasta/rice/couscous Lasagna Chips/wedges Bread/toast				
Beans/lentils				
Fruit-canned/fresh/Juice Milk/soymilk Custard/ice cream/yoghurt				
PROTEIN				
Meat/steak/chop/sausages Chicken Cheese Quiche Eggs (regular/n-3) Fish-fresh/frozen/canned Soy products/tofu				
VEGETABLES				
Carrot Peas/beans Broccoli/zucchini Cabbage/cauliflower				
FAT				
Margarine/oil/dressing Peanut butter/nuts Avocado/olives				
Butter/cream				

COMPOSITE MEALS: (frozen dinners)

Part 5: Main Meal (Continued)

Prompts	Type	Cooking method	Serving size	Frequency
CARBOHYDRATE				
Potato/pumpkin/mashed Sweet potato/corn Pasta/rice/couscous Lasagna Chips/wedges Bread/toast				
Beans/lentils				
Fruit-canned/fresh/Juice				
Milk/soymilk Custard/ice cream/yoghurt				
PROTEIN				
Meat/steak/chop/sausages Chicken Cheese Quiche Eggs (regular/n-3)				
Fish-fresh/frozen/canned Soy products/tofu				
VEGETABLES				
Carrot Peas/beans Broccoli/zucchini Cabbage/cauliflower				
FAT				
Margarine/oil/dressing Peanut butter/nuts Avocado/olives Butter/cream				

COMPOSITE MEALS: (frozen dinners)

Part 5: Main Meal (Desserts/Drinks)

Prompts	Type	Cooking method	Serving size	Frequency
CARBOHYDRATE				
Rice				
Bread/toast				
Fruit pie/pastries				
Pudding/cake/cheesecake				
Sago				
Beans/lentils				
Fruit-canned/fresh/Juice				
Milk/soymilk				
Custard/ice cream/yoghurt				
PROTEIN				
Cheese				
Eggs (regular/n-3)				
Soy products/tofu				
VEGETABLES				
Rhubarb				
FAT				
Margarine/oil/dressing				
Peanut butter/nuts				
Avocado/olives				
Butter/cream				
Other Foods				
Tea/coffee				
Sugar/milo				
Cordial/soft drink				

Part 6: Takeaway/Restaurant Meals

Prompts	Type	Serving size	Frequency
McDonald's			
• Quarter pounder			
• Burger			
• Fries			
• shake/sundae			
Kentucky Fried Chicken			
• fried chicken			
• roast chicken			
• nuggets			
• fries			
Pizza			
• pan			
• thin-based			
• toppings			
• soft drink			
Asian food			
• Chinese			
• Japanese			
• Thai			
• Vietnamese			
Fish and chips			
• battered and fried			
• grilled			
• potato scallops			
• fries			
Other			
• soft drink			
• Indian food			
• Italian food			
• Mexican food			

Part 7: Evening Snack Foods

Prompts	Type	Serving Size	Frequency
CARBOHYDRATE			
Bread/toast/fruit loaf Muffin/crumpet Biscuit/crackers/cake Fruit/juice			
Milk/Soymilk Custard/ice cream/yoghurt			
PROTEIN			
Cold meat/chicken Cheese Eggs (regular/n-3) Salmon/tuna			
VEGETABLES			
Salad Cooked Canned			
FAT			
Margarine/oil/dressing Peanut butter/nuts Avocado/olives Butter/cream			
Other Foods			
Tea/coffee Sugar/milo jam/honey/vegemite Cordial/soft drink			

Part 8: Food Frequency Checklist (only tick required if accounted for)

Type of food	Serving size	Frequency
Bread		
Biscuits/cake Crisps		
Fruit/dried fruit		
Fruit juice Beans/legumes		
Milk/yoghurt		
Ice Cream		
Soft drink/cordial Jam/honey/spreads		
Lollies/chocolate		
Cheese 20g = 1 slice, 1party cube, 2tbsp grated Eggs (regular/n-3 enriched)		
Avocado		
Fish (white/oily) Nuts		
Alcohol		

