Establishing evidence for practice in medical nutrition therapy: a case study of the impact of a high amylose resistant starch diet on clinical indicators of the insulin resistant syndrome

Vanessa Brenninger
University of Wollongong

ESTABLISHING EVIDENCE FOR PRACTICE IN MEDICAL NUTRITION THERAPY: A CASE STUDY OF THE IMPACT OF A HIGH AMYLOSE RESISTANT STARCH DIET ON CLINICAL INDICATORS OF THE INSULIN RESISTANT SYNDROME

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VANESSA BRENNINGER
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CERTIFICATION

I, Vanessa Brenninger, declare that this thesis, submitted in fulfilment of the requirements for the award of Master of Science – Research, in the Department of Biomedical Sciences, University of Wollongong, is wholly my own work unless otherwise referenced or acknowledged. The document has not been submitted for qualifications at any other academic institution.

Vanessa Brenninger

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iii List of abbreviations

ANOVA: analysis of variance

ANZFA: Australia and New Zealand Food Authority

AUC: area under the curve

BMI: Body Mass Index

CA: Conversation Analysis

Ca: Calcium

CHO: Carbohydrate

Chol: Cholesterol

Clamp: Hyperinsulinaemic Euglycaemic Clamp

CSIRO: Commonwealth Scientific and Industrial Research Organisation

DAA: Dietitian's Association of Australia

DF: Dietary Fibre

DH: Diet History

DXA: Dual-energy x-ray absorptiometry

E: Energy

EE: Energy Expenditure

EI: Energy Intake

GI: Glycaemic Index

HARS: High Amylose Maize Starch

HDL: High Density Lipoprotein

Hood: Delta-trac metabolic monitor hood (indirect calorimetry)

Ht: Height

IR: insulin resistance

kJ: kilojoule

LDL: Low Density Lipoprotein

MRNA: Messenger ribonucleic acid

MUFA: Monounsaturated Fatty Acids

n-3 FA: Omega 3 Fatty Acids

n-6 FA: Omega 6 Fatty Acids

NHMRC: National Health and Medical Research Council

NIDDM: Non Insulin Dependant Diabetes Mellitus

NSP: non-starch polysaccharides (can be soluble and insoluble)

PAI-1: plasminogen activator inhibitor-1

Ptn: Protein

PUFA: Polyunsaturated Fatty Acids

RCT: randomised controlled trial

RIA: Radio-immuno Assay

RMR: Resting Metabolic Rate

RQ: Respiratory Quotient

RS: Resistant Starch

SCFA: Short Chain Fatty Acids

SFA: Saturated Fatty Acids

TG: triglyceride

WHO: World Health Organisation

Wt: Weight

iv Acknowledgements

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v Abstract

INTRODUCTION

In the context where current strategies employed by health professionals are not able to slow the increasing rates of obesity, diabetes mellitus and insulin resistance, collectively known as the insulin resistance syndrome (metabolic syndrome, syndrome X), evidence-based practice is central to implementing appropriate and targeted guidelines to the individual. The central hypothesis argued here is that for evidence based practice to have relevance there is value in collecting this evidence from both quantitative and qualitative research methodologies. The aim of this thesis is to explore a number of aspects of research that produce evidence for the management of diet related disease. It uses as a reference point, a randomised controlled trial investigating the feasibility and efficacy of the incorporation of high amylose maize resistant starch on clinical, and dietary outcomes in an overweight sample of the population. Current research aims to develop the optimal nutrient mix for the insulin resistance syndrome, however, the challenge and focus now should be to make the benefits achievable in the 'real world' (Storlien, Tapsell, Fraser, Leslie, Ball, Higgins, Helge and Owen 2001). To this end, a rigorous framework addressing dietetic and lifestyle issues was included in the randomised controlled trial.

The nutrient of choice for the intervention trial was resistant starch (RS); a form of carbohydrate that reaches the lower gastrointestinal tract undigested and is consequently fermented. Resistant starch is composed of two polysaccharide forms; amylose and amylopectin. The beneficial effects are particularly evident from the amylose form

compared to the more readily digested amylopectin. It demonstrates probiotic and dietary fibre-like characteristics hypothesised to be beneficial for people with the insulin resistance syndrome, hypercholesterolaemia and colon cancer due to its reduced availability as a source of energy, reduced energy density and its ability to lower colonic pH. Therefore RS has potential to be used in the dietary management for reducing risk factors for the insulin resistance syndrome.

METHODOLOGY

Three preliminary studies were performed to enable the accurate recording of significant lifestyle variables. The first employed sociolinguistics to conceptualise how and why inaccuracy in reporting of dietary intake occurs. Secondly, a lifestyle history questionnaire was developed to examine possible sources of baseline variation between subjects in the study. Finally, an intervention trial survey was designed to analyse subject's experiences post-intervention such as barriers to adherence.

Following these, a dietary intervention trial was conducted in overweight (BMI: 25-35kg/m^2) adult volunteers. Subjects with any of the following were excluded: diabetes mellitus (fasting blood glucose level ≥ 6.1mmol/L), known hypercholesterolaemia or hypertension, inflammatory bowel disease, coeliac disease, renal disease, current smokers, pregnancy and those reporting a significant weight change in the previous 6 months. Twenty-five volunteers were randomly assigned to receive advice on either a diet high in RS or to a control diet low in RS. Control groups were maintained at a level of 6 grams of various types of RS, based on the Australian average consumption, while the RS group received 25 grams of RS derived from commercially manufactured RS

containing an high amylose to amylopectin ratio.

Subjects recorded foods used to achieve differences in RS using a daily checklist form. Foods recorded on daily checklist forms were analysed by counting. Repeated diet history (DH) interviews were performed in weeks 0, 3, 6, 9 and 12. Dietary data were entered into a nutrient analysis software package, *FoodWorks* (v2.10.136, Xyris Software, Highgate Hill, Brisbane) for further statistical comparisons. To estimate the accuracy of reporting dietary intakes the ratio of reported energy intake to estimated basal metabolic rate (BMR) was calculated. This method provides an index for comparison with cut-off limits that assess the validity of the reported energy intakes.

Baseline metabolic and biochemical indicies were compared to those at 12 weeks after intervention. Insulin resistance was measured by hyperinsulinaemic euglycaemic clamp. Fasting respiratory quotient (RQ) and resting metabolic rate (RMR) was measured by indirect calorimetry. Fasting plasma glucose, insulin, triglycerides, total cholesterol, high-density lipoprotein (HDL) and low-density lipoprotein (LDL) cholesterol were measured by standard assays. Body mass index (BMI) was calculated by weight in kilograms divided by height in meters squared and body composition was assessed by dual-energy x-ray absorptiometry (DXA).

In the same subjects the acute response to RS diets and control diets were performed by a meal challenge (breakfast and lunch) at 12 weeks. The following variables were collected from participants while fasted and then postprandially on an hourly basis thereafter: RQ, RMR, plasma glucose, insulin, triglyceride excursions and satiety.

Statistical comparisons were made within groups initially and on completion and between groups over time using a statistical software package, *JMP* (Version 3.2, SAS institute Inc, Cary NC, 1989-1996).

In addition, as derived from the preliminary studies, subjects completed lifestyle history questionnaires initially in week 0 and an intervention trial survey at 12 weeks. Survey responses were reviewed using content analysis to identify themes and applying a ranking of significance based on frequency of their occurrence.

RESULTS

Of the twenty-five subjects randomly assigned with random numbers to a high or low amylose-rich RS diet, twenty-two completed the trial. Twenty of these were classified as insulin resistant. The two subjects who were not insulin resistant had been randomly assigned to the high RS diet group. The discontinuing participants caused groups to become mismatched for gender, BMI and HDL cholesterol. In addition this caused the RS and control groups to be significantly different for insulin sensitivity with a mean and standard deviation of 6.01 ± 0.79 versus 3.51 ± 0.42 mg/kg.min respectively at week 12 (p=0.006). There were no significant effects of 12 weeks intervention with control or RS diets on body composition (% change in body fat 6.3 versus 1.7 respectively, p>0.05) and metabolic variables (change in insulin sensitivity 2.8% versus –8.4% respectively, p>0.05) despite reported compliance to the dietary goals for intervention foods.

Assessment of the meal challenges displayed a smaller rise in glucose excursion in response to the RS pretreated group challenged with either low or high RS meals. The differences between fasting glucose response to a breakfast meal was significantly affected by the intervention diet (p=0.016). There was also a significant effect of test meal composition on insulin excursion reflecting an increased insulin response to low RS meals in both groups (p=0.04). The remaining variables measured during meal challenges were not significantly affected by meal composition or intervention diet.

The lifestyle history questionnaire identified several variables, such as weight cycling and level of physical activity in the intervention group that may produce variation in response and further may explain the equivocal results. The final survey confirmed previous reports that individualised treatment is more effective and that the provision of foods in an intervention trial enhances compliance to dietary regimens.

The preliminary study of diet history interviews emphasised the need for the interviewer to listen for verbal cues such as “probably” and “it depends”. These were most prominently identified in relation to energy dense foods and thereby assisted the interviewer in obtaining more accurate dietary descriptions. Visual displays of food quantities also needed to be available for more precise reporting of problematic meals to recount such as dinner. The diet history interview data collected during the intervention trial indicated a mean score for valid reporting for weeks 0, 3, 6 and 9, though greater under-reporting resulted in a decline in validity at week 12.

DISCUSSION

After 12 weeks the lack of significant differences between control and intervention groups in terms of changes in body composition, serum lipids, substrate utilisation and fasting plasma glucose/insulin levels suggested that, at least with this profile of subjects, there is no effect of habituation with 25g RS in the diet. This may reflect the impact of dosage (25g RS estimated for bowel health may not be enough for metabolic health), the small sample size of the study and/or attrition rates. An increase in insulin resistance of about 10% in the RS group was consistent with the data (mean change = -9.8%; 95% confidence limit: 29 + 9) however, approximately 40 subjects would have been required to detect an effect of this magnitude using the current protocol. A reduction in the insulin excursion when challenged with the high RS meals was reasonable considering what is known about RS metabolism, however this significant result was not reflected in the glucose values overall, nor did it translate to a metabolic benefit from chronic exposure. Overall, with the consumption of relatively moderate quantities of RS, and given that reported meal patterns and intakes of some nutrients varied over the duration of the trial, the metabolic effect could be explained by a variety of differentials.

Human metabolic and behavioural variability are significant factors to consider in trials establishing the evidence for the optimal nutrient mix for the metabolic syndrome. First, there is diversity among humans in their genetic predisposition to disease. Second there are numerous points within a clinical trial where error in measurements may occur.

In current practice clinicians are asked to support their approach to the management of diet related disease with evidence-based guidelines. To date the most recognised form of best evidence is in the RCT, which presents limitations in relation to assessing the effect of dietary intake on the management of chronic disease as demonstrated here. The results of the thesis reported here using a RCT as its basis and made relevant to the 'real world' through the collection of naturalistic practice based evidence, showed that the effects of high amylose RS on the insulin resistance syndrome were equivocal. The reasons for this may be explained in the way in which outcomes were measured and assessed.

Results from the preliminary work on the collection of dietary data supported the need for research that studies the way outcomes are measured and assessed. The verbal descriptors used by participants were shown to correlate with their difficulty in reporting accurate food intake. This thesis demonstrates that problematic reporting of caloric intake was typically associated with energy dense foods. As diet-disease relationships need accurate recording of dietary intake to demonstrate cause and effect, qualitative studies such as this are fundamental to improving accurate gathering of energy intake. The methods developed here for identifying accurate reporting and applied to this randomised controlled intervention trial can be used in further trials and applied to clinical practice.

Results gained in clinical trials of dietary manipulation need to be able to be reproduced in the real world to have significant outcomes on the incidence of type 2 diabetes and the metabolic syndrome. Hence, to establish the evidence for practice in medical

nutrition therapy[1] information from both objective scientific[2] research and naturalistic[3] observations have been collected and analysed. Holistic patient care is necessary if individuals are to adapt recommended dietary guidelines to their modern lifestyle. Despite limitations in the relatively short duration of the RCT presented here, it serves as a template to analyse the outcomes of dietary intervention in the long term. To prove RS as a therapeutic dietary agent in the control of risk factors for the insulin resistance syndrome, further investigations using combined methodologies are indicated.

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[1] Medical Nutrition Therapy refers to the application of nutrition knowledge and clinical data in the management of diet-related disease using an evidence based approach (Franz 2003)

[2] Scientific – The scientific (positivist) paradigm uses a reductionist stance, examining mostly laboratory-based interventions with a predetermined question of causality between stable, tangible variables (Guba and Lincoln 1981 and 1985).

[3] Naturalistic – With regards to the experimental environment in human feeding research, naturalistic research studies the free-living environment. Naturalistic implies a less precise, less accurate and less controlled evidence though greater in ecological relevance when compared to intervention or laboratory formed evidence. They are constructed in the natural environment where behaviour is less disrupted, there are no controlled manipulations and allow for a variable environment (Blundell and Stubbs 1997).

vi Structure of the thesis

Well-recognised confounders in human based research vastly dictate the challenge in establishing sound evidence-based practice. These aspects reflect the reality of human variability, the need for individualised therapies and the existence of lifestyle derived confounders such as diet and activity levels and the problems associated with gathering information on these factors. The challenges raised form the ambiance for this thesis, taking the theoretical position that establishing the evidence from a dietetic perspective must draw on the scientific and naturalist dichotomies in the research context. Current human research does not commonly combine these modalities of analysis. The RCT is positioned as high-level evidence, yet inadequately captures less tangible attributes of human variability that naturalistic research can identify. The reductionist approach enforced by a RCT does not detect or accommodate for non-quantifiable and often significant personal environmental barriers to individual adoption of recommended lifestyle modifications. However, non-RCT forms of research are often perceived to be insufficient in rigor and robustness to base clinical practice upon.

The RCT, the accepted design for establishing evidence based practice, is of limited value on its own. This is because the extent of human variability from both biological and social influences makes it difficult for studies of a size feasible in practice to produce definitive results where biological outcomes are tested. Evidence based practice would benefit from research that includes both qualitative and quantitative methodologies so that practitioners have a range of information on which to base their decisions.

This thesis hypothesises that researchers should provide naturalist evidence in a complimentary fashion when researching diet-disease relationships with more widely accepted scientific (positivist) high-level evidence such as the RCT for appropriate integration into clinical practice. This hypothesis is tested through a RCT complimented by observational naturalistic research. The diet-disease relationship chosen for this comparison and testing was carbohydrate manipulation in an overweight insulin resistant population.

vii Publications and presentations related to this thesis

◈ ***Full Manuscripts Published in Refereed Journals***

1. Barnard, JA, Tapsell, LC, Davies, PSW, **Brenninger, VL,** Storlien, LH (2000) Relationship of high energy expenditure and variation in dietary intake with reporting accuracy on 7 day food records and diet histories in a group of healthy adult volunteers. *European Journal of Clinical Nutrition*.

2. Tapsell, LC, **Brenninger, VL** and Barnard, JA (2000), Applying conversation analysis to support accurate reporting in the diet history interview. *Journal of the American Dietetic Association* 100, 818-24.

◈ ***Conference Proceedings and Presentations***

1. **Brenninger, VL** (2002) Carbohydrates and the metabolic syndrome. Oral presentation. *Queensland Dietitians Association of Australia, Yeppoon, August 2002.*

2. Ngai, HHY, **Brenninger, VL**, Tapsell, LC, Brown, IL (2001), The acute effect of resistant starch on postprandial satiety in an overweight population. Oral presentation and proceedings publication. *Nutrition Society of Australia, Canberra, December 2001*.

3. **Brenninger, V**, Tapsell, L, Barnard, J (2001), Assessing energy intake: qualitative and quantitative methods account for variations. Oral presentation and proceedings publication. *Public Health Association of Australia Annual Conference, Sydney, September 2001*.

4. **Brenninger, VL**, Tapsell, LC (2001), Considerations for dietary intervention trials in an overweight population. Poster presentation and proceedings publication. *4th International Conference on the Scientific Basis of Health Services, Sydney, September 2001*.

5. **Brenninger, VL**, Tapsell, LC, Jenkins, AB, Barnard, JA (2001), Food sources of starch: implications for an intervention study involving resistant starch. Poster presentation and proceedings publication. *DAA 20th National Conference, 'Nutrition and Dietetic Practice: Reflections and New Horizons', Adelaide, May, 2001*.

6. Ngai, H, Tapsell, L, **Brenninger, V**, (2000), Resistant Starch: the acute effect on postprandial substrate oxidation and satiety; implications for obesity. Poster presentation and proceedings publication. *Masters in Dietetics Research Day, University of Wollongong, November 2000.*

7. **Brenninger, VL**, Tapsell, LC, Barnard, JA. (1999), Assessing usual dietary intakes: straightforward vs problematic reporting. Oral presentation and proceedings publication. *2nd South-West Pacific Nutrition and Dietetic Conference*, Auckland, *September, 1999*.

8. Barnard, JA, Tapsell, LC, **Brenninger, VL**, Higgins, J, Jenkins, AB, Davies, PSW and Storlien, LH (1999), Accurate reporting of diet and physical activity: identifying "ideal" subjects for dietary intervention trials. Oral presentation and proceedings publication. *2nd South-West Pacific Nutrition and Dietetic Conference, Auckland, September, 1999.*

9. Tapsell, LC, Barnard, J, **Brenninger, V**, Higgins, J, Jenkins, AB, Davies, PSW and Storlien LH (1999), Dietary reporting in 'free-living' individuals: implications for intervention trials. Poster presentation. *Diet and the Metabolic Syndrome. The Swedish Nutrition Foundation 21st International Symposium, Ystad, August, 1999.*

◈ ***Awards***

1. Poster Presentation Award (2001) *Dietitians Association of Australia, 20th National Conference, Adelaide, SA*. (**Brenninger, VL**, Tapsell, LC, Jenkins, AB, Barnard, JA (2001), Food sources of starch: implications for an intervention study involving resistant starch.)
2. Poster Presentation Award (2001) *Student Research Day, University of Wollongong, Wollongong, NSW*. (**Brenninger, VL**, Tapsell, LC, Jenkins, AB, Barnard, JA (2001), Food sources of starch: implications for an intervention study involving resistant starch.)
3. Poster prize (2000), Major projects (MSc Nutr. Diet.) University of Wollongong. (Ngai, H, Tapsell L, **Brenninger, V**, (2000), Resistant Starch: the acute effect on postprandial substrate oxidation and satiety; implications for obesity.

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1. Introduction

In recent years establishing the evidence for the dietary management of disease has been the subject of continued debate. One of the main challenges has been establishing adequate control in research processes. There is variation in dietary patterns and in health status between and within individuals during the course of their lives. An overweight participant from the research described in this thesis, once said *" I just don't know what to do…my husband can eat twice as much as me and he's built like a stick…I just can't seem to lose the weight."* As a clinician with an interest in evidence based nutrition therapy, these expressions of desperation or feelings of hopelessness provided strong motivation to pursue knowledge of this apparent enigma. It was not difficult to become part of the participants' lives and to fully appreciate the physical and mental improvements that could be gained from finding a feasible and efficacious dietary solution to the adverse health effects they experience. While scientific research may unveil this solution, ultimately we treat individuals, whose social environment may lead to marked variations in response to intervention. Most importantly, the source of these variations is multidimensional and therefore requires a combination of research disciplines to capture.

This thesis links physiology to sociology using a dietetic perspective. Many factors influence food consumption patterns. These include knowledge of food and nutrition,

income, food prices, the price of other products and services, individual taste and preferences (Variyam and Blylock 1998). In any study of the dietary management of disease, it is important to consider the impact of these factors on variations in responses. It is also important to understand the disease and its links with dietary intake.

The insulin resistant syndrome (or syndrome X, or metabolic syndrome) refers to the co-occurrence of obesity, glucose intolerance, insulin resistance, dyslipidaemia and hypertension, all risk factors for coronary heart disease and type 2 diabetes mellitus (Meigs 2000). Insulin resistance is the linking characteristic between heart disease, diabetes mellitus and obesity (Reaven 1993, 1994, 1988a, DeFronzo and Ferrannini 1991, Daly and Landsberg 1991), and dietary factors are implicated in all cases. This thesis focuses on a particular aspect of the dietary management of insulin resistance syndrome, taking as its study population, overweight adults. While a number of clinical outcomes are assessed, the thesis also considers social and behavioural differences that may influence these clinical outcomes, a range of which will now be introduced.

This chapter introduces the concept of human variation as a central tenet to the problem of establishing evidence for the dietary management of disease. With this backdrop, it provides a brief overview of the main aspects covered in the thesis, beginning with how evidence is established, some cardinal dietetic issues, primarily measuring dietary intake and follows with the social context of food consumption patterns. The chapter concludes with issues related to the dietary management of insulin resistance syndrome (covered in Chapter 2), with a consideration of opportunities provided by resistant starch in the diet.

1.1 Providing evidence for the dietary management of disease

Research evidence for the relationship between diet and disease takes many forms. Whether the evidence is considered sufficient to translate to practice has become the subject of a substantial amount of work by regulatory bodies. One example of imprecision in research targeting healthful dietary patterns is in the field of epidemiological investigations, where the effects of exposure to a food or nutrient on disease risk lack precise quantitative descriptions (Marshall and Chen 1999). Evidence may be considered less biased if there were greater accuracy in measuring the effect of exposure, and the ability to adjust for confounding variables made achievable. Terms such as 'relative risk', 'dose response' and 'threshold points' are less accepted as informative descriptors due to these problems in generating evidence and only add to the burden of publishing findings (Marshall and Chen 1999).

Epidemiological studies assume an important role in clarifying diet-disease relationships and generate findings that are useful in developing public health recommendations. However, the consumption of a food or nutrient is often correlated with the intake of another food or nutrient (Barker, McClean, Thompson and Reid 1990 and Kant, Schatzkin and Ziegler 1995 cited in Williams, Prevost, Whichelow, Cox, Day and Wareham 2000) or with lifestyle factors (Margetts and Jackson 1993 cited in Williams *et al* 2000). The observed relationship may be either a singular effect, or may be that the single food or nutrient is acting as a marker for an overall lifestyle and dietary patterns (Williams *et al* 2000).

Generating evidence for healthful dietary patterns or 'evidence-based nutrition' requires an understanding of the limitations of research. It is good practice to reflect on the value of the study's findings and think carefully about those studies classified as 'good evidence' (Truswell 2002, National Heart Foundation 1999). Levels of evidence are used in review processes by scientists (Kuntz and Oxman 1998), clinicians (DAA), Government regulatory bodies such as the Australian and New Zealand Food Authority (ANZFA 2000) and funding organisations including the National Health and Medical Research Council (NHMRC 1998). They are used in making respective practice-based and grant awarding decisions.

Quality evidence based research is of utmost importance in fields such as weight loss (Egger, Camerson-Smith and Stanton 1999). Currently RCTs are graded at the top of the hierarchy for levels of evidence used by the National Health and Medical Research Council (NHMRC), Cochrane reviews, ANZFA and the National Heart Foundation. All of these organisations and many more internationally, have significant influence on the way in which research is conducted as they have both financial and publication power. The NHMRC is a significant funding source of Australia's research, accounting for approximately one-quarter of all health research nationally (Anderson 1997). The RCT, however, is problematic in evidence-based nutrition as, unlike a therapeutic drug that can easily fit within the confines of the RCT, dietary intervention trials involve complex systems of food intake (Truswell 2002). Many of the factors that may aid dietary management include behavioural aspects, promoted through intensive therapy (Ash 2002), however these are regarded more observational and therefore less credible in the evidence hierarchy. Nevertheless, it is believed that the strongest form of evidence for

practice lies in the randomised controlled trial, where the test diet is compared with a control.

One of the biggest problems in establishing this form of evidence, however, is that of variation in response within the study population. This may be due to genetic factors, considering that families tend to have a similar risk for chronic diseases, sharing both their genes and environment (Simopoulos 1995). Although these two interacting factors are difficult to separate from one another, an Australian study focussing on osteoporosis, found that genetic variance accounted for as much as 75% of the variance in bone density (Morrison, Qi, Tokita, Kelly, Crofts, Nguyen, Sambrook and Eisman 1994). Heritability is principally defined as the "proportion of the total variance that can be explained by genes" (Suzuki, Griffiths, Miller, Lewontin 1989 cited in Simopoulos 1995:157). Still, the effect of lifestyle on measures of chronic disease management is ubiquitous. Genetic variation appears to describe the differences in susceptibility to chronic disease (Childs 1990, Childs 1988) while the interaction of our environment upon this genetic susceptibility such as through diet, accounts for the manifestation of chronic diseases (Elliott and Ong 2002, Maffeis, Pinelli and Schutz 1996).

Investigations targeting chronic diseases, such as in obesity (Bouchard 1989), diabetes mellitus (Kobberting and Tillil 1990), coronary artery disease (Berg 1994), cancer (Friends 1990, Peltomaki, Aaltonen, Sistonen *et al* 1993, Aaltonen, Peltomaki, Leach *et al* 1993, Hall, Lee, Newman *et al* 1990, Sikora 1994) and osteoporosis (Morrison *et al* 1994), have supported the theory of heritability. Heritability may vary between populations and similarly the environment differs between regions. It is therefore

sensible that dietary recommendations should vary between populations (Simopoulos 1995). An example of such recommendations is the *Recommended Dietary Intakes* of nutrients established for populations (NHMRC 1991). Murphy (2001) discussed the importance of sources of variability between people, such as lifestyle, that needed to be considered for the basis of these figures. In the American guidelines, setting of nutrient requirements neglects to account for variation that exists due to chronic disease, as they are based on healthy populations (Murphy 2001). The other important sources of variability considered, though not relied on explicitly in setting the American *Recommended Dietary Allowances*, were age, gender, life-stage such as puberty, menopause, pregnancy, body size, medical history and genetic susceptibility. The latter was derived from information gathered on family history (Murphy 2001).

In understanding human variability, we must first appreciate the evidence supporting aspects of similarity (Shea, Churchill, Edwards, Holdaway, Henry, Hovers, Kuhn, Mithen, Pettitt and Wiseman 1998). Brent James (2001) argues one of the difficulties in explaining research outcomes is attributable to situations where researchers cannot easily decipher which variable caused the effect. Thus, while variations in response to dietary management may prove problematic when attempting to explain results, improved clinical outcomes remain a worthy target.

1.2 Measurement and assessment of dietary intake

Studies providing evidence for the effectiveness of dietary intervention rely upon participant compliance with dietary targets. Large-scale clinical trials have shown that individualised approaches are more effective than general advice in achieving targets

(Tuomilehto, Lindstrom, Eriksson, Valle, Hamalainen, Ilanne-Parikka, Keinanen-Kiukaanniemi, Laakso, Louheranta, Rastas, Salminen and Uusitupa 2001, DPP 2002), however this evidence is derived through interviews assessing self-reported intake. Accurate and reliable methods that assess dietary intake are therefore an essential component of such studies. It is important to emphasise however that dietary manipulation is an iterative process targeting specified health outcomes. Endeavoring to obtain accurate records of dietary intake have led dietitians and other allied health professionals to apply ethnographic approaches to provide insight into 'how' people present information verbally through patterns of 'talk' (Tapsell, Pettengal and Denmeade 1999, Tapsell, Brenninger and Barnard 2000, Robinson 1998, Robinson 2001, Pilnick 1998, and Perakyla and Silverman 1991). Aside from dietetic research in this area, pioneered by Tapsell in 1992 (Tapsell 2000), studies involving general practitioners (Robinson 2001, Robinson 1998), pharmacists (Pilnick 1998), and counsellors for alcoholics anonymous or HIV/AIDS (Perakyla and Silverman 1991) all acknowledge that questions and probes are perceivably improved by findings from conversation analysis, a form of ethno-methodology (Watson 1996, Psathas 1995, Psathas 1979).

Earlier work on the diet history interview clarified the way subjects structured their talk on reporting dietary intake. Reporting of dietary intake was presented within a story like fashion subsequently coined the term 'story-telling'. The interviewer naturally directed the story-telling to improve the data collated on a usual day's intake before it was entered into dietary analysis software. Studies by Tapsell (1997a, 1997b, 2000) reported that breakfast appeared to be a readily narrated in response to the dietitian's request for

the patient to start from the beginning of day and to continue reporting their intake through to the remainder of the day. Verbal acknowledgement or cues by the dietitian such as “mhmm” and “yes” were enough to allow the participant to continue their narration of the day’s intake before the dietitian would go back to the beginning and clarify minor details, frequency of items and variations.

Although breakfast could be described in a straightforward report, dinner meals presented a greater challenge for the participant and data collector. Further work in this area found that forms of hedging, by saying ‘it depends’, or guesswork, indicated by the term ‘probably’ were used most during accounts of the dinner meal, suggesting greater variability in food choice patterns at this meal (Brenninger 1998, Tapsell, Brenninger and Barnard 2000). Hedging also appeared in the reporting of lunch. Questioning in a summative fashion at the end of the interview with a food frequency checklist also resulted in responses using ‘it depends’ and ‘probably’, but this may be related to the form of questioning. Overall, conversation analysis of recorded diet history interviews provided insights for interviewers as to where possible inaccuracy of reporting is located. A complete comparison on methods used to collect dietary data, including the diet history interview, is shown in the methodology of this thesis.

Clinical intervention trials use the diet history interview as a central component of the measurement and assessment of dietary intake, leading to the establishment of dietary advice. The data obtained from this process would provide yet another example of potential variation in the study population. In this thesis, emphasis is placed on additional work targeting accuracy in dietary reporting and validating the dietary data as

a form of quality assurance.

1.3 The social context of dietary intake

Converting theory to practical recommendations for prevention, treatment and management of certain diet-related diseases must take into account interpersonal variation of metabolic profile, environment and lifestyle history. Lifestyle is a known source of variability (Murphy 2001). Humans may choose which dietary recommendations they will abide by or may have pre-existing barriers to change, unlike animal and cellular interventions. Hence, recommendations not deemed feasible by subjects do not alter clinical outcomes. As an example, the attempt to lose weight using currently recommended strategies such as eating fewer calories and exercising more is reported in only 34% of American trying to lose weight. Of the 34%, there is a tendency to display demographic characteristics such as increased level of education and being a non-Hispanic white (Kruger, Galuska, Serdula and Jones 2004). Part of the criticism surrounding weight loss research is the view that research needs to become more holistic (Wing, Goldstein, Acton, Birch, Jakicic, Sallis, Smith-West, Jeffery, and Surwit 2001). A review derived from the National Institute of Diabetes and Digestive and Kidney Diseases declared four priority areas for future obesity and physical activity research (Wing *et al* 2001). These four areas included:

- Environmental factors related to obesity, eating and physical activity
- Adoption and maintenance of healthful eating, physical activity and weight
- Aetiology of eating and physical activity, and
- Multiple behaviour change

The feasibility of diet manipulation and factors that increase resistance to dietary changes are therefore a key component of dietary research. Feasibility can be examined from many different viewpoints such as psychological and sociological. Many behaviour change theories focus on individual psychological traits, such as self-efficacy. An individual's self-efficacy is their own assessment of their ability to successfully perform the desired behaviour (Bandura 1977). Self-efficacy was believed to be a rich area of opportunity to investigate (Brownell and Wadden 1992) considering that it may be a powerful predictor of a treatment's feasibility thereby an important construct in the treatment of obesity. Consequently further work on self-efficacy emerged by Clarke, Cargill, Medeiros and Pera (1996), then by Fontaine and Cheskin (1997) and indicated overall that this relationship was inconclusive. Similarly other potential predictors of weight management in obese people including age, gender, age of onset, glucose tolerance, personality and locus of control have generally produced equivocal findings (Fontain and Cheskin 1997).

Associated with self-efficacy is the theory named readiness to change. There is a considerable body of evidence that support the notion that various factors may contribute to the effectiveness of health recommendations. These include frameworks such as the transtheoretical model (stages of change) (Prochaska, Redding and Evers 1997), personality types (O'Neill 2001) and behavioural science (Wing *et al* 2001). In this thesis, while such psychological aspects are not directly measured, the areas will be initially explored through surveys of factors within participants' lifestyles, which may affect their ability to adjust to dietary change. In this way a more holistic approach to the question of feasibility will be attempted.

The literature shows that dietary compliance compared to non-compliance can produce better outcomes such as greater weight loss on low calorie and very low calorie diets, however the paucity of predictors currently limits the incorporation of individual characteristics to guide dietary treatments (Martin, O'Neil and Binks 2002). Overall the social context of dietary intake affect feasibility and efficacy and their influence may further introduce variation in response, thereby an aspect needing consideration. Properly planning a dietary intervention trial now requires an understanding of the diet-related conditions.

1.4 Diet and insulin resistance: opportunities with resistant starch

Insulin resistance is the one factor linking all co-morbidities of the metabolic syndrome – obesity, heart disease and diabetes mellitus (Reaven 1988a). Dietary saturated fats may be linked to the development of insulin resistance and polyunsaturated fats may provide some protection (Storlien *et al* 2001). In contrast, research on the effects of different forms of dietary carbohydrate (CHO) is relatively undeveloped. Resistant starch (RS) is a form of CHO producing desirable metabolic outcomes in humans (Behall and Howe 1995, Brown, Wang, Topping, Playne and Conway 1998, Brown 1996, Brown 1997, Muir, Lu, Collier and O'Dea, unpublished). Lower acute post-prandial insulin and glucose responses have been found with diets containing high-amylose maize starch (Byrnes, Brand Miller and Denyer 1995, Raben, Tagliabue, Christensen, Madsen, Holst and Astrup 1994). Various studies have looked at the effect of RS in the diet, bearing in mind that not all of these studies have used 'gold standard' measures of insulin resistance, nor have they accounted for the impact of background diet on metabolic outcomes. The general population consumes less than one quarter

of recommended intake of RS, and while the market has grown, food products have mostly targeted bowel health (Baghurst, Baghurst, and Record 1996). The final test, assessment of the impact of diet on metabolism under free-living conditions, is rare. Under these conditions, variations in lifestyle factors may also exert significant effects on metabolic outcomes.

One of the ways of examining these variations from an environmental perspective is to consider different populations. Between different regions of the world, there are obvious differences in longevity. Less well-financed regions tend to suffer more from infection and poor nutrition, while cosmopolitan societies live for longer without these health concerns (Crews and Gerber 1994). Patterns of chronic degenerative diseases and longevity vary across the world today and the "likelihood is that they have varied throughout hominid evolution" (Crews and Gerber 1994:154). Where the life expectancy of a population extends into 70 and 80 years of age, chronic degenerative diseases, such as mature-onset diabetes mellitus, various cancers, coronary heart disease and cerebrovascular disease lead mortality and morbidity statistics (Crews and Gerber 1994). These differences in life expectancy display variation between populations simply through the processes of age and the consequential degenerative processes leading to mortality and morbidity.

Many chronic degenerative diseases such as diabetes mellitus were diagnosed using a blood glucose value defined by inadequate evidence (Harris, Hadden, Knowler and Bennett 1985, Foster 1989). These initial values for diagnosis of health conditions are usually based on retrospective or prospective population data. However, it cannot be

inferred that if a person is above or below a critical value, that they will unconditionally develop identical outcomes to another person with a similar diagnosis. One pertinent illustration of this point is the current debate surrounding the management of people diagnosed with impaired glucose tolerance or impaired fasting glucose (Shaw and Chisholm 2003, Diamond, Chauhan, Kruger and Subramanian 2003). Whether there is a benefit from early intervention is unclear.

Once there is evidence that a nutrient can support health promotion, another interface exists in generating a recommended dose or requirement which will promote optimal health outcomes without causing deleterious effects. Take for example the *Recommended Dietary Intakes* (RDI) of nutrients. Here the estimated requirements for macro- and micronutrients are based on the amounts required by 'most' of the population (Truswell 1990), a value which varies according to each nutrient (NHMRC 1991). For example, the RDI for protein is estimated to apply for 97.5% of the population, while vitamin B6 has a 33% safety margin in-built (NHMRC 1991). Clearly, variation among our nutrient needs exists, both between and within each person and each population. It is important to acknowledge the deviations to the rule in diet-disease relationships as these may provide greater insight into disease manifestations and overall, will add up to be a significant number of people in each state or country.

Grouping people into disease or disease-free categories has numerous implications. One for example, is the availability of treatment and financial support offered to an individual diagnosed with diabetes mellitus as compared to people classed as impaired glucose tolerance. Applying fiscal importance to the threshold for diagnosis of chronic

disease, such as diabetes, negates the rationale that each value is a point along a continuum. However, the goal post has moved and definitions of disease status, such as diabetes mellitus, have been reviewed and redefined since their establishment (Colman, Thomas, Zimmet, Welborn, Garcia-Webb and Moore 1999). Similarly there are new guidelines for hypertension prevention, detection and management (Chobanian, Bakris, Black, Cushman, Green, Izzo, Jones, Materson, Oparil, Wright, and Roccella 2003). The cut-off values for metabolic and clinical parameters have changed with both technological advances and improvements in expertise (Crews and Gerber 1994). Chronic non-infectious degenerative diseases are the outcome of complex, poorly defined series of events, beginning at an unidentified point then progressing over a large proportion of an individual's life. These chronic diseases appear to be the interaction between an individuals genes, their environment, personal life history and importantly, medical technology (Hutt and Burkit 1986 cited in Crews and Gerber 1994). Such complex interactions are problematical in establishing aetiologies "since most people with these disorders have sub-clinical diseases and many disease-free individuals share features, or risk factors, in common with those affected" (Crews and Gerber 1994:155).

Variability between subjects from metabolic, social and dietary perspectives is compounded by the variation that occurs within individuals over time. Both chronic and acute measures of metabolism are needed in establishing the reasonable estimate of each person's metabolic make-up. In reality, this estimate is contaminated by subjects displaying controlled behaviour during measurement, both in terms of their food intake and in their physical activity. The effect of intervention generates a critique of research findings that have attempted to address weight loss. Some researchers report that high

fat, added sugar and low fibre intakes rather than energy intake cause obesity (Miller, Niederpruem, Wallace and Lindeman 1994). However, Tucker and Peterson (2000) suggests that people who consume an unstable energy intake and food intake in general are less able to adjust their metabolisms accordingly and become more overweight. In support, research on substrate utilisation indicate that it takes time to adjust to the proportion of macronutrients consumed (Schrauwen, van Marken, Lichtenblet, Saris and Westerterp 1997). It may be postulated that in many controlled, rather than free-living, intervention trials, people tend to lose weight due to the stabilisation of their food intake and ability of their metabolism to adjust more easily to this stability. For this reason, free-living intervention trials would provide a more accurate scenario and application to diet-disease relationships. This school of thought continues to support the need for naturalistic forms of evidence to account for non-clinical confounders.

Establishing evidence based practice for the treatment of obesity, insulin resistance and diabetes is complex. There are numerous limitations which question the strength of our findings, one of which appears to be that researchers tend to remain focussed on questions that are answerable by their research skills sets. For example, once animal model and cellular outcomes necessitate a clinical trial, employing the same scientific approach in humans may transmit very different outcomes (Baghurst *et al* 1996, Edwards 2002, Mitchell 2002). In addition, employing a positivist approach alone to investigate diet-disease relationships displays initial confidence in the hypotheses despite our knowledge that inconsistency between animal and human based research exists. Once the null hypothesis is accepted, environmental and behavioural conditions may no longer be accessible for comparison and discussion. It is attractive then, that we

best enumerate answers for the metabolic syndrome by focussing our research efforts on an interdisciplinary approach (Tobin and Miller 2001). With all this in mind, this thesis addresses the task of establishing evidence for the management of diet related disease, using as a case study, the impact of a high amylose resistant starch diet on clinical indicators of insulin resistant syndrome.

2. Diet and Insulin Resistance

The following literature review discusses two primary metabolic conditions that are major targets of this thesis: obesity and insulin resistance. Current management focuses on changes in the environment and lifestyle, often blamed for the expression of symptoms in aging and genetically susceptible people. At an individual level, patients with these chronic diseases are counselled by health professionals to improve their general eating patterns and lifestyle, with the ultimate aim of remaining asymptomatic. Health professionals desire the same outcomes, though also consider other instigators for this aim, such as reducing the cost of illness including the reliance on medication or need for hospitalisation. An introduction to the metabolic position implicated by obese and insulin resistant classifications is outlined.

2.1 Insulin resistance syndrome

The insulin resistant syndrome, alternately known as 'syndrome X', lacks consensus for diagnostic criteria and an operational definition (Sterne 1997). Although, Reaven (1988a) outlined that the syndrome consisted of resistance to insulin-stimulated glucose uptake, glucose intolerance, hyperinsulinaemia, hypertension, increased very-low density lipoprotein, triglycerides and decreased high-density lipoprotein cholesterol. Insulin resistant syndrome exists in lean and obese individuals, though a greater number found to have insulin resistant syndrome tend to be the latter (Sterne 1997). The insulin resistant syndrome is also defined with regard to its 'features' and its 'outcomes'. The 'features' include the aforementioned disorders of glucose and lipid metabolism, hypertension, obesity and an unfavourable body fat distribution. The elements considered 'outcomes' of insulin resistant syndrome are type 2 diabetes mellitus and

atherosclerosis, including coronary artery disease. Insulin resistance is believed to be the underlying condition promoting the cluster of disorders that manifest (Reaven 1988a). Hypertension has also gained attention as the initiator of the syndrome, by causing vascular rarefraction in skeletal muscle (Julius, Gudbrandsson, Jamerson, Tariq Shahab, Andersson 1991 cited in Sterne 1997) leading to insulin resistance (Sterne 1997). However Meigs (2000) reports that, from a cluster analysis, blood pressure is only loosely associated with the primary components of this syndrome.

Evidence supports that obesity is not an outcome of insulin resistance, rather the opposite (Sterne 1997). Overweight is defined as a BMI 25-30 kg/m^2 and obesity as a BMI >30 kg/m^2 (WHO 1997). It is a clear definition; though the distinction between associated management and health risks are not as easily separated. Therefore, both terms will be referred to as obesity from this point on. Obesity is recognised as a global public health concern (WHO 1998). Since 1966, 3622 peer-reviewed studies were found in MEDLINE that included the topics obesity, diabetes mellitus and cardiovascular disease (Tobin and Miller 2001). Because of their public health significance scientists are relentless in targeting obesity, type 2 diabetes mellitus, cardiovascular disease, along with other diseases such as cancer, gastrointestinal diseases and arthritis (WHO 1998). Recent data indicate that the metabolic syndrome is far more common even among children and adolescents than previously reported and that its prevalence increases directly with the degree of obesity (Weiss, Dziura, Burgert, Tamborlane, Taksali, Yeckel, Allen, Lopez, Savoye, Morrison, Sherwin and Caprio 2004).

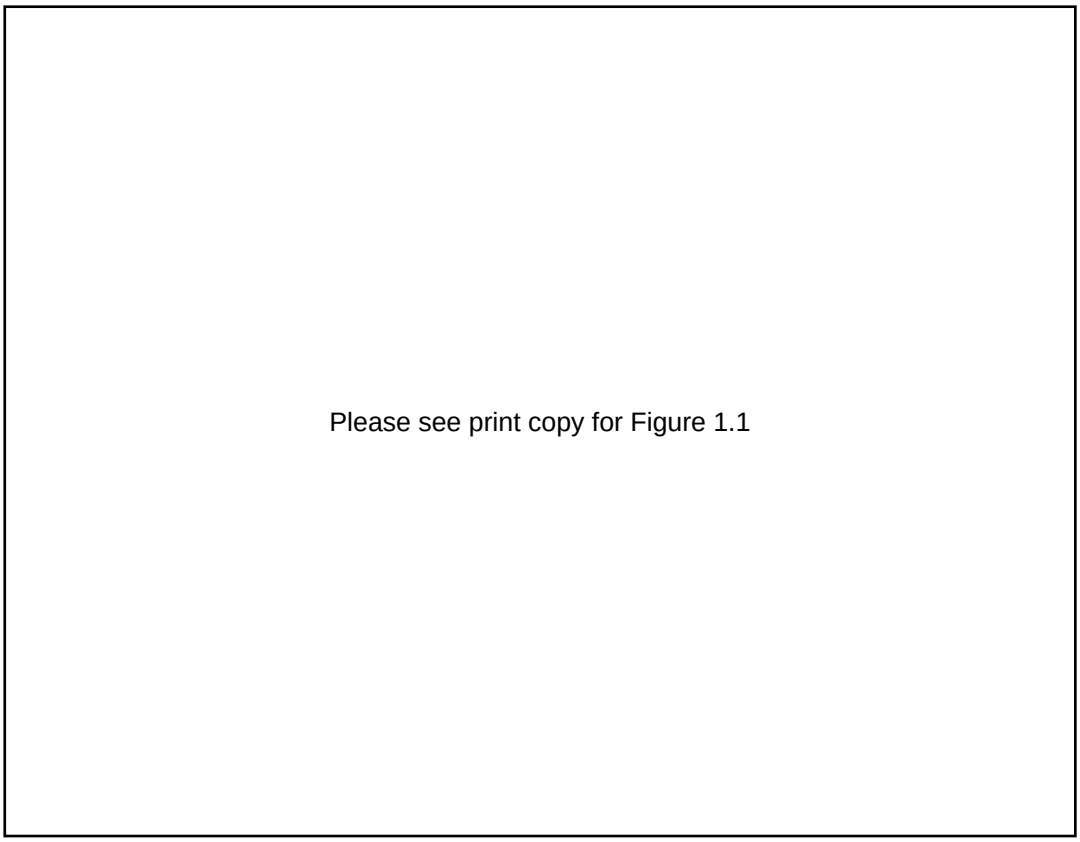
Associations between body weight, body fatness or adiposity, insulin resistance, hormones and all other components of the metabolic syndrome are important to consider as mediators in shifting the energy balance equation. For example, a current position held is that improving insulin sensitivity may reduce the prevalence of metabolic syndrome abnormalities, including obesity (Pan and Storlien 1993). Therefore, the following sections will discuss the means by which dietary manipulation alters any one of these, and ultimately lead to the gap for an investigation into resistant starch on metabolism.

Some important considerations used as a marker of the severity of various health conditions are morbidity, mortality, and the costs associated. The World Health Organisation declared obesity as one of the four major epidemics for the new millennium. Globally, an estimated 1.2 billion people are overweight or obese, a figure that is increasing rapidly (WHO expert Committee 1995 in WHO 1998). A staggering 200 million people were classed as obese in 1995, a figure that has escalated to 300 million according to the latest estimates by the World Health Organisation (WHO 2002). Eighteen percent of Australia's population alone is classified as obese, while the figures within America are even higher (WHO 1998), a trend that is evident in other Westernised countries and gaining momentum (Kopelman 2000). In addition, Americans are currently spending more than $33 billion per annum on weight loss products and services (Cleland, Graybill, Hubbard 1998).

With regard to diabetes mellitus, the prevalence of this condition is also growing rapidly, currently estimated to affect 8.0% in men and 6.8% in women in Australia (Dunstan, Zimmet, Welborn, De Courten, Cameron, Sicree, Dwyer, Colagiuri, Jolley, Knuiman, Atkins and Shaw 2002) and 150 million people worldwide (King, Aubert and Herman 1998 cited in Dunstan *et al* 2002). In addition, 17.4% of men and 15.4% of women either have impaired glucose tolerance or impaired fasting glucose (Dunstan *et al* 2002). Progress in defining a cure remains limited, although changes in lifestyle and food consumption are thought to be the main causes of metabolic abnormalities, such as obesity, a major component of the metabolic syndrome (WHO 1997).

Diabetes mellitus is perhaps the most serious outcome of developing insulin resistance and the metabolic syndrome. There are many forms of diabetes mellitus that differ in severity, usual age of the subject at onset, pregnancy-induced onset, and whether it is associated with tissue wasting or overweight morphology. Overweight patients diagnosed with diabetes have commonly been classed as type 2 diabetes mellitus and are classically portrayed by the following diagram of development (Figure 1.1).

Figure 1.1 Flow diagram for the development of type 2 diabetes mellitus.



An abnormality in the control of food intake is hypothesised the most likely influence on the development of obesity (Schutz, Flatt and Jequier 1998). It is established however, that the types of food and the range of nutrients consumed are all important in influencing insulin action (Storlien *et al* 2001). The shuttle of nutrients into cells or for the provision of energy achieves orderliness when energy intake is in balance with energy expenditure in normal weight humans. This balance is worked on an acute (Dionne and Tremblay 2000), daily- (Schrauwen, Wagenmakers, van Marken Lichtenbelt, Saris and Westerterp 2000) and longer-term (Schrauwen *et al* 1997, Schrauwen *et al* 2000) basis. When the energy equilibrium is disrupted, that is too much

substrate provided and/or insufficient energy expended, the overflow of nutrients can cause unfavourable use of metabolic pathways, such as De novo lipogenesis (Hellerstein 1999), which alter blood fats to become more saturated (Hudgins, Hellerstein, Seidman, Neese, Diakun and Hirsch 1996 cited in Hellerstein 1999). Greater proportions of saturated fatty acids incorporated into cell membranes tend to result in insulin resistance (Storlien, Pan, Krisketos, O'Connor, Carson, Covney, Jenkins and Baur 1996b).

There are differences in responsiveness to diet (Denke, Adams-Huet and Nguyen 2000). The study by Denke *et al* (2000) is an example of responsiveness in a trial of butter versus margarine consumption examining effects on triglycerides, and other blood fats, in a familial setting. Margarine reduced low-density lipoproteins, which are beneficial for lowering heart disease risk in both adults and children, while butter increased triglycerides in adults, potentially detrimental for heart health. However, despite achieving compliance, the authors confirmed in their own findings that approximately 19% of participants were not responsive to the dietary manipulation, which they believe could be attributable to genetic factors. Their free-living intervention trial is similar to the findings of other studies, where the prevalence of participants who do not respond to dietary change has been estimated to be 15-20% (National Diet-Heart Study Research Group 1968, Denke and Grundy 1994; Shenberger, Helgren, Peters, Quiter, Johnston and Hunninghake 1992; Denke 1994; Quivers, Driscoll, Garvey, Harris, Harrison, Huse, Murtaugh and Weidman 1992). Similarly, changes in cholesterol were influenced by body weight. Overweight people, regardless of age or sex-bias, were unable to achieve the same cholesterol reduction with dietary manipulation as the lean participants (Denke

et al 2000). They concluded that, in both children and adults, lean and overweight, a person's body weight predicted their dietary responsiveness.

An inability of obese and overweight people to respond to dietary manipulation for cholesterol lowering may be reflected similarly in other metabolic studies with varying outcomes. The likelihood that this population under-reported (Johnson, Goran and Poehlman 1994 and Lichtman, Pisarska, Berman, Pestone, Dowling, Offenbacher, Weisel, Heshka, Matthews, Heymsfield 1992 cited in McManus, Antinoro and Sacks 2001) could possibly be true in the investigations regarding responsiveness. Alternately, these people may report true accounts of their consumption for the particular period in question, then eat differently during the study period. Another line of reasoning is that 'misreporting' is the justification used for insignificant results. This latter issue of misreporting dietary intake will be revisited in the dietary methodology section of this thesis.

2.2 Impact of dietary management

We must be aware, that each time we consume food a complex interaction of macro- and micro- nutrients takes place (Huijbregts, Feskens, Räsänen, Fidanza, Nissinen and Kromhout 1997, Leahy, Croniger and Hanson 1999). When you add the confounder, obesity combined with insulin resistance, the mechanisms surrounding fuel utilisation become increasingly more difficult to determine and amend. It is therefore fundamentally important, in the study of diet on metabolism, to separately consider the main three macronutrients in food; fat, protein and carbohydrate, as each may displace the other when manipulated. The following literature will review potential effects of these macronutrients, ending with an overall review on energy balance and fuel utilisation.

2.2.1 Fat

The nutrient highest in energy density is fat, delivering over two times the energy per weight than its companions in food, carbohydrate and protein (Yao and Roberts 2001). Foods rich in fat provide us with fat-soluble vitamins, some antioxidants, and polyunsaturated fats, which may, in combination with low saturated fat intake, reduce the risk for cardiovascular disease (Dixon and Ernst 2001). A great deal of research in the quality of different types of fat and their health sustaining attributes repeatedly negate the well publicised message that, fat is unfavourable to health. Reducing total fat has been the mainstay of weight loss campaigns, diabetes management, or 'healthy eating' regimens for many years, as for example, the placement of oil in the 'eat least' section of the healthy eating pyramid (Nutrition Australia 2000). All high fat foods are very energy dense, although ongoing research supports that some classes of fat are

less easily mobilised for energy (DeLany, Windhauser, Champagne and Bray 2000) and may differ in there capacity to promote insulin resistance syndrome morbidities (Kraegen and Storlien 1989, Vessby, Uuisupa, Hermansen, Riccardi, Rivellese, Tapsell, Nälsén, Berglund, Louheranta, Rasmussen, Calvert, Maffetone, Pedersen, Gustafsson and Storlien 2001, Storlien, Krisketos, Calvert, Baur and Jenkins 1997a, DeLany *et al* 2000).

2.2.1.1 Forms and categories of fat

Dietary fat can be categorised into three subdivisions by their level of saturation. The three classes of fats or fatty acids are: monounsaturated fatty acids (MUFA), polyunsaturated fatty acids (PUFA), and saturated fatty acids (SFA) (Eschleman 1996). Within these are further divisions, including trans-fatty acids that act similar to SFA, and perhaps the more well known, n-3 and n-6 fatty acids within the PUFA family of fats. The saturation level and the pathway or enzymes that the various fat subtypes use, can account for the vast differences that each type impart on our metabolic profile.

2.2.1.2 Mechanistic research

A vast body of research indicates that high fat diets and saturated fat promote insulin resistance (Storlien, Kriketos, Jenkins, Baur, Pan, Tapsell and Calvert 1997b). The common view that the consumption of fat makes you fat appears to stem from the energy density of fat and its efficient storage as adipose tissue compared to fuels such as carbohydrates (Flatt 1978, Hill, Melanson and Wyatt 2000). Dietary fats only lose approximately 3% of their energy when stored within the body, as opposed to carbohydrates that exhaust more than 20% of their potential energy in their

conversion to fat for storage (Flatt 1978, Guthrie and Picciano 1995). Fat further upholds a damaging image by its failure to induce greater fat oxidation (Surina, Langhans, Pauli and Wenk 1993, Flatt 1995) in addition to lacking appropriate satiation (Green, Burley and Blundell 1994; Blundell, Burley, Cotton and Lawton 1993). Therefore, it is plausible that the consumption of fat is a risk factor for subsequent weight gain (Heitmann and Lissner 1995).

Fat intake cannot take sole responsibility for this weight gain, especially in light of the fact that not all fats act uniformly in metabolic pathways. One class of unsaturated fatty acids, the polyunsaturated fatty acids, have even displayed at the cellular level, the potential to induce "leaky" membranes, causing augmented mitochondrial or sodium-potassium pump activity, and perceivably increase metabolic rate (Else and Hulbert 1987, Else and Hulbert 1989). Fatty acids exert varying effects on their storage as fat, their capacity to promote weight gain or metabolic disorders, and their ability to alter the transcription of specific genes (Clark and Jump 1996).

Both n-6 and n-3 fatty acids compete for the same metabolic pathway for desaturation and elongation. Without consumption of n-3 fatty acids, n-6 fatty acids easily enter into metabolic pathways, which lead to their incorporation into cell membranes (Raatz, Bibus, Thomas and Kris-Etherton 2001). Diets high in n-6 have demonstrated elevated triglyceride accumulation in muscle tissue and increasing liver triglyceride production, which interfere with glucose metabolism (Kraegen and Storlien 1989). Therefore, n-6 fatty acids appear capable of impairing insulin action (Kraegen and Storlien 1989; Pan and Storlien 1993). This is also true for high fat feeding, but more specifically with

saturated fat, as these are poorly used for energy and poorly mobilised once stored (DeLany *et al* 2000).

2.2.1.3 Clinical and population research

In terms of effects on energy balance, fats can be viewed in two ways. Firstly, fats can have detrimental effects on energy balance in excessive amounts, and secondly, the proportion of the types of fats can also have detrimental or advantageous effects (Vessby *et al* 2001, Storlien *et al* 1997b). However, dietary fat quality may alter insulin sensitivity in healthy subjects (Vessby *et al* 2001). These encouraging results were demonstrated in a study where saturated fatty acids were decreased and monounsaturated fatty acids were increased over a three-month intervention. This multi-national trial was an affiliation between five centres studying a total of 162 healthy subjects ranging from normal weight to obese (BMI 22-32kg/m^2) and consuming isoenergetic diets. The effect of this fatty acid manipulation was not however transferred to insulin secretion, nor apparent when fat intake exceeded 37% of energy intake (Vessby *et al* 2001).

Dietary fat and lipids are widely distributed throughout the food supply, and hidden within many foods, beverages and supplements that are readily available for consumers. Certain high-fat foods play a role in weight gain and obesity in susceptible populations (Rolls 1995; Lissner, Levitsky, Strupp, Kalkwarf and Roe 1987; Rolls, Kim Harris, Fischman, Foltin, Moran, Stoner 1994). This hazardous image has led to the development of low- or no-energy fat alternatives. No-energy fat replacers are poorly

metabolised and absorbed (Blundell and Stubbs 1997), thereby attempting to satisfy the palate, while disguising a less rich, less hazardous alternative.

A prospective trial conducted in a large population of 84 204 women with type 2 diabetes mellitus, found that an increase in trans fatty acids and decrease in PUFA lead to the progression of type 2 diabetes. On the other hand, total fat, SFA and MUFA did not explain any rises or decline in type 2 diabetic status over a 14-year period of investigation (Salmeron, Hu, Manson, Stampfer, Colditz, Rimm and Willett 2001).

In Western societies, concerns for under-nutrition have been superseded by the highly prevalent threat posed by over-nutrition (Prentice and Jebb 1995; Albanes 1998). Excessive food and energy intake has been met with an infiltration of low-fat foods and energy replacers. It has been suggested that rather than develop these energy replacers, resources should be redirected into marketing fruit and vegetables (Stanton 1999). This author reported that manufactured functional foods or suitable alternatives may be useful. However, the food industry strongly dictates the food supply available to the consumer, despite suggesting that they market foods that consumers demand (Stanton 1999). One example where functional foods have shown their beneficial place in the food supply is in improving folic acid (folate) intakes through folate-fortified breakfast cereals and supplements. It appears that the use of these are regarded most effective for reducing elevated plasma total homocysteine concentrations, a risk factor for vascular disease (Riddell, Chisholm, Williams and Mann 2000).

Though there are obvious disadvantages in the area of food labelling required, marketing and the money to be made by industry, we require scientists to perform research on functional foods (Stanton 1999). There is potential in developing our knowledge in metabolism or science interests and for potentially valuable work that demonstrates the efficacy of these functional foods (Stanton 1999). The challenge for scientists is to identify individual components of foods that can prevent health concerns and promote the quality of life (Heasman and Mellentin 2001). "A key goal of functional food science is to understand and target particular 'biomarkers' or endpoints for disease and illness and the food components that act upon these" (Heasman and Mellentin 2001:15)

Despite industry filling a perceived need for fat replacers, the importance of dietary fat in determining weight loss is a controversial issue. Some research has found a lack of weight loss following a reduction in dietary fat intake, which suggests that dietary fat does not perform a role in the development of obesity (Willett 1998). There is sufficient evidence that the current public health recommendation to lower fat intake to <30% of energy intake is upheld as appropriate and worthwhile (Hill, Melanson and Wyatt 2000). However, given the vast amount of supplementary evidence on fat sub-types now available, it is important to move beyond the debate regarding high fat intake producing obesity (Hill *et al* 2000). It is important that the variation in fatty acids ratio, individual contribution as energy and displacement of fat overall with an intervention trial are monitored, recorded and minimally changed if fat is not the targeted nutrient for manipulation.

2.2.2 Carbohydrates

Fats and carbohydrates (CHO) are two main sources of energy for humans. Defining set amounts of each of these fuels and their subtypes requires further qualification. There is evidence that particular types of these nutrients may promote or prevent the onset of diabetic complications and other aetiologies related to the metabolic syndrome. Insulin resistance, which is central to the metabolic syndrome, is recognised by hyperinsulinaemia and normoglycaemia or hyperglycaemia (Krentz 1996). Fundamentally, it is as an inability to effectively metabolise CHO (Moore 1997).

2.2.2.1 Classification and sources of resistant starch

Not all CHOs are equivalent in terms of digestion and absorption. As with fats, dichotomies exist, such as labelling them as 'good' and 'bad' (Aronne, Edman and Willett 2001). Vegetables and high-fibre whole grains are the food forms of CHO that tend to have a lower glycaemic load and therefore considered 'good', while the CHO's labelled as 'bad' are primarily high glycaemic index or refined and processed CHOs (Aronne *et al* 2001). Additionally, this macronutrient is grouped into 'available' and 'unavailable' CHOs (Jones 1997). For example, sugars would be placed in the available CHO category, while non-starch polysaccharides and resistant starch in the unavailable class. Comparative with this is the simple (monosaccharides) versus complex (polysaccharides) distinction, which refers to sugars and starches respectively (Eschleman 1996, Jones 1997). As with many dichotomies however, the meaning can be interpreted differently in different situations (Jones 1997). A potato is regarded as 'good' if considered as a vegetable and a source of complex CHOs, while 'bad' when placed in regard to their high glycaemic index. In addition, within the categories there

are problems. Some CHOs are both available and unavailable, there is no consensus on whether complex CHOs include the CHOs in dietary fibre (cellulose, hemicellulose and pectins) (Jones 1997) and there are moderate glycaemic index foods. There are many ways to categorise CHOs, however table 2.2.2.1 shows the main classification of dietary carbohydrates (Baghurst *et al* 1996) according to structure.

Table 2.2.2.1 The main dietary carbohydrates

Please see print copy for Table 2.2.2.1

More protein, more fat and less CHO in the diet may decrease appetite, yet the type of CHO chosen appears to be more important on satiety, than the percent of total CHO eaten (Aronne *et al* 2001). The 'glycaemic index' (GI) of foods is an attempt to categorise different sources of CHO with the same metabolic (blood glucose) response (Jenkins, Wolever, Taylor, Barker, Fielden, Baldwin, Bowling, Newman, Jenkins and Golf 1981, Wolever and Bolognesi 1996, Wolever, Jenkins, Jenkins and Josse 1991, Brand-Miller 1994, Brand-Miller 1995). Foods such as white rice, cracker biscuits or white bread, with reference to GI are categorised as 'high' GI foods indicating that they are likely to quickly deliver its glycaemic impact, producing elevated blood glucose and insulin levels. However, the American Diabetes Association (1999) suggests that the amount rather than source of dietary CHO is clinically more significant for the treatment of type 2 diabetes mellitus, considering that GI concept varies from person to person, and warrants further assessment towards standardisation (Aronne *et al* 2001). Another problem exists in the limited range of foods with a low GI (Hoebler, Karinthi, Chiron, Champ and Barry 1999) suitable for diabetes management. This is further supported by the comparison of CHO-rich foods their ability to produce different insulin responses following injection (Holt, Brand Miller and Petocz 1997). However, taken together with other concepts, this tool shows that not all CHOs are equal.

2.2.2.1.1 Resistant starch

Resistant starch is composed of two polysaccharide forms; amylose and amylopectin, which differ in structure. Amylose is essentially linear, while amylopectin is branched (Annison and Topping 1994) as shown in figures 2.2.2.1.1.1 and 2.2.2.1.1.2 following.

Figure 2.2.2.1.1.1 Amylose structure

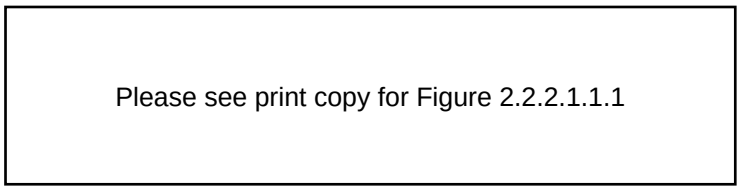
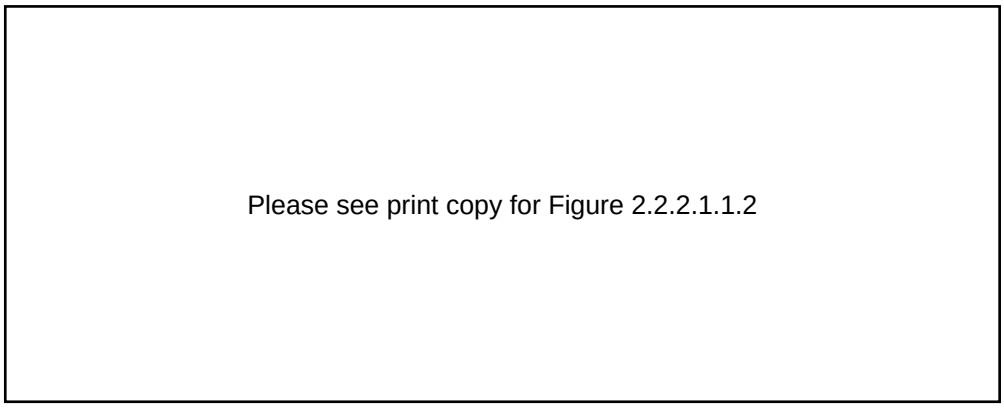


Figure 2.2.2.1.1.2 Amylopectin structure



Resistant starch is a polysaccharide (Crittenden 1999, Baghurst *et al* 1996). A common characteristic that defines RS is that starch or starch fragments remain undigested in the upper gastrointestinal tract (Granfeldt, Drews and Björck 1995). It remains debatable whether RS fulfils all criteria to be classed as a prebiotic (Gibson and Roberfroid 1995, Brown *et al* 1998). Due to its inability to be broken down in the small intestine it is fermented in the colon and produces beneficial effects from stimulating growth and activity of bacteria. It has been proposed that these bacteria act as probiotics, which then provide therapeutic benefits (Goldin and Gorbach 1992). Further examination in to the components of RS show that high amylose starch acts differently due to its lack of enzyme availability (less branched structure). The explanation for this is unknown,

though amylose has a tendency to recrystallize or interact with lipids (Berry 1986, Holm, Björck, Ostrowska, Eliasson, Asp, Larsson and Lundquist 1983).

Resistant starch is a source of dietary fibre (Brown *et al* 1998, Brown 1998) and it appears to act like dietary fibre (Brown 1998), making studies on fibre of interest also. Some time ago, an association was found between dietary fibre intake and improvements in glucose and lipid metabolism in humans (Anderson and Chen 1979). Alterations in glucose and insulin responses have also been shown in studies where the amount and source of CHO, including starches and dietary fibre, were varied (Wolever and Bolognesi 1996). A form of carbohydrate, high amylose resistant starch may be beneficial for people with metabolic syndrome symptoms due to its inability to be digested from the small intestine and smaller energy contribution compared to other carbohydrates, fat and protein (Brown 1998).

Brown (1998) summarises the many affects that high amylose RS promotes through digestion, absorption and physiological performance within humans and animals. These nutritional attributes include:

- Reducing blood glucose and insulin responses
- Lowering available energy
- Promoting bowel health
- Acting as a fermentable substrate for some bowel microflora
- Acting as a functional prebiotic for probiotic organisms
- Increasing the production of volatile fatty acids in the large bowel including

acetate, propionate and particularly butyrate (also known as short-chain fatty acids)

- Increasing faecal output
- Lowering levels of secondary bile acids
- Apparent increase in bowel length
- Source of dietary fibre for coeliac sufferers, and
- Acting like a dietary fibre.

Many of the beneficial effects from RS have been shown to result from the production of short-chain fatty acids through fermentation of dietary fibre, thereby playing a role in bowel health (Anderson and Chen 1979, Alamowitch, Boillot, Boussairi, Ruskone-Fourmestraux, Chevalier, Rizkalla, Guyon, Bornet and Slama 1996). Interestingly, some studies have shown links between colon cancer and insulin resistance (Tran, Gupta, Goh, Mehrotra, Chia, Naigamwalla, Bruce and Giacca 2000; Slattery, Benson, Berry, Duncan, Edwards, Caan and Potter 1997). Food chemists and physiologists have discovered that RS (high-amylose variety) is not readily available CHO (Brown 1996). It is therefore potentially beneficial for people with insulin resistance who have difficulty managing CHO as an energy source.

The relationship between the metabolic syndrome and a diet high in RS is not well understood. The majority of Australia's population consume only 5-7g of RS per day, though the Commonwealth Scientific and Industrial Research Organisation (CSIRO), Australia, are currently recommending 20g daily for benefits from RS on colon cancer prevention. Further interest into the usefulness of this carbohydrate lead to animal

studies and short-term human trials investigating glycaemic control and insulin resistance, where beneficial effects have emerged (Muir, Lu, Collier and O'Dea 1994a; Brown 1998, Byrnes *et al* 1995, Noakes, Clifton, Nestel, Leu and McIntosh 1996). There is reason to believe that such a dietary treatment may help those with these metabolic abnormalities, though no long-term human intervention trial had been performed to reinforce and demonstrate the beneficial effects within free-living insulin resistant humans.

Studies examining the effects of unavailable complex CHO, primarily referring to dietary fibre, have found that by varying the amount of this food component at a meal can decrease hunger and energy intake at the following meal although these effects are modest. Dietary fibre appears to effect intestinal transit time, increase postprandial satiety and perhaps alter glucose metabolism (Rossner, Zweigbergk, Ohlin and Ryttig 1987, Rigaud, Ryttig, Angel and Apfelbaum 1990, and Mickelsen, Makdani, Cotton, Titcomb, Colmey, Gatty 1979 cited in Miller *et al* 1994). Resistant starch may also be a part of these effects seen, given that they are usually inseparable from fibre. However, as the effects have only been modest, if we increase the amount of RS without altering the bulk or energy density of the food, the effect could presumably be even less. This question remains unanswered and is a part of the research presented here. The manufactured form of RS is easily incorporated into foods and does not noticeably alter the texture, volume, density or palatability. If it were able to exert an effect on the metabolism and eating behaviour of overweight people, RS could easily be integrated into a healthy diet.

Studies utilising CHO-rich foods, and in particular, those containing RS, have a limited focus. These include effects in animal models (Wiseman, Higgins, Denyer and Brand-Miller 1996; Kabir, Rizkalla, Champ, Lou, Boillot, Bruzzo and Slama 1998; Zhou and Kaplan 1997), single food tests (Behall and Howe 1995) or studies involving men only (Behall and Howe 1995; Howe, Rumpler and Behall 1996). Meanwhile, the potential health effects from recommendations for bowel health (20g RS/day) need further evaluation with reference to the metabolic syndrome. Resistant starch in the diet also needs to be evaluated in free-living conditions, rather than in short-term studies (Baghurst *et al* 1996) and in both men and women.

Some food sources of RS include whole or partially milled grains and seeds, known as type I RS. Raw potatoes, green bananas, and high-amylose maize are known as type II, while retrograded starch formed during processing of starch or cooked and cooled foods, including bread and Cornflakes, make up type III. Lastly, type IV includes chemically modified starches (Brown, McNaught and Moloney 1995; Crittenden 1999). An increasing number of products are becoming available in supermarkets that contain high-amylose maize; however, the amount of RS in these products and other sources of RS mentioned above remains insignificant.

2.2.2.2 Mechanistic studies

Animal models used to measure metabolic outcomes from intake of RS do not always simulate the effect that RS will produce in humans (Baghurst *et al* 1996). So far, benefits in cholesterol metabolism that are linked to dietary fibre in humans have not been as pronounced in the rat model (Baghurst *et al* 1996). One reason may be that

rats with 'the metabolic syndrome' have not been bred yet. In humans, metabolism and single foods or meal challenges have been investigated, however, Baghurst *et al* (1996) promote the idea that the 'natural' free-living eating patterns are not necessarily studied and may not translate to the same metabolic outcomes, especially when the population studied do not have metabolic disorders. Nevertheless, a brief collection of animal and human studies, relevant to RS follows.

In general, foods containing starch that are more slowly digested and absorbed along the length of the small intestine tend to depress the post-prandial glucose and insulin responses (Jenkins, Wolever, Kalmusky, Guidici, Giordano, Pattern, Wong, Bird, Hall, Buckely, Csima and Alick-Little 1987). Higgins, Vos and Storlien (1998 unpublished findings) reported that the type of complex CHO effects insulin and glucose responses and therefore insulin sensitivity in rats. Starches low in RS cause prolonged elevation in plasma glucose and insulin concentrations compared to starches high in RS. Starch structure appears to have an impact on insulin sensitivity. A rat study comparing glucose and insulin response in amylose and amylopectin diets, over an 8-week crossover design study, showed no significant difference in glucose tolerance between groups. Insulin response however was 50% higher in the high amylopectin compared with high amylose-fed rodents (Wiseman *et al* 1996).

The support for metabolic benefits from RS in animal studies is strengthened by Brynes *et al* (1995) who found that in rats fed high amylose diets compared to those on low amylose diets, insulin responses were smaller. Wiseman and colleagues (1996) found that starches high in amylopectin are absorbed more quickly than high amylose starches.

This rapid absorption of amylopectin appeared to produce a non-reversible insulin resistant state in rats during long-term feeding (Wiseman *et al* 1996), though the extent of insulin resistance may vary in accordance with both type of maize and the age of the animal (Brown 1996). Acute postprandial glycaemic and insulin responses were lower in rats on high-amylose maize starch diet (Byrnes *et al* 1995).

Resistant starch, when fermented in the colon, produces three primary fermentation products called short-chain fatty acids (SCFA). SCFA are the major anions of the colonic (large intestinal) content, primarily in the forms of acetate, propionate, and n-butyrate (Cherbut, Ferrier, Roze, Anini, Blottiere, Lecannu and Galmiche 1998). In humans, the concentration of these is 57:21:22% respectively (Cummings, Pomare, Branch, Naylor and Macfarlane 1987). SCFA have been found to change colonic motor patterns in rats and increase transit rate, with local nerve fibres and polypeptide YY also involved in this effect (Cherbut *et al* 1998). SCFA stimulate polypeptide YY in blood. Intraluminal procaine infusion has been shown to suppress the SCFA effect indicating that a local neural mechanism is involved (Cherbut *et al* 1998). Polypeptide YY works to inhibit gastric emptying and small intestinal motility (Cherbut *et al* 1998) which may be important for production of SCFA.

Each of the SCFAs acetate, propionate and n-butyrate are produced in different concentrations and perform various functions. N-butyrate is a preferred fuel source for colonocytes and cell differentiation, illustrating its role as an effective agent in reducing the risk of colon cancer. Propionate, a SCFA, has been used in the animal model demonstrating its ability to defend against hypercholesterolaemia. Various mechanisms

enable propionate to lower cholesterol (Moundras, Behr, Demigne, Mazur and Remesy 1994). Acetate also appears to have a similar hypocholestolaemic effect (Beynen and Lemmens 1987). A study of fermentable polysaccharides in rats found that dietary fibres known to decrease ileal absorption of bile acids and promote excretion have the most potent cholesterol lowering effect (Moundras *et al* 1994). A summary of how RS compares to soluble and insoluble non-starch polysaccharides is given in Table 2.2.2.2 below. In general, sources of insoluble non-starch polysaccharides, such as wheat are most responsible for faecal bulking and hastening intestinal transit, whereas RS is associated with fermentation reliant actions in the lumen (Muir 1999).