Part 9: Food Preparation Practices

6.1 Butter/Margarine

What type do you usually use?

a) Butter
b) Dairy Blend
c) Margarine - polyunsaturated, regular
e) Margarine - monounsaturated, regular
f) Margarine - monounsaturated, reduced fat
g) Margarine - polyunsaturated, reduced fat
h) Canola margarine
i) Gold'n Canola
j) Soy margarine

6.2 Oil/Fat in Cooking

What type of oil/fat do you use in cooking?

a) Butter
b) Dairy blend
c) Margarine - polyunsaturated, regular
d) Margarine - polyunsaturated, reduced fat
e) Margarine - monounsaturated, regular
f) Margarine - monounsaturated, reduced fat
g) Lard or dripping
h) Olive oil
i) Canola oil
j) Soybean oil
k) Gold'n Canola
l) Other vegetable oil _____

6.3 Fat on Meats/Chicken

How much fat is trimmed from meat before cooking/eating?

a) None
b) 25%
c) 50%
d) 75%
e) All

How much skin do you eat on chicken?

a) None
b) 25%
c) 50%
d) 75%
e) All
f) Other, please specify: _____

6.4 Salt

a) All the time during cooking
b) All the time at the table
c) Some of the time during cooking
d) Some of the time at the table
e) Never during cooking
f) Never at the table
g) I don't use salt at all

What do you consider to be a serve of salt? _____

APPENDIX D: 3 DAY FOOD RECORD IN STUDY 3

THE UNIVERSITY OF WOLLONGONG
METABOLIC RESEARCH CENTRE
ILLAWARRA DIETARY INTERVENTION STUDIES

3 DAY FOOD RECORD/DIARY

We need as much detail as possible so these diaries can be of use to estimate your usual consumption. Please help by checking that you have supplied the following information as you record each meal.
Measuring cups, spoons and small kitchen scales are supplied to you, so please use them to record amounts.
A sample record is enclosed as an example of one volunteer's diary.

Breakfasts

Cereal – type, brand, amount. Measure amount milk, sugar added. Also type of milk.

Toast/Bread – which type, brand is useful.

Spreads – measure your usual spread by the teaspoon as it goes on – this can be your reference each day. This amount may vary for crumpets/toast, compared to bread as hot toast/crumpets soak up more butter/margarine.

Toppings – did you have jam, honey, etc., amount/teaspoons if possible.

Tea/Coffee – how do you have it? Measure your usual dash of milk once to see how much you add. Tell us type of milk and amount of sugar added, if any.

Fruit/Fruit Juices – amounts. Please specify brand of juice and whether 100%, or if it is a fruit drink (not juice).

Morning/Afternoon Teas – record how many cups of tea, coffee, and amount and type of milk. Biscuits, etc. – how many, type.

Lunches

Sandwiches – type of bread, spread used (may need to ask if you are using canteen). Was spread usual amount you would use? What type of fillings – estimate number of slices of meat, cheese. If it is a salad sandwich, what is actually in there – beetroot, meat, etc. as well?

Take-aways – try to estimate quantities as best you can. Include type of cooking oil.

Evening Meals

Raw-weight of cooked meat. If it is a meal for 4, estimate how much of the meal you ate (i.e. 1/3, ¼).

- How was meat cooked?
- How much, and what type of oil/margarine was used?
- Did you eat fat on meat?
- Did you eat skin on chicken?
- What vegetables, salad, rice, pasta was served with meat and how much?
- What salad dressings, butter, cream was added?

Desserts

- Brand of ice-cream. How many scoops or tablespoons?
- Fruit/tinned fruit – quantities?
- Yoghurt – brand, amount?
- Cheeses – what types, how much?
- Commercial products – brands?
- Home-cooked goods – i.e. apple crumbles, etc. Recipe would be helpful.

Drinks - Remember to record wine, soft drinks, juices, etc.

Also remember that we are not judging you by what you eat. The records are needed because this is a scientific project. To make it a valid study we need the truth, so don't be afraid to write down everything you eat and drink.