Table 2.2.2.2 Summary of the physiological effects of RS and soluble and insoluble non-starch polysaccharides (NSP) on large bowel function.

Please see print copy for Table 2.2.2.2

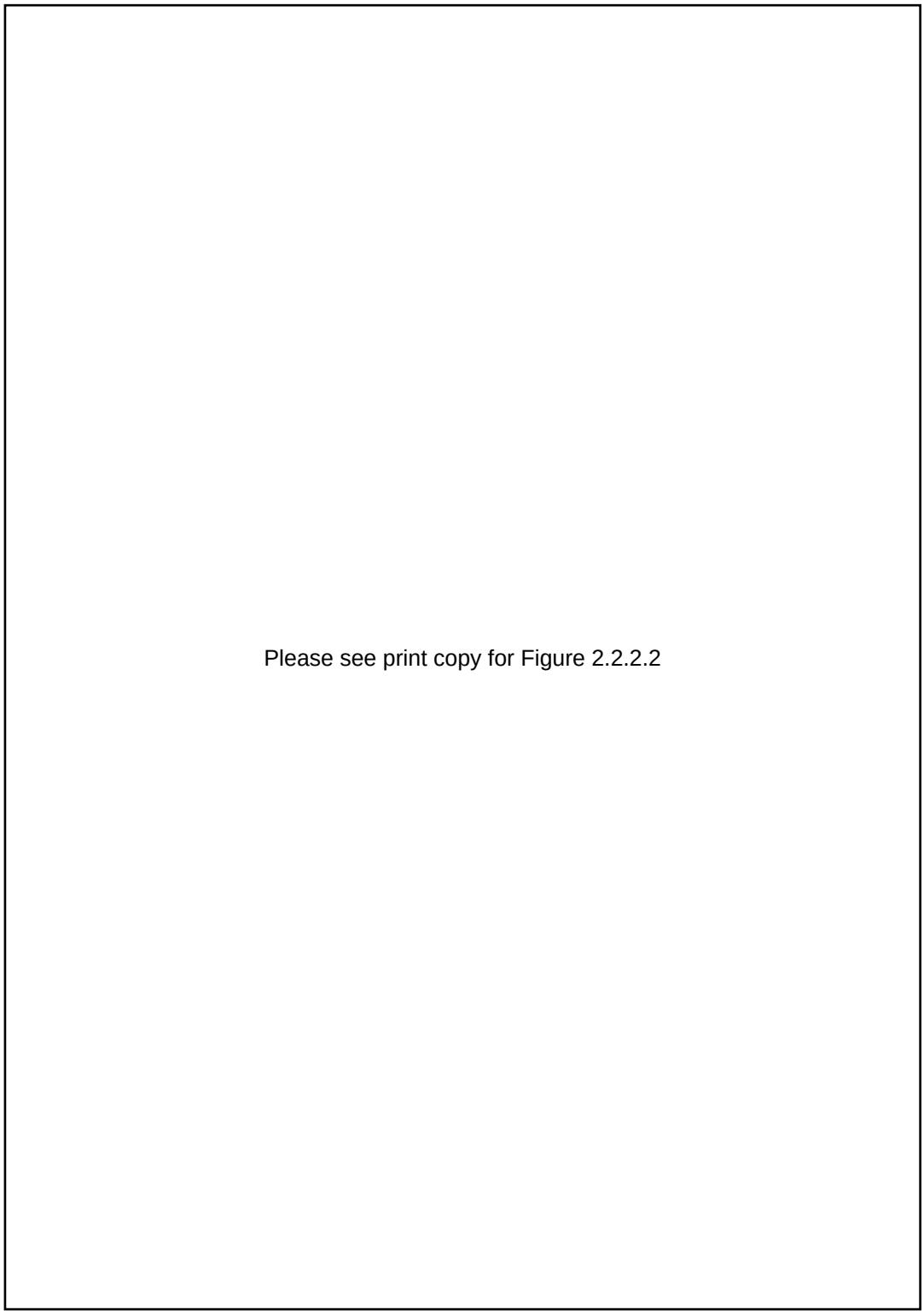
Source: Muir (1999:S17). Abbreviations: short chain fatty acids (SCFA); concentration (conc); positive effect (+); negative effect (-); unknown (?).

Fermentable dietary fibres including RS, create an acidic pH within the gut that help lower cholesterol by limiting the concentration of soluble bile acids. Calcium phosphate

complexes bind to microorganisms, which in turn enhance resorption and steroids subsequently become insoluble (Remesy, Levrat, Gamet and Demigne 1993). However, Crittenden (1999) argues that additional studies are required to conclude that prebiotics, which may include RS, can clearly benefit those with hyperlipidaemia. That is, evidence suggests that fermentation of polysaccharides leading to an acidic pH is not achieved by RS (Crittenden 1999). It is also debated whether RS is a prebiotic (Gibson and Roberfroid 1995). Figure 2.2.2.2 following depicts the metabolic pathways that follow the consumption of RS in humans. Although many of these mechanisms are yet to be linked with the metabolic syndrome, some are (see shaded boxes).

A three-week cross-over design study in 11 subjects comparing 5g to 39g of RS intake (high amylose) per day showed an increase in faecal output and lowered faecal pH following the high RS dietary period (Phillips, Muir, Birkett, Zhong, Jones, O'Dea and Young 1995). This study used weighed food records pre-intervention, and starch in faeces acted as a biological marker of compliance of dietary intake. Significantly, higher concentrations of acetate and butyrate from high RS compared to the low RS diet were observed (Phillips *et al* 1995). Another study showed increase faecal excretion of butyrate from high-amylose maize starch (Noakes, Clifton, McIntosh, Le Leu, Nestel 1995). The amounts of SCFA in faeces may underestimate actual amounts produced in the large bowel and it is suggested that the absorption of SCFA may be augmented at a lower pH in both animal and human models (Sellin, DeSoignie and Burlingame 1993, Phillips *et al* 1995). A change in pH has also been demonstrated to have an impact upon cholesterol metabolism (Remesy *et al* 1993).

Figure 2.2.2.2 Proposed mechanisms of fermentable carbohydrate and short chain fatty acids in human metabolism.



Source: Crittenden RG (1999)

The by-products of RS consumption, SCFAs have been targeted further in animal investigations. Using a 14-day cross-over design, a study in dogs compared the effects of a high to a low fermentable fibre diet (Massimino, McBurney, Field, Thomson, Keelan, Hayek and Sunvold 1998). They concluded that improvements in glucose homeostasis are observed in healthy dogs when they ingest fermentable fibres. They identified an increase in plasma glucagon-like polypeptide 1 (GLP-1), insulin and reduced plasma glucose in high fermentable fibre-fed dogs. Similar positive outcomes have resulted from simply adding SCFA to total parenteral nutrition formulations in rats following 80% small bowel resection (Tappenden, Thompson, Wild and McBurney 1997). The mechanisms postulated for these outcomes are outlined in the respective studies. In summary, the high fermentable fibre diet promoted significantly greater maximal glucose uptake capacity for D-glucose in the jejunum (Massimino *et al* 1998), while the addition of SCFA augmented intestinal proglucagon messenger RNA, GLUT2 messenger RNA, mucosal mass and ileal uptakes of D-glucose (Tappenden *et al* 1997). Glucagon-like polypeptide 1, a gastrointestinal peptide, inhibits glucagon release and gastric emptying and stimulates insulin release. Human studies have shown that when given subcutaneously before a meal, it lowered the postprandial rise in blood glucose concentrations in 12 insulin requiring diabetic patients (Juntti-Berggren, Pigon, Karpe, Hamsten, Gutniak, Vignati and Efendic 1996). However the short circulating half-life of less than one minute limits the clinical utility of GLP-1. The mechanism in which diet modulates proglucagon expression and GLP-1 secretion remains unknown (Massimino *et al* 1998).

The vast effect of various foods and particular nutrients on appetite, eating behaviour, and consequently energy balance, is investigated more readily now with the inception of our ability to measure leptin (Raynaud, Brun, Perez-Martin, Sagnes, Boularan, Fedou and Mercier 1999). Concerning specific types of CHO, our understanding of their contribution to appetite and energy balance is negligible, and inadequate to draw any conclusions (Stubbs, Mazlan and Whybrow 2001). The knowledge that CHO subtypes exert different effects on metabolism (Jenkins *et al* 1981, Wolever 1991, Brand-Miller 1994, Brand-Miller 1995) has emerged in the last two decades and gained real momentum in the literature since. Perhaps the under-developed knowledge in how CHO can abet or impede metabolism is due to the understanding of its dietary roles that have only expanded into several new areas in the last 20-30 years (Schneeman 2001). Traditional roles include the provision of energy and bulk, while new areas include the glycaemic effects of CHO-rich foods; use of fermentable CHO for a healthy bowel; some changes in physical characteristics of gut content, such as viscosity; and provision of a range of physiologically active phytochemicals that may be involved in lowering the risk of chronic disease (Schneeman 2001).

Another reason contributing to the lack of evidence to support the exact effects of various CHOs on appetite, feeding behaviour and energy balance is attributable to there being numerous confounding effects that need to be controlled in such investigations. Effects such as the energy density of foods, presence of other nutrients in foods, the moisture content of food items being compared, sensory or organoleptic attributes of foods, and the psychological, physiological and genetic predisposition of the subjects involved in the investigation (Stubbs *et al* 2001).

2.2.2.3 Clinical and population research

Clinical and population research on the effects of CHO manipulation is useful for insights into the actual attempts to implement some of the mechanistic and animal based findings. Armed with the knowledge that not all CHO's act the same way metabolically and chronic disease progression may be an avenue that this evidence could influence, has lead to a number of studies in CHO-disease relationships.

Research to date indicates that a low-fat, high-CHO dietary prescription appears to attenuate postprandial lipidaemia in those with type 2 diabetes mellitus. That is, hypertriglyceridaemic effect and multiple risk factors for coronary heart disease were accentuated from a high-CHO diet (Chen, Coulston, Zhou, Hollenbeck and Reaven 1995, Berry 1997). The current literature regarding CHOs suggests that slowly digested CHOs in the diet may have significant benefits (Brown 1996) including reduced risk of colon cancer and reducing serum lipids and cholesterol (Crittenden 1999). Resistant starch (high in amylose to amylopectin ratio) may then have a positive role in the dietary treatment of the metabolic syndrome. However, to form strong conclusions, additional long-term, valid, free-range, human studies are imperative. In particular, the dietary intervention that hopes to establish diet-disease relationships requires thoughtful collection and assessment of dietary intake data (Heerstrass, Ocke, Bueno-de-Mesquita, Peeters and Seidell 1998) and adherence. To date, one of the problems associated with the management of diabetes has been the lack of adherence to the diets, such as those high in CHO and low in fat, over a long period (Brinkworth, Noakes, Keogh, Luscombe, Wittert and Clifton 2004, Lo and MacLean 1995, Toobert and Glasgow 1991, Rolls 1995). Similarly, more than 30% of American adults are attempting lose

weight which, given the number of overweight and obese accounts for only half of those that would benefit from weight loss, with many relying on unsafe or ineffective strategies (Kruger *et al* 2004).

In people with diabetes mellitus, the benefit of including less readily digestible CHO may be to aid postprandial effects, that is, slowly absorbed starch containing foods can reduce postprandial insulin responses and improve blood lipids. However, individual foods have primarily been assessed (Muir, Young and O'Dea 1994b). Lintas Cappelloni, Bonmassar, Clementi, Del Toma and Ceccarelli (1995) studied seven males and three female subjects with type 2 diabetes mellitus. Subjects had an average body mass index of 24kg/m^2 and were not on medication for the management of blood glucose levels, but used diet to manage their condition. Subjects were randomly assigned to isocaloric and isoglucidic test meals two weeks apart at lunchtime. All four meals contained between 41-60% of total dietary fibre in the form of non-starch polysaccharides. The first period of *in vitro* starch hydrolysis (20 minutes) was highly correlated with glycaemic plasma responses in this population. Rice and barley meals were similarly digestible, containing starch that was predominantly readily digestible (83-88%) and 6% RS. Pasta meals were less digestible and had higher amounts RS, 14% and 11% for pasta and pasta with fibre respectively. The higher amounts of RS were postulated to be a consequence of gelatinisation and enzyme hydrolysis of the starch during processing.

One study that provided evidence to establish the effects of CHOs, in terms of the GI on diabetes management, and that also completed dietary intake assessments was a

comprehensive trial by Järvi, Karlström, Grandfelt, Björck, Asp and Vessby (1999). This group of researchers investigated improved glycaemic control, lipid profiles and normalised fibrinolytic activity in a dietary intervention trial involving 5 men and 15 women with type 2 diabetes mellitus. The intervention evaluated the effects of two diets, with distinct differences in GI, to establish whether the GI approach is useful in a realistic long-term diabetic diet. Subjects were free-living, with BMI up to 27kg/m^2. The dietary prescription was: 54-55% CHO, 18% protein, 27-29% fat (9% sat, 12% mono, 7% poly) and for an 1820-1880kcal diet, it included 205-215g starch and 34-38g dietary fibre. A low GI (57U) diet and a high GI (83U) diet were only calculated from CHO sources though all food was provided during the study. The study was two consecutive 24-day periods, crossover design. The authors (Järvi *et al* 1999) provided descriptive dietetic methods with all foods weighed and prescribed for appropriate energy levels. The differences in GI were achieved by altering chemical starch structure or botanical food structure within the diets.

The low GI diet showed improved metabolic outcomes, including reduction in circulating glucose, insulin, low-density lipoprotein cholesterol, and normalisation of plasminogen activator inhibitor-1 (PAI-1) and increased insulin sensitivity (assessed euglycaemic clamp) compared to a high GI diet. PAI-1 production could inhibit fibrinolysis contributing to thrombus formation (Sterne 1997). However, improvements were also seen in many of these after the high GI diet. According to the authors, the results seen for the high GI diet were comparable to the average of a meta-analysis of studies using the GI concept whose low GI diets were similar to the value of their high GI diet. Incremental area of calculated glucose and insulin was approximately 30% less

after the low GI diet. Low-density lipoprotein cholesterol decreased in both groups, especially low GI. In both groups, cholesterol and serum apolipoprotein concentration decreased. However non-esterified fatty acid concentration did not change among fasting measures between diets. Non-esterified fatty acid levels were on average 40% higher at 120 and 180 minutes, and 31% lower at the 300 minutes measurement for low GI compared to high GI.

The GI was used in the context of a complete diet, rather than meal challenge and the authors assert that the study indicates that the GI is a useful concept in the management of this chronic metabolic disorder, diabetes mellitus. That is, the low GI diet improves glucose homeostasis and lipid metabolism (Järvi *et al* 1999).

Another study that investigated glucose and lipid metabolism, by means of examining substrate utilisation after short-term feeding, also provided evidence supporting less readily digested CHO. Two groups of healthy males (age 18-34 years), completed two weeks on a diet high in CHO and either low RS or high RS (high amylose) foods, followed by a meal test similar to their intervention diet. Respiratory quotient (RQ) and blood samples were taken post-prandially and analysed for glucose, insulin, free fatty acids, cholesterol and total lipid concentrations. Following the dietary intervention, results indicated a significant decrease in fasting free fatty acids. In the high RS group compared to the low RS group there was a trend for free fatty acids to be higher two hours after the meal challenge and RQ to be lower three hours post-meal (0.09 ± 0.02 vs. 0.95 ± 0.01, $p < 0.03$). The authors state that if the low RS subjects were oxidising 50% fat and 50% CHO, the shift in substrate utilisation in the high RS group would

equate to 67% fat and 33% CHO, suggesting an acute increase in fat oxidation (Higgins *et al* 1998 unpublished).

In contrast, this phenomenon established by Higgins *et al* (1998) could not be demonstrated in hyperinsulinaemic men (Howe *et al* 1996). Their study measured the impact of high amylopectin or high amylose and overfeeding or energy maintenance on 13 hyperinsulinaemic men and 9 control men in a 14-week crossover design. RQ was unchanged by subject type or diet. However, in response to a starch tolerance test, both groups displayed a significant reduction in glucose and insulin ($p<0.04$) response following high amylose consumption.

Another part of the picture that may affect chronic disease progression, such as obesity can be described with respect to CHO and its utilisation compared to other macronutrients. Studies by Abbott, Howard, Christin, Freymond, Lillioja, Boyce, Anderson, Bogardus and Ravussin (1988) and Acheson, Schutz, Bessard, Anantharaman, Flatt and Jequier (1988) found that for both protein and CHO, the rate of oxidation effectively matches intakes of these nutrients. Schrauwen *et al* (1997) have since recognised that even though the storage capacity for fat is 100 times greater than that for CHO, normal weight persons (n=12, men and women) were able to adjust fat oxidation to meet intakes within one week. However, this primarily related to shifting from a low-fat diet (30% energy from fat) to a high-fat diet (60% of energy from fat) while maintaining energy balance. Subjects on average appeared to consume 29 ± 1% energy from fat, 54 ± 2% from CHO and 16 ± 1% from protein. One limitation of this study was that the sole use of one 3-day food record to provide the dietary data.

However support of this concept, in the acute sense, is that some change in substrate utilisation does take place when fat replaces CHO in a meal, as the RQ is primarily associated with the CHO consumed (Flatt 1995).

Hyperglycaemic episodes in diabetic people were no longer believed solely the response to high sugar foods despite Hollenbeck, Coulston and Reaven (1986a,b) linking impaired glycaemic control with a high intake of simple sugar (sucrose). This evidence allows clinicians to offer greater freedom to clients with an obvious affection for sweets or that "cup of tea with one", while remaining conscious that sugar intake warrants discussion in managing insulin resistance. In addition to this, Holt *et al* (1997) measured the insulin score for some foods, compared to the GI method and showed that variation exists among CHO rich foods. However, one of the richest sources of sugar, jellybeans, produced the highest mean insulin score. In contrast, white bread similarly produced a higher score compared to the many foods tested (Holt *et al* 1997). Many other studies have similarly discussed the deleterious effect that sucrose has on the aetiology of insulin resistance and obesity in humans (Coulston, Hollenbeck, Donner, Williams, Chiou, Reaven 1985, Reiser *et al* 1979), and rats (Hallfrisch, Cohen and Reiser 1981). Other studies have shown variable effects on insulin from the consumption of foods high in sugar (Holt *et al* 1997) or impaired insulin action with sucrose feeding in rats (Storlien, Kraegen, Jenkins and Chrisholm 1988).

2.2.3 Protein

Protein is not primarily used for energy, as the body requires this nutrient foremost for its growth and repair functions. Though gaining publicity for its potential weight loss

effect (Skov, Toubro, Rønn, Holm and Astrup 1999), this macronutrient has been investigated far less compared to fat and carbohydrate with respect to metabolic abnormalities. Possibly due to our ability to acutely maintain protein balance and subsequently the reasoning that body weight is regulated by variations when fat and CHO are metabolised (Flatt 1988). Conversely, protein earns its position in the discussion regarding the metabolic syndrome, as one of the aetiologies that may evolve from diabetes mellitus is renal dysfunction; otherwise known as diabetic nephropathy, which requires a low protein intake (Brodsky 1998). To demonstrate the delay in protein research evolution, Munro originally cited the factorial method, the first technique systematically used to estimate a human adult's requirement for protein, in the literature in 1985.

2.2.3.1 Forms and categories of protein

Protein is needed for cell growth and repair, formation of enzymes, antibodies, transport proteins, hormones and other substances that regulate body processes (Eschleman 1996, Read 1997). Compared to fats and carbohydrates, the structure of protein is more varied and complex (Eschleman 1996). Protein is made up of various proportions and combinations of 20 different amino acids (Read 1997, Eschleman 1996). There are ways of classifying protein, such as essential or indispensable and non-essential or dispensable which refers to whether they can be synthesised by the body (non-essential) or only obtained through food (essential) (Eschleman 1996, Read 1997). The daily requirement for protein is actually our need for essential amino acids (Read 1997, Rutishauser 1997). Again, there are problems with attempting to dichotomise, for example, when an impairment in metabolism causes amino acids that are ordinarily

non-essential to become essential (Eschleman 1996). Considering this, and the difficulty in measuring protein requirements accurately (Read 1997) most researchers have discussed their findings simply in terms of protein overall rather than with respect to the amino acid composition of the diet. The following commentary will review some of the research on dietary protein intakes with relevance to this thesis.

2.2.3.2 Mechanistic research

Research surrounding the response to manipulating dietary protein intake has become more prominent since the emergence of evidence supporting weight loss as a consequence of low-carbohydrate, high-protein, high-fat diet (Foster, Wyatt, Hill, McGuckin, Brill, Mohammed, Szapary, Rader, Edman and Klein 2003). Part of the potential for weight loss with a high-protein intake is due to the acute metabolic responses seen in parameters such as insulin. Similarly, by reducing the availability of a cuisine that provides a high glycaemic load, hyperinsulinaemia would be infrequent and perhaps slow the incidence of insulin resistance syndrome (Colagiuri and Brand Miller 2002). Yet there has been controversy surrounding the manipulation of dietary protein in insulin resistant people (Gannon, Nuttall, Saeed, Jordan and Hoover 2003), which could include many overweight individuals.

One animal study compared a low protein intake (~6% of total energy) to a control group receiving approximately 17% of energy as protein over a three-month period. The study showed that the response of the low-protein group to an oral glucose tolerance test gave a lower insulin level (Reis, Carneiro, Mello, Boschero, Saad and Velloso 1997). These researchers believe that the hypoinsulinaemia seen in protein malnutrition is due

to the diminished amount of β-cells and a reduced insulin output per β-cell (Reis *et al* 1997).

Another part of the hypothesis is possibly that the glucose-induced insulin secretion that accompanies malnutrition could reflect a defect in the ability of glucose to increase calcium uptake and/or to decrease calcium efflux from β-cells (Carneiro *et al* 1995 cited in Reis *et al* 1997). Weight loss due to high-protein, low-CHO diets also has an effect on calcium metabolism. It may be postulated, though not proven that calcium leaches from the skeleton to neutralise acidic ketones which may result from this type of diet. A recent RCT comparing the Atkins diet (low-CHO, high-protein, high-fat diet) to a conventional (low kcal, high-CHO, low-fat diet) diet showed that urinary ketones were not significantly different despite similar weight loss in both groups by 12 months (Foster *et al* 2003). Nevertheless, rapid weight loss can accelerate bone deterioration leading to osteoporosis (Aronne *et al* 2001).

2.2.3.3 Clinical and population research

Of late, an emergence in high-protein, low-CHO diets has transpired; encouraged for weight loss and maintenance once a perceived desired body weight is achieved (Skov *et al* 1999). Some of the benefits from a high-protein compared to a high-CHO diet over a six-month intervention in an overweight population, were greater weight loss, greater fat loss, and significantly improved triglycerides and free fatty acids (Skov *et al* 1999). However, the high-protein diet (25% protein as energy) meant to be assessed with urinary nitrogen, was not reported on within the article. In addition, the total energy

intakes of the high-protein group were lower throughout the trial, compared to the high-CHO group, making the authors conclusions less straightforward.

A diet high in protein may manifest in people consuming fewer CHOs. If people reduce or limit their CHO intake, their blood glucose levels would decline, the pancreas would not need to produce the insulin response required when given high-glycaemic loads, and a shift towards mobilising fat stores or circulating fatty acids or even ketosis as seen in the 'Dr. Atkins' New Diet Revolution' diet, would result (Aronne *et al* 2001). This explanation is plausible, though still requires energy manipulation which may be challenging, especially since protein is readily found in foods that contain saturated fats or are energy dense, such as sausage meats, full cream dairy foods, and peanut butter. Increasing protein intake usually increases saturated fat intake, leading to the aforementioned deleterious effects (Wolever 1999). Aside from this, animal protein has been shown to increase cholesterol, though vegetable proteins do not (Carroll 1982 cited in Wolever 1999).

High protein consumption promotes the progression to chronic renal failure (Walker, Bending, Dodds, Mattock, Murrells, Keen and Viberti 1989 cited in Wolever 1999). However, this does not indicate that a low-protein diet should be consumed. In humans with diabetes, where there is an insufficient concentration of insulin, dietary protein restriction would be detrimental despite concerns for diabetic nephropathy, as there would be greater losses in body protein (Nair, Ford, Ekberg, Fernqvist-Forbes and Wahren 1995). In addition, detrimental effects have been shown in free-living insulin-dependent people with diabetes consuming a moderate dietary restriction of protein to

0.6g/kg of ideal body weight per day over a three-month period (Brodsky 1998). The effects seen included an increase in adiposity during weight maintenance and reduced muscle strength (Brodsky 1998).

2.3 Establishing the ideal nutrient mix

From the preceding synopsis of evidence surrounding diet-disease relationships, it appears that chronic diseases are affected by dietary treatments. However, many variables warrant consideration in the promotion of an optimal nutrient mix for these conditions, as far reaching as the cut-off points for diagnosis to the impact of lifestyle on trial attrition or adherence to dietary regimens.

There continues to be disagreement on the importance of amount versus the sources of nutrients and energy, however where mechanistic and animal research comes to fruition in the context of free-living human trials, the distinction between many of these variables is blurred. In addition, measurement at this level is often compromised due to the great deal of variability introduced and the lack of control over feeding (Blundell and Stubbs 1997). People that are obese or insulin resistant are likely to vary in the severity of their condition and co-morbidity status. This variability probably contributes to individualised treatment being more successful than general advice (Tuomilehto *et al* 2001, DPP 2002). Recommendations need to be adapted to the patient's circumstances and ability to adhere to certain dietary and lifestyle regimens (Aronne *et al* 2001). Despite these problems, human studies produce the necessary evidence for public health initiatives. To begin, if we endeavour to come up with a prescription that is feasible and flexible enough to adjust for differences in humans who are at risk of the metabolic

syndrome, then the following characteristics would be worthy of consideration. The macronutrient composition of the diet can affect food intake, body weight, body composition, hunger and satiety (Rolls 1995).

The balance of evidence suggests that diets high in fat and saturated fat produce insulin resistance (Storlien *et al* 1997), promote fat storage as adipose tissue (Flatt 1978, Hill *et al* 2000), are less satiating (Blundell *et al* 1993, Green *et al* 1994), do not immediately shift to greater oxidation as fuel (Surina *et al* 1993) and are poorly mobilised once stored (DeLany *et al* 2000). If the diet is high in the polyunsaturated fat n-6, interference with glucose metabolism is also reported (Kraegen and Storlien 1989) while n-3 fatty acids enriched diets benefit insulin action (Storlien, Baur, Kriketos, Pan, Cooney, Jenkins, Calvert and Campbell 1996a). Diets that are moderate or low in fat (<30% energy) remain suitable (Hill *et al* 2000). Yet, up to 37% of energy as fat, predominantly monounsaturated fatty acids (that is 23% of energy) and low in saturated fat (< 8% of energy) can also be beneficial for insulin sensitivity (Vessby *et al* 2001).

Compared to fat, the evidence surrounding the amount of CHOs appears to be far more controversial (Daly, Vale, Walker, Alberti and Mathers 1997). Research reports that high-CHO diets attenuate hypertriglyceridaemia (Chen *et al* 1995, Berry 1997), one of the components of the insulin resistance syndrome (Reaven 1988a). As the type of fat within a moderate fat diet becomes more important, so do the types of CHOs on clinical outcomes (Aronne *et al* 2001).

Evidence is building that supports that, CHOs, such as dietary fibre, when consumed, are accompanied by a slow rise in glucose and insulin (Jenkins *et al* 1987), and may promote improvements in lipid metabolism (Anderson and Chen 1979). Complex CHOs that are not readily available for energy also have the capacity to decrease hunger and energy intake at a subsequent meal possibly due to their effect on intestinal transit time and increase postprandial satiety (Rossner *et al* 1987, Rigaud *et al* 1990 and Mickelsen *et al* 1979 cited in Miller *et al* 1994). Further, fermentable CHO's, such as RS, may lower pH (Phillips *et al* 1995, Noakes *et al* 1995) consequently improving cholesterol metabolism (Remesy *et al* 1993) and may produce an acute shift to greater fat oxidation than readily absorbed CHO (Higgins *et al* 1998). Last, sucrose, a readily digestible CHO, has been shown to impair insulin action in rats (Storlien *et al* 1988), and when consumed in a food form such as jelly beans, produce a significantly high insulin response to its intake compared with other foods (Holt *et al* 1997). Perhaps this insulin response is one of the reasons for CHOs oxidation matching its intake readily also demonstrated with protein (Abbott *et al* 1988, Acheson *et al* 1988).

Protein is not a primary nutrient used for energy, and while high-protein diets have received recent attention for the potential to encourage weight loss (Skov *et al* 1999), its increase may accelerate bone deterioration and osteoporosis (Aronne *et al* 2001). Likewise, too little protein may lead to protein malnutrition and reduce insulin output from β-cells (Reis *et al* 1997) or increase adiposity during weight maintenance and reduce muscle strength (Brodsky 1998). Further, support for moderate protein intake stems from evidence surrounding high protein consumption promoting the progression to chronic renal failure (Walker *et al* 1989 cited in Wolever 1999). Increasing protein

intake usually increases saturated fat intake, leading to the aforementioned deleterious effects. Aside from this, animal protein has been shown to increase cholesterol; vegetable proteins do not (Carroll 1982 cited in Wolever 1999). Overall, body weight regulation is believed to be more affected by variations when fat and CHO are metabolised than protein (Flatt 1988).

An interpretation of the overall message from the abundant research on this diet-disease relationship could be simplified as follows. Within energy balance, the moderate intake of CHO, fat and protein remains preferential, as increasing intakes have the potential for producing deleterious effects on metabolism. Casting our focus on the types of each macronutrient, protein is less well documented, though fat and CHO sub-types will exert a substantial effect through various pathways. Saturated fat, trans-fatty acids, n-6 fatty acids, and readily available CHO appear to be detrimental in excess and may influence the results of dietary intervention trials.

2.3.1 The impact of foods and cuisines on the diet-disease relationship

As with the conversion from mechanistic studies to human feeding trials, there is another translation to be made. That is, repackaging the information from nutrient into food or cuisine forms, which again introduces variability. Some studies have already touched on this area. One study on mortality in fifteen cohorts over twenty years (Huijbregts *et al* 1997) examined the World Health Organisation (WHO) guidelines for prevention of chronic disease. Results showed that healthy eating was associated with reduced mortality in men (13%) aged 50-70 years. Based on this evidence, the researchers also felt that dietary patterns as a whole are more important than a specific

dietary component or single nutrients in relation to mortality. Similarly, a study focussing on the effects of foods on a metabolic indicator of diabetes by Ekblond, Mellemkjær, Tjonneland, Suntum, Stripp, Overvad, Johansen and Olsen (2000) advocated the use of foods rather than nutrients in building evidence.

Evidence from Dutch and Finnish males cohorts from the Seven Countries Study, where a 30-year follow-up survey was administered, showed that certain food categories, such as fish, potatoes, vegetables and legumes, protected against type 2 diabetes mellitus (Feskens, Virtanen, Rasanen, Tuomilehto, Stengard, Pekkanen, Nissinen and Kromhout 1995 cited in Ekblond *et al* 2000). Contradicting these, a prospective study in women promoted evidence that the development of this disease does not appear to relate to specific foods or macronutrients (Lundgre, Eengtsson and Blohme 1989 cited in Ekblond *et al* 2000). However, the role of foods on type 2 diabetes mellitus progression was supported by a large cross-sectional study (Ekblond *et al* 2000). Their findings indicated that poultry, fruit and cereals appeared to be protective against glycosuria, a predictor of type 2 diabetes mellitus (Ekblond *et al* 2000).

A theory surrounding sugar consumption with respect to colon cancer and circulating insulin levels has also evolved (Shapiro 1998). One particular study showed that sugar intake was associated with biliary tract cancer, thought to be a consequence of increased gallstones that increase the risk for this type of cancer (Moerman, de Mesquita and Runia 1993). In addition, according to Edward Giovannucci, an injection of insulin into laboratory rats with colon cancer appeared to promote the tumour's progression (Shapiro 1998). Perhaps this is a consequence of a diet high in animal fat, less fruit and

vegetables and higher processed food consumption, already related to both disorders (Shapiro 1998). This hyperinsulinaemia–cancer disease relationship could account for the correlation between a typical Western diet and colon cancer, though lacks sufficient evidence to prove such a theory (Giovannucci quoted in Shapiro 1998). It is also believed that the fructose component of sucrose (sugar) is responsible for an increase in triglycerides from the liver, transported in very low-density lipoproteins (Reaven 1988b). Interestingly, this appears to further link RS with potential benefits in states of insulin resistance, as RS has been shown to reduce the risk of colon cancer. The gap in knowledge between insulin resistance and a Westernised diet continues to prompt further research, while our understanding on the pathology of such chronic diseases grows simultaneously.

The previously mentioned mechanistic and animal studies have provided many reasons to continue investigating the manipulation of the types of CHOs, such as RS, in our attempts to achieve an optimal diet for the metabolic syndrome. Few human studies have been published that assess the effects of high amylose RS on disease. A study such as Järvi *et al* (1999), invoke a plausible explanation for how available CHO impact on metabolism in a free-living context. High-amylose maize starch is not readily available in the small intestine; hence the available energy will be reduced compared to starch that is fully digestible in the small intestine (Brown 1996). Starch acts as a substrate for microbial fermentation, on which microorganisms that produce SCFA, rely upon. Postprandial insulin output was reduced by 15% after a meal that had 33% of its CHO as high-amylose maize starch compared with low-amylose maize starch control (Noakes *et al* 1995). Thereby, high-amylose maize resistant starch is again suggested to be

beneficial in reducing insulin requirements in an IR population. Despite this, no studies have illustrated significant weight loss in subjects as the result of consumption of RS, though the lack of evidence for this is believed to be almost certainly a consequence of the limited length of measured intervention time (Brown 1996).

Resistant starch has received attention for its benefits in bowel health and cancer rather than its role in glucose, lipid metabolism and insulin responses (Baghurst *et al* 1996). Of the investigations and indicators of disordered metabolism, RS has fundamentally been compared to other starches and non-starch polysaccharides in humans and in rats. However, long-term dietary intervention is lacking. In addition, a factor that confounds metabolic research in humans is the way dietary information is collected and analysed. Therefore, an objective of this study is to present clear dietary intake data. The present study also will discuss whether the introduction of high RS foods is sustainable over a 3-month intervention period in an IR population.

Australians consume approximately five grams of RS daily, though in a review compiled by Baghurst *et al* (1996), 20g/day was recommended to deliver bowel health advantages. The potential health effect from this amount of RS needs to be evaluated in free-living conditions, rather than short-term studies (Baghurst *et al* 1996). Health effects that warrant further research include metabolic and hormonal processes and satiety (Baghurst *et al* 1996). Continued efforts to expose a dietary regimen that is optimal for management of the metabolic syndrome also requires further attention.

In summary, insulin resistance is identified as the origin or link between these disorders, collectively known as 'the metabolic syndrome' (Defronzo and Ferrannini 1991; Modan Halkin, Almog, Lusky, Eshkil, Shefi, Shitrit and Fuchs 1985). This disease exhibits a cycle, for example, people with type 2 diabetes mellitus experience impaired CHO, fat and protein metabolism (Krentz 1996; Moore 1997) and in turn, or as a result, elevated postprandial glucose and insulin from high-CHO diets contribute to the development of insulin resistance (Byrnes *et al* 1995). The detrimental repercussions of high circulating fatty acids on insulin resistance are part of this complex system. Dietary manipulation is therefore appropriate to consider in treatment and "the challenge is to put the complex pattern of evaluation and care together and deliver it, appropriately customised, to all who need it." (Keen 1997:xxiii)

3. Methodology

The previous chapters outlined three broad areas including, how evidence is established and the diet-disease relationship from both biological and sociological aspects for consideration in clinical prescriptions by health professionals. All of these have an effect on the data generated for the dietary management of disease. From this summation of the literature, we can recognise that our efforts are best utilised within an interdisciplinary framework in research (Tobin and Miller 2001), thereby addressing both the feasibility and efficacy in dietary management of disease. Using as a case study, the impact of a high amylose RS intake on clinical indicators of the insulin resistant syndrome, the combination of approaches used to establish holistic evidence can be demonstrated. The first part of this methodology is given to dietetic issues such as how we may better address the problem of mis-reporting dietary intake. This is followed with the development of methods to measure the social context of diet-disease relationships. Next, the intervention itself is provided, whereby the physiological and anthropometrical parameters are described in the context of a RCT.

3.1 The randomised controlled trial: establishing the evidence

As discussed previously, the RCT is seen to provide the ultimate evidence for treatment strategies. Thus, it is appropriate to apply a RCT methodology in the study of RS in the metabolic syndrome. Within this syndrome, obesity is associated with many lifestyle-related diseases. This suggests that understanding the relationship between diet and obesity will be problematic. Broadening the type of methods used to establish clinical evidence is imperative in human investigations. This thesis is based on an analysis of data derived from a RCT assessing the feasibility and effectiveness of a high resistant

starch diet that is consumed under 'free living' conditions, on the metabolic outcomes in insulin resistant subjects.

In addition to formulating a set of research questions, a robust study design is required to verify whether RS has a potential place in the dietary treatment of the metabolic syndrome. This chapter on methodology outlines considerations for the study designs and subsequently for methods applied throughout the study. In human studies both validated physiological and biochemical measures are available. However, measures that capture the fluid nature of diet, life history and other metabolic variables, should be assessed by methods that mimic or comprehend their fluctuating characteristics.

With reference to duration of the trial, assessing the feasibility and efficacy of RS in an overweight population, moderate to long-term studies would be required. A number of chronic dietary intervention trials in humans have investigated the effects of two diets high in either soluble or insoluble dietary fibre (Wolever, Hegele, Connelly, Ransom, Story, Furumoto, and Jenkins 1997). For example, a study conducted by Wolever *et al* (1997) investigated the effects of dietary fibre intakes on dyslipidaemiain using a 4-month crossover design separated by 2 months wash out period in 32 otherwise healthy men and postmenopausal women. The authors classified 15 weeks as sufficient time to establish chronic effects. The meal challenge test day included 10 consecutive hourly plasma measures. It was interesting to note however that the meal challenge test day included in their research was administered within the final two weeks of the intervention, though a contradiction to this was made in the methods of the manuscript. If the former is true, plasma measures were taken at approximately week 13. In the

current study, meal challenges will be completed within one to two weeks of completing 12 weeks of daily consumption of the intervention foods. Similarly, 10 consecutive hourly measures will be followed.

Kennedy, Bowman, Spence, Freedman and King (2001) have reviewed some of the studies on popular diets and their relationship to health, nutrition and obesity. The following table (Table 3.1.1.1) adapted from literature in the Kennedy *et al* (2001) review, addresses, in part, the rationale behind the use of 12 weeks for a dietary intervention trial on metabolic profile adjustments.

Table 3.1.1.1 Duration of study used in dietary intervention trials manipulating dietary intakes in overweight and obese subjects

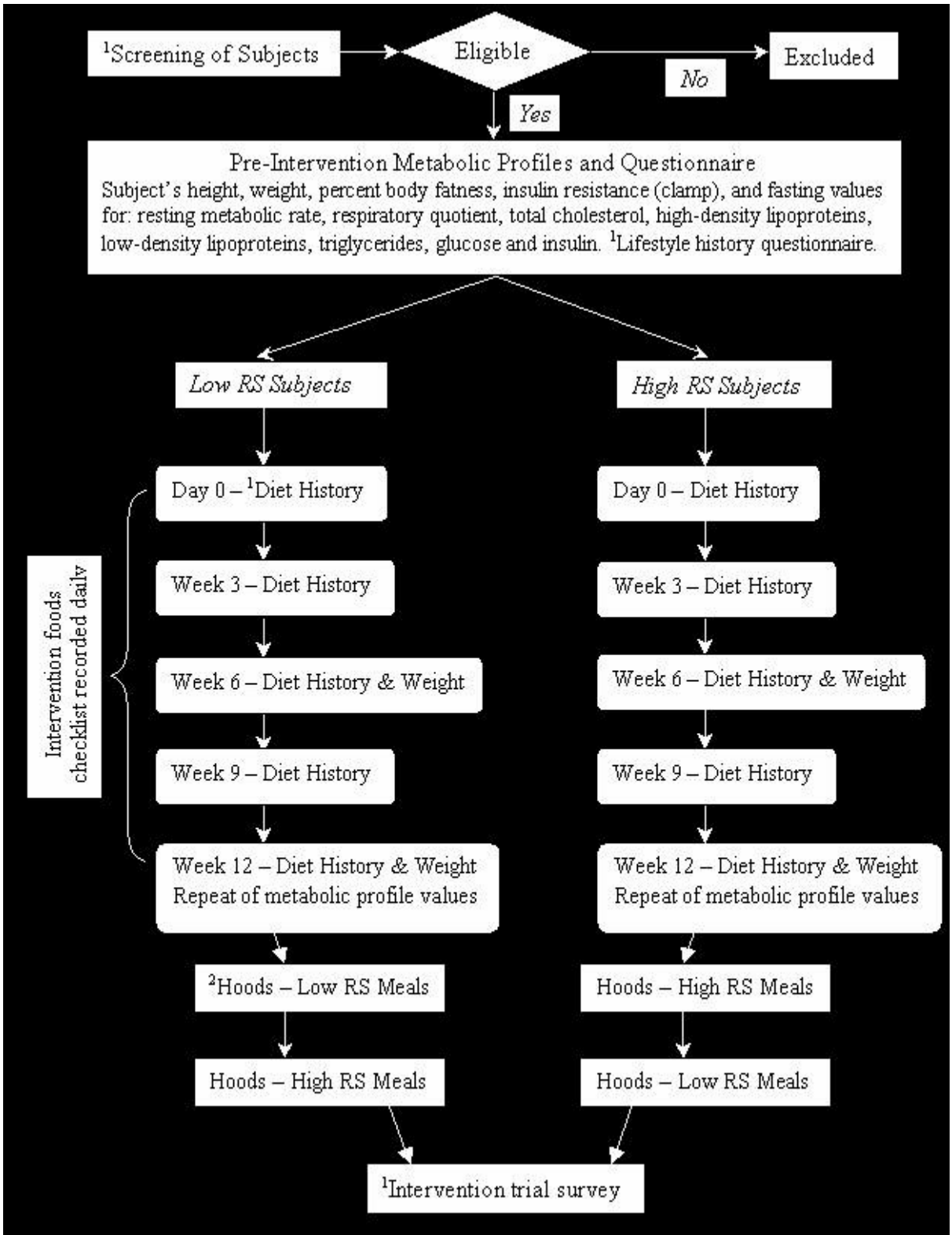
Please see print copy for Table 3.1.1.1

Please see print copy for Table 3.1.1.1

The average number of participants in these trials, excluding Barnard *et al* (1992) who studied thousands of participants for a three-week period, was 20.76 participants. Studies of 12 weeks duration, shown in six of the aforementioned references, were common among studies that investigated overweight participants and their body composition changes and therefore seemed reasonable for the proposed intervention trial. In addition, a multi-national trial between five centres on the effects of dietary fatty acids on insulin sensitivity used a trial of 90 days in duration to examine this relationship (Vessby *et al* 2001). This study used 162 healthy subjects ranging from normal weight to obese (BMI 22-32kg/m^2) and isoenergetic diets.

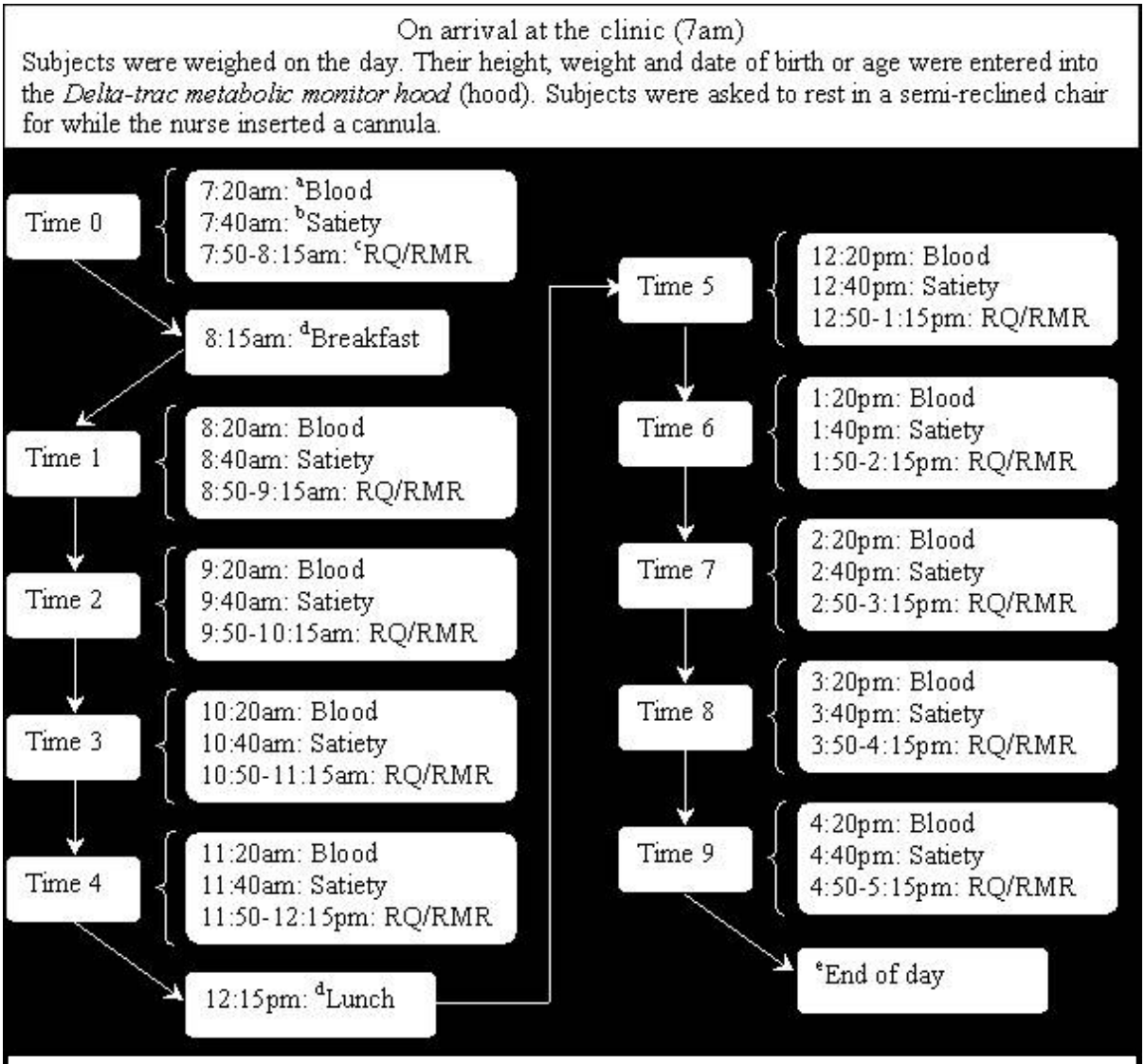
The design of the study in this thesis is displayed graphically in figures 3.1.2 and 3.1.3. During the course of the study for each participant, the three month commitment to the intervention was preceded by a screening questionnaire (appendix 1) and screening blood glucose test, height and weight measures, completed in the morning following a 12 hour fast. The recruitment of subjects was staggered over a period of 12 months for (July 1999 to July 2000). As clusters of subjects were randomised to both groups, this reduced bias due to seasonal differences between groups.

Figure 3.1.2 Summary of intervention trial study design.



[1] The screening criteria, lifestyle history questionnaire, diet history protocol and the intervention trial survey were developed through the research completed in the methods development phase.
[2] The hoods occurred on completion, with ~1 week in between. The protocol is shown in figure 3.1.3, following.

Figure 3.1.3 Summary of acute, meal challenges study design. Both days completed by all participants were identical, differing only in the content of high-amylose maize resistant starch in the foods. The following is a timed example of a typical schedule.



[a] All blood was collected in EDTA tubes, centrifuged immediately, and plasma drawn off for analysis of glucose, insulin, total cholesterol, high-density lipoprotein, low-density lipoproteins and triglycerides at time point zero, then, glucose, insulin and triglycerides at each subsequent hourly interval.

[b] Satiety scales used to measure satiety are shown in Appendix 9.

[c] Respiratory quotient (RQ) and resting/postprandial metabolic rate (RMR) data was immediately checked for correctness and averages for the final 15 minutes of each session calculated.

[d] Breakfast and lunch ingredients and overall nutritional values are shown in Appendix 6.

[e] Participants were offered more food of beverages before leaving the clinical area. Connecting pieces, ventilation tubes and hoods were washed with warm soapy water and methylated spirits.

To examine the long-term effects of high amylose RS, an intervention trial of approximately 12 weeks in duration would be required. In addition, meal challenges would be required to examine acute effects. The study population would have characteristics of the insulin resistant syndrome so that application of any outcomes would address the appropriate population and prevention or management of this disorder. The test diet should contain 20-25g of high amylose maize starch to be compared with approximately 5g of various types of resistant starch in the control diets. Metabolic variables of interest include fasting and meal-based insulin, glucose and lipid concentrations, metabolic rate, substrate utilisation and satiety. Long-term outcomes include similar plasma values at the fasting level, insulin sensitivity and body fat content.

The subjects were not in a weight loss trial, as this would have promoted greater variability depending upon the amount of weight lost prior to the acute meal challenge. It was also the aim of the investigator to assess cholesterol following an intervention using RS so as to assess its impact in an overweight group. This would not have been possible in the context of a weight loss trial due to the fact that even mild weight loss can reduce total cholesterol levels (Di Buono 1999). The question of cholesterol lowering was important also in the domain of a trial manipulating CHOs, as this macronutrient has previously been labelled as having a detrimental affect on cholesterol profiles, which required clarification in this research alike.

People are not simply cultured cells and are not forced to comply with identical raring strategies that are employed in animal models, where there are tight controls such as

measurement of intake over all aspects of the experiment. However, through these forms of research, scientists have both developed validated physiological and biochemical methods to classify deviation in human responses. In addition, we have ethnographic measures that capture the variable and fluid nature of diet, life history and other metabolic mediators with methods that mimic the nature of humans. Human metabolic responses to dietary manipulation are diverse though usually discussed with reference to the way in which the manipulation can influence one or two metabolic parameters. If we consider that there is a reason why each person varies from one another at the outset, and consequently their response to feeding varies, then simplifying research methods does not reflect nor preserve human characteristics and scientific evaluation.

3.1.1 Aims and hypotheses

Aim: To establish the evidence for practice in medical nutrition therapy information from both objective scientific research and naturalistic observations needs to be considered.

Hypotheses: The central hypothesis is that for evidence based practice to have relevance there is value in collecting this evidence from both quantitative and qualitative research methodologies.

Specific research aims and their respective hypotheses:

1) *Aim:* To demonstrate variation in reporting of dietary intake.

   Hypothesis: Patients in an intervention trial will report evidence of variation in dietary habits;

2) *Aim:* To identify human lifestyle characteristics of participants that may affect the feasibility (compliance) and efficacy (metabolic improvements) of chronic disease management.

   Hypothesis: Based on lifestyle factors, patients will report a range of barriers to dietary compliance;

3) *Aim:* To identify and compare following an intervention, changes in insulin sensitivity, fasting substrate utilisation, glucose, insulin, lipids, body composition and food patterns.

   Hypothesis: There will be significant differences in metabolic and dietary profiles between subjects randomly allocated to a high RS group or the low RS, control group;

4) *Aim:* To evaluate the acute (1-day) impact of meals representative of the intervention by measuring substrate utilisation, lipid, glucose and insulin metabolic responses and satiety profiles.

   Hypothesis: There will be a significant difference in metabolic response to acute challenges of meals differing in RS amounts;

5) *Aim:* To compare differences in reported dietary intakes between groups in the intervention trial.

   Hypothesis: There will be significant differences in energy and nutrient intakes between dietary groups in an intervention study;

6) *Aim:* To assess the validity of reported dietary intakes during the intervention trial.

   Hypothesis: There reported dietary intakes during the dietary intervention trial will be valid for energy.

3.2 Methods development

Energy balance is an important aspect of many nutrition related health concerns (Wahlqvist 1986), yet it is unable to address the impact of dietary patterns on disease progression. An interaction of macro- and micro- nutrients takes place when we consume food (Huijbregts *et al* 1997, Leahy *et al* 1999). Therefore, as people consume foods and not nutrients, we need to continue research into the effects of foods on chronic diseases (Ekblond *et al* 2000). Indeed, we already appreciate that the types of food and the range of nutrients consumed are all important in influencing insulin action (Storlien *et al* 2001). In particular, evidence shows that certain food categories, such as poultry, fruit, cereals (Ekblond *et al* 2000), fish, potatoes, vegetables and legumes (Feskens *et al* 1995) are protective against the chronic degenerative disease; type 2 diabetes mellitus (Feskens *et al* 1995, Ekblond *et al* 2000).

The previous studies may have been limited to food categories selected by the researchers, thereby reducing the variety of responses. Dietary variety augments the adequate supply of essential nutrients while reducing the likelihood of excess exposure to adverse dietary factors, such as excess sodium intake in people with high blood pressure (Wahlqvist 1986). Hence, the completeness of data on food consumption is becoming more important in all forms of health research. The quality of data collected on aspects of dietary intake are improving with both the development of the methodologies used (Tapsell *et al* 2000) and computer software, such as *FoodWorks* (v2.10.136, Xyris Software) that accommodate for the complexity of food composition. However, inaccuracy in reporting dietary intake remains a primary limitation of

understanding diet-disease relationship (Tapsell *et al* 2000, Tapsell *et al* 1999, Johnson 2000).

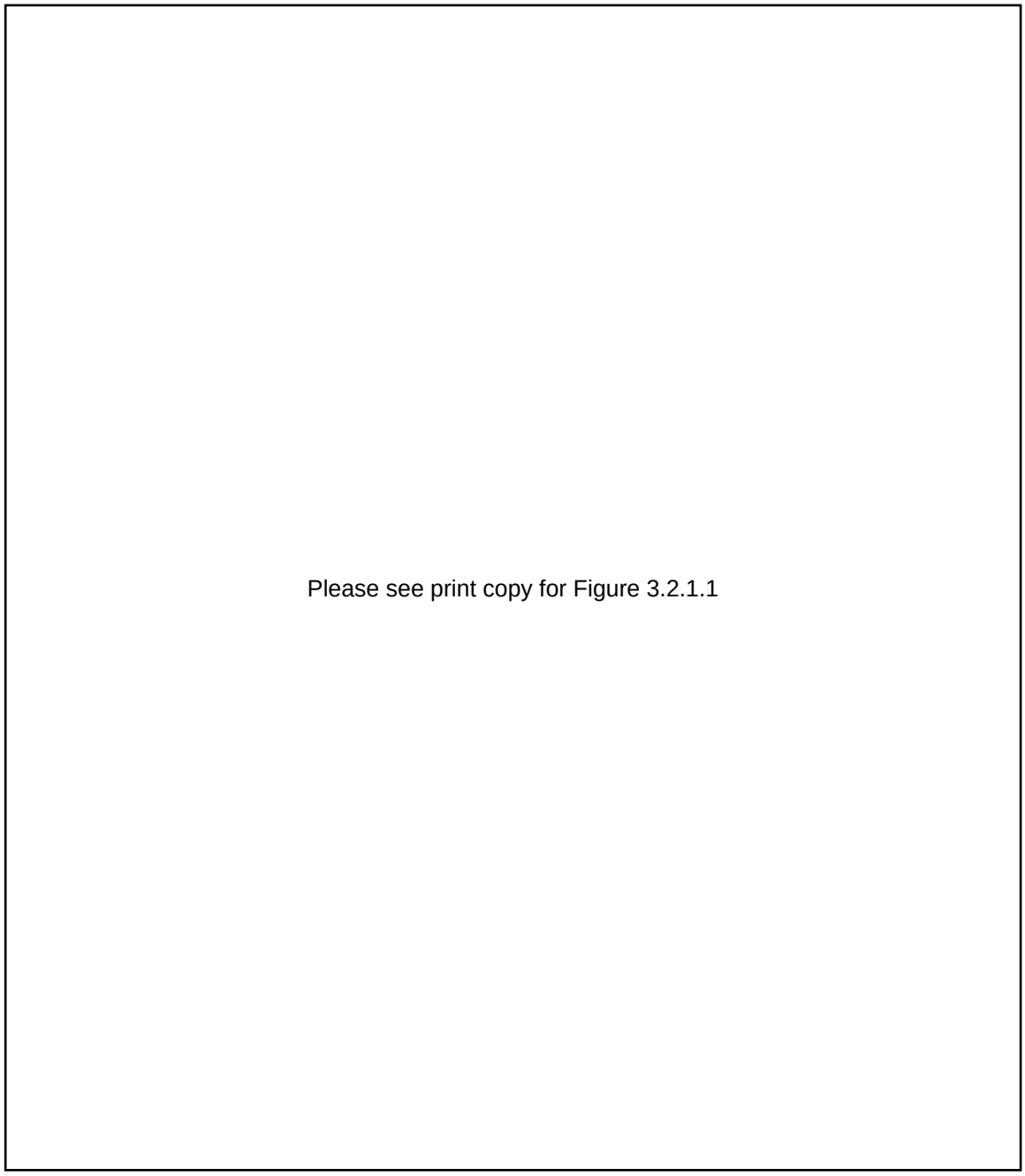
There is limited understanding about the relationship between the initiation of chronic diseases, such as type 2 diabetes mellitus, and dietary patterns or food nutrients (Ekblond *et al* 2000). To add to the challenge of such studies is that lifestyle characteristics are also believed to influence meal patterns and disease status (Wing *et al* 2001). To fully understand this relationship between diet and disease, comprehensive sets of dietary data, that allows the researcher to appreciate the meal-related context in which foods are consumed, warrants investigation. The following methods development aim to promote interviews conducive to the accurate and complete reporting of usual dietary intake. In addition, the survey instrumentation was developed to account for the relevant social or lifestyle context of manipulating and reporting of dietary intake, adding another perspective for the outcomes from the subsequent RCT.

3.2.1 Diet history interview

Inaccurate reporting of dietary data is a real problem in nutrition research. A sociological window into how people might mis-report, can be studied using conversation analysis (CA). This technique was appropriate to use on the DH, as its basic theoretical position is that "social actions are meaningful for those who produce them and that they have a natural organization that can be discovered and analyzed by close examination." (Psathas 1995:2). By analysing recorded diet history interviews in this way, interview techniques could be developed to improve accuracy of reporting. Components of the CA process are illustrated in the following flow diagram (Figure

3.2.1.1).

Figure 3.2.1.1 Process of conversation analysis



Sources: Tapsell, Brenninger and Barnard (2000:820) Reprinted with permission from JADA.

In developing a diet history method for use in the RCT, CA was applied to data collected under a pilot study.

a) Subjects and recruitment

Four sets of archival tape recorded interview data from a study comparing energy expenditure from calculations based on doubly labelled water excretion with energy intake from DH interviews (Raaschou 1997) were originally available. This data set was supplemented with an additional ten subjects recruited under similar conditions for studies, completed by two dietetic students (Barnard JA, Brenninger, VL) for energy balance and dietary methodology research respectively. All volunteers were English speaking, non-pregnant, and relatively healthy, recruited from the Illawarra population through advertisement (Table 3.2.1.2).

Table 3.2.1.2 Characteristics of subjects (n = 14)

Please see print copy for Table 3.2.1.2

b) Data collection procedures

Diet history interviews were video-taped and audio-recorded. All tapes were transcribed, verbatim, by an external source. The transcripts were analysed qualitatively using the CA method described in figure 3.2.1.1. Brenninger, VL, completed analysis with the support of Barnard, JA, Tapsell, LT and Gardener, R (an independent researcher of the school of linguistics), during analytic sessions with the recordings and

their respective transcriptions. Brenninger viewed videotaped recordings for analysis of non-verbal communication (data not shown).

During the DH interview, the dietitian made available plastic food models, figure 3.2.1.2, a food portion book and a product information folder that displayed a range of current supermarket foods labels. The audiotapes were 90-minute high position (TDK SAX high position IEC II/ Type II 90) and videotapes were TDK HS180 (VHS E-180/ 258m) high quality standard videotapes. Of the interviews, one of the subset of ten participants was not successfully recorded on the videotape.

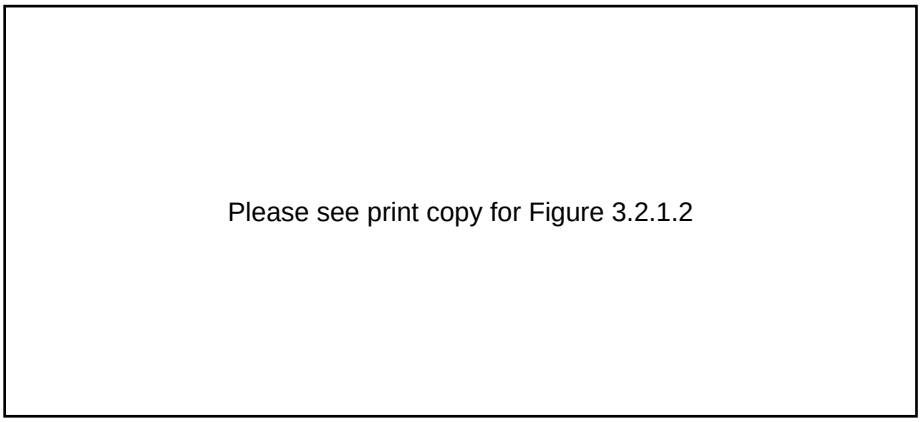


Figure 3.2.1.2 Diet history interview in progress.

c) Data analysis

All analyses were performed by at least two researchers and key observations were established by consensus. Notes were made on the transcripts for the following identifiable traits as they appeared:

i. Phases in DH interview, for example, breakfast, lunch, and dinner.
ii. For each meal component, which of the two parties indicated the meal category.
iii. Hesitation and pauses in the interactions, verified by visual evidence.

iv. Repaired statements.

v. Offer of information on quantity of food or beverage, frequency eaten, and type or brand.

vi. Discussion of food ideas, displays of nutritional knowledge and other talk not directly food listings.

vii. "Marked talk" such as the offer of a reason for the foods eaten; additional information (stories); hesitations, pauses and laughter attached to the talk surrounding foods or quantity and amounts consumed.

viii. Evidence of collaboration or negotiation between the subject and dietitian, for instance, by reference to food models and portion size photographs to provide the estimated amount usually served and eaten.

ix. Simple "Listing" of foods. These were utterances where the subject displayed no additional stories, hesitations, nor other "marked talk".

x. The structure of utterances used to deliver information on certain foods, and whether this significantly deviated from talk on other foods.

The method of discovering these phenomena in 'talk-in-interaction' resulted from a process of repeated examination through both reading the transcripts and while listening to the audiotapes simultaneously (Psathas 1995). Defining all the variations and structural similarities between the utterances themselves and turns at talk followed this macro-level of analysis, where key phenomena were first observed. As a result, clearly identifiable patterns in the actual structure of talk-in-interaction clarified the key observations.

The next stage involved hypotheses testing based on identification of patterns in the talk. This time, a search for regularity of cases and 'deviant' cases was undertaken to 'prove the rule'. The 'deviant' case was significant. Unlike all other consistently observed patterns this was organised in a different fashion, and the task of the analyst was to discuss why this was so and its negative consequences. In this way deviance came to confirm the "rule" that all other transcripts conformed to.

Once this level of analysis was complete, key patterns of talk were scrutinised for their function or purpose on each observed occasions. This analysis was done by an individual researcher (VB), and later verified with another researcher (JB). The regularity of the pattern was also verified through counting of each occasion throughout the transcripts. For instance, the use of verbal cues associated with reducing the confidence applied to the utterance of talk may have appeared to cluster around certain meals. An hypothesis that once confirmed through consensus, could be further supported by calculating the density of the cue's use throughout the all meals.

The terms "probably" and "it depends" were previously shown to be qualitative indicators of potential inaccuracy in dietary reporting, especially in reference to meals (Brenninger 1998). Additional analysis was undertaken on the use of these terms in reference to food items. This was performed by firstly gaining insight into commonly eaten foods through content analysis. Use of the terms in reference to the food item was then calculated throughout the entire transcripts. Results were tabulated and graphed. In addition, food items that attracted "marked" talk, that is, additional talk which displayed elaboration, stories, explanations, hesitations and/or laughter, were highlighted during

this analysis and denoted with an asterisk (*) on a bar chart.

Variability in food choice patterns may be another indicator of inaccurate reporting. We further examined written records of DHs linked with the taped interviews. Data on 8 of the 14 were available. Food items described and manually recorded by the dietitian were listed and tabulated. Once all eight potentially analysable DH interview recording sheets were evaluated, content analysis could be applied to the tabulated data. Content analysis was used to categorise types of food combinations for each meal. The number of times these appeared in accounts of breakfast, lunch and dinner was then assessed for each individual DH. The range of food combinations was then identified and a variation score determined as the mean number of food combinations reported in each meal (Brenninger, Tapsell and Barnard 1999).

3.2.2 Survey of participants

Randomised controlled trials are placed at the top of the hierarchy for establishing evidence on the consequences of diet on metabolism. There is a gap however, between this step and the implementation of dietary therapy in 'free-living' conditions (Tapsell 2001, Jancin 2001, Nestle, Wing, Birch, DiSogra, Drewnowski, Arbor, Middleton, Sigman-Grant, Sobal, Winston and Economos 1998). Clinical measures of metabolic responses are important; nevertheless research on chronic disease sanction the use of complimentary forms of evidence. Food is consumed not nutrients (Ekblond *et al* 2000), similarly, we treat individuals not populations. Greater research attention should be directed at issues related to sustaining healthful eating habits and strategies for modifying unhealthy behaviours (Wing *et al* 2001).

"If dietary change were simple, then dissemination of information would automatically lead to behaviour change. However, this has not occurred for any dietary behaviour" (Nestle *et al* 1998:S50). Self-reported questionnaires have been reported to produce accurate accounts of anti-retroviral therapy compliance by comparison with clinical outcomes (Greer 2001). There were various reasons for lack of adherence to the drugs in this trial, though in relation to dietary trials, non-compliance is a significant and complex multifactorial problem (Johnson, Bazargan and Bing 2000). Lifestyle behaviours and strategies to manage diet-related conditions share a strong association (Wing *et al* 2001). Here, we report on a survey completed subsequent to a 12-week dietary intervention trial that aimed to determine barriers to the feasibility of clinical trials from a participant's perspective. Subjects diagnosed with type 2 diabetes mellitus involved in another trial conducted in the same institution were used in the development of this instrument through focus groups.

According to Barton (2000), work examining the relationship of the RCT and observational studies do not suggest a change to the hierarchy of evidence, rather offer support for a flexible approach where the two forms compliment each other as tested within this thesis. Qualitative research in medical research is more popular than ever before (Barbour 2001, Mays and Pope 2000). This rise in awareness of these methods is perhaps a response to the lack of adherence to dietary regimens that have the potential to offer relief from growing epidemics such as the insulin resistance syndrome. Focus groups are one form of research that have been implemented previously to study factors that influence decisions about what to eat and reporting dietary intake using various dietary assessment methods. The researchers found evidence that reporting accuracy

may be compromised by several issues, though the research was able to help "expand what is known about participant-introduced bias by documenting the experience of reporting from the participants' perspective" (Vuckovic, Ritenbaugh, Taren and Tobar 2000).

Three focus groups were conducted among type 2 diabetes mellitus sufferers (n=20) who were involved in a 12-month fat modified dietary intervention trial. Focus group questions (appendix 2) were derived from the literature reviews of the three student Dietitians[1] for the fulfilment of a research major project. Facilitators[2] (VB and JB) were instructed to address the following issues pertinent to the success of dietary changes made or to be made: social support, eating out, dietary changes, personal food preferences, family meal patterns and preferences, food preparation, meal planning, cooking methods and shopping. Content analysis was completed by the three Dietetic student researchers and results used for the formulation of a survey to be distributed to all participants of the trial.

A self-administered survey was chosen as a convenient means of addressing the social and environmental impacts contributing to the clinical outcomes, including dietary adherence, of the subsequent intervention trial. Intervention foods were chosen carefully for the free-living study population, though the inclusion of a qualitative measure was appealing considering the well documented lack of adherence to dietary regimens in

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[1] Eronen M, Olsen M and Morgan-Jones S, were involved in the research project for the completion of their degrees in a Masters of Science, Nutrition and Dietetics, 1998.

[2] VB (Brenninger V), facilitated two focus groups, while JB (Barnard J), facilitated one focus group.

people with diabetes mellitus (West 1973, and Turnbridge and Wetherill 1970 cited in Hauenstein, Schiller and Hurley 1987; Haynes, Taylor, Sackett, 1979 cited in Insull 1992) and insulin resistance (Brinkworth *et al* 2004).

There are various means for assessing the quality of qualitative research methods (Mays and Pope 2000). In particular, deciding upon the survey's content and designing a survey require careful consideration (Fink 1995, Nelson and Margetts 1997). The principals that can be employed are outline in Fink (1995) and Nelson and Margetts (1997). On a broader level, aspects such as content, types of question, wording, question sequence, layout, method of administration, recording of responses, coding and pre-testing are the major aspects to take into account (Nelson and Margetts 1997). More specifically, the following guidelines (Fink 1995) for survey questions were considered in the producing the current survey.

- Use of complete sentences
- Avoid abbreviations
- Avoid slang and colloquial expression
- Be careful of jargon and technical expressions
- Have the questions reviewed by experts
- Have the questions reviewed by potential respondents
- Adopt or adapt questions that have been used successfully in other surveys
- Use shorter questions when you need to save time, minimise reading, or are satisfied with brief answers
- Use loaded questions, if necessary, but be cautious
- Avoid biasing words and phrases

- Avoid two-edged questions
- Avoid negative questions

The survey (Appendix 3) included a number of open- and closed-ended questions and was distributed to 10 health professionals [1] for review. Changes were made accordingly and a second review completed by 3 academic health professionals [2]. The development of a survey that allowed both open- and closed-ended responses from participants appeared least likely to add more to the time commitment required of subjects, though able to provide the forum necessary for the participant's opinions to be expressed. This form of raw data could also be easily analysed by the researcher later, following the completion of testing all of the participants within the trial.

The survey data was analysed by qualitative content analysis. Content analysis is a flexible approach that begins with the concept of process or social context. The analyst performs 'reading' of the text produced by the subject, seeks theory through locating patterns of meaning and codes them accordingly. Although quantitative content analysis looses much of the flexibility found in its qualitative form, this was also used a means of quantifying categories numerically and applying a ranking of significance to accounts or themes (May 1993). Using both forms of this method enable some of the limitations with this form of research to be overcome and enhances rigor of the analysis (Seale and Silverman 1997). The former allows for a complete interpretation as it flexible enough

[1] 4 Dietitians (research and clinical); 4 Senior Lecturers (science and nutrition); 1 Science Post Doctoral Student; 1 Science Postdoctoral Fellow.

[2] 2 Research Dietitians; 1 Senior Nutrition Lecturer.

to deal with all the information, not simply that which can be simplified into categories. The latter enhances reliability and verification of categories (May 1993) as it is a "defensible correspondence between the transformed accounts and the way the information was meant in its original form" (Garfinkle 1967: 190-1 cited in May 1993). In qualitative research, no method can ensure absolute reliability and validity, though when used with the acknowledgement of these limitations, they compliment and contribute to research (Seale and Silverman 1997).

3.3 Study population, sampling, screening and recruitment

Previous studies on the effects of RS on metabolic processes, so far provide a limited spectrum of evidence. Researchers have concentrated on the effects in animal model studies (Wiseman *et al* 1996; Kabir *et al* 1998; Zhou and Kaplan 1997); in feeding studies using one type of food (Behall and Howe 1995) and in clinical trials with men only (Behall and Howe 1995; Howe, Rumpler and Behall 1996). It is therefore important to go beyond these limitations and address relevant population outcomes from groups classes as overweight or obese and most at risk of developing further symptoms of the insulin resistance syndrome.

Overweight and obesity are known to cause ill health; nevertheless, the conditions are commonplace in our society (Caterson 1997). Globally, an estimated 1.2 billion people are overweight or obese, a figure that is increasing rapidly (WHO Expert Committee 1995 in WHO 1998). A staggering 200 million people were classed as obese in 1995, a figure that has escalated to 300 million according to the latest estimates by the World Health Organisation (WHO 2002). Prevention of obesity is therefore desirable, and

the current proportion of the Australian population that is already overweight or obese strongly indicates that research into dietary treatment is a high priority on public health agendas. It is therefore commonsense to include this group and screen more people with a body mass index (BMI) above 25kg/m^2 into studies that hope to address some of their related detrimental health and social outcomes.

Obesity is seen as the symbolic or phenological characterisation of the metabolic syndrome; this cluster of abnormalities includes resistance to insulin-stimulated glucose uptake, glucose intolerance, hyperinsulinaemia, hypertension, increased very-low density lipoprotein triglycerides and decreased high-density lipoprotein cholesterol (Reaven 1988a). The disorders within this cluster trace back to an underlying metabolic disturbance known as insulin resistance. Although the recruitment of obese and overweight individuals was suitable and advantageous in this study, it was equally important to exclude people with type 2 diabetes mellitus or those taking medication for cholesterol lowering from participating in the investigations. Furthermore, it would be ethically incorrect to postpone treatment for diabetes mellitus or cholesterol lowing for the duration of the investigations. For these reasons, the study population for this research was determined as most susceptible to developing the type 2 diabetes mellitus. These were, overweight or obese individuals with reduced or normal insulin sensitivity. Recruitment then relied upon screening for a fasting blood glucose level below that for diagnosis of diabetes mellitus. The subjects were also selected based on being overweight or obese using the WHO (1997) and definitions of a BMI of 25kg/m^2 up to 35 kg/m^2.

To recruit these subjects, an interview administered survey was regarded the option that could basically attend to all selection criteria while offering an affordable tool that is easily administered. For body mass index measures and fasting glucose, completed in the screening, would ensure that the participant would not have to commence diabetes mellitus management during the trial. These again are obtainable via inexpensive, easily accessible methods. The research facility routinely used a mobile stadiometer, recording data to the nearest 0.1cm, while electronic bathroom scales, accurate to 0.1kg, were available for the measurement of body mass. The determination of fasting blood glucose using an *Accutrend* glucometer was analogous to hospital, general practitioner and home blood glucose monitoring techniques and therefore considered appropriate in the context of this study.

a. Recruitment

Subjects were recruited for the study by advertisement throughout the University of Wollongong, Illawarra Technical and Further Education (TAFE), and from previous study volunteer lists that had consented to be contacted for future studies held at the University of Wollongong. Inclusion criteria were fasting blood glucose below 6.1mmol/l (determined by *'Accutrend' glucometer*, Boehringer Mannheim, Germany), and a body mass index between the range of 25-35kg/m^2. Height was measured without shoes, to the nearest 0.1cm, using a *Stadiometer* (SECA, model no. 220, Germany). Weight was measured in light clothing without shoes, to the nearest 0.1kg, with electronic bathroom scales to one decimal place (*OHAUS*, Model GT410, Florham Park, NJ 07932, made in the USA). Exclusion criteria included poor bowel health, certain medications, pregnancy, smoking, special dietary needs or high alcohol intake,

highly variable activity patterns and recent weight loss (Appendix 1). Potential subjects also needed to be English speaking and aged between 18-60 years.