THE UNIVERSITY OF WOLLONGONG
METABOLIC RESEARCH CENTRE
ILLAWARRA DIETARY INTERVENTION STUDIES

SAMPLE FOOD RECORD

PLEASE RECORD EVERYTHING THAT YOU EAT AND DRINK FOR 3 DAYS

DAY: THURSDAY EXAMPLE ONLY
DATE: 29/4/99

TIME OF DAY	TIME	DESCRIPTION OF AMOUNT OF FOOD OR DRINK	HOW PREPARED/ COOKED
BREAKFAST	8a.m.	¾ cup Special K	
		1 cup Lite-White Milk	
		1 Buttercup Wonder White toast	spread with 1 teaspoon Canola marg
		1/2 teaspoon Vegemite	
MORNING TEA / SNACKS	10a.m.	4 Cruskit Biscuits	spread with 4 teaspoons peanut butter
		Cup of tea	with 2 tablespoons Lite White Milk

SAMPLE FOOD RECORD

PLEASE RECORD EVERYTHING THAT YOU EAT AND DRINK FOR 3 DAYS

DAY: THURSDAY EXAMPLE ONLY
DATE: 29/4/99

TIME OF DAY	TIME	DESCRIPTION OF AMOUNT OF FOOD OR DRINK	HOW PREPARED/ COOKED
LUNCH	12.30	2 sandwiches – 4 slices wholemeal bread filled with 2 slices Soccerball ham	spread with total of 3 teaspoons Canola marg
		½ avocado	
		1 small tomato	
		½ lettuce leaf	
		5 slices cucumber	
AFTERNOON TEA/ SNACKS	2p.m.	1 banana	
	3p.m.	40g dry roasted peanuts	
		glass of cordial (diet)	

SAMPLE FOOD RECORD

PLEASE RECORD EVERYTHING THAT YOU EAT AND DRINK FOR 3 DAYS

DAY: THURSDAY EXAMPLE ONLY
DATE: 29/4/99

TIME OF DAY	TIME	DESCRIPTION OF AMOUNT OF FOOD OR DRINK	HOW PREPARED/ COOKED
DINNER	6.30pm	1 x cod fillet (120g cooked)	fried in 1 tablespoon Canola oil
		2 medium potatoes (200g cooked)	boiled
		¾ cup broccoli	steamed
		½ cup carrot	
		1 slice white bread	spread with ¾ teaspoon Canola marg
SUPPER / SNACKS	8.30pm	Tinned peaches in natural juice (3 halves)	
		1 banana	
		2 scoops Dairy Bell ice-cream	
	9.15pm	Cup of coffee	with 2 tablespoons whole milk
		1 granita biscuit	

APPENDIX E: PARTICIPANT INFORMATION IN STUDY 3

[date]

Dear Diabetes Service Client

You are offered a position in the University of Wollongong/Illawarra Area Health Service research project to provide ***"dietary intervention in the treatment of Gestational Diabetes Mellitus".*** The project aims to assess the benefits and achievability of an individualised dietary plan that is based on current research knowledge. The results of the project will contribute to improvements in the dietary management processes for women with Gestational Diabetes to benefit pregnancy outcomes and reduce risks to both mother and child.

If you agree to take part you will be randomly assigned to one of two dietary advice groups. All members of both groups will be provided with an indivi dualised diet plan (negotiated with you and based on your usual food intake), but for each group, the information will be packaged in different ways. You will be required to follow the diet plan for the duration of your pregnancy. You will supply and consume your own food at home.

This will require close contact with an Accredited Practicing Dietitian (APD), who will regularly monitor your progress and provide you with support. Diet methods and research procedures that will be used during the study are set out below, along with possible risks and burdens:

At your first appointment and at 4-weekly appointments at the Diabetes Centre

* A dietary interview to report and discuss your food intake (approximately 2 hours) at a time convenient to you.

* Your height and your weight will be recorded at the initial appointment and your weight at each appointment thereafter.

At your second appointment at the Diabetes Centre *(within a week of your first appointment)*

* A dietary plan will be provided with instructions and food lists for you to follow. The plan will be based on your regular diet. Advice regarding appropriate food choices, cooking and recipe formulation will also be given as well as answers to any questions you may have.