Eligible subjects for the study were randomised into intervention groups using random numbers (Daniel 1991). However, to ensure that both groups would be equal in terms of commencement date, if half of the subjects commencing in the first week were randomly assigned to one of the diets, the remaining volunteers would be automatically allocated to the other intervention group. Therefore, the groups would regularly recruit equal numbers of subjects concurrently. The power of the study could not be determined due several reasons including, the lack of human studies involving RS, lack of studies using appropriate measures of insulin resistance (euglycaemic hyperinsulinaemic clamp) or lack of metabolically similar subjects (overweight or obese and insulin resistant). However, a short-term feeding study (traditional starch versus high amylose RS) showed significant changes in substrate utilisation during an acute meal challenge, between 2 groups of 12 healthy males. In this study, a difference in the group responses was observed three hours post-prandially, where the RS group produced an acute shift towards greater fat oxidation ($p < 0.03$) (Higgins *et al* 1998). The problem here is the use of healthy, insulin sensitive males that would be more sensitive to dietary changes and able to adjust fuel utilisation quickly (Thomas, Peters, Reed, Abumrad, Sun and Hill 1992 cited in Miller *et al* 1994, Schrauwen *et al* 1997). Another study in non-obese subjects (3 men and 8 women) comparing 6 types of bread, varying in there level of high amylose RS also showed beneficial effects from its consumption on glucose and insulin responses post-prandially (Muir *et al* 1994).

Accutrend screening

Once subjects passed the telephone screening questionnaire (appendix 1) they were asked to attend the University of Wollongong one morning for their consent to the study, height, weight and fasting blood glucose measurements. Subjects were asked to fast for 12 hours prior to the blood glucose test, though were allowed to drink plain drinking water *ad libitum*. The subject's hand was warmed with warm water for 2-3 minutes and dried with tissues. The site was made sterile with alcohol, pierced with a sterile lancet and the first drop of blood wiped away with a dry tissue. The next drop of blood was allowed to drop, without pressing the finger, onto glucose steristrips inserted into a pre-calibrated *Accutrend* glucometer (Boehringer Mannheim, Germany). The resulting glucose level was recorded to one decimal place in mmol/L. If the subject attained a value greater than 6.1mmol/L, they were excluded from entering the trial, counselled on the risk of diabetes mellitus, and advised to visit their family doctor for further tests.

Lifestyle history questionnaire screening

Two students (Barnard J and Brenninger V) developed questions for a lifestyle history questionnaire, based on pilot research comparing reported energy intakes with energy expenditure and an appreciation of possible sources of between subject variations. A copy of the questionnaire is given in Appendix 4. It considers a range of potential mediators of metabolism, such as weight cycling, family history of obesity and general physical activity questions. Question items on barriers to exercise were taken from Department of the Arts, Sport, the Environment and Territories (1992), *Pilot Survey of*

the Fitness of Australians. Australian Government Publishing Service, Canberra. In addition, food knowledge questions were developed to expose possible areas of concern in reporting (sensitive foods) and to identify whether better food knowledge or portion size estimation equated to more accurate dietary intake. Examples from a published portion size atlas (Nelson, Atkinson and Meyer 1997) are shown in Appendix 5. Food and nutrition related questions were derived from conversation analysis outcomes of recorded interviews (Brenninger 1998, Tapsell, Brenninger and Barnard 2000, and Barnard, Tapsell, Davies, Brenninger and Storlien 2002).

An additional self-reported account of lifestyle and medical history variables that may accounts for variations in responses or to test the homogeneity of the groups is important. The considerations for survey construction and data interpretation is discussed previously (see section 3.2.2).

3.4 Dietary intervention

Alterations in glucose and insulin responses have also been shown in studies where the variable amounts and sources of CHO were utilised (Wolever and Bolognesi 1996). One form of CHO, RS may potentially cause similar effects in humans due to reduced availability of energy and its fermentable nature. These have been outlined in section 2.2.2.1.1. In particular, the high amylose variety of RS is not readily available CHO (Brown 1996). It is therefore potentially beneficial for people with insulin resistance who have difficulty managing CHO as an energy source.

Australians consume approximately 5-7g of RS per day, though the Commonwealth Scientific and Industrial Research Organisation (CSIRO), Australia, are currently recommending 20g daily for benefits from RS on colon cancer prevention. Further investigations into the usefulness of this CHO have lead to animal and short-term human studies in glycaemic control and insulin resistance, where beneficial effects emerged (Muir, Lu, Collier and O'Dea 1994 cited in Brown 1998, Byrnes *et al* 1995, Noakes *et al* 1996). Considering the emergence of links between cancer and insulin resistance (Shapiro 1998), the recommendation for RS intake to promote bowel health (20g/day) seems an appropriate level to begin with.

Although the various studies refer to applications in the management of obesity, insulin resistance and dyslipidaemia, they use doses that may be unattainable in the real world considering the average Australian intake of RS. Using the recommendation derived for bowel health (20g RS/day) is probably achievable yet may not be appropriate for effects in the metabolic syndrome, though this is yet to be determined. In addition, study populations have healthy, normal weight adults and unequal numbers of male to female subjects are studied which limits the representation of the population at large (Lancet editorial 2001). This study was set in free-living conditions, and using both men and women to overcome the problem of unsuitably extrapolating chronic expectations from short-term studies (Baghurst *et al* 1996).

Many readily available foods contain detectable amounts of RS. The amount can vary greatly for the one type of food, depending on the degree of processing, cooking method, length of time cooked and storage conditions. Australians are amongst the

highest consumers of RS, eating in the range of 3.5-6.0g RS daily (EURESTA 1994). As a group, consumables such as kibbled or raw grains, unprocessed fruit such as bananas, starch-containing foods such as bread and breakfast cereals, and processed foods with chemically modified starches, are recognised as the main sources of RS. However, if consumed individually these foods contribute very little RS.

The amount of RS considered tested in the current study was similar to that promoted for bowel health and bowel cancer prevention. As recent cancer research suggests a link with insulin resistance and hyperinsulinaemia (Shapiro 1998) the cancer prevention levels may be a good starting point. This target level of 20-25g of RS intake per day was also considered appropriate in terms of achievability in the diet. Previous researchers (Phillips *et al* 1995) have used higher levels of RS, however, the investigations were usually short-term and did not test feasibility or efficacy of RS doses in the diet under "free living" conditions. The studies were also unable to meet their targeted RS intake without resorting to unconventional foods and products unlikely to become available in our supermarkets.

3.4.1 Long term dietary changes

An intervention trial length of 12 week was specified to test whether the high amylose RS diet would produce metabolic changes and determine, on a more practical level, the feasibility and adherence to the dietary manipulation. In addition to the numerous work compiled on the diet-disease relationship, which have utilised a 12-week intervention (see table 3.1.1), three months is believed a sufficiently long period of time for assessing dietary influence on insulin action (Storlien *et al* 2001).

Completing acute measures or meal challenges following an adaptive period to the intervention foods has been a design used in previous studies testing RS in humans (Higgins *et al* 1998, Howe, Rumpler and Behall 1996). The intervention design used in the following research, (see figures 3.1.2 and 3.1.3) considered these studies, in addition to the feasibility of completing multiple meal challenge days with regard to clinic availability and subject burden. Measuring the acute response of overweight and obese people to similar foods within their dietary treatment offers a means of interpreting whether acute and longer-term exposure to high amylose RS are interrelated. Often, acute studies are performed to provide evidence for subsequent long-term clinical trials, however in the area of the insulin resistant syndrome, whether acute responses translate into chronic benefits is poorly understood. Providing the alternative dietary treatment in a meal challenge, provides evidence on substrate adaptation and may support the chronic outcome measure of insulin resistance.

The primary means of manipulating dietary intake warrant examination in any intervention study. In clinical settings, dietary intake is commonly assessed using a diet history interview, which assesses usual food consumption (Rutishauser 1997, Nelson and Bingham 1997). Close monitoring of nutrient intakes and their absolute and proportional amounts are important data to observe as they may act as confounding variables. If the inclusion of intervention foods causes displacement of other nutrients, the research question becomes problematic.

In terms of nutrient displacement, if subjects successfully reduce the percentage of energy from fat in their diets, they consume a higher proportion CHOs (Rolls 1995). This macronutrient shift may affect hunger, satiety, or food intake (Rolls 1995). Likewise, an increase in RS may cause a reduction in readily available CHO if the foods substituted are similar to those they are replacing. In a large cross-sectional study, that recruited 32807 subjects, showed that dietary habits, and in particular certain food items, were positively associated with predictors of type 2 diabetes mellitus (Ekblond *et al* 2000). The authors felt that this research is relevant as people consume foods not nutrients and that insight into the consequences of foods on the development of type 2 diabetes mellitus should be researched further (Ekblond *et al* 2000).

The study described here comprised a 12-week dietary intervention trial with the control group consuming foods with a low RS starch content and the experimental group consuming equivalent foods with a high RS (high amylose/amylopectin ratio) content. All other dietary variables were controlled except for the difference of 20g RS in the diet of the experimental group. Dietary advice was individualised based on an understanding of usual intakes obtained from the DH interview. Target foods were included as appropriate to achieve the study goals. Equivalent food choices are indicated in table 3.4.1. Subjects were blinded to their randomly allocated diet, and intervention foods.

Table 3.4.1 Foods provided in intervention trial

Control diet	***Intervention diet***
Buttercup white English muffin	Wonder White English muffin
Buttercup white sandwich bread	*Hi Maize* enhanced bread
Green's de'lites Blueberry 97% fat free sweet flavored muffins	Hi Maize enhanced *White Wings* 97% fat free Banana/Apricot muffin
(Manufacturer) Wine gums	*Green's* fruit snacks
Uncle Toby's Nutrigrain breakfast cereal	*Uncle Toby's* Grinner's breakfast cereal
Heinz canned spaghetti	*Heinz* fibre increased spaghetti
Pauls Vaalia yoghurt	*Pauls* Vaalia breakfast yoghurt
Reduced fat milk drink (no brand)	*Sanitarium* Up & Go drink

3.4.2 Meal challenge tests

The aim of the meal challenges was to provide an understanding of the acute (1-day) impact of meals representative of each intervention condition, by measuring substrate utilisation, lipid, glucose and insulin profiles and satiety. Specifically measuring these parameters were due to the following reasons.

Respiratory quotient (substrate utilisation changes) was important to measure given the recent development shown in the Higgins *et al* (1998) data. This showed the potential for high amylose RS to produce a shift to increased fat oxidation 3 hours after the meal compared to the normal starch meal. While metabolic rate was to automatically measured with RQ, it also provides indirect information on diet-induced thermogenesis.

Respectively, protein, CHOs and fat have high, intermediate and low potential to increase energy expenditure (Dionne and Tremblay 2000). Although, more importantly, a low resting metabolic rate is associated with risk of weight gain (Ravussin, Lillioja, Knowler, Christin, Freymond, Abbot, Boyce, Howard and Bogardus 1988 cited in Dionne and Tremblay 2000).

In brief, substrate utilisation or oxidation is measured through indirect calorimetry (see section 3.5.4.1 and figure 3.5.4.1.1 for more detail) and is known as the respiratory quotient (RQ). This technique involves the measurement of oxygen consumption and carbon dioxide production using a transparent, flow-through, ventilated hood. Substrate use can be determined from the respiratory quotient (RQ; VO2/VCO2). A high RQ (approaching 1.0) is indicative of CHO oxidation and a low RQ (approaching 0.7) is indicative of fat oxidation (Melby, Ho and Hill 2000).

Assessment of circulating glucose and insulin were all important to assess the glycaemic and insulinaemic effects of the foods, as demonstrated in meal challenge tests in previous research in humans (Raben *et al* 1994). Measurement of triglyceridemic excursions would allow any concerns for the potential of CHO to produce hypertriglyceridaemia, a condition of the insulin resistance syndrome.

A study conducted on 6 men over one week in a whole body indirect calorimeter reported that both protein and CHO were able to similarly affect subsequent energy intake. For instance, if CHO balance were achieved with CHO stores, a negative impact on the following day's energy intake would occur (Stubbs, Harbron, Murgatroyd and

Prentice 1995). Although a more detailed discussion follows (see section 3.5.5), the use of subjective satiety ratings appeared to be relevant in this context of CHO manipulation, also shown in previous research (Raben *et al* 1994).

A breakfast and a lunch with water ad libitum was measurable and fairly representative of usual food consumption patterns. The meals themselves were designed to provide an approximate total energy intake 4000kJ. This intake reflected no more than two thirds of usual consumption for women, which has been used in other studies (Millen, Quatromoni, Copenhafer, Demissie, O'Horo and D'Agostino 2001). Overfeeding may disguise any shift in fuel utilisation, though women are usually believed to be smaller eaters. Likewise meals should deliver 3900kJ in each day's test, using commonly available foods.

Glucose, insulin, triglyceride, respiratory quotient, metabolic rate and satiety excursions were also assessed at one hourly intervals for 10 hours during the test meals at the end of the 12 weeks diets.

Two meal challenge tests were applied one week apart at the end of the 12-week intervention. In each meal challenge, subjects from both groups consumed consecutive breakfast and lunch meals, either high or low in resistant starch (25g or 5g RS respectively). Details of meals provided are outlined in Table 3.4.2.

Table 3.4.2 Composition of meal challenges

Control Meals	Intervention meals
Breakfast 1 blueberry muffin 1 regular English muffin 15g Olive Grove margarine 1 tsp honey	Breakfast 1 *Hi Maize* banana Muffin 1 *Wonder White* English muffin 15g Olive Grove margarine 1 tsp honey
Total RS	9.53g
Lunch 3 slices *Buttercup* bread 15g Olive Grove margarine 30g lean leg ham 1½ leaves lettuce 25g Jelly babies	Lunch 3 slices *Hi Maize* enhanced bread[1] 15g Olive Grove margarine 30g lean leg ham 1½ leaves lettuce 25g *Green's* fruit snacks
Total RS	15.21g

[1] *Hi Maize* enhanced bread and sweet muffins were specifically produced with added *Hi Maize* for the study.

Both meal challenges provided about 3900kJ and the difference in RS was 20g. All other dietary variables were constant. Tables 3 and 4 in Appendix 6 indicate the nutrient composition of all components of the meal challenges. Monounsaturated fatty acids are the predominant type of fat found in *Olive Grove* margarine as used in the acute meal challenges. This type of fat was chosen as it is steadily metabolised (McCargar, Clandinin, Belcastro and Walker 1989). Ethically, using this type of fat was appropriate as olive oil is beneficial in lowering atherogenic risk

factors in healthy subjects (Ruiz-Gutierrez, Morgado, Prada, Perez-Jimenez and Muriana 1998). Water was allowed ad libitum, though all water consumed were recorded for each person on each meal challenge day (data not shown).

3.5 Clinical procedures and outcome variables

There is a need to address a multifaceted problem with multidisciplinary research (Tobin and Miller 2001). Recent reviews on the establishment of evidence for clinical practices (Barton 2000) suggests that a broad approach to data collection enables aspects of practice above and beyond clinical outcomes to be addressed. For example, we may address the feasibility of the approach as an adjunct to collating efficacy data. In our case, although RS could prove useful in dietary treatment of disorders, practitioners need to know if the metabolic outcomes are supported with evidence of effects in normal practice. In this light, to understand whether subjects felt that an intervention was feasible, an additional self-reported account of lifestyle and medical history variables would account for variations in responses or tests and, could be easily included in data collection.

In terms of clinical outcomes from the actual dietary intervention, it is plausible to hypothesise from the previously discussed literature (see chapter 2) that the consumption of high amylose RS may produce a decline in fat mass or reduce weight gain and promote insulin sensitivity. If however, shifting of body weight occurred in one or both of the diet groups, it would be difficult to decipher the mechanism of action from an intervention effect. While some may argue that separating out one effect is less important and that promoting several benefits is not problematic in research (James

2001), too much weight change could blur the hypotheses. In this study, weight stability was targeted.

Despite weight stability, changes in body composition over time may still prevail and could add to the evidence supporting or rejecting the null hypotheses. Body composition and in particular, central adiposity, may have a large impact on insulin sensitivity (Lamarche 1998). An increase in muscle tissue mass to the proportion of fat mass in this area could therefore provide a greater concentration of insulin sensitive tissue, in this sense, fat mass may be utilised for fuel in the high RS consuming group. For this reason, body composition should be assessed before and on the completion of the intervention trial. The length of the intervention trial will also be important, as a short-term intervention would not be able to demonstrate any changes in body composition.

The central metabolic hypothesis was that dietary RS could influence the management of the metabolic syndrome, insulin sensitivity, fasting levels of cholesterol and its components; triglyceride and glucose would need to be analysed pre- and post-intervention. However, hypertension, a component of the metabolic syndrome, is probably not as crucial to measure considering the debate surrounding whether it is a consequence or instigator leading to insulin resistance (Sterne 1997). In support of this debate, a factor analysis on underlying patterns of the syndrome have shown that blood pressure is only loosely associated with the primary components of this syndrome (Meigs 2000).

With reference to the dietary variables to be measured, energy intake, total macro-nutrients, fat (monounsaturated, polyunsaturated and saturated fatty acids) and CHO subtypes (starch and sugar), alcohol, dietary cholesterol, calcium and phosphorus have been chosen for analysis. The macronutrients will be expressed as percent of energy also. Inclusion of these as dietary variables were based on research implicating the nutrient in the diet-disease relationship (see section 2.3: Establishing the ideal nutrition mix) and the limitations of the dietary analysis software available at the time of data entry. Currently, not all databases associated with *FoodWorks* (v2.10.136, Xyris Software, Highgate Hill, Brisbane), nutrient analysis software are complete for the micronutrients zinc and folate. Nor did they include n-3, n-6 or trans-fatty acid data.

Within energy balance, the moderate intake of CHO, fat and protein remains preferential, as increasing intakes have the potential for producing deleterious effects on metabolism. With reference to the types of each macronutrient, protein is less well documented, though fat and CHO sub-types exert substantial effects on various metabolic measures. In particular saturated fat, trans-fatty acids, n-6 fatty acids, and readily available CHO, such as sugar have all been associated with several detrimental metabolic outcomes when consumed in excess. These include reduced insulin action (Storlien *et al* 1997, Storlien *et al* 1988), hyperinsulinaemia (Holt *et al* 1997), glucose metabolism (Kraegen and Storlien 1989), adiposity and weight gain (Flatt 1978, Hill *et al* 2000), substrate oxidation (Surina *et al* 1993), poor mobilisation once stored (DeLany *et al* 2000), satiety (Blundell *et al* 1993, Green *et al* 1994) and dyslipidaemia (Chen *et al* 1995, Berry 1997). While less readily available and fermentable CHOs, monounsaturated fatty acids and n-3 polyunsaturated fatty acids may lead to the

following beneficial effects. Importantly, they may promote insulin sensitivity (Vessby *et al* 2001, Storlien *et al* 1996a), improve glucose and insulin responses (Jenkins *et al* 1987), decease hunger and food intake (Rossner *et al* 1987, Rigaud *et al* 1990 and Mickelsen *et al* 1979 cited in Miller *et al* 1994), decrease adiposity or body weight, fat oxidation (Higgins *et al* 1998) and decrease cholesterol or dyslipidaemia (Anderson and Chen 1979, Remesy *et al* 1993).

Animal protein can increase cholesterol (Carroll 1982 cited in Wolever 1999) and often they are in foods containing saturated fat (Wolever 1999). This suggests that plant sources of protein should be encouraged as a moderate protein intake is important to avoid complications from protein malnutrition (Reis *et al* 1997), and potential effects on weight management and adiposity (Brodsky 1998, Skov *et al* 1999). These dietary issues are important to consider as variables and also measured as accurately as possible for analysis.

3.5.1 Body weight and body composition

"Obesity is a chronic condition characterised by an excess of body fat" (Nöel, Arterburn and Mulrow 2000:329). Obesity is a risk factor for a cluster of chronic health conditions, indicating that two important characteristics to measure in a dietary intervention trial such as this are variables that define obesity in general, and body fatness.

3.5.1.1 Body mass index

Body mass index (BMI) is a commonly used indicator of mortality and morbidity risk from diseases including cardiovascular disease, diabetes mellitus and certain cancers (Garrow 1986, Bray 1996, World Cancer Research Fund and American Institute for Cancer research 1997 and Seidell 1998, cited in Trichopoulou, Gnardellis, Benetou, Lagiou, Bamia and Trichopoulos 2002). The BMI is the official international standard used for measuring and identifying overweight and obesity (WHO 1997). The limitations of this instrument, including that discussed in table 3.5.1 under 'anthropometric', primarily relate to the body's composition. BMI is an insensitive predictor of body composition (Lukaski 2001), which is believed to be a better determinant of health (Segal, Dunaif, Gutin, Albu, Nyman and Pi-Sunyer 1987 cited in Lukaski 2001). For example, in a study on men and women, BMI was shown to be a poor predictor of the percentage of body fat in individuals, especially when they were below a BMI of 30kg/m^2 (Frankenfield, Rowe, Cooney, Smith and Becker 2001). This lead to misclassification of many below a BMI of 30kg/m^2. Similarly, approximately half the number of subjects, regardless of gender, classified as overweight according to BMI (BMI > 27.3kg/m^2) were in fact obese (Smalley, Knerr, Kendrick, Colliver and Owen 1990 cited in Lukaski 2001).

Nevertheless, BMI is closely associated with the incidence of several chronic disease (Kopelman 2000). This classification tool has proved to be useful in large cross-sectional studies that hope to provide initial information on diet and health-related outcomes (Trichopoulou *et al* 2002). Indeed, one of the major causes of ill health, obesity, is generally a classification applied from measuring BMI despite this tool's

many limitations compared with other means of assessing fatness (Arterburn and Nöel 2001, Little and Byrne 2001, Frankenfield *et al* 2001). Therefore, omitting the collection of BMI data in a study concerning overweight and obesity would be unsystematic.

The formula used to calculate BMI (body mass index) was BMI = weight (kg) / (height (m))^2 (WHO 1997). BMI was assessed during screening, where height was measured without shoes, to the nearest 0.1cm, using a *Stadiometer* (SECA, model no. 220, Germany). Weight was measured in light clothing without shoes, to the nearest 0.1kg, with electronic bathroom scales to one decimal place (*OHAUS*, Model GT410, Florham Park, NJ 07932, made in the USA).

3.5.1.2 Dual X-ray Absorptiometry

Body composition, especially fat mass, is assessable via numerous methods. These consist primarily of hydro-densitometry (underwater weighing), dual energy x-ray absorptiometry (DXA or DEXA), bioelectrical impedance, near infrared spectroscopy, sum of skin folds, measurement of naturally occurring isotopes (K), neutron activation analysis or simply through BMI (Caterson 1997). A review of body composition techniques by Forbes (1999) provided a basis to define the most appropriate technique (Table 3.5.1 adapted from Forbes 1999). Within the table, an asterisk identifies two compartment model devices; multi component models with two asterisks and any other techniques are left unmarked.

Table 3.5.1 Body composition techniques: advantages and disadvantages

Please see print copy for Table 3.5.1

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In light of the aforementioned pros and cons, the chosen technique to determine body composition in addition to BMI, as it has been shown to be a poor predictor of body fatness (Frankenfield *et al* 2001, Lukaski 2001) was DXA (or 'DEXA'). The technique is based on the principle that X-ray beams of two different energies are differentially attenuated by body tissues of different densities (Mazess, Barden, Bisek and Hanson 1990). A total body DXA scan involves very low-dose radiation (ranging from 0.05 to 1.5 mrem) and takes approximately 20 minutes to perform. The subject lies on a bed while the X-ray beam scans from head to foot. A trained operator performs the measurement (Brenninger V). This procedure is believed to have greater accuracy for determining body composition than other methods such as bio-electrical impedance (O'Connor 1997).

DXA, a relatively new technique has been successfully used to assess overweight women (Houtkooper, Going, Sproul, Blew and Lohman 2000) and is described as a convenient, safe and non-invasive technique that provides a precise measure of lean soft tissue masses and total bone mineral content (Mazzess *et al* 1990, Russell-Aulet, Wang, Thornton and Pierson 1991). It also provides a more sensitive means of assessing change in body composition in postmenopausal women compared to underwater weighing and a multi-component model when using up-to-date software (Houtkooper *et al* 2000).

There are however, some limitations to consider in the use of DXA, despite its emergence as a possible "gold standard" at several conferences (Roubenoff, Kehayias, Dawson-Hughes and Heymsfield 1993). These include the following:

- It may not be sufficiently accurate in infants (Roubenoff *et al* 1993), though debated by others (Speakman, Booles and Butterwick 2001).
- DXA may be limited in its capacity to provide comparable results between thin and obese participants due to its sensitivity to anteroposterior thickness of the body (Johnson and Dawson-Hughes 1992, Bulh, Heymsfield, Russell-Aulet, Wang, Pierson and Lichtman 1991).
- Extremes in hydration of the body are a problem as the instrument assumes that lean body mass is hydrated at a level of 0.73 mL per gram, though many body composition instruments cannot adjust for hydration. Likewise, exclusion of the head from soft tissue analysis due to the lack of bone-free soft tissue visible to the X-ray beams is suggested (Roubenoff *et al* 1993).

In the proposed investigations, body composition comparison from pre-intervention to post-intervention in obese or overweight people are necessary and achievable using DXA. The limitations mentioned are of little concern in the context of this study, with the exception of hydration. In addition, exclusion of the head's composition in the analysis of groups will be unnecessary and may have introduced instrument operator bias and within-subject changes would not necessarily benefit. It may also be seen as inconsistent with evidence that recognises that thoracic and arm regions of the body are prone to imprecision for the same reason (Roubenoff *et al* 1993). DXA software makes a reasonable estimate for these regions by interpolating the probable lean and fat composition of the soft tissue component for the thorax and arms from that of the immediately adjacent tissues (Speakman *et al* 2001).

The radiation dose associated with a DXA scan is relatively small (Mazzess *et al* 1990, Engelen, Schols, Heidendal, and Wouters 1998) and regarded as safe, providing only a radiation dose of < 5 mrem for a whole body scan (Roubenoff *et al* 1993). The *Norland XR-36* DXA machine, housed at Wollongong Nuclear Medicine, Wollongong, will be used for this purpose.

The *Norland XR-36* DXA machine, housed at Wollongong Nuclear Medicine, Wollongong, was used to determine body fat and fat distribution. Example output generated by the DXA scan can be viewed in Appendix 7.

3.5.2 Disease biomarkers: lipids, insulin and glucose

In the broadest sense, a biomarker is any substance, structure, or process that is measured in body fluids or tissues that independently reflects the intake of a food component. Biomarkers assess the incidence or biological behaviour of a disease and may predict or influence health (Katan 1998 cited in Johnson 2000, Milner 1999). The assessment of lipids, insulin and glucose as biomarkers for the insulin resistance syndrome are appropriate considering the preceding review of the literature (chapter 2).

3.5.2.1 Blood collection

Disodium ethylenediaminetetraacetate (EDTA) is an anticoagulant that is used in tubes to collect whole blood for the purposes of measuring insulin, glucose, triglycerides and lipoproteins from the plasma component of blood. This was an important ethical factor to consider, as the amount of blood taken from the subjects may have become an issue during the final measures if several different tubes were used to provide the

analytical material. Heparin tubes may have also been useful for measuring lipoprotein, however the more important aspect of the study was that the initial and final measures were comparable and the direction of change be considered more than the actual values. According to the National Cholesterol Education Program Adult Treatment Panel Guidelines, plasma levels may be multiplied by 1.03 to convert the value to its equivalent serum concentration, as this is what their risk levels are based upon (Report of the National cholesterol education program expert panel on detection, evaluation and treatment of high blood cholesterol in adults, 1988). This is only a consideration however, and the individual change is currently the research question.

3.5.2.2 Plasma analysis

Plasma analyses were undertaken for total cholesterol, high-density lipoprotein cholesterol, triglycerides, glucose and insulin, using standard laboratory procedures at baseline and 12 weeks. Low-density lipoprotein cholesterol was calculated using the Friedewald formula: LDL = total cholesterol – triglycerides ÷ 5 – high-density lipoprotein level (Dons 1994).

Using laboratory assays to determine endocrine values requires cautious interpretation (Dons 1994). Statistical concepts may help here, where the 'sensitivity' and 'specificity' of the assays are important terms to consider. That is, one of these attributes may increase and compromise the other. There are however, no known acceptable levels documented for sensitivity and specificity of tests. Together, these work to detect the endocrinological changes imagined, even though, if we suppose that the change is real, another confounding factor adds an element of uncertainty to our interpretation of

results. This additional confounder can be labelled ‘random error’ or ‘coefficient of variation’ or ‘precision’. If the precision of the assay is larger than the percent change detected between the comparable values, then it is possible that the change does not exist at all or is of no clinical significance (Dons 1994). The coefficient of variation between two identical assay kits may be two to three folds greater than seen in intra-assay values, which is problematic for studies such as this that require several kits for each variable. The flaw in this method may be minimised, however this remains a limitation of laboratory procedures. It also fuels the debate that scientific evidence should not dominate over observational data.

Once the whole blood was collected in EDTA tubes, it was immediately centrifuged at 3500rpm for 10minutes at 4^{o}C. The plasma, then drawn off with an unused disposable pipette, was stored on ice in *eppendorf* tubes. All plasma sample duplicates were frozen at -80^{o}C. Plasma samples collected for insulin assays were frozen within 1 hour of taking the sample. The nurse collecting the blood used a checklist for bloods taken and any problems that occurred while taking the blood or time delay was recorded.

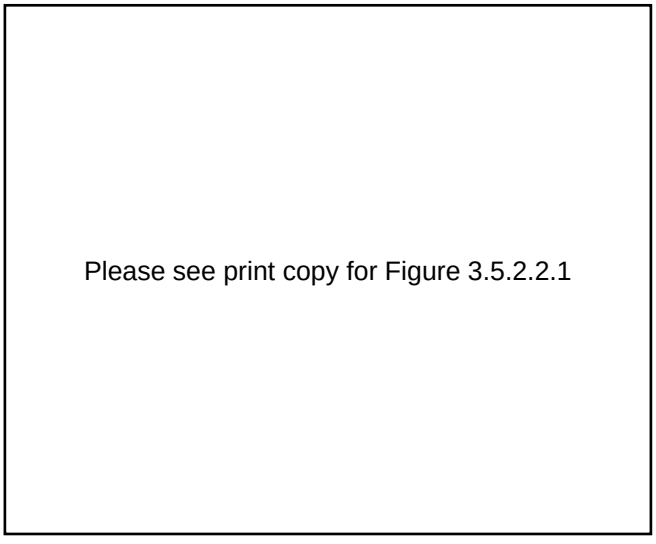

Figure 3.5.2.2.1 Timed blood collection.

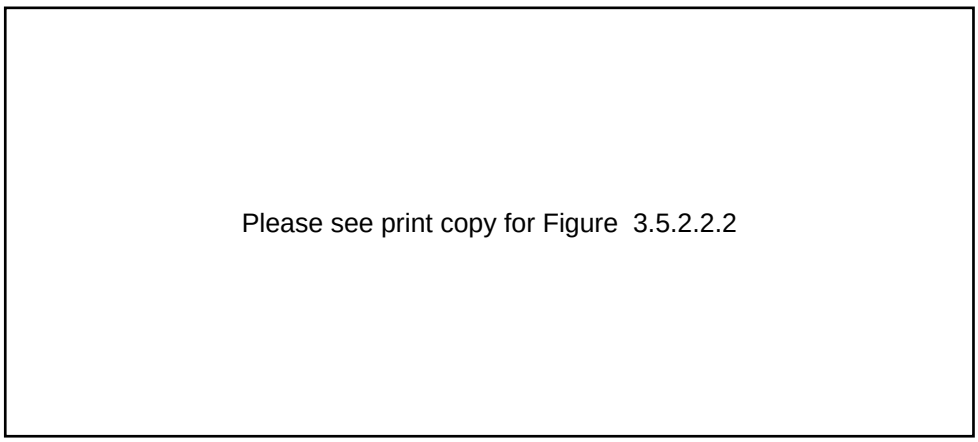

Figure 3.5.2.2.2 Transferring plasma from an EDTA tube to eppendorf tubes

The insulin assays were analysed with a *Linco* human insulin specific radio immuno-assay (RIA) kit (*Linco* Research Inc.). Plasma were thawed on ice in eppendorf tubes, vortexed, then centrifuged for 2 minutes at 1.5 rev/min x 1000. Standard procedures were followed subsequently. Centrifugation of samples following the overnight fast were done in a *Sorvall*® RT 6000D, at 3500-3600 rev/min x 1000 for 30 mins with chamber temperature at –4^{o}C. Where any problems were incurred, tubes were dealt with similarly and duplicates ran so that inaccurate results could be ruled out. Plasma glucose and all aforementioned plasma lipids were measured using the *Cobas Mira* and standard accepted assay kits. Specifically, total and pre-prepared HDL plasma cholesterol and triglyceride levels were determined by the oxidase, colourimetric assays (Boehringer Mannheim, Germany). Specifically, plasma glucose was determined by the appropriate oxidase, peroxidase colourimetric method (Boehringer Mannheim, Germany).

Communications with the laboratory technician for the *Cobas Mira* confirmed that calibration dye tests for the *Cobas Mira* were completed monthly, presenting good results for precision, in the range of 0.6 to 1.4%. Standard kit coefficient of variation could vary from 0.7 to 2.7% depending on within run or between day and sample medium.

3.5.3 Insulin sensitivity

A number of studies investigating IR or type 2 diabetes have used methods such as the oral glucose tolerance test to assess variations in insulin and glucose metabolism (Reaven 1988a). However, the euglycaemic hyperinsulinaemic glucose clamp ("clamp") is considered the "gold-standard" for assessment of insulin action (DeFronzo, Tobin and Andres 1979, Zierler 1999). This direct method for studying human insulin sensitivity and can be performed in hyperglycaemic conditions, but is usually tested under steady state euglycemic, hyperinsulinaemic technique (Walker, Fulcher, Sum, Orskov and Alberti 1991).

3.5.3.1 Euglycemic hyperinsulinaemic clamp

Insulin sensitivity was assessed at baseline and 12 weeks using the euglycemic hyperinsulinaemic clamp technique (DeFronzo *et al* 1979, Zierler 1999). Insulin infusions were adjusted based on an assessment of individual body composition and glucose levels were clamped at 4.5 mmol/L. Insulin resistance was classified by *'M'* values less than 7mg/kg.min (DeFronzo *et al* 1979).

In this technique, plasma insulin is acutely raised and maintained at approximately 100 microU/ml by a prime-continuous infusion of insulin. The plasma glucose is then held constant at a basal level of 4.5 mmol/L by a variable glucose infusion using the negative feedback principle (DeFronzo *et al* 1979). Under these conditions of steady-state euglycaemia, the glucose infusion rate equals glucose uptake by all body tissues and is therefore a measure of whole body sensitivity to exogenous insulin (DeFronzo *et al* 1979).

The indwelling cannula in the cubital fossa of the left arm was used for the infusion of glucose and insulin, while blood was collected from a retrograde positioned indwelling cannulae in the right arm (aided by continual gentle warming of the hand and arm). The data sheet used to calculate insulin and glucose infusion rates is provided in Appendix 8. The subject was reclined in a comfortable bed during the procedure, which lasted approximately 3 hours. Due to residual infused insulin reaction, blood glucose usually declines, therefore subjects were subsequently fed carbohydrate foods and remained under observation in the a clinical area for the period immediately following the final "clamp" measurement until blood glucose levels were back to 4.5mmol/L.

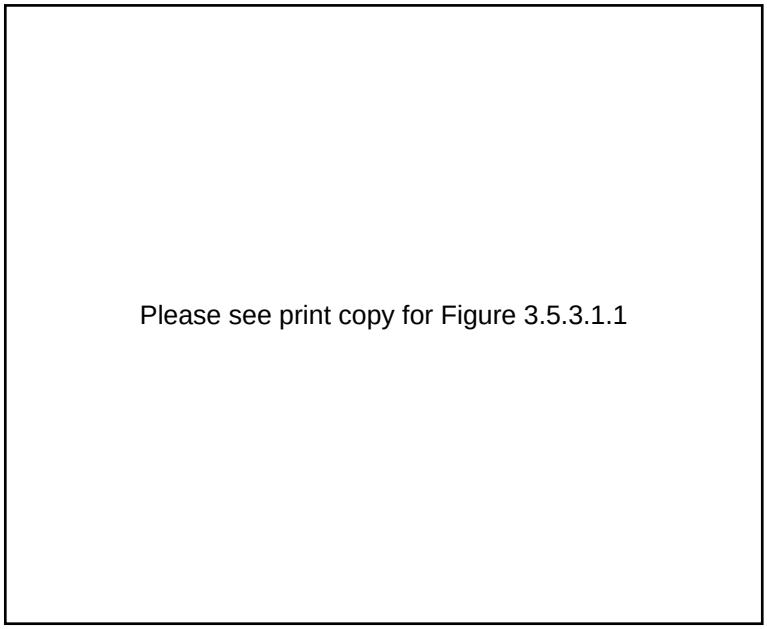

Figure 3.5.3.1.1 Euglycaemic hyperinsulinaemia clamp.

3.5.4 Substrate utilisation

An important component of research in metabolism is to determine changes in fuel utilisation and possible energy balance adaptations from intervening with target nutrients, in this case RS. Obesity is regarded as a surplus of energy intake to expenditure (Melby *et al* 2000). To measure energy intake, calorimetry methods are required. There are two types of calorimetry. The first is known as direct calorimetry that assesses energy expenditure by measuring the amount of heat produced by the body (Webb 1991 cited in Melby *et al* 2000). Limitations include accessibility to the instrument (whole room calorimeter), the long duration required for detecting changes in heat, and the lack of ability to simultaneously assess substrate utilisation changes (Melby *et al* 2000).

The second method available for measuring energy balance features is indirect calorimetry. Doubly labelled water, labelled bicarbonate and respiratory gas exchange are the usual forms of indirectly measuring this value in research. The following list outlines the various advantages of indirect calorimetry using respiratory gas exchange:

- Easily accessible in the department where the research was conducted, due to the affordability of the monitoring instruments
- Technically less difficult than direct calorimetry
- Both energy expenditure and substrate utilisation values can be assessed simultaneously
- Two subjects can be assessed on the one machine each day

There are advantages in choosing doubly labelled water for assessing energy expenditure only compared to respiratory gas exchange, though these were easily negated considering the cost and world shortage in the supply of doubly labelled water (Westerterp 2000). There is also an increased burden on the subjects, such as collecting three urinary samples, when so many measurements of other variables are accompanying.

3.5.4.1 Indirect calorimetry

Therefore, of the types of indirect calorimetry, respiratory gas exchange was primarily chosen due to its accessibility, as this apparatus has been utilised in metabolic studies undertaken at the University of Wollongong. Also, the ability to measure both desired variables at the same time with this apparatus reduces subject burden. The indirect calorimetry was performed using the Datex Metabolic Monitor (Datex, Finland).

This technique involves the measurement of oxygen consumption and carbon dioxide production using a transparent, flow-through, ventilated hood. From these measurements, estimates of energy expenditure and substrate utilisation can be determined. Substrate use can be determined from the respiratory quotient (RQ; VO2/VCO2). A high RQ (approaching 1.0) is indicative of CHO oxidation and a low RQ (approaching 0.7) is indicative of fat oxidation (Melby *et al* 2000).

Respiratory Quotient was assessed at baseline and 12 weeks using the Datex Metabolic Monitor (Datex, Finland) over a 25-minute period. Respiratory quotient was also assessed on the day of the test meals, starting in the fasted state, and repeating measures for 25 minutes every hour for 10 consecutive hours (Figure 3.1.1.3).

In this study, subjects were asked to arrive fasted and then seated in a semi-reclined position. Once the subject has rested for 20 minutes, a baseline indirect calorimetry measurement was performed (25 minutes duration). Subjects were measured for 25 minutes every hour for a total of 10 consecutive hours including the fasting measure. The first 10 minutes of each session was discarded and the remaining 15 minutes, excluding any unreliable RQ measures, were averaged.

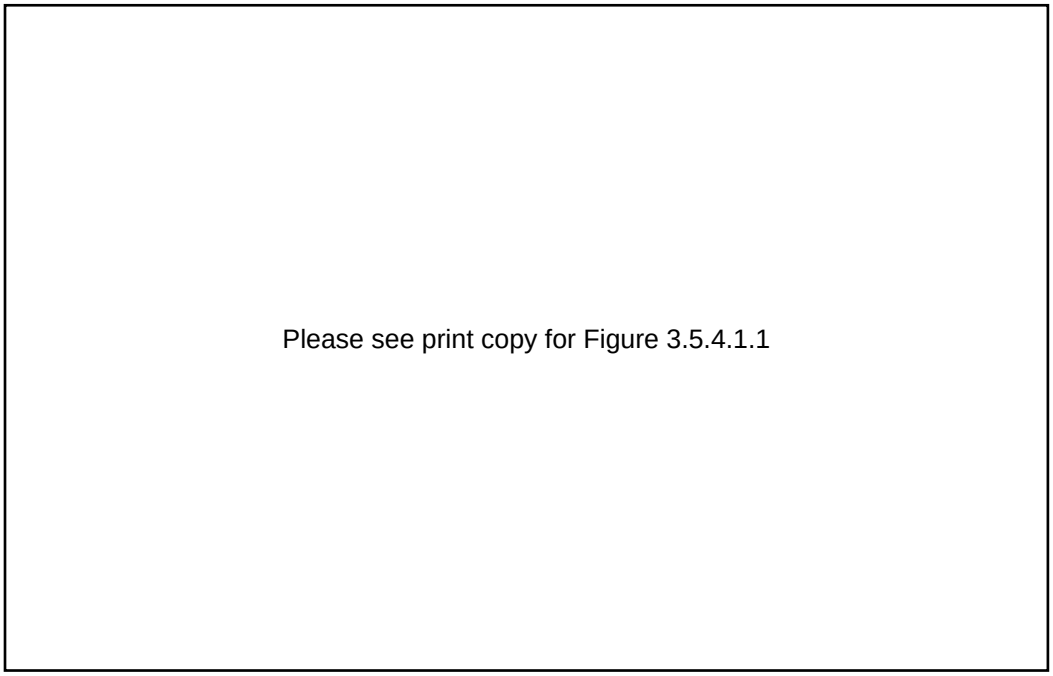

Figure 3.5.4.1.1 Use of the Datex Metabolic Monitors for indirect calorimetry assessment (subjects 1 and 3); completion of satiety scales (subject 2).

3.5.5 Satiety

"Satiety refers to the reduction of hunger and the termination of eating, which generally mark the end of a meal, and represents the interplay of psychological, physiological, and metabolic events." (Rolls 1995:960S). More protein, more fat and less CHO in the diet may decrease appetite, yet the type of CHO chosen appears to be more important on satiety, than the percent of total CHO eaten (Aronne *et al* 2001). Studies examining the effects of unavailable complex CHO, primarily referring to dietary fibre, have found that various loads of this food component at a meal can decrease hunger and energy intake at the following meal. That is, dietary fibre appears to effect intestinal transit time and increase postprandial satiety, although these effects are modest (Rossner *et al* 1987, Rigaud *et al* 1990 and Mickelsen *et al* 1979 cited in Miller *et al* 1994). In contrast,

satiety has been shown to decrease in response to resistant starch in a meal compared to normal starch (Raben *et al* 1994), though the authors report that differences in texture and palatability may have influenced these findings. It is possible however that with the reduction glycaemic and insulinaemic impact shown in the study by Raben *et al* (1995) may result in lower satiety. Health effects that warrant further research include metabolic and hormonal processes and satiety (Baghurst *et al* 1996).

The use of visual analogue scales to assess satiety is one that has been successfully implemented in previous meal challenge studies (Holt, Delargy, Lawton and Blundell 1999, Romon, Lebel, Velly, Marecaux, Fruchart and Dallongeville 1999, Speechly and Buffenstein 2000). One limitation of this assessment is that overweight people tend to display poorer sensitivity to satiety or appetite (Friedman 1995, Speechly and Buffenstein 2000), therefore limiting the capacity of these scales to detect differences. Also, satiety scales yield data including inter-individual variability, that may reduce statistical power, therefore lessen the chance of determining subtle significant differences (Romon *et al* 1999).

3.5.5.1 Survey instrumentation

There are a number of confounders when investigating feeding behaviours and appetite which may also impact on measure of satiety. Factors such as the energy density of foods, presence of other nutrients in foods, sensory or organoleptic attributes of foods, and the psychological, physiological and genetic predisposition of the subjects involved in the investigation (Stubbs *et al* 2001). It is therefore important to maintain consistency in the presentation and preparation of foods provided during the meal challenges.

The psychological, physiological and genetic predisposition of the subjects would not be confound with subject comparisons between meal challenges. With regard to between group comparisons, recruitment of similar subjects and, randomisation to groups will expectantly distribute subjects evenly between groups.

During each meal challenge, subjective satiety scores were assessed using 100mm visual analogue scales, where 0% (extremely hungry) was anchored on the left and 100% (extremely full) anchored on the right (Appendix 9). These were administered at baseline (fasting) and hourly intervals during the test meal period. Subjected were asked to mark each scales with an "X" representing where they felt in the continuum between 0 and 100% for each survey item. Complete satiety data were obtained for only 7 subjects due to procedural difficulties and these data were therefore not analysed.

3.6 Dietary assessment and monitoring

Dietary intake may be assessed by a variety of methods, although few researchers are confident that the quality of analysable dietary data produced from these methods is adequate (Kohlmeier 1994). It has been reported that the most difficult variable to measure in energy balance studies is habitual food intake (Westerterp 2000) making research into diet-disease relationships a challenging one. Given this, the following review of dietary assessment methods complimented by work completed on inaccuracy in reporting dietary intake, and finally, methods for addressing the validity of dietary data, will be considered. These components, supported by previous dietary intervention trial research, will provide the evidence for the selection of method, measurement design and validity testing used within the current study.

In brief, dietary intake was assessed using a DH interview at baseline, and at 3, 6, 9 and 12 weeks in the intervention. In addition, subjects were asked to complete a checklist on the consumption of test foods within the trial for a measure of compliance (Appendix 10). Data were entered into the nutrient analysis software program *FoodWorks* (v2.10.136, Xyris Software, Highgate Hill, Brisbane), using the Australian Nutrient database, NUTTAB 95 (Commonwealth Department of Health, Canberra). The validity of the DH interview data was assessed by comparing the DH interview to Goldberg and Black (Goldberg, Black, Jebb, Cole, Murgatroyd, Coward and Prentice 1991) cut-off limits, in addition to a comparison using basal metabolic rate (from indirect calorimetry).

3.6.1 Dietary methods

An individual's food intake will vary on a daily, weekly and seasonal basis (Nelson 1997). To compound this variations is another aspect of variability, on the subject of how much an individual's intake differs will vary from person to person (Food and Nutrition Board, Institute of Medicine 2000). Subjects that consume high average intakes will also tend to show more variation in their intake patterns that those with lower average intakes (Nusser, Carriquiry, Dodd and Fuller 1996 cited in Food and Nutrition Board, Institute of Medicine 2000). Barnard *et al* (2002) supported this phenomenon. "To have consistency, dietary intake data should reflect typical food patterns of the individual. Memory lapses, inaccurate knowledge of portion sizes, and over- or under-estimating of amounts consumed jeopardize the reliability of any food intake method." (DeHoog 1996:369). Therefore dietary intake is not easily analysed. Nevertheless, diet history interviews, food records, food frequency questionnaires, 24

hour recalls and checklists are well known assessment techniques used (Nelson and Bingham 1997). These techniques, outlined in the following table (table 3.6.1) will demonstrate support for the diet history interview's use in the current dietary intervention trial.

Table 3.6.1 Review of dietary assessment methods

Please see print copy for Table 3.6.1

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There are a number of strengths outlined regarding the DH interview. In FRs, meticulously weighing food may frustrate subjects and complicate meal planning (Aronne *et al* 2001). It is important that individual preferences and lifestyle be a function within any nutritional plan formulated (Aronne *et al* 2001). Hence, the flexibility of the DH techniques is perhaps its most appealing characteristic as it allows researchers to assess the variability that appears to be so problematic. The DH provides a basis for making changes within a persons usual pattern of intake (Eschleman 2000), making it particularly appropriate for dietary intervention trial such as the current study. Personal communication with Noakes (1999) confirmed that regular assessments are essential in dietary intervention trials, suggesting that monthly intervals would be too great a period for adequacy of dietary data. Three-weekly intervals between each diet history interview were proposed for the current study. More regular intervals would have significantly increased subject burden considering the large number of measures that were already proposed, and thereby a concern for maintaining subject numbers until the completion of the trial.

Research to improve dietary methods its fundamental to the study of diet-disease relationships (Nelson 1997). As mentioned in table 3.6.1, the DH interview can be compared for validity with Goldberg cut-off limits (reviewed later). The application and limitations of validity measures such as this are addressed elsewhere (Nelson 1997, Nelson and Bingham 1997, Westerterp 2000). However, within the current study, where data from indirect calorimetry would be readily available, resting metabolic rate measures were also planned for comparison with reported energy intakes. “While the comparison of reported energy intake with estimated basal metabolic rate does not solve

the problem of underestimation of food intake it enables plausible intakes to be separated from those which are clearly underestimates. This is particularly important when food intake data are used to assess dietary adequacy in individuals or groups." (Rutishauser 1997:69).

Other methods for testing validity are presented in table 3.6.1. This is a principal concept in dietary research considering the likelihood of measurement error (Nelson and Bingham 1997). Obesity and overweight populations are believed to be a problematic study group due to the findings that they under-report intake (Johnson, Goran and Poehlman 1994 and Lichtman *et al* 1992 cited in McManus *et al* 2001, Nelson and Bingham 1997, Johnson 2000). Results inconsistent with these findings have also been reported (Poppitt, Swann, Black and Prentice 1998). Also, under-reporting is more likely to occur with 24 hour recalls than the DH or food records (Black 1982 cited in Nelson and Bingham 1997) and may not be related to a physical characteristic, but rather food types such as high fat (Heitmann, Lissner and Osler 2000) and sugary foods (Poppitt *et al* 1998).

3.6.2 Criterion validity of dietary data

An objective measure of EE, provided through the indirect calorimetry method employed (flow-through, ventilated hood system), enabled comparison of reported EI from the DH interview with the EE determined analytically. The EI reported in the initial DH interview was correlated with the fasting resting metabolic rate assessed in the initial assessment for the trial and the final (week 12) values. For the final DH, reported EI was similarly correlated with initial and final indirect calorimetry data. Data

analysis, expressed as rho (r) and significant at $p < 0.05$.

The validity of the DH interview was examined through a comparison of reported EI, derived from the DH interview data, with Goldberg and Black (Goldberg *et al* 1991) cut-off limits, and subsequently EI was compared with metabolic rate estimates (EE) assessed through indirect calorimetry. Energy intakes were assessed using a DH interview at baseline, and at 3, 6, 9 and 12 weeks in the intervention. Raw data were then entered into the nutrient analysis software program *FoodWorks* (v2.10.136, Xyris Software, Highgate Hill, Brisbane), using the Australian Nutrient database, NUTTAB 95 (Commonwealth Department of Health, Canberra) before evaluated using Goldberg cut-off limits.

A physical activity level factor of 1.55 was assigned for all participants as it would have been too cumbersome to warrant the inclusion of a physical activity questionnaire given the period of the intervention trial. If the questionnaire had been used, subjective physical activity levels can be applied (light, moderate or heavy activity) with reference to the FAO/WHO/UNU document Protein and Energy Requirements. Basal EE, were derived from Schofield equation (Schofield, Schofield and James 1985). The ratio of the EI and derived EE value incorporating an estimated physical activity level was assessed with the Goldberg upper and lower cut-off limits. A value for EI: EE within the range of 1.17 to 2.06 classified the participant as an ‘accurate reporter’. Discrepancies above or below this range provided the basis for ‘inaccurate reporter’ categorisation. Data analysis is represented as mean EI:EE with standard deviation and with reference to reporting categories over time.

At the group level, this instrument is able to determine overall bias associated with reported energy intakes (Black 2000). The need for a PAL is one limitation, though the PAL value chosen was anticipated to be representative of this population and less significant given that the group would be compared against themselves and all subjects instructed to maintain their level of physical activity for the duration of the intervention trial. Another limitation surfaces with the Schofield equation's use within the calculations, as BMR of obese subjects may be overestimated and fail to detect under-reporters. This misclassification could also prevail at the individual level, where the cut-off level may be inappropriate considering individuals that have high energy requirements (Black 2000). Despite these considerations, this tool has been useful in investigating 'low energy reporters' and helps to direct researchers in identifying individuals who provide poor data (Black 2000).

3.6.3 Relative validity of dietary data

An objective measure of EE, provided through the indirect calorimetry method employed (flow-through, ventilated hood system), was used to compare reported EI from the DH interview. The EI reported in the initial DH interview was correlated with the fasting resting metabolic rate assessed in the initial assessment for the trial and the final (week 12) values. For the final DH, reported EI was similarly correlated with initial and final indirect calorimetry data. Data analysis was expressed as rho (r) and significant at $p < 0.05$.

3.6.4 Achievement of dietary targets

With regard to manipulation based on personal likes and dislikes, the following method was chosen. All participants were provided with each of the foods and beverages available, with recommended amounts based upon what they usually ate, for example, the amount of yoghurt. If a product was not suited to the individuals likes or usual dietary patterns, some of the alternative and preferred food choices for intervention were offered as a substitution, for example, another slice of bread. For the purposes of analysis of DH interview data, all subjects were asked to maintain a constant level of physical activity throughout the intervention that was consistent to their pre-intervention physical activity behaviour. In addition, both intervention food appreciation and fluctuations in physical activity were examined in the non-compulsory intervention trial survey that subjects received on completion of their final metabolic measures.

Daily compliance to *Hi Maize* intervention foods was measured using the checklists provided. The foods and amounts specified were entered into an Excel spreadsheet, then the amount of RS provided for each food over the 12-weeks calculated. This total value was then converted to a daily RS intake. Outcomes were expressed as mean, standard deviation and range.

The groups, provided with equivalent foods to achieve normal or high RS intakes, could still encounter possible displacement of foods, and therefore cause a discrepancy in nutrient intakes. An examination of dietary intakes at 3 weekly intervals beginning from an initial pre-intervention assessment would produce sufficient evidence for a repeated measures analysis. This comparison of nutrient changes over time between dietary

groups and within subjects from baseline values was taken as significant at an α level of 0.05. The values compared included: energy intakes (EI), percent contribution of macronutrients and fat subtypes to EI, including alcohol, and absolute amounts of macronutrients, fat subtypes, dietary fibre, starch, sugar, calcium, phosphorus, and dietary cholesterol.

3.6.5 Identification of major food sources of starch

In addition to the general manipulation of dietary intake and its 3-weekly interval assessments, variability of initial consumption of RS in all participants was an important consideration. As mentioned earlier, there are a number of sources of RS available and each of these contributes only small amounts of RS. For the purposes of evaluating the feasibility of RS incorporation in diets, it was necessary to investigate the sources of starch already present in the trial participant's diets. As the effectiveness of increasing this agent in dietary management of the metabolic syndrome was also a consideration, the pre-intervention DH interview seems most appropriate to examine.

Subjects underwent an initial DH interview with a trained dietitian (Brenninger V). Dietary data were analysed using *FoodWorks* (v2.10.136, Xyris Software) containing the Australian nutrient database AusNut (ANZFA). Foods were grouped into categories, and the percent contribution of these groups to total dietary starch was assessed. As a quality assurance measure, Goldberg cut-off limits (Goldberg *et al* 1991) were applied to assess accuracy of reporting overall energy intakes and results expressed as mean and standard deviation.

3.7 Social context of dietary intake

As mentioned in section 3.2.2, assessing metabolic change as a consequence of dietary manipulation requires more than statistical documentation for the benefits to be transferred to clinicians and subsequently the general public. The following two sections, 3.7.1 and 3.7.2, address the social context of dietary intake.

3.7.1 Lifestyle history questionnaire

Progress in defining a cure remains limited, although changes in lifestyle and food consumption are thought to be the main causes of metabolic abnormalities, such as obesity, a major component of the metabolic syndrome (WHO 1997). Lifestyle is a known source of variability (Murphy 2001); therefore the use of a lifestyle history questionnaire was appropriate for the context of this study. Refer to section 3.3 for more detail of this questionnaire.

3.7.2 Participant survey

Dietitians and clinicians require knowledge of the feasibility of the dietary intervention to the extent as that for the efficacy of the intervention. A number of measures, both quantitative and qualitative were utilised for gaining insight into this component of the hypothesis and theory on human variability. An opportunity for the subjects to express any concerns about the feasibility of the incorporation of the intervention foods or about the measurement of metabolic or dietary variables was provided through a semi-quantitative survey. The intervention trial survey is shown in Appendix 3.

The pre-piloted intervention trial survey was completed subsequent to the 12-week dietary intervention trial (see 3.2.2). Its aim was to determine barriers to the feasibility and efficacy of clinical trials from a participant's perspective. The participants were offered the anonymous intervention trial survey on completion of the 12 weeks and asked to return it in the envelope provided. Survey data were then collated and where applicable, content analysis performed. Results were expressed as a percent of the total number of respondents and with descriptions where applicable.

3.8 Analysis of intervention trial data

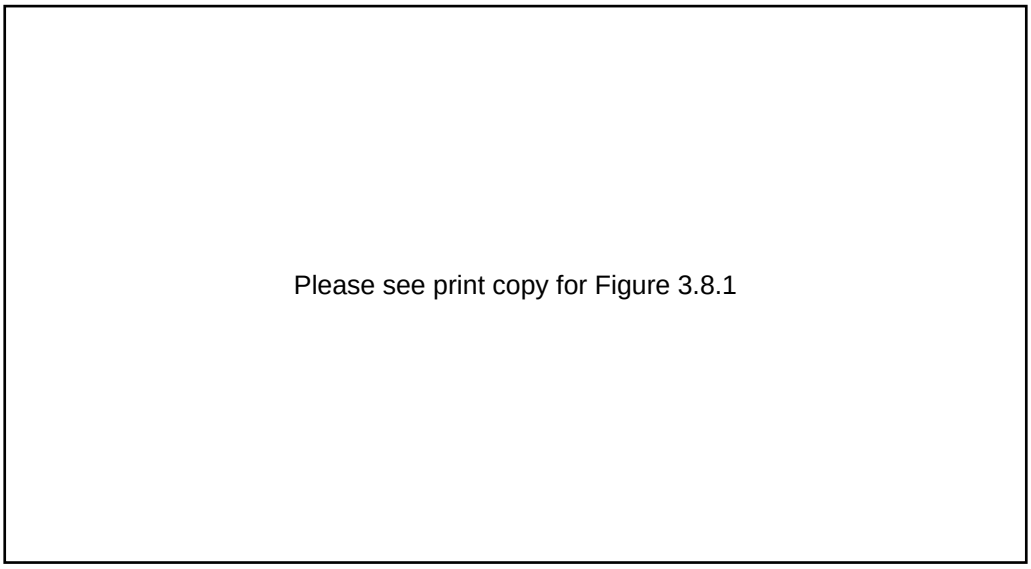
Distributions of variables were tested for normality using the Shapiro-Wilk test. One-way ANOVA was used to test the similarity between groups at baseline and 12 weeks. Changes over time within and between groups were assessed by repeated measures ANOVA. Differences between groups at the endpoint were assessed by ANOVA, or ANCOVA when adjusting for potential baseline confounders. Test meal glucose, insulin, triglyceride and RQ time profiles were compared between test meal types and groups using compound MANOVA. A small number of missing values in these data sets were estimated by linear interpolation between adjacent values. Respiratory quotient, metabolic rate, glucose, insulin, triglyceride and satiety areas under the curve were analysed likewise. Analysis were completed using statistic software computer package JMP (Version 3.2, SAS institute Inc, Cary NC, 1989-1996).

3.8.1 Impact of social factors

Optimal nutritional status is a balance between our nutrient requirements and the adequacy with which we meet these. DeHoog (1996) illustrated how this balance is

the consequence the interaction between a number of variables on both sides of the equation (Figure 3.8.1). In particular, the left hand side of the diagram reinforce that dietary intake is influenced by its social context.

Figure 3.8.1 Basis for the social content of optimal nutrition.



Source: DeHoog (1996) The assessment of nutritional status. In: Mahan LK and Escott-Stump S (Editors) Krause's food, nutrition and diet therapy (9th edition). WB Saunders Company, United States of America. Chapter 17 p362.

Social factors measured through both the lifestyle history questionnaire and intervention trial survey will provide insight into discussion on the feasibility of this dietary manipulation and another level of interpretation of metabolic outcomes. In the instance where variability exists, survey outcomes will be used to help explain some of these differences.

3.9 Ethics

The University of Wollongong human ethics committee granted ethical approval. Examples of the participant information sheet and consent forms are presented in Appendix 11.

4. Results

A principal theme of the methodology section was to address how evidence based nutrition therapy captures metabolic variation in responses between individuals and the social context of these responses. The study of the feasibility and efficacy of a high amylose RS diet in an overweight, insulin resistant population requires a broad appreciation of a range of sciences, from physiology to dietetics and sociology. The various questions addressed through those disciplines draw on a range of methodologies, employing both and quantitative and qualitative methods. The presentation of results therefore creates a challenge, which is addressed by the initially presenting work on methods development, followed by the clinical intervention outcomes, and finally, social commentary results.

4.1 Methods development

4.1.1 Diet history interview

One of the biggest challenges for conducting an intervention trial is the assessment and monitoring of dietary intake. In clinical studies, this is mostly done through a diet history interview, making human communication an important area of understanding. Work on communication in the diet history thus comprised the main part of preliminary research for this thesis. A study of talk is a useful approach to addressing communication issues. Talk is an appropriate medium to gain insight into how humans construct meaning, produce order and 'make sense' (Psathas 1995). Studies involving general practitioners (Robinson 2001, Robinson 1998), pharmacists (Pilnick 1998), and counsellors for alcoholics anonymous or AIDS (Perakyla and Silverman 1991)

acknowledge that well designed questions and probes perceivably improved by findings from conversation analysis.

In the thesis presented here, research on the DH interview expanded on previous published studies (Tapsell 1997a, 1997b, 2000) and began as part of a major project undertaken within a Masters of Science course (Brenninger 1998). A number of publications extending from this Masters research were developed during the course of the thesis (Brenninger, Tapsell and Barnard 2001, Tapsell, Brenninger and Barnard 2000, Brenninger *et al* 1999, Barnard *et al* 2002), bearing in mind the relevance to the central study. The main findings from the thesis were that subjects used the term "probably" and "it depends" when describing certain food consumption patterns.

a) Additional observations from conversation analysis

Further analysis was conducted on the tape-recorded DH interviews from the original pilot study sample during the course of this thesis.

Subjects: Table 4.1.1.1 displays the subject characteristics of the group examined by DH interview and energy balance using doubly labelled water. Subjects comprised 7 females and 7 males volunteers aged 22 – 59 years with a range of body weights (BMI 19 – 33 kg/m^2) (Table 4.1.1.1).

Table 4.1.1.1 Baseline subject characteristics for group overall [a]

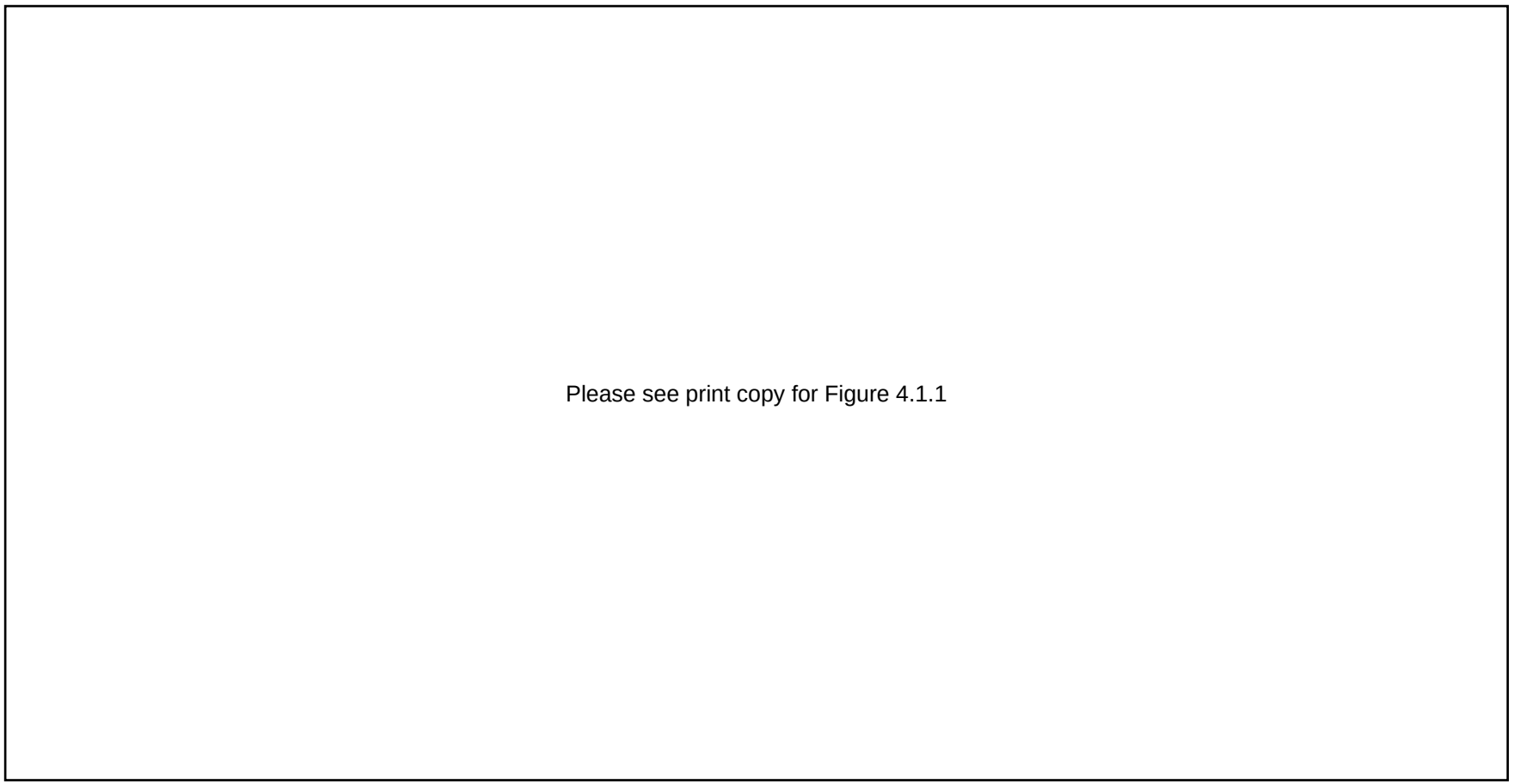
Please see print copy for Table 4.1.1.1

[a] Values for four of these participants were provided by Raaschou (1997) in a previous study, though at the same time as all their data were collated, and previously reported in Barnard *et al* (2002). [b] Mean and standard error of the mean; kg: kilograms.

The expression "probably" is a modal term, known to serve the function of lessening the degree of certainty of the statement (Coates 1986, Knapp and Watkins 1994). As with the word "probably", the utterance "[it] depends" was strategically placed with a similar association to a particular type of phrase and order of dialogue. The phrase "[it] depends" was observed repeatedly whenever subjects were indicating areas of variability in food and beverage intake. This word or phrase is believed, in linguist disciplines, to reduce the commitment to what the person is communicating to another (Coates 1986). We refer to this as 'hedging'. Thus, in developing the interview schedule for the DH, note was taken that particular care should be given when these utterances were heard by the interviewer. Clarification of serving size or frequency of consumption would be undertaken. Either way, the presence of these expressions provided "evidence in the talk" of variation with an individual's usual food consumption patterns.

Having made observation of the use of ‘it depends’ and ‘probably’ in the talk displayed through DH interviews, a summary of the pattern of use throughout the interview provided an indication of possible variation or quantification difficulties in food choices (Figure 4.1.1). All instances of the use of “probably” or “it depends” were identified in the transcripts. These instances were then quantified in reference to actual foods or beverages discussed. Content analysis was then applied to the resulting food categories and the number of instances that each of the hedging and modal phrases applied to each category was tabulated (Figure 4.1.1).

Figure 4.1.1 Instances of use of "it depends" and "probably" in fourteen dietetic interviews with reference to specific food categories



Overall, this analysis indicated that most of the variation in single food items consumption was likely to occur with bread/sandwiches and take-out/eat-out foods, and to a lesser extent, vegetables/potato, meat and fish. The use of the term "probably", that has previously been discussed with reference to problematic quantification or estimation of amounts or frequency consumed (Tapsell *et al* 2000, Knapp and Watkins 1994), was commonly linked with talk on pasta, rice, red/meat/pork, vegetables/potatoes, and bread/sandwiches.

Focussing on these meal descriptions then, the main food combinations, or cuisines reported were analysed. Three, four and seven different categories were identified in the breakfast, lunch and dinner meals respectively (Table 4.1.1.2). The range of different cuisine types and the mean variation score increased from breakfast to lunch. The breakfast meal was much less variable in cuisine choices (range 1 – 3, variation score 1.625) and dinner was the most variable (range 2 – 6, variation score 4.125). This continued the analysis identifying the likely location of greatest variation in food consumption patterns throughout the day. Data on four participants could not be included in the analysis due to unavailability of the interviews in transcript form. In addition, two shift workers in the remaining sample of ten subjects consumed snacks as opposed to 'meals' shown by both the dietitian and the participants being unable to clearly define each meal, therefore data from these two participants were not represented in this analysis.

Table 4.1.1.2 Cuisine categories identified in breakfast, lunch and dinner meals (n = 8)

Breakfast	**Lunch**	**Dinner**
Cereal/ fruit/ yoghurt	Sandwich	Soup
Toast only	Takeaway meal (not a	Meat and vegetable
Eggs/ leftovers	sandwich)	Pasta meal
	Leftovers/ soup	Takeaway/ pizza
	Yoghurt/ fruit	Rice dish
		Restaurant meal
		Vegetarian meal

b) Implications for the intervention trial

These findings suggest that the DH interview will display considerable variation in the eating habits of subjects, volunteering for the intervention trial. They also provide insights into areas of the interview which would require additional probing and cognitive support (for example, with the use of food models) to ensure reporting which is as accurate as possible.

4.1.2 Participant survey

4.1.2.1 Study participants

The preliminary work on the DH interview indicated the potential for a large variation in behaviours within a study sample. Following the observations from conversation analysis, a set of questions was devised to characterise subjects, not only in terms of eating habits, but also with respect to food preparation, exercise and weight maintenance patterns. The questionnaire was developed and tested by another student

(Barnard), but utilised questions in diet developed by this author (Brenninger) based on the conversation analysis work reported in previous sections of this thesis. Characteristics of subjects undertaking the intervention trial, so derived would act to provide a description of the variation in the study sample with respect to lifestyle factors. This would be relevant to the overall questions of feasibility and efficacy of dietary interventions in the free-living context.

Twenty participants of the twenty-five subjects who began the intervention trial (Table 4.2.2) completed the questionnaire (n=20; Age: μ (SD)= 42.3 (13.3) years; Weight: μ (SD)= 84.9 (17.0) kg; Height: μ (SD)= 169.3 (9.7) cm). Invalid answers and null responses were not recorded within the calculations for the mean and range. Where participants answered 'never' or 'zero', the responses were included in the resulting mean and range of values.

a) Weight History

Dietitians assessing a person for dietary treatment would normally take a weight history to establish a possible dietary explanation for weight gain. At the time of assessment the self-reported mean weight of the sample was 84kg, ranging from 58 – 129kg. The mean lowest adult weight reported by the group 65kg, ranging from 44 to 100kg. Most respondents indicated that their highest weight was also their current weight. Despite their present overweight or obese status, only one respondent stated that they were substantially overweight as a child or adolescent, two did not know and the remaining 17 reported that they were not substantially overweight in childhood.

The most prominent weight change experienced, was an increase in weight with age, followed by a steady weight gain during adulthood (usually began after having children or mid-thirties or forties); post-pregnancy weight gain; weight cycling; weight gain resulting from changes in activity and diet; and miscellaneous incidents prior to weight gain (spider bite incident, travelling, fluctuating beer consumption). In the three months preceding the survey, ten participants had remained at a constant weight; six had experienced a slow increase of approximately 3 – 5kg, while two had experienced some weight loss of approximately 4kg. In addition, at least one of the respondent's immediate families had been substantially overweight in 65% of cases.

Three out of 10 respondents acknowledged weight cycling phases of losing and regaining weight that were not attributed to their menstrual cycle. Seven reported a previous mean weight loss of 6.13kg (range, 1 – 15kg). The most weight ever regained, reportedly ranged from 1 – 11.6kg with a mean of 5.27kg.

In response to whether diet influences body weight, all respondents believed that there were some foods that should be avoided if a person was trying to lose weight. The dominant theme was that foods high in fats were the main cause of obesity. Next were sugary/ sweet foods followed by takeaway foods. Alcohol or nuts represented by single responses only. One person did not deliver a response listing food types to be avoided. Environmental factors were implicated consistently as important influences on weight gain.

b) Exercise Patterns

When asked to describe usual exercising pattern, four respondents indicated that it was non-existent (sedentary); nine replied that their exercise was much the same from week to week, and six noted that it was variable. One individual indicated it was both the same and variable. The reasons offered for variable exercise patterns were due to the person's workload or other commitments, the season or cold weather, the type of sport being dependant on the season or basic changes. Two respondents discussed variations within the activities. The extent of effort in exercise also varied for the group (Table 4.1.2.1).