Between each 4-weekly appointment (at home)

* Measure and record your food intake over 4 consecutive days including one weekend day. You will be provided with a food diary, kitchen scales and measuring cups and instructed in their use.

Support meetings will be arranged by agreement at times convenient to you (at least bi-weekly)

Potential Benefits

You will receive an individualised dietary plan from a dietitian, aimed at controlling your weight, blood glucose, cholesterol and triglyceride levels as well as reducing your risks of detrimental pregnancy outcomes, such as having a large-for-age baby, premature delivery, caesarian section and special care requirements for the newborn.

A summary of your dietary analyses will be kept in your Wollongong Hospital patient notes for reference by other health professionals.

All other information collected will be stored on computer or in locked files under number codes to ensure your confidentiality. Reporting of this information at conferences and in scientific journals will be in general terms and will not identify individuals.

If you agree to take part you have the right to discontinue the project at any time. Non-participation or withdrawal will not affect your treatment or the duty of care provided to you at the Diabetes Centre.

The people involved in the research are located at either the University of Wollongong or the Wollongong Diabetes Centre and include:

Dietitian and PhD student at the University of Wollongong

Manager of the Smart Foods Centre at the

University of Wollongong

APDSenior Dietitian at the Wollongong Diabetes Centre

Manager of the Wollongong Diabetes Centre

Area Manager of the Illawarra Diabetes Service

If you have any questions about this research please contact at the
Smart Foods Centre, University of Wollongong, or at the Wollongong Diabetes Centre.
If you have any concerns about the research being conducted please contact the Human Research Ethics Committee on

APPENDIX F: CONSENT FORM IN STUDY 3

Project: ***Dietary Intervention in the Treatment of Gestational Diabetes Mellitus***

Researchers:

I have received and read the information sheets for the research project "*Dietary intervention in the treatment of Gestational Diabetes Mellitus*". is conducting the research at the Wollongong Diabetes Centre as part of her PhD research with the University of Wollongong. explained the project to me and answered my questions.

I understand that participation in the project will require me to:

a) describe my food intake in detail to a dietitian

b) measure and record my food intake for short periods at home

c) follow a prescribed dietary meal plan

I have been advised of the potential burdens associated with these diet methods and research procedures.

I have been informed that no individual data will be identifiable in the publication of results from this study in the form of a PhD thesis, scientific journal article or conference seminar.

I understand that my participation in this research is entirely voluntary and that I am free to withdraw my consent at any time. My decisions will not affect my treatment or my relationship with the Wollongong Diabetes Centre in any way.

If I would like to discuss this research further I can contact at the Wollongong Diabetes Centre or at the Smart Foods Centre, University of Wollongong. If I have any concerns about the way the research is being conducted I can contact the Human Research Ethics Committee on.

Dietary Intervention as Treatment of Gestational Diabetes Mellitus

I consent to participate in the research being conducted by and co-workers as it has been described to me in the information sheets. I understand the data collected will be used for a PhD thesis, scientific journal articles and conferences, and I consent for the data to be used in this manner.

…… ……../……../……...

Signed Date

……

Name (please print)

APPENDIX G: RECRUITMENT ADVERTISEMENT IN STUDY 4

Do you have type 2 Diabetes and would like to participate in a study of how it is managed by diet?

The Smart Foods Centre at the University of Wollongong is seeking volunteers for a study on the dietary management of type 2 Diabetes Mellitus.

If you fit all these criteria, we would like you to contact us:

- Aged 35-70years
- Diagnosed and treated for at least 2 years
- Generally well
- Not on insulin therapy
- No food allergies

The study involves working closely with research dietitians at the University and the Illawarra Diabetes Service in testing the how well and why certain approaches to dietary management might work best for people with type 2 diabetes. Using guidelines for dietary management based on the best available scientific evidence, we will be concentrating on developing your usual eating patterns over a 6-month period, starting in January 2003. If you would like to register your interest and find out more, please contact Marian Bare at the Smart Foods Centre on .

APPENDIX H: SCREENING SURVEY IN STUDY 4

Dietary Management of Type 2 Diabetes Mellitus

The Eatwell Study

In this questionnaire general questions are asked about yourself, your health and the food you eat. The information that you provide is confidential. If you have any concerns or have difficulty in answering any of the questions please do not hesitate to contact any of the researchers named in the information package.

1. Title: Dr Mrs Mr Miss Ms
2. Full Name: _____
3. Address: _____

   _____
4. Phone No.: Home: _____

   Work: _____

   Mobile: _____
5. Date of birth: _____day _____month _____ year
6. Country of birth_____ Language spoken at home_____
7. Highest level of education_____
8. Occupation_____
9. Height _____Ft _____Inches **OR** _____cm
10. Weight _____St _____lbs **OR** _____kg
11. Has your weight changed more than 3 kgs (7lbs) in the last 6 months?
    (Please tick (✓) one box)

    Don't know

    No

    Yes - it has gone up by _____ lb. or _____kg

    Yes - it has gone down by _____ lb. or _____kg
12. Do you smoke cigarettes? (Please tick (✓) one box)

    No

    Yes, 1-10 per day

    Yes, 11-20 per day

    yes, more than 20 per day

13. On average, how many alcoholic drinks (eg. number of middies of beer, glasses of wine, sherry, port, nips of spirits) would you have each day during a typical week?

    (Please tick (✓) a box)

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    (Please tick (✓) one box)

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(Please tick (✓) a box)

	None	1	2	3	4	5 or more
Monday						
Tuesday						
Wednesday						
Thursday						
Friday						
Saturday						
Sunday						

14. Have you ever been advised that you have a **high** HbA1c reading (a measure of blood glucose or 'sugar')?

YES NO NOT SURE

15. Have you ever been advised that you have a **high** cholesterol or triglyceride reading (a measure of blood fat)?

YES NO NOT SURE

16. Have you ever been advised that you have a **high** blood pressure reading?

YES NO NOT SURE

17. Please indicate any recent measurements of these items below (if known):

Test	Date	Result	Treatment (Medications, diet, no treatment etc)
HbA1c			
Cholesterol			
Triglycerides			
Blood pressure			

18. Do you take any medications for your blood sugar, cholesterol, triglycerides or blood pressure?

YES NO NOT SURE

If YES, Please specify_____

_____

_____

19. List any medications taken **occasionally (eg. For headache, arthritis, hay fever, indigestion)**

Medications	**Dose**	**How often**

20. List any medications not already listed that you are taking **regularly**

Medication	**Dose**	**How often**

21. Which of the following health/medical conditions have been diagnosed by a doctor? (Please tick (✓) one or more boxes)

High blood pressure	Migraine
Angina	Asthma
Heart disease	Menopause
Stroke	NONE
Diabetes	
Arthritis	other… please specify _____
Gout	_____

22. Do you currently follow a special or modified diet?

YES NO NOT SURE

If yes, do you follow a prescribed carbohydrate meal plan?

YES NO NOT SURE

If you do follow a prescribed carbohydrate plan, please indicate the number of serves of carbohydrate you consume each meal

Breakfast: Morning Tea : Lunch :

Afternoon Tea : Dinner : Supper :

23. If you are following another form of special diet, please specify what this is:

_____

_____

24. Who advised this diet? (e.g. doctor, self, dietitian)

_____

25. Do you have any known food allergies, intolerances or aversions to certain foods?

YES NO NOT SURE

Food type: _____

26. Do you eat any of the following foods? (Please tick & list amount)

	Amount	**How Often**
☐ white fish	_____	_____
☐ oily fish (salmon, tuna, sardine, mackerel)	_____	_____
☐ soy beans	_____	_____
☐ soy milk	_____	_____
☐ soy yogurt	_____	_____
☐ soy cheese	_____	_____
☐ Soy drinks	_____	_____
☐ soy & linseed bread	_____	_____
☐ soy & linseed breakfast cereals	_____	_____
☐ peanuts	_____	_____
☐ walnuts	_____	_____
☐ other types of nuts	_____	_____
please specify type: _____		
☐ oils	_____	_____
please specify type/brand: _____		
☐ margarine/butter	_____	_____
please specify type/brand: _____		

Are there any of the above foods you will **NOT** eat

YES , all of them YES, some of them NO, I will eat most foods

Please specify individual food items you prefer not to/will not eat:

_____

27. On average, how many times a week would you eat meals away from home?
(i.e.: Visit a restaurant, take-away food or have meals prepared by friends?)