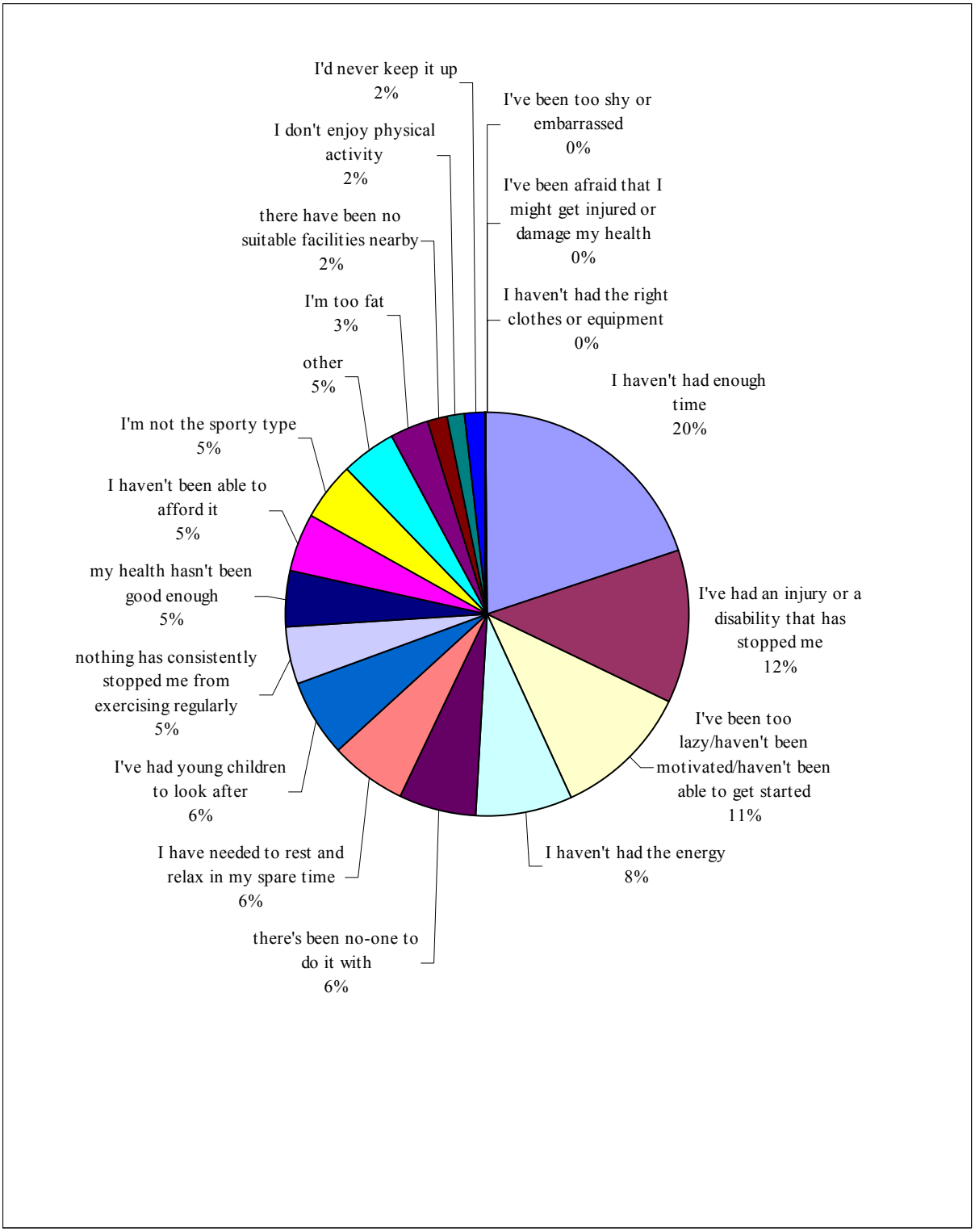
Table 4.1.2.1 Frequency per week by level of effort for 20 minutes of continuous exercise

Effort level (20 minutes continuous)	Number of responses				
	Not applicable	**0 times/ week**	**> 0 times/ week**	**Mean times/ week**	**Range of times/ week**
Light effort[1]	4	9	7	1.9	2 – 7
Light-moderate[2]	4	7	9	2.3	1 – 10.5
Moderate[3]	4	7	9	2.4	1 – 9
Moderate-hard[4]	4	10	6	1.8	1 – 10
Hard or very hard[5]	4	15	1	0.1	2

[1]Light effort (e.g. strolling on level ground); [2]light to moderate effort (e.g. gardening – weeding, trimming); [3]moderate effort (e.g. slow cycling, slow jogging, walking uphill); [4]moderate to hard effort (e.g. swimming laps, running cross country); [5]hard or very hard effort (e.g. competitive cycling or rowing, fast running).

Of the 19 respondents, most (n = 11) did not change exercise patterns in the 3 months before the trial, four did, and the remaining 4 answered ‘not applicable’. Reasons for these changes were also highly individual. The influence of exercise to aid weight loss was believed to be very important for most (n = 14), or ‘important’ for some (four), and ‘kind of important’ for two. “Lack of time” was recognised as the most important barrier to exercise (Figure 4.1.2.1).

Figure 4.1.2.1 Number of responses for each reason that subjects refrained from exercise



c) Eating Patterns

All participants generally ate three meals daily. Apart from the four who indicated 'it varied', the mean number of times per week for breakfast, lunch and dinner were consumed were 6.3, 6.9 and 6.9 respectively. Only one person listed less than seven times per week for two of these meals (specifically, breakfast 4/week and lunch 6/week). Breakfast was the most variable in terms of frequency of consumption. Of these meals, the numbers of times each were described as takeaway food or eaten out of the home was very rare for breakfast (mean = 0.01/week, n = 18). In contrast, the mean number of times these were described for lunch and dinner were 1.4/week (n = 18) and 3.3/week (n = 18) respectively.

Thirteen subjects felt that they ate regular meals and seven ate meals in no particular pattern. With reference to snack foods, four ate regular snacks, eleven ate snacks in no particular pattern, and five rarely consumed snacks. One person did not respond. These patterns were believed to fluctuate with workload, work shifts, exercise patterns, or other activities.

d) Food preparation and familiarity with food

The participants of the survey prepared their own breakfast, on average, 5.6 times per week (range: 0 – 7/week). They prepared their own lunch a mean of 4.4 times per week (range: 0 – 7/week) and dinner on 4.0 occasions through any given week (range = 0 – 7/week). Ten participants solely did the grocery shopping for the household. Four respondents shared the shopping, regularly, four occasionally completed the shopping, and two respondents never did it. Eight of eighteen individuals had tried a new food

product recently including different margarines (n = 5), or individually listed foods such as bread, new drinks, ice blocks, tahini, Asian sauces, and noodles.

In general, the survey population preferred to eat the following foods on a daily basis: vegetables (9), fish (7), meat (6), fruit (6), chicken/white meat (5), pasta (4), bread (4), cereal/ Weet-bix® (3), carbohydrates (2), a variety (2), yoghurt/dairy products (2). Many other individual responses were given. When asked why they preferred these, the dominant theme exposed was that the foods were tasty, enjoyed or satisfying (n = 10), believed to be healthy (n = 7), due to habit (n = 3), for cooking reasons (n = 2) or to allow for treats (n = 1).

The opposing question was then asked. "Which foods would you prefer to avoid eating on a day-to-day basis?" In order of highest number of responses to lowest, takeaway/fried foods was most frequently named (n = 7). This was followed by fatty/oily foods/high in saturated fat (n = 4), spicy foods (n = 2), peas (n = 2) and meats/deli foods (n = 2). The remaining responses were actual food dislikes and bland foods, in single responses only. The participant's avoidance to these foods, due to reasons such as 'dislike' (n = 5), adverse reaction (feel heavy/sick) (n = 4), believed to be unhealthy (n = 3), and equally (n = 2) lacked energy, bland, weight gain, tasty, or expensive.

The participants beliefs surrounding 'good' and bad' foods were then investigated. In general, vegetables (n = 16), fruit (n = 15), bread (n = 6), pasta/rice, lean meat/meat, carbohydrates, fish, and low fat foods received the greatest responses (shown in order of

highest to lowest). These foods were reported to be nutritious, required for good health, promoted through literature or ads, low fat or containing good dietary fats, fibrous, and related to body weight. Foods in the 'not good' classification primarily included: high fat or deep fried foods, (n = 12), takeaway/ snack foods and sugar (n = 5 for each). Reasons for their classification were linked to their containment of fats (n = 7), relationship to heart disease or cholesterol (n = 6), lack of nutritious nature (n = 4), high in sugar, or related to an overweight status (n = 3).

Actual consumption of some foods was described, including typical dinner foods and amorphous foods. Pasta was eaten on average 1.6 times per week for 16 subjects (range: 0.3 – 3/week). It was 'too difficult to judge' the number of times pasta, rice and alcohol, was consumed on a weekly basis by two respondents, and one participant regarding milk in cereal. Mean reported weekly rice intake (n = 17) was 1.4/week (range: 0.3 – 7/week). Average weekly bread consumption (n = 20) was 6.7 (range: 3 – 7/week), while margarine or butter was consumed (n = 16) 6.2 times per week (range: 2.5 – 7/week). Mean alcohol intake (n = 15) was 3.9/week (range: 0 – 7/week), though two rarely consumed alcohol. Milk in cereal (n = 16) averaged 5.4/week (range: 1 – 7/week), again two rarely used milk in their cereal. Vegetables (n = 19) were reported to be eaten 5.9/week (range: 1 – 9/week). One rarely ate vegetable, three reported that they rarely ate fruit, which on average, was consumed (n = 17) 5.7/week times per week (range: 0.5 – 14/week).

Conceptualising the way in which this group recognises volume or quantities, presented the need for a series of open-ended questions based on amounts consumed of a few

common foods. A complex array of answers from the survey group showed that an obstacle between reporting of dietary intake and how the dietitian documents it could be through the lack of food models or measuring devices.

Six participants found that the amount of pasta and rice was too difficult to estimate. This was also the case for vegetables (5), bread and fruit (2), margarine/butter and alcohol (3), and milk in cereal (1). The remaining respondents indicated for pasta (n = 12) an average of 1.2 cups cooked was eaten (0.66 cup raw) which is equivalent to 182g cooked (70.5g raw), ranging from 0.75 cup cooked to a large bowl (~372g). Rice was believed to be consumed in similar quantities: (n = 11). The mean was 1.3 cups cooked (0.34 cups raw), ranging from 0.25 cup raw to 2 cups cooked. Responses to the bread question on the other hand produced a mean of 4.2 slices or 1.7 rolls per occasion (range: 2 to 11 slices).

The reported intake of margarine or butter when eaten was 2.8 teaspoons or 0.71 tablespoons (n = 13, range: 1 teaspoon to 3 tablespoons). Two stated that they rarely ate this type of food. The mean alcohol intake reported (n = 16, including 3 that specified zero) was 2.8 full strength middies of beer or 2.9 x 140ml wine. There was a wide range reported from no alcohol to 2177ml-beer intake. Another food, which tested participant's ability to define amounts, like pasta and rice, was the milk poured into breakfast cereal. The mean of sixteen responses given was 0.70cups (175 ml), ranging from ½ cup to 1½ cups, though one subject stated that they rarely used milk in cereal. Interestingly, defining the amount of vegetables proved more difficult to ask about than expected, leading to seven invalid responses. The remaining six responses, on average

equalled 1.1cups (256kJ) (range: ¾ cup to 2 cups). Finally, fruit consumption was reported on average 2.3 pieces for the sixteen subjects (range: 1 – 7 pieces).

e) Implications for the intervention trial

Although participants in this study were all overweight, this survey provided evidence of variation in a number of areas. On average though, the study sample had been within the healthy weight category until their mid-thirties or forties and/or before pregnancy. Environmental factors appeared to be largely related to excess body weight, which supported the need for addressing physical activity and energy intakes. Exercise patterns varied between and within subjects that could be a problem for the study. The most distinct reason for limited exercise was a "lack of time". Although all participants had a body mass index greater than 25kg/m^2, they showed knowledge gained through various mediums, targeting weight loss. The subjects consumed three meals on average per day and for most, there was no particular pattern on snacks nevertheless this probably indicates stability in consumption patterns which would aid the intervention. The recognition of portion sizes, in particular amorphous foods such as rice, was reasonably well answered, though reported alcohol intake showed great variation. Most importantly, this survey suggested the communication between the dietitian and the participant would need facilitation by portion size photographs, food models and a number of cups, spoons and example food packages, to ensure accuracy of dietary reporting.

4.2 Dietary intervention trial – Study participants

Twenty-eight candidates met the overweight (BMI > 25) and eligibility requirements. Three subjects were unable to be cannulated due to poor veins, fainting, and nausea. Of the remaining 25 subjects who began the trial, two dropped out for personal (2) reasons. One subject did not complete the trial due to lengthy illness and antibiotic treatment. Thus, complete data were obtained from 22 subjects (12F, 10M) for the 12-week intervention. Of these 20 were classified as insulin resistant (M < 7mg/kg.min) (DeFronzo *et al* 1979).

4.2.1 Demographic and social profile

All participants (10 males, 12 females) were from the Illawarra region, with an age range of 20 to 60 years. All were non-smokers. Volunteers were free from bowel complications for at least 3 months before screening for the trial. Of the females, no volunteers were pregnant or considering pregnancy for the subsequent 3 months.

4.2.2 Baseline clinical characteristics

Baseline data for all subjects who completed the chronic intervention are presented in table 4.2.2. Following dropouts, gender was mismatched between intervention groups, and BMI at baseline in the control group (30.2 ± 0.9) was significantly ($p = 0.02$) higher than in the RS diet group (27.5 ± 0.8). This was accompanied by significantly reduced HDL cholesterol (0.97 ± 0.07 versus 1.19 ± 0.08, $p = 0.05$) and insulin sensitivity (3.42 ± 0.43 versus 6.01 ± 0.79, $p = 0.006$). However, both groups were overweight (BMI > 25), and all bar two subjects (in the RS group) were insulin resistant (M < 7mg/kg.min)

(DeFronzo *et al* 1979). Exclusion of these from the analyses had no effect on any inferences (not shown).

Table 4.2.2 Effects of 12 weeks intervention with control and RS diets on body composition and metabolic variables (mean ± sem)

	Control Group (5F/6M)			Intervention Group (7F/4M)			Diet effect [1]
Variable	Baseline	12 weeks	%Change	Baseline	12 Weeks	%Change	% Baseline (95% CI)
Age (yr)	42.6 ± 3.4	NA	NA	43.4 ± 4.8	NA	NA	NA
Body Weight (kg)	87.0 ± 4.4	87.8 ± 4.4	0.8%	78.6 ± 2.6	79.6 ± 2.8	1.3%	0.4 (– 1.2, 2.0)
BMI (kg/m^2)	30.2 ± 0.9	30.2 ± 0.9	0.0%	27.5 ± 0.7	27.5 ± 0.8	0.3%	0.3 (– 1.6, 2.2)
% Body Fat	36.6 ± 2.7	39.0 ± 2.7	6.3%	37.7 ± 3.2	38.3 ± 4.0	1.7%	– 1.2 (– 6.4, 3.9)
Total Cholesterol (mmol/l)	4.4 ± 0.2	4.3 ± 0.3	– 1.0%	4.6 ± 0.3	4.5 ± 0.3	– 3.3%	– 2.4 (– 12.2, 7.4)
HDL Cholesterol (mmol/l)	0.97 ± 0.07	0.98 ± 0.07	1.7%	1.21 ± 0.09	1.19 ± 0.08	– 2.2%	– 3.3 (– 19.0, 11.6)
Triglycerides (mmol/l)	1.50 ± 0.28	1.99 ± 0.52	33%	1.11 ± 0.16	1.33 ± 0.21	20%	– 24 (– 117, 69)

NA: not applicable. [1] Percent of baseline value in the Intervention diet group.

Table 4.2.2 continued: Effects of 12 weeks intervention with control and RS diets on body composition and metabolic variables (mean ± sem)

	Control Group (5F/6M)			Intervention Group (7F/4M)			Diet effect [1]
Variable	Baseline	12 weeks	%Change	Baseline	12 Weeks	%Change	% Baseline (95% CI)
RMR (kJ/day)	1776 ± 115	1744 ± 97	– 1.8%	1642 ± 77	1642 ± 73	0.0%	1.9 (– 5.4, 9.3)
RQ	0.82 ± 0.03	0.83 ± 0.01	0.9%	0.82 ± 0.01	0.83 ± 0.01	1.7%	0.9 (– 6.1, 8.2)
Fasting Plasma Glucose (mmol/l)	5.38 ± 0.22	5.39 ± 0.22	0.2%	5.06 ± 0.21	5.09 ± 0.19	0.5%	0.2 (– 7.9, 8.3)
Fasting Plasma Insulin (mU/l)	15.3 ± 2.7	16.6 ± 2.6	8.4%	11.1 ± 1.5	12.3 ± 1.5	10.8%	– 0.7 (– 41, 40)
Insulin sensitivity (mg/kg.min)	3.42 ± 0.43	3.51 ± 0.42	2.8%	6.56 ± 0.92	6.01 ± 0.79	– 8.4%	– 9.8 (– 29, 9)

NA: not applicable. [1] Percent of baseline value in the Intervention diet group.

4.3 Effects of long term dietary changes

4.3.1 Changes in clinical outcomes

The effects of 12 weeks intervention with control or high amylose RS diets on body composition and metabolic variables are summarised in table 4.2.2. There were no significant effects of intervention on any measured variables either within or between groups. The estimated effects of the RS versus the control diet are presented in the last column of table 4.2.2 as percentage change from baseline levels in the RS group with 95% confidence limits. The RS diet resulted in an estimated 10% decrease in average insulin sensitivity, but the data cannot exclude a 9% increase with 95% confidence. Approximately 40 subjects would have been required for 80% power to detect an effect of that magnitude using the current protocol. Similar results were obtained when insulin sensitivity was expressed per kilograms of fat free mass (not shown).

4.3.2 Response to acute meal tests

a) Subjects

Five subjects either failed to complete both meal tests, or had failure of cannulations during one of the procedures. Baseline characteristics of those subjects with complete plasma data are summarised in table 4.3.2.1. As with the complete groups (Table 4.2.2) gender was mismatched between groups, associated with significantly increased BMI and decreased HDL cholesterol and insulin sensitivity at baseline in the control compared to the RS group.

Table 4.3.2.1 Baseline body composition and metabolic variables in subjects with complete acute meal test data (mean ± sem) [a]

Variable	Control Group (5M, 5F)	Intervention Group (2M, 5F)
Age (yr)	44.9 ± 2.8	44.9 ± 6.0
Body Weight (kg)	86.9 ± 4.8	78.1 ± 3.7
BMI (kg/m^2)	30.4 ± 0.9	27.5 ± 1.0 [b]
% Body Fat	38.3 ± 2.4	38.2 ± 4.1
Total Cholesterol (mmol/l)	4.4 ± 0.2	4.6 ± 0.4
HDL Cholesterol (mmol/l)	1.0 ± 0.1	1.2 ± 0.1 [b]
Triglycerides (mmol/l)	1.5 ± 0.3	1.2 ± 0.2
RMR (kJ/day)	1753 ± 125	1618 ± 106
RQ	0.83 ± 0.03	0.80 ± 0.02
Fasting Plasma Glucose (mmol/l)	5.3 ± 0.2	4.8 ± 0.1
Fasting Plasma Insulin (mU/l)	16.3 ± 2.8	9.3 ± 1.5
Insulin sensitivity (mg/kg.min)	3.2 ± 0.4	6.8 ± 1.3 [b]

[a] Subjects with complete insulin, glucose and triglyceride meal test data. Some of these subjects had incomplete RQ and Satiety data due respectively to the subjects' intolerance of the calorimeter hood and procedural problems (see legends to relevant figures and tables below). [b] Significant difference between groups ($p < 0.05$). M: male, F: female

b) Meal test responses

The effects of prior intervention diet and test meal composition on the metabolic responses to the meal tests are summarised in Table 4.3.2.2. As expected, glucose, insulin and RQ showed significant variations over time in response to the meals (Figure 4.3.2.1, A to D), but triglycerides did not. There was a strong effect of chronic diet group on glucose responses to the meals independent of test meal composition. This effect was detected as an interaction of chronic diet group with time that reflects an increased glucose concentration in the control group during the first half, but not the second of the meal profile (Figure 4.3.2.1A). There was no effect of chronic diet composition on glucose AUC (p = 0.13), consistent with the apparent tendency for higher glycaemic responses in the high amylose RS group during the second half of the meal profile. Since fasting glucose concentrations tended to be elevated in the low RS (LRS) group both before and after diet treatment (Table 4.2.2, Figure 4.3.2.1A), glucose responses to meals were also analysed as differences from fasting levels (delta). There was no significant effect of diet group on delta glucose over the whole meal profile (p = 0.22). However, the delta glucose response to the breakfast meal alone was significantly affected by diet group (p = 0.016, see Figure 4.3.2.1A). The trends in Ln(insulin) were qualitatively similar to those of glucose (Figure 4.3.2.1B) but were not formally significant (Table 4.3.2.2). However, a significant effect of test meal composition on insulin was detected, reflecting an increased insulin response to low RS meals (Figure 4.3.2.1B). Although this effect on insulin was not associated with any similar effect on glucose, there was no evidence of any discordance between glucose and insulin levels induced by meal composition when the individual area under the curves for glucose and insulin were examined together (Figure 4.3.2.2).

Table 4.3.2.2 Effects of chronic (intervention) diet and acute meal composition on plasma glucose, insulin and triglycerides, and RQ during meal tests[a]

		Effects				
Variable	**n**	**Time**	**Meal**	**Time*Meal**	**Time*Diet**	**Meal*diet**
Glucose	17	**0.002**[1]	0.25	0.2	**0.007**[1]	0.76
Ln(Insulin)	17	**<0.0001**[1]	**0.04**[2]	0.28	0.63	0.46
Triglycerides	12	0.25	0.15	0.72	0.21	0.55
RQ	15	**0.01**[2]	0.82	0.45	0.35	0.29

[a] Results are presented as significance levels (p values) of effects in a compound MANOVA with repeated measures in time and meal composition and a main effect of chronic diet composition. n: number; *: where the two variables are combined in the analysis; RQ: respiratory quotient; Ln: log of plasma insulin values. [1] Significant at ($p < 0.01$). [2] Significant at ($p < 0.05$).

Figure 4.3.2.1 Glucose (A), Ln (Insulin) (B), Triglyceride (C) and RQ (D) responses to low/normal RS (N) and high amylose RS (R) test meals in subjects pre-treated with low RS (Low) or high amylose RS (Hi) diets for 3 months. Results are presented as mean ± sem.

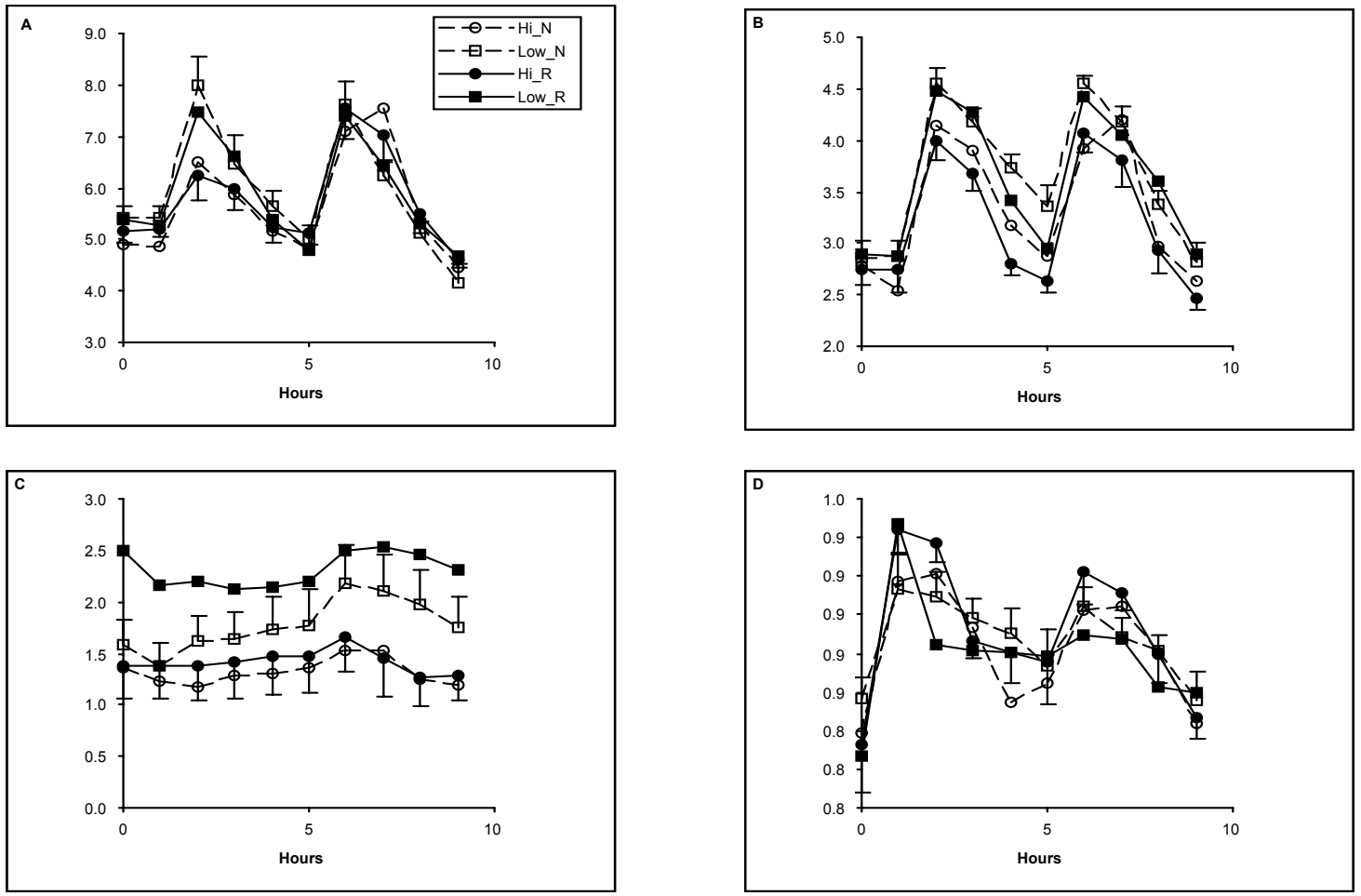
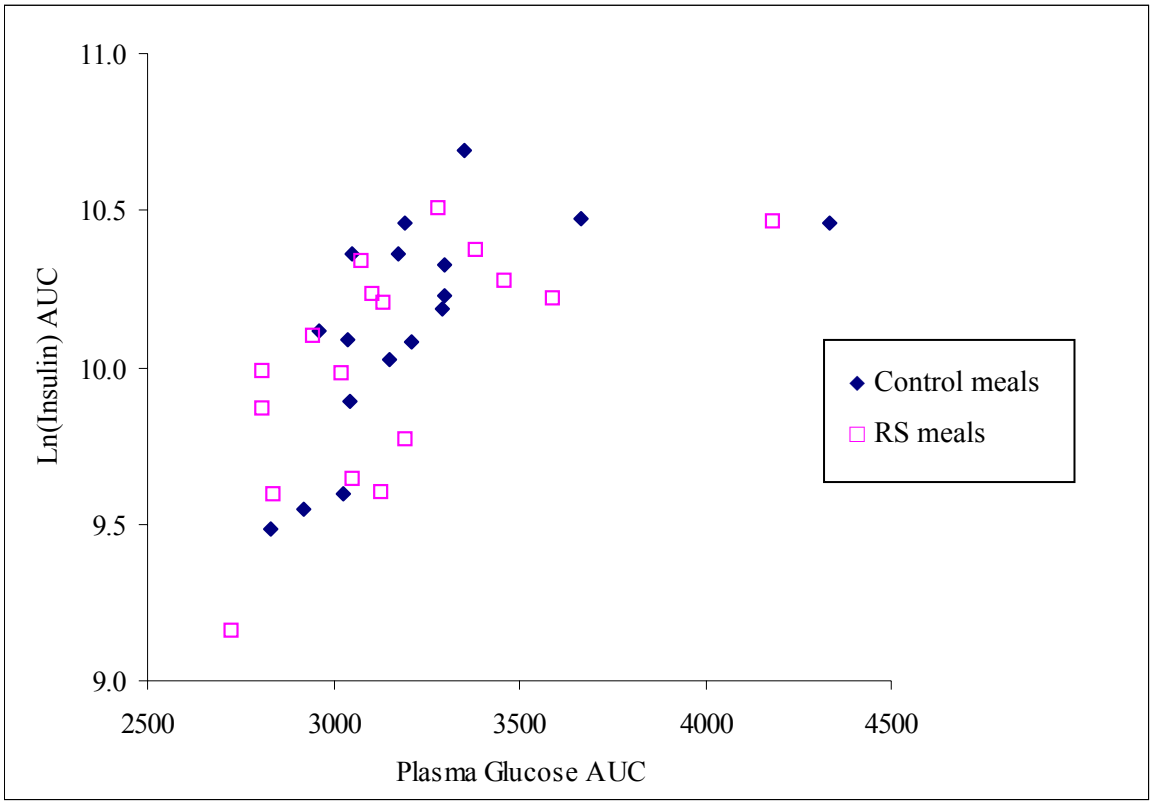


Figure 4.3.2.2 Relationships between Ln(Insulin) AUC and plasma glucose AUC during control and high amylose RS meals in 18 subjects completing both meal tests.



4.4 Analysis of dietary data

a) Baseline nutrient intakes

Dietary analysis involved in-depth analysis of repeated diet history interviews. The following table (Table 4.4.1) summarises the mean, standard error of the mean and range for each group for baseline diet history interviews. Overall, there were no significant differences detected for all comparisons made between diet groups for both absolute amounts of nutrients and the percent of energy derived from macronutrients.

Table 4.4.1 Baseline diet composition from the diet history interview (mean ± sem) and range

	Control Group (6M, 5F)				Intervention Group (4M, 7F)			
Nutrient	Mean	SEM	Minimum	Maximum	Mean	SEM	Minimum	Maximum
Energy Intake (kJ)	9796.73	1150.91	4745.00	19590.00	9769.73	962.49	6418.00	15834.00
%Carbohydrate	43.78	1.65	36.90	53.30	45.32	0.68	41.70	49.00
%Protein	19.29	0.83	13.40	22.70	19.03	1.26	14.10	26.40
%Fat	32.56	0.96	27.61	38.70	31.08	0.74	26.50	34.90
%Polyunsaturated fatty acids	16.55	0.81	11.90	20.30	18.46	1.91	10.00	29.20
%Monounsaturated fatty acids	40.55	1.39	31.70	45.10	39.88	1.10	35.40	48.30
%Saturated fatty acids	42.91	1.60	35.70	50.50	41.67	2.22	32.50	54.40
%Alcohol	2.40	0.62	0.00	6.30	2.73	0.69	0.00	7.40
Carbohydrates (g)	269.87	36.90	134.40	578.00	278.20	29.59	167.40	484.90
Protein (g)	109.04	12.04	63.20	210.10	105.85	8.43	61.40	154.70

No significant differences between groups ($p < 0.05$) were found. High amylose maize starch group, n = 11; Control group, n = 12; kJ: kilojoules; %: percent contribution of energy.

Table 4.4.1 continued. Baseline diet composition from the diet history interview (mean ± sem) and range

	Control Group (6M, 5F)				Intervention Group (4M, 7F)			
Fat (g)	85.51	9.22	38.20	157.60	83.17	9.52	47.90	147.50
Polyunsaturated fatty acids (g)	13.10	1.82	4.60	28.90	12.90	1.44	7.80	22.10
Monounsaturated fatty acids (g)	31.48	3.54	14.90	59.80	28.92	2.65	17.60	45.70
Saturated fatty acids (g)	33.53	3.66	14.10	54.10	31.42	4.55	14.70	61.10
Alcohol (g)	7.64	2.05	0.00	22.60	9.23	2.66	0.00	27.20
Dietary fibre (g)	26.46	3.22	12.10	51.10	26.64	1.59	17.60	33.90
Sugar (g)	114.46	23.35	48.10	293.00	125.49	13.87	75.50	206.20
Starch (g)	149.27	19.05	85.20	315.70	145.44	16.52	81.80	236.30
Cholesterol (mg)	315.27	38.27	124.50	578.00	291.80	30.07	118.80	444.10
Calcium (mg)	1116.16	104.30	735.10	1882.70	1088.61	123.19	619.80	1883.20
Phosphorus (mg)	1773.72	166.96	1084.00	2911.00	1795.91	146.80	1115.60	2739.80

No significant differences between groups ($p < 0.05$) were found. High amylose maize starch group, n = 11; Control group, n = 12; kJ: kilojoules; %: percent contribution of energy.

b) Changes in dietary intakes over time between intervention groups

Although groups were provided with matching foods to achieve normal or high RS intakes, possible displacement of foods, and subsequently, nutrient displacement were a possibility. An examination of dietary intakes regularly produced the following results (Table 4.4.2).

Table 4.4.2 Comparison of nutrient changes over time between dietary groups and within subjects (n = 22).

Repeated measures	Between subjects	Within subjects	Within subjects	Description of analysis findings for significant differences if applicable
Wilk's Lambda	Diet	Time*Diet	Time	
Energy (kJ)	0.4966	0.8399	0.1778	
% Carbohydrate	0.1939	0.7373	0.1283	
% Protein	0.2079	0.9036	0.0563	
% Total fat	0.1630	0.8992	0.3541	
% Polyunsaturated Fat	0.9372	0.2642	0.1738	
% Monounsaturated Fat	0.3306	**0.0365** [a]	**0.0363** [a]	Groups were not parallel over time and the %MUFA intake changed with time
% Saturated Fat	0.5376	**0.0284** [a]	**0.0089** [a]	Groups were not parallel over time and the %SFA intake changed with time
% Alcohol	0.8017	0.2129	0.2690	

kJ: kilojoule; %: percent of energy that the nutrient contributes; CHO: carbohydrate; PUFA: polyunsaturated fatty acids; MUFA: monounsaturated fatty acids; SFA: saturated fatty acids; g: grams; mg: milligrams; [a] significantly different ($p < 0.05$).

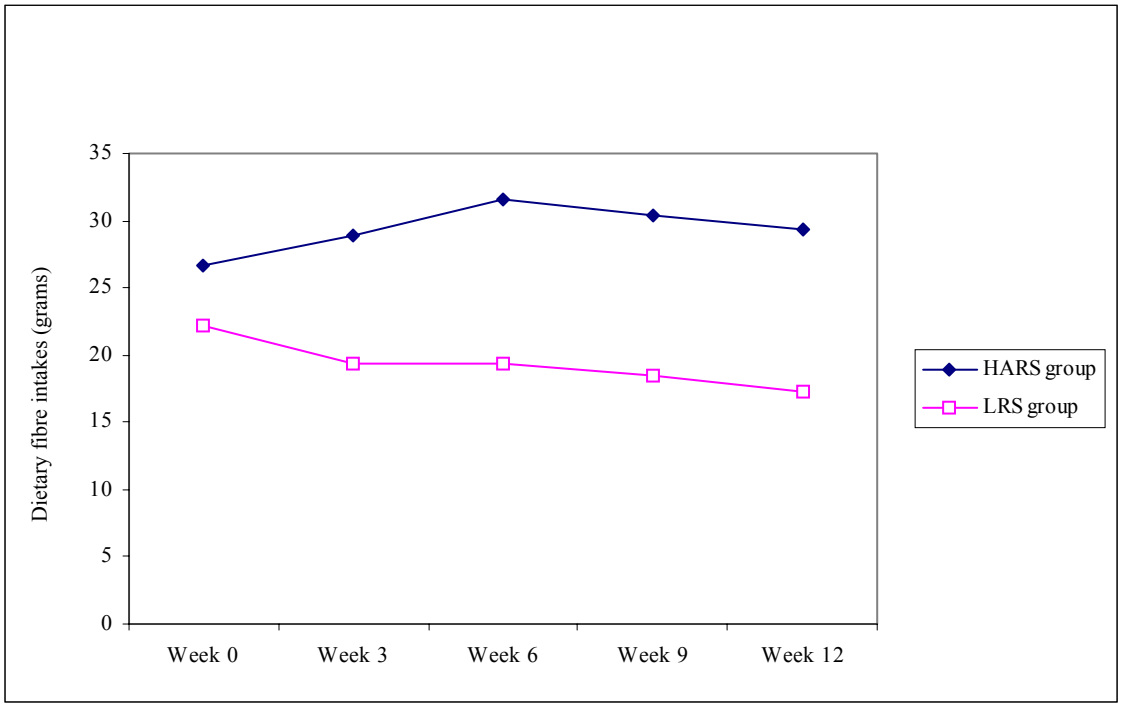
Table 4.4.2 continued. Comparison of nutrient changes over time between dietary groups and within subjects (n = 22).

Repeated measures	Between subjects	Within subjects	Within subjects	Description of analysis findings for significantly different variable
Wilk's Lambda	Diet	Time*Diet	Time	
Carbohydrate (g)	0.2981	0.9839	0.1978	
Protein (g)	0.9852	0.8538	0.5138	
Total fat (g)	0.9624	0.8955	0.0965	
Polyunsaturated Fat (g)	0.6265	**0.3400** [a]	**0.0258** [a]	Groups were not parallel over time and the actual amount of PUFA (g) changed with time
Monounsaturated Fat (g)	0.9890	0.9875	0.1376	
Saturated Fat (g)	0.5570	0.5574	0.1079	
Alcohol (g)	0.6602	0.0739	0.4060	
Dietary Fibre (g)	**0.0225** [a]	0.1230	0.6041	Dietary fibre (g) intake was significantly different between groups, though intakes were parallel between groups over time and constant over time
Sugar (g)	0.1904	0.7921	0.0528	
Starch (g)	0.5891	0.1884	0.6104	
Cholesterol (mg)	0.4276	0.8711	0.1150	
Calcium (mg)	0.6268	**0.0354** [a]	**0.0053** [a]	Groups were not parallel over time and the amount of calcium (g) intake changed with time
Phosphorus (mg)	0.8690	0.0534	**0.0168** [a]	Groups were just parallel over time, however the amount of phosphorus (g) changed with time

kJ: kilojoule; %: percent of energy that the nutrient contributes; CHO: carbohydrate; PUFA: polyunsaturated fatty acids; MUFA: monounsaturated fatty acids; SFA: saturated fatty acids; g: grams; mg: milligrams; [a] significantly different ($p < 0.05$).

As an example of the change in intake with time, figure 4.4 shows the pattern of dietary fibre intakes reported during the diet history interviews between intervention groups. In summary, there were no significant differences between baseline nutrient intakes between intervention trial groups.

Figure 4.4 Dietary fibre intakes by dietary intervention group measured at 3-weekly intervals five consecutive measures (n = 15)



However, over the intervention period of 12 weeks, from baseline to completion, inclusive, five diet history interviews were conducted at 3-weekly intervals. Their subsequent analysis, showed an overall difference ($p < 0.05$) in dietary fibre intake (see Figure 4.4), though all remaining measured nutrients varied over time, differing slightly for percent monounsaturated fatty acids, percent of saturated fat, absolute amount of polyunsaturated fatty acids, calcium and phosphorus. Where groups were not parallel, graphically, intakes usually crossed over suggesting that there would be no clear impact

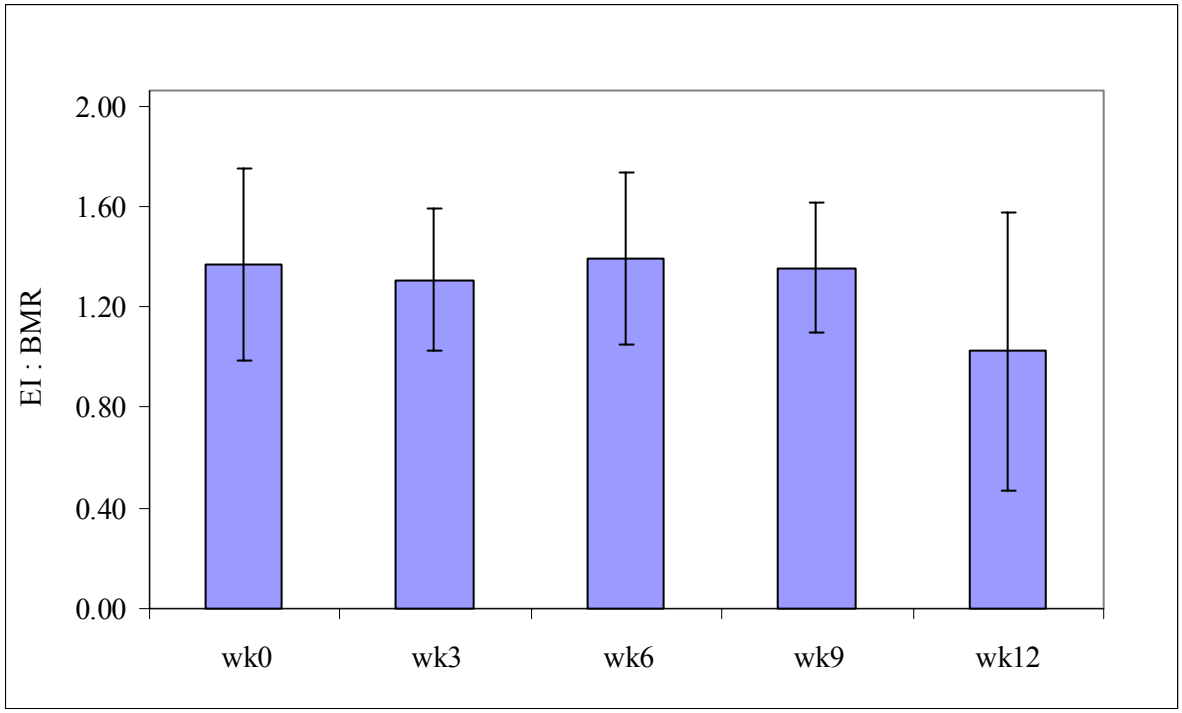
of these intakes on the metabolic outcomes, or where amounts changed over time, both groups changed similarly.

4.4.1 Validity of dietary data

a) Accuracy of reporting energy intake from the diet history interview

Goldberg cut-off limits were used to estimate the accuracy of reporting dietary intakes, where the ratio of reported energy intake to estimated basal metabolic rate (BMR) provides an index. Estimated BMR was derived from the Schofield equation (Schofield *et al* 1985), and an applied physical activity factor of 1.55. The limits were, a ratio of EI to estimated BMR value below 1.17 classified the subject as an "under-reporter", and if the ratio was above 2.06, the classification would be "over-reporter". Values in between 1.17 – 2.06 achieved "valid" categorisation. The following two figures (figures 4.4.1.1 and 4.4.1.2) display the reporting accuracy for all participants diet histories completed and represented in categories over time.

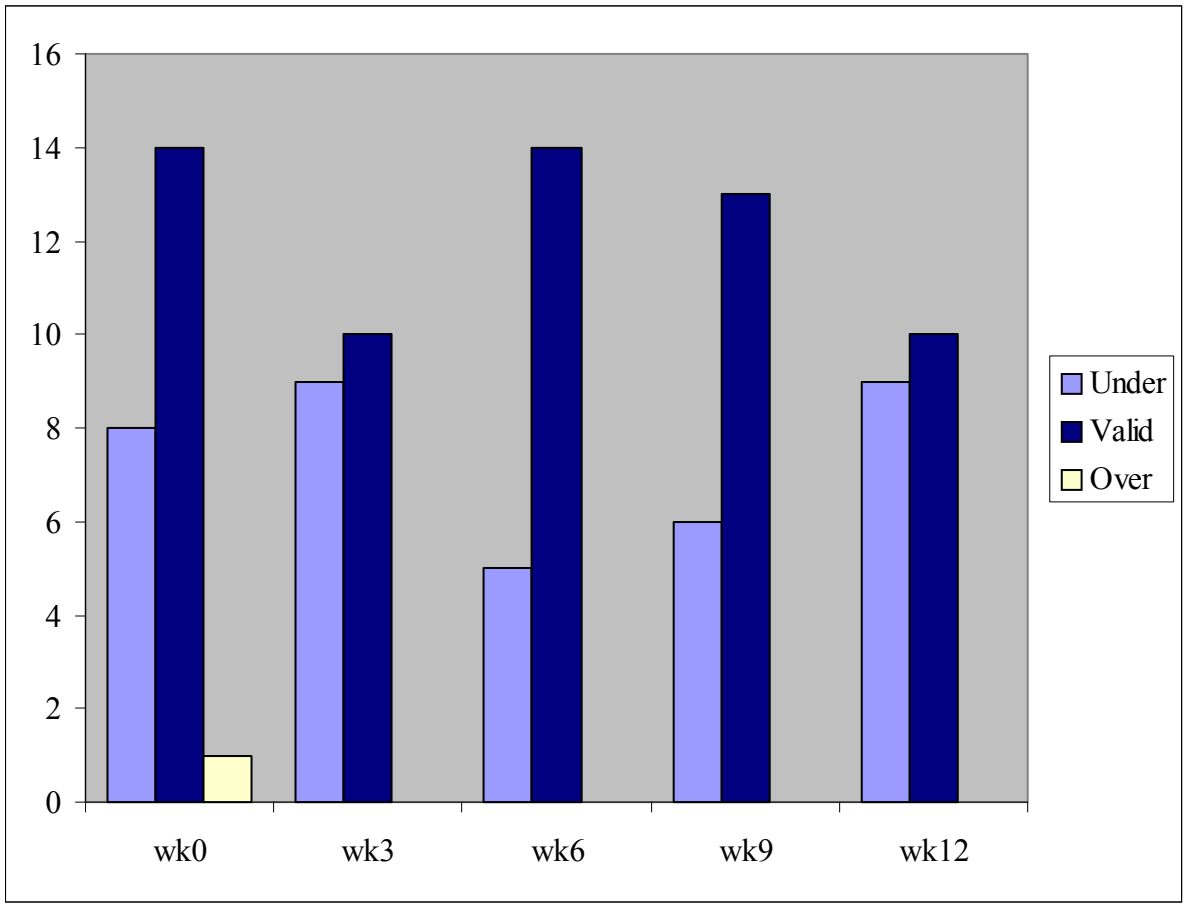
Figure 4.4.1.1 Diet history interview assessment of energy intake compared with basal metabolic rate using Goldberg cut-off limits [a]



[a] Diet history reported energy intake to an estimated basal metabolic rate ratio, shown as the mean (±SD) of all diet histories analysed for each of the weeks indicated. <1.17 is classed as underreporting, and > 2.06, over-reporting.

Figure 4.4.1.1 shows a marked decline in the ratio in the final interview. All other dietary interviews analysed for baseline, weeks 3, 6 and 9 maintained on average, "valid" reporting. More precisely this following figure, 4.4.1.2, separates out the under-, valid and over-reporters. The darkest bars represent "valid reporters" which appear to decline gradually, while the number of "under-reporters" increase from week 6 to 9 to completion (week 12). This observation is perhaps due to respondent burden. The sole over-reporter in the initial, pre-intervention interview was also the youngest participant. This result is arguably the result of less awareness about food preparation and quantities eaten as the participant did not prepare or shop for food.

Figure 4.4.1.2 Comparison of reporting accuracy according to Goldberg cut-off limits classifications by 3-weekly assessments, where 'under', 'valid and 'over' refer to under-reporting, valid reporting and over-reporting respectively



b) Relative validity of reported dietary intakes

The energy intake reported in the initial DH interview was not well correlated with the fasting resting metabolic rate assessed in week 0 (n = 22). Alternately, this energy intake value significantly correlated with the final, week 12, resting metabolic rate (r = 0.505, p = 0.017). For the final DH, reported energy intake did not correlate with week 0 or week 12 resting metabolic rate, however, the preceding energy intake reporting during the week 9 meeting significantly correlated with both week 0 (r = 0.486, p = 0.041) and week 12 (r = 0.499, p = 0.035) metabolic rate measurements (n = 18). This is

perhaps due to the lower number of under-reporters in the week 9 dietary intake assessments.

4.4.2 Achievement of dietary target

Checklists for intervention foods, self-administered daily and known sources of naturally occurring RS were used to calculate the average RS intake per day. The high RS group averaged 27g of RS per day and minimal (assumed 5g of RS/day) RS intake in the control group. Therefore, the checklists showed compliance to the intervention foods. Some participants used the checklists as a record of dinner and other meals, then used these as a point of reference to aid recall during the subsequent DH interview.

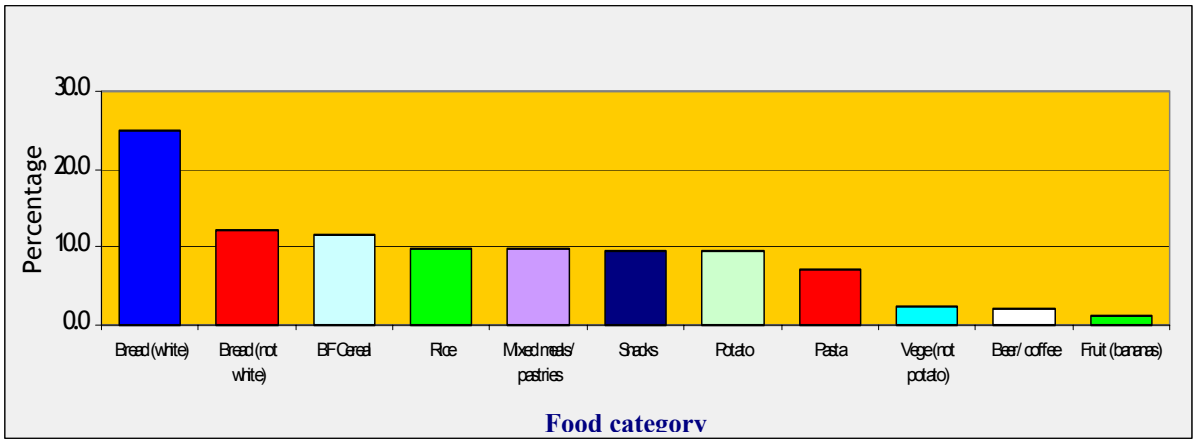
4.4.3 Major food sources of dietary starch

It is important to know which foods to manipulate dietetically. With the knowledge that less than half of the participants mis-reported their baseline dietary intakes, the identification of high starch foods consumed by a study sample as potential delivery agents of dietary RS could be assessed. This analysis was completed before one subject's discontinuation as it only relied upon pre-intervention data; therefore, the data set included 23 diet history interviews (Brenninger, Tapsell, Jenkins and Barnard 2000).

Carbohydrate (CHO) intake per day was 269.2 ± 107.7 g, which represented 44.5 ± 3.8 % of energy intake (EI) from CHO, range 36.9 – 50.1%. Starch intake was 145.9 ± 56.6 grams, range 81.79 – 315.73 grams per day per subject. The primary sources of starch in the diets were white bread, other breads and breakfast cereal, collectively contributing 48.7% of total intake (see Figure 4.4.3). EI was 9668 ± 3481 kJ, range 4745 – 19590 kJ.

Nine subjects were classified as inaccurate reporters, however they were not significantly different to the valid reporters with respect to BMI ($p > 0.05$) or gender.

Figure 4.4.3 Percent contribution of starch from various sources in the diet of 23 subjects



In this study sample, bread and breakfast cereal provided the main potential agents for RS delivery. At present white bread is the main commercial source, yet non-white breads and a wider range of breakfast cereals may increase its accessibility in the diet. Other sources of RS, such as rice, mixed dishes, snacks, potato and pasta may however, introduce variability in total RS intakes. Whilst the degree of under-reporting of energy in this study is of concern it is unlikely to weaken these findings since under-reporting is more likely to related to fat intake (Heitmann *et al* 2000) and sugar intake (Poppitt *et al* 1998).

4.5 Correlations between energy intake, BMI and fat mass from initial to week 12

Overall, the group showed no linear relationship between EI and BMI. BMI did not relate to percent fat mass (%FM). Though an increase in reported EI corresponded to a

decrease in %FM (r_s = –0.54, p = 0.0082), suggesting that higher %FM may promote underreporting though %FM was not significantly different between valid and under-reporters. Females compared to males tended to exhibit a greater percentage of fat mass and similarly had smaller reported EI in the DH interviews than males did, both significant ($p < 0.05$). Overall, under reporters were not significantly different ($p > 0.05$) in BMI, percent fat mass or gender to valid reporters.

4.6 Participant views on feasibility of dietary approaches

Eleven participants (46%) returned the anonymous survey. The survey, shown in appendix 11, was necessary and useful in this context to supply data on the feasibility of the intervention and in capturing participant's views and barriers to acknowledge in future dietary intervention trials. Discussion of the current trial outcomes may be more fully developed from the results of these exploratory findings. For instance, although participants were asked to maintain the same level of exercise as they were doing prior to the trial, which 73% confirmed that they did, three said that it varied (sometimes more, sometimes less), and one of the eleven reported that they did less exercise during the trial.

Regular contact with the dietitian in this study was performed on a monthly basis and five of the eleven participants reported that regular contact with a health professional or other participants was important, five felt that they didn't require regular contact and one didn't know. This reiterates how participants vary from one another and that adequate contact can be determined on an individual basis.

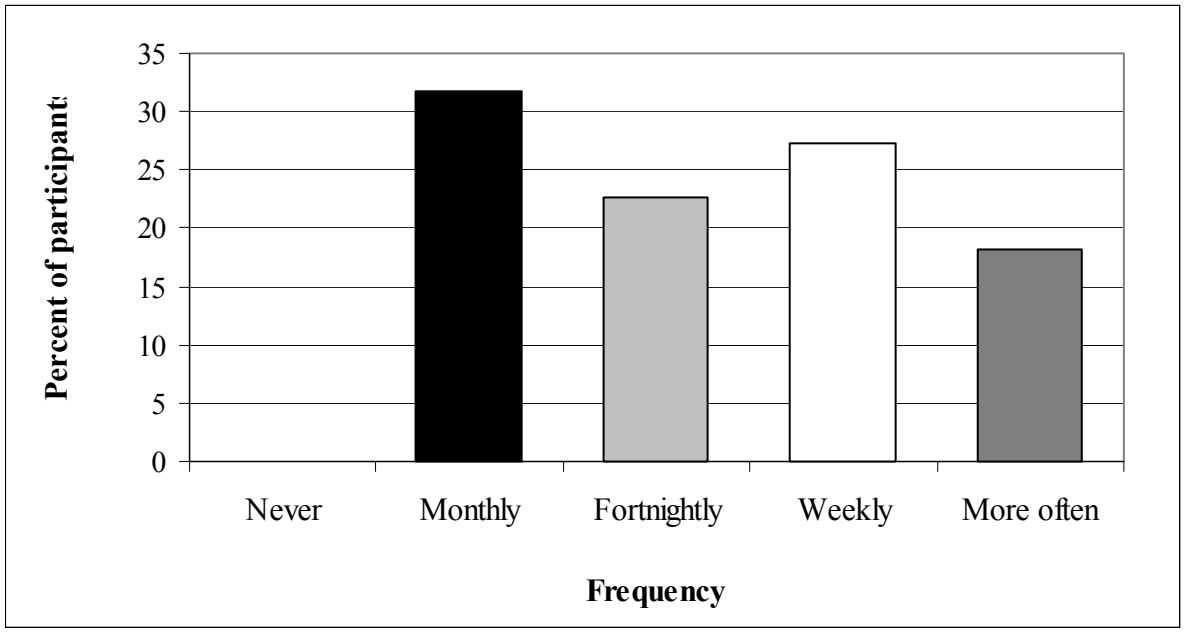
Three believed that regular contact with the dietitian helped attain goals, while writing down daily consumption of intervention foods on checklists was equally as helpful and two participants felt commitment to the study was able to help them attain the goals set. Other responses were given, such as establishing a routine and having the foods and amounts given, though only one subject each represented these. No adaptation occurred or was needed for most subjects (7). However, it is also relevant that no-one found the food goals "very difficult" to adhere to, in fact, nine of the eleven found the dietary goals "acceptable" to "very easy" and only two found the goals "difficult".

The participant felt that out of all the options (self, family, friends, researchers or dietitian) that they had the most influence on their ability to adhere to the dietary intervention (10 of 11). The next favourably rated option was the dietitian. No adaptation occurred or was believed to be needed according to most subjects (7).

For the current intervention trial, most (82%) felt that there was "no difference" for the time required to prepare meals, expense required to shop for foods (73%), time required to shop for foods (82%) and planning of their meals (82%). Despite these figures, some participants felt that they ate more food (64%), the remaining participants (37%) stated that there was no difference in the amount. The dietary interventions were perceived as feasible and these types of carbohydrate rich foods may be a deterrent to weight gain in 67% whom thought that they were eating more. Body weight did not significantly change during the intervention trial.

The participants adhered well to the trial's requirements; nevertheless, barriers to complying with all food goals were explored. The most prominent response was that eating out created a difficult environment to sustaining the daily or weekly food goals. When it was most difficult to adhere to the diet appeared to be occasions that differed from there routine; such as on holiday/ travelling (5), eating out/ special occasions (7). Though some participants found it hard to eat the foods when they didn't feel hungry (3) or when working long hours (1) though this person also felt that it was difficult when their routine changed. The following illustration (Figure 4.6) displays the frequency that "eating out" occurred, expressed as percentage.

Figure 4.6 Frequency of 'eating out' as percent of participants (n = 11)



Although two people marked the response that it was difficult to adhere to the diet, all respondents stated that they did adjust to meet the food requirements. They also felt that these requirements were met within one week of commencing the trial (10 out of the 11). We would expect from data on the low or average RS intake (EURESTA 1994),

that an expectation to reach 25–30g/ day could change usual intakes. The use of matching foods, only differing in the amount of RS, for each dietary group was a strategy employed to equalise any displacement of usual foods in either group. Whether the intervention was significantly different to their normal diets, was divided among the respondents, and one was unsure. It seems that the quantity of bread and bread products were challenging to fit into their usual diet and canned spaghetti was disliked most of all. Equal in numbers for foods most liked included bread, English muffins and yoghurt, followed by sweet muffins.

The best aspect of the trial received a variety of responses including: helping others and research (3), leaning about personal health (3) and diet (2) or receiving food as part of the trail (2). Similarly, there were a variety of responses with respect to the worst study attribute, though the indirect calorimetry procedure (7), which included needles, was the most significant, followed by time requirements (4) and measuring food intake (3). Two participants had no complaints. Last, the reasons exposed by participants through an open-ended question that lead them to volunteer for the research included: to help others and the researchers (7), learn about their own health and diet or health concerns (5), general interest (3) and free food (1).

4.7 Summary of results

With reference to the main aim of the study, the intervention trial survey and checklist analysis showed that the trial was feasible in terms of achieving food goals within one week of commencement. The results from the trial metabolically suggest high amylose RS does not affect metabolism chronically. However, there was a small effect of

chronic RS consumption on the glycaemic responses to breakfast meals. The significant and non-significant finding are problematic from the outset considering that the groups became mismatched for insulin sensitivity and BMI at baseline due to attrition of subjects throughout the study. An increased number of subjects, length of trial, or amount of RS may have provided conclusively that the beneficial post-prandial insulin response from acute exposure to RS compared to control meals was without doubt a true result.

The results therefore indicate wide-ranging evidence for diet-disease relationships, from its principals of collection to metabolic outcomes. We discovered through conversation analysis of the interviews that the diet history interview is important to capture meal patterns and food sources of nutrients. In addition, and supported by the lifestyle history questionnaire, dinner meals required further probing by the interviewer while offering appropriately sized food models or photographic displays. Analysis of dietary intake revealed, on average, "valid" reporting for baseline, and the following three interviews, though not week 12. We may postulate, from the collection of naturalist data, that this was due to the burden felt by participants towards the end of the trial and the suggestion for increasing the length of the trial for assessment of chronic metabolic effects impracticable.

5. Discussion

Research in the area of the diet-disease relationship is complex being influenced by both human genetic and behavioural variables. Previous work has tended to focus on either qualitative or quantitative analysis. The increasing rates of obesity and diabetes in our society imply limited success of currently recommended lifestyle modifications to the general population. The social context within which lifestyle modifications are recommended to an individual is not captured within the randomised controlled trial, an accepted cornerstone of evidence based practice. To address this, presented in this thesis is a methodological concept designed to capture human behavioural, social and metabolic data of a dietary intervention within a free-living overweight insulin resistant population.

This thesis has addressed a number of hypotheses regarding the establishment of evidence for practice from dietary intervention trials. It has been demonstrated here that for evidence based practice to be most relevant, collecting evidence from both qualitative and quantitative research methodologies is warranted. This thesis therefore has implications for future therapeutic and research practices.

This chapter follows the sequence employed in the abstract, beginning with an examination of the role of the randomised controlled trial and naturalistic evidence. A discussion on the development of evidence for health and disease management in view of the data generated by this thesis follows. Last, recommendations for further work in this area will conclude this thesis.

5.1 Diet and insulin resistance: opportunities with resistant starch

The impact of our environmental and its variable nature can be illustrated through the debate surrounding functional foods, which includes RS enriched foods. One view is that the food industry sets the agenda, deciding upon the food selection available to the consumer rather than meeting consumer driven needs (Stanton 1999). With an enormous number of items in supermarkets, it is common for consumers to try new foods or change their pattern of intake to experience some of this wide and ever changing food supply. In fact, consumers may displace traditional less processed foods for new products that are highly processed, well marketed and potentially contribute to the incidence of obesity. Currently, many consumers do not display a healthy eating pattern and neglect to follow recommendations regarding daily intake of fruit and vegetables (Magarey, Daniels and Smith 2001). Therefore, in some instances, functional foods such as RS or suitable alternatives may be useful. It is against this backdrop that research into the efficacy of these functional foods is warranted (Stanton 1999).

The increasing incidence of overweight and obese people in Australia's population is possibly due to small decreases in physical activity and small changes in food intake by many, rather than extreme inactivity and excessive food intake among just a few (NHMRC 1997). An increased consumption of high amylose RS may play a role in the dietary treatment and prevention of obesity and insulin resistance by delaying the delivery of carbohydrate via fermentation into short chain fatty acids. The evidence supporting this view has developed from animal studies, short-term meal challenges with humans, and indirectly through research demonstrating the health benefits of short chain fatty acids on bowel health and colon cancer prevention (Baghurst *et al* 1996).

The amount of research on the effects of RS on insulin resistance in humans, however, is limited, especially with respect to the long-term consequences, providing a suitable gap for this thesis whereby, foods enriched with RS were tested in a clinical trial. The primary aim of the intervention was to assess the feasibility and efficacy of consuming high amylose maize RS on metabolic outcomes in an overweight population. In particular, the study was aimed at revealing any potential correlation between the chronic consumption of RS and improvements in metabolism, and secondly, if an adaptation to RS produces acute metabolic and subjective satiety responses to meal challenges. The specific measurable objective was to test the effects under free-living conditions of the long-term ingestion of 25g/day RS contained in commercially available foods on fasting and postprandial metabolic responses in a group of overweight, insulin resistant subjects.

5.1.1 Effects of long term dietary intervention on clinical outcomes

After 12 weeks, the lack of significant differences between control and intervention groups in terms of changes in body composition, serum lipids, substrate utilisation and fasting plasma glucose/insulin levels suggested that, at least with this profile of subjects, there is no effect of habituation with 25g RS in the diet. This may reflect the impact of dosage (25g of RS estimated for bowel health may not be enough for metabolic health) or the small sample size of the study. Unexpectedly an increase in insulin resistance of about 10% in the RS group was observed however, after attrition of subjects from both groups baseline metabolic characteristics were mismatched. Further, given the relatively small study size, the results displayed that approximately 40 subjects would have been required to detect an effect of this magnitude using the current protocol. Overall, with

the consumption of relatively moderate quantities of RS, and given that some dietary components, such as meal patterns and specific nutrients varied in consumption over the duration of the trial, the metabolic effect could be explained by a variety of differentials for which discussion will follow.

a) Impact on body composition

Dual energy X-ray absorptiometry was chosen to examine whole body proportion of fat mass. This machine was selected primarily to produce data that limits human error compared with other methods such as conventional skin fold evaluation (Forbes 1999). Despite a mismatching of groups at baseline for BMI, there was no significant difference in fat mass to fat free mass ratio between dietary treatments. Considered alone, this may reflect that the potential acute increase in fat utilisation reported in previous human work (Higgins *et al* 1998) does not appear to translate into a chronic shift in total fat mass. The acute meal challenges in the current study also do not support greater fat utilisation from RS consumption in this type of study group and meal composition (discussed later). Alternately, this assessment could not detect specific adipose tissue shifts, such as from visceral stores. Visceral fat is a potent modulator of insulin action on hepatic glucose production and gene expression (Barzilai, She, Lui, Vuguin, Cohen, Wang and Rossetti 1999). Likewise, abdominal adiposity has been suggested to be "the most prevalent dominator of highly atherogenic dyslipidaemic and hyperinsulinaemic insulin-resistant states in affluent, sedentary societies." (Lamarche 1998). This author (Lamarche 1998) demonstrated that abdominal obesity was a leading predictor of insulin resistance, hyperinsulinaemia, hypertriglyceridaemia, low HDL cholesterol and an increased level of small, dense LDL particles. Considering this, a

precise measure of visceral and/or abdominal adiposity by computer tomography and waist to hip ratio would have been preferential. However, had there been a change in adiposity over the intervention period, it should have been reflected in insulin action measured by the clamp, a finding not observed.

b) Impact on insulin sensitivity

The use of the euglycemic hyperinsulinaemic glucose clamp, as with the use of an RCT, strengthens the scientific outcomes. The clamp is a known gold standard as it delivers highly reproducible results and a reliable assessment of tissue sensitivity to insulin (DeFronzo *et al* 1979). As previously noted, there was no significant benefit shown from the consumption of RS over 12 weeks on measures of insulin sensitivity. Surprisingly, attrition of subjects created a significant difference between groups for this parameter also. This may have effected the response of groups to meals and perhaps why the repeated acute exposure to RS did not produce the theorised outcomes. Nevertheless, the 'clamp' has limitations with regard to being an indication of whole body insulin action and not specific organ insulin sensitivity. When insulin sensitivity was determined using the homeostasis model assessment (HOMA) as described by Jenkins, Samaras, Carey, Kelly and Campbell (2000), the clamp outcomes were confirmed.

5.1.2 Acute meal challenge effects following chronic dietary interventions

Following 12 weeks of RS intake, the glucose response to an acute challenge with either high amylose RS or control breakfast meals was reduced compared to participants receiving 12 weeks of the control diet, though not significant overall (Table 4.3.2.2). In

contrast, there was a small but significant effect of acute RS meals to reduce post-prandial insulin levels. The relationship between individual area under the curve values for glucose and insulin (Fig 4.3.2.2) appeared to correlate well reinforcing that there is a mild relative hypoglycaemic effect (with reduced insulin) from RS intake as supported by previous research in 21 men (Howe *et al* 1996). This glucose mediated effect was shown to have dissipated by the time of the lunch meal leading to a number of possible explanations. The breakfast response may reflect a phenomenon of glycaemic control mechanisms at play at this point in the day, such as following a period of fasting, with the low glucose response resulting from a low glycaemic load prior to the day of meal challenges. More likely though, it is due to non-significant baseline differences in the plasma glucose levels between diet groups, amplified at breakfast by the higher insulin resistance in the control group. However, if this is factual then other metabolic processes must diminish or reverse the effect later in the day. Our understanding of these findings is partly addressed by recent research on meal challenge studies that found a 'second meal effect' (Axelsen, Arvidsson, Lenner, Lonnroth and Smith 1999), however the current study would have required different study design features for appropriate comparison.

Satiety remains a difficult parameter to measure successfully in subjects participating in the meal challenges. In the current research, the assessment of subjective satiety scores was difficult to assess for all subjects at hourly intervals therefore not analysable. As with investigators that suggest obese people misreport their dietary intake (Heitman and Lissner 1995, Black, Pretice, Goldberg, Jebb, Bingham, Livingstone and Coward 1993, Lichtman *et al* 1992) it is plausible to suggest that satiety scales could also be

misreported in the current investigation had all the data been available. A more metabolically relevant explanation that may have influenced results is that overweight people tend to display poorer sensitivity to satiety or appetite (Friedman 1995, Speechly and Buffenstein 2000), therefore limiting the capacity of these scales to detect differences. If real, there would be a shift toward the mid-point of the satiety scale measures and thereby less likely to reach significant differences between meal challenges. Lack of responsiveness has previously been investigated (National Diet-Heart Study Research Group 1968, Denke and Grundy 1994, Shenberger *et al* 1992; Denke 1994; Quivers *et al* 1992) and may account for up to 20% of subjects also. The hormone leptin, believed most representative of satiety levels, may be an alternative means in future trials to better depict the potential relationship between RS and satiety, overcome the potential for mis-reporting and may make visible differences which exist in a persons responsiveness.

5.1.2.1. Limitations of acute meal challenge outcomes

There were several limitations to address within the present research. In general with respect to metabolism, the blood collection for the analysis of each parameter is cross-sectional and whether this can be regarded as a sound representation of a subject's metabolism overall is debatable. There is also contention surrounding substrate utilisation (RQ values). Subjects may have climbed the stairs rather than taken the elevator before arriving at the metabolic unit. It has been established that following high-intensity exercise, the need to replenish the body's bicarbonate ion concentration causes RQ to be substantially less than true cellular RQ (Melby *et al* 1997). Although not reported on, this phenomenon presumably occurs in less intense exercise, and

although the use of the stairs initially seemed inconsequential, the current trial's subjects were overweight and obese, thereby increasing energy expended for this task in comparison their a lighter counterpart. Therefore all methods of minimising physical exertion prior to examination of substrate utilisation should be a consideration in future trials. Last, in the present study the nitrogen value was estimated as a constant for all participants rather than calculated from urinary nitrogen excretion, therefore the non-protein RQ values may have been under- or over-reported for some subjects.

Under-reporting will be addressed in relation to the discussion on dietary assessment, yet remains a noteworthy limitation of any research involving diet-related disease. Another area of concern is the paucity in assessment on subject's responsiveness to change and their genetic influence. This has already been addressed through the discussion on satiety. Overall, the genetic predisposition of participants is becoming an increasingly more important factor to consider, however, this could not be assessed within the current research.

The interpretation of the quantitative results relies heavily on the outcome of statistical analysis of the gathered data. According to Sterne and Smith (2001) an interpretation of the findings in the context of the study and available evidence is more important than if statistical significance was achieved. High amylose RS may earn its position within a diet adjusted for other nutrients, such as saturated fat, though is it possible that if a larger dose had been prescribed, displacing a proportion of available carbohydrate, a different result would have been seen. If however, removing all forms of readily available carbohydrate had lowered the glycaemic impact of the diet, then the ability to

isolate the impact of RS alone would have been compromised. It can be postulated that the amount of readily available carbohydrates in the participant's diets was a factor that may have limited the attainment of statistical significance between metabolic variables measured.

5.1.3 Overall impact of a high amylose resistant starch diet on clinical indicators of insulin resistance syndrome

Overweight, insulin resistant male and female adult volunteers were recruited to perform the trial within a 'free living' environment to ensure the applicability of findings to the 'real world'. The use of this study population had distinct advantages in establishing treatment relevance. The challenges facing recruitment of the overweight population, however, proved numerous and several volunteers discontinued, though the compliance with consumption of intervention foods was not problematic. The resulting smaller sample size reduced the power of the study, particularly as the variation in individual responses was quite large. Furthermore, the groups became mismatched at baseline due to participant discontinuation throughout the study. However the rate of attrition could not be attributed to the composition of the intervention diets. The resulting data showed that no significant effects of the chronic high amylose RS diet were observed in any fasting responses after 12 weeks habituation. There were possible, but unlikely, effects of chronic RS consumption on measured glycaemic responses to breakfast meals, and there was a small but significant effect of acute RS meals to reduce post-prandial insulin levels as previously discussed. This study is the first to have examined the effects of chronic RS consumption on this set of metabolic parameters and can therefore be used as a reference point for further investigations.

5.2 Measurement and assessment of dietary intake

Dietary intake is commonly assessed in the clinical context using the diet history interview (Rutishauser 1997, Nelson and Bingham 1997). There are alternative dietary assessment tools, however this method also provided descriptions of usual meal patterns (Rutishauser 1997, Nelson and Bingham 1997) upon which the intervention foods were introduced with consideration for food displacement and changes to meals. The intervention conducted here appeared to be feasible with good adherence to the dietary prescriptions. Adherence was assessed via checklist for recording daily intakes of intervention foods, a tool that was also a useful supplement to the diet history.

Most people underestimate their usual dietary intake, though perhaps not intentionally (Mertz 1991). Some researchers have supported the opinion that obese people in particular underestimate their dietary intake to a greater extent (Heitman and Lissner 1995, Black *et al* 1993, Lichtman *et al* 1992). One investigation found that older women underreported more than older men, and in the men the physiological variables were unrelated to accuracy of reporting, though in the women, underreporting increased with increasing adiposity (Johnson *et al* 1994). Obese men have been shown to underreport due to under-recording of food intake and under-eating, with particular bias towards underreporting fat intake (Goris, Westerterp-Plantenga and Westerterp 2000). In contrast, Barnard *et al* (2002) has attributed reporting inaccuracy to energy expenditure and not obesity. While others report that mis-reporting is a widespread problem (Black, Goldberg, Jebb, Livingstone, Cole and Prentice 1991), and unrelated to BMI

classification (Lindroos, Lissner, Mathiassen, Karlsson, Sulivan, Bengtsson and Sjöström 1997, Barnard *et al* 2002).

In the intervention trial within this research, subjects were not significantly different in their ability to accurately report energy intake with respect to BMI, gender or dietary group ($p>0.05$). In addition, only nine of the twenty-three overweight and obese subjects were inaccurate reporters of energy intake at baseline, thereby providing further support that BMI classification does not indicate likelihood of under-reporting.

It seems contradictory to exclude obese subjects from interventions that aim to benefit them. Indeed, the health of obese people cannot be studied if they are excluded from research on the basis that they may misreport dietary intake (Johnson 2000). Rather, there is likely to be variations in a person's ability to report an accurate account of their food intake regardless of their phenotype. By comparison with cut-off limits, the diet history interviews analysed here were on average validly reported for weeks 0, 3, 6 and 9, though overall, a greater level of under-reporting occurred in the final week (week 12). The primary reason believed responsible for this decline related to respondent burden at this time and subject fatigue. That is, all of the final measures were completed around the time of the week 12 diet history and this created a time limitation which may have influenced the diet history interview process. It was interesting to note, upon analysis of the checklists, and during the interviews, some participants (approximately 8) used written cues on their checklist for dinner meals to aid their recall of variations in meal types.

All types of dietary assessment methods have their limitations (see table 3.6.1). For example, under- and over-reporting may occur when using 24 hour recalls and food frequency questionnaires (DeHoog 1996) due to the restrictions that they place on data collection and consequential presentation of results that may not represent usual intake (DeHoog 1996, Nelson and Bingham 1997). Similarly, food records may be atypical of usual intake as they measure only a short period of actual consumption (Rutishauser 1997). To achieve a precision of 10% within an individual to be representative of usual intake, at least 4 weeks of food records are required (Basiotis *et al* 1987, cited in Westerterp 2000). Food records are also believed to be the most demanding on subjects compared to other methods (Rutishauser 1997), may affect usual eating habits (Westerterp 2000), reduce food intake (Rutishauser 1997) or show under-reporting of sensitive foods (Westerterp 2000). Under-reporting in general may occur with the measurement of dietary intake (Nelson and Bingham 1997).

Assessing variation in food intake was an important aspect of this thesis as it needed to obtain data collected from a flexible approach that allowed for the impact of 'free-living' conditions. It was also necessary to enhance the quality of data collected, rather than be parsimonious with such an important aspect of establishing diet-disease evidence. Therefore, the use of the diet history interview was appropriate and provided an ample