(Please tick (✓) one box)

6-7 times per week (most days)

3-5 times per week

1-2 times per week

1-2 times a fortnight

1-2 times a month

4-6 times a year

rarely (<6 times a year)

Never

28. Do you supplement your diet with any of the following? (Please tick (✓))

Vitamins &/or minerals

Vitamin E capsules Dose per day _____

Fish oil capsules Dose per day _____

Cod liver oil Dose per day _____

Evening primrose oil Dose per day _____

Others (please specify) _____

I do not supplement my diet

29. Do you eat fish? (Fresh fish - including shellfish, or canned fish)

YES

NO

If so, how frequently? (Please tick (✓))

Daily

Weekly

Fortnightly

Monthly

Never

I understand that the information provided will be used only for the purpose of determining my suitability to participate in the Eatwell Study. Completion of this questionnaire does NOT ensure that I will meet all the requirements for the study.

I understand that the Smart Foods Centre regularly conducts studies such as this one which ask for volunteers. I would like the information in this questionnaire:

to be kept in a confidential file at the Smart Foods Centre for consideration in future research projects.

OR

to be destroyed immediately.

Signed _____ Date _____

Thank you for your participation!

APPENDIX I: DIET HISTORY QUESTIONNAIRE IN STUDY 4

Code:
Date:
Site:

diet history questionnaire

Return to:
Smart Foods Centre
University of Wollongong
Northfields Av, Wollongong NSW 2522. Australia
Phone:
Fax:

Smart Foods Centre
ARC Key Centre of Teaching and Research
University of Wollongong

Interviewer: _____

DOB: _____ Age: _____

Ht: _____cm Weight: _____

BMI: _____ _ BMR: _____

Medications: _____

History of health conditions: _____

Supplements: _____

Physical activity level: _____

Core Food Choices: Please indicate the ***type*** of foods you select in these categories

Food group	Type	Food group	Type
Milk (full fat, skim)		Spread (margarine etc)	
		Oils (olive, canola)	
Bread (white, grain)			
		Drinks (sweetening)	

Part 1: Breakfast

How often do you eat this meal?_____Home_____Away_____

Breakfast Cereals/Porridge		
Type	**Amount**	**Frequency**
Milk with cereal		
Sugar with cereal		

Toast/Bread/Muffins etc (including toppings)		
Type	**Amount**	**Frequency**
Spread with toast		
Topping on toast		

Eggs and other cooked dishes		
Type	**Amount**	**Frequency**
Oil/fat		

Other Foods (including drinks, fruit, yoghurt)		
Type	**Amount**	**Frequency**

Part 2: Light Meal. **Lunch or Dinner** (Circle)

How often do you eat this meal?_____Home_____Away_____

Sandwiches/Rolls		
Description (include all components)	**Amount**	**Frequency**
Spreads		
Added salt		

Salads		
Description (include all components)	**Amount**	**Frequency**
Dressings		

Soups		
Description (include all components)	**Amount**	**Frequency**
Soup mix		
Added salt		
Bread		

Other foods (including drinks, fruit, takeaway meals, cakes)		
Description	**Amount**	**Frequency**

Part 3: Main Meal. **Lunch or Dinner** (Circle)

How often do you eat this meal?________________________Home_______Away___________

Main dishes (include all components)	Amount	Frequency
Oils/spreads		
Dressings		
Sauces		

Other foods (include drinks, bread, side dishes, desserts, fruit)		
Type	**Amount**	**Frequency**

Part 4: Foods consumed outside meals

How often do you eat snacks?_____Home_____Away_____

Type	**Amount**	**Frequency**

Part 5: Food Frequency Checklist

Food category	Amount	Frequency
Bread/crumpet		
Biscuits		
Crispbreads/crackers		
Cakes/scones/muffins/pastries		
Pancakes		
Beans/legumes Fruit		
Fruit juice Soft drinks/cordials		
Chocolate/lollies Chips		
Alcohol		
Milk		
Yoghurt		
Ice cream Cheese		
Dip/cream cheese/cheese spread Soy milk		
Soy yoghurt Eggs/omega eggs		
Salmon/tuna (fresh/canned) Sardines/Mackerel		
White fish varieties		
Oysters Walnuts		
Pecans Other nuts		
Seeds		

Part 6: Food Preparation Practices

6.1 Butter/Margarine
What type do you usually use?
Butter
Dairy blend
Margarine - polyunsaturated, regular
Margarine - polyunsaturated, reduced fat
Margarine - monounsaturated, regular
Other_____

6.2 Oil/Fat in cooking
What type of oil/fat do you use in cooking?

Butter	Olive oil
Dairy blend	Canola oil
Margarine - polyunsaturated, regular	Soybean oil
Margarine - polyunsaturated, reduced fat	Gold'n Canola
Margarine - monounsaturated, regular	Other _____

6.3 Fat on Meats/Chicken
How much fat is trimmed from meat before cooking/eating?
a) None
b) 25%
c) 50%
d) 75%
e) All
How much of the skin on chicken to you remove before cooking/eating?
a) None
b) 25%
c) 50%
d) 75%
e) All
Other, please specify: _____

APPENDIX J: FOOD RECORD IN STUDY 4

Code:
Date:
Site:

3-day food record

Return to:
Smart Foods Centre
University of Wollongong
Northfields Av, Wollongong NSW 2522. Australia
Phone:
Fax:

Smart Foods Centre
ARC Key Centre of Teaching and Research
University of Wollongong

Breakfast and Morning Tea Date:_____

Food	Amount

Lunch and Afternoon Tea Date:____________________

Food	Amount

Dinner and Supper Date:_____

Food	Amount

APPENDIX K: PARTICIPANT INFORMATION IN STUDY 4

Dietary Management of Type 2 Diabetes Mellitus

The Eatwell Study

You are kindly invited to participate in the Eatwell Study conducted by the Smart Foods Centre, Department of Biomedical Science, University of Wollongong and the Illawarra Diabetes Service, Illawarra Health. The project aims to assess the benefits and achievability of different dietary approaches in the management of type 2 diabetes mellitus. The results of this research will contribute to better understanding of the processes behind the dietary management of type 2 diabetes and thereby more effective treatment.

If you consent to participate you will be asked to:

Complete a screening questionnaire to assess your suitability for the study

For this you will be required to provide details of your medical history and dietary habits to the researchers at the University.

Attend an information evening at the University of Wollongong at the start and completion of the six month study period

On these occasions you will be given further information about the study and will have the opportunity to meet and ask questions of those members of the team conducting the research.

Attend the University clinic at the start of the study, after 3 months and 6 months

* On each of these occasions you will be required to provide a fasted blood sample of approximately 40ml (about 1.5 tablespoons). A qualified practitioner will collect the blood from your arm and you may experience some discomfort and possible bruising.

* Your weight, height, waist circumference and blood pressure will be measured.

Attend either the Illawarra Diabetes Service in Wollongong or the University clinic (depending on your group allocation) **at monthly intervals**

* On each of these occasions a dietitian will conduct a dietary interview. This will require you to give a detailed report of your usual food intake - approximately 1 hour.

* You will be required to keep a 3 day food record prior to these interviews

* You will receive dietary advice supporting the management of diabetes

Receive telephone calls at 2 weekly intervals to see how you are going on the diet

Try to follow the dietary instructions as best you can and to advise the researchers of any problems you may encounter in doing so

If we are able to offer you a place in the study and you accept, you will be randomly allocated to one of three dietary advice groups. All members of each group will be provided with an individualised meal plan that meets current dietary recommendations and fits with your usual food preferences as best as possible. You will be required to follow this advice as best you can for the 6 months duration of the study. As the advice is based on your normal routines, and we are testing its feasibility, you will still be purchasing and preparing your own food as before.

Following the meal plan will require close contact with an Accredited Practicing Dietitian (APD), who will regularly monitor your progress and provide you with advice and support. This programmed, individualised attention over a 6-month period is one of the major benefits you will receive throughout the study. When the study is complete we will ensure you have continued support through the Diabetes Service. A summary of your dietary analyses, measurements of height, weight, blood pressure and blood pathology results will be kept in your patient notes at the Illawarra Diabetes Service for reference by health professionals in your continued care.

All other information collected will be stored on computer or in locked files under number codes to ensure confidentiality. Reporting and publication of this information as a PhD thesis, scientific reports, in journals and at scientific conferences will not identify any individual.

If you agree to take part you have the right to discontinue the project at any time. Non-participation or withdrawal will not affect in any way your association with the University of Wollongong or the Illawarra Diabetes Service.

The people involved in the research are located at either the University of Wollongong or the Illawarra Diabetes Service in Wollongong and include:

Assoc. Prof. Manager of the Smart Foods Centre at the

University of Wollongong

Research Fellow at the Smart Foods Centre

Dietitian and PhD student

Senior Dietitian, Illawarra Diabetes Service

If you have any questions about this research please contact A/Prof
or at the Smart Foods Centre on or at the
Illawarra Diabetes Service on If you have any concerns about the research being conducted please contact the Human Research Ethics Committee on .

APPENDIX L: CONSENT FORM IN STUDY 4

Dietary management of Type 2 Diabetes Mellitus:

The Eatwell Study

Associate Professor

Smart Foods Centre, Department of Biomedical Science,
University of Wollongong

Illawarra Diabetes Service, Illawarra Health

I have been given information about the Eatwell Study and discussed the research project with one of the above named researchers. I understand that is involved in this research as part of a PhD program supervised by Associate Professor in the Smart Foods Centre, Department of Biomedical Science at the University of Wollongong.

I understand that, if I consent to participate in this project I will be asked to:

• complete a screening questionnaire with details of my medical history and dietary habits

• attend an information evening at the University and the start and completion of the study

•attend the University clinic at the start of the study, and after 3 months and 6 months to:

provide a fasted blood sample of approximately 40ml (1.5 tablespoons), and

have my weight, height, waist circumference and blood pressure measured

Depending on my allocation, attend either the Illawarra Diabetes Service in Wollongong or the ESRC clinic at the University at the allocated time, at monthly intervals to:

Undergo a diet history interview and keep a 3 day food record prior to these interviews.

Receive dietary advice on the management of diabetes

Receive phone calls at 2 weekly intervals to see how I am going on the diet

Try to follow the dietary instructions as best I can and to advise the researchers of nay problems I may be encountering in doing so.

I have been advised of the potential risks and burdens associated with this research, which include some potential bruising with the collection of blood and the need to keep to a dietary pattern as best I can. I have had an opportunity to ask any of the above named researchers any questions I may have about the research and my participation.

I understand that my participation in this research is voluntary, I am free to refuse to participate and I am free to withdraw from the research at any time. My refusal to participate or withdrawal of consent will not affect my treatment in any way with the University of Wollongong or the Illawarra Diabetes Service.

If I have any enquiries about the research, I can contact
at the Smart Foods Centre on or at the Illawarra Diabetes Service on
, or if I have any concerns or complaints regarding the way the research is or has been conducted, I can contact the Complaints Officer, Human Research Ethics Committee, University of Wollongong on .

By signing below I am indicating my consent to participate in the research entitled the Eatwell Study, conducted by and colleagues as it has been described to me in the information sheet. I understand that the data collected from my participation will not identify me. It will be used for the purposes of research that will be published in reports, scientific journals and conferences and I consent for it to be used in that manner.

Signed Date

..../...../.....

Name (please print)

.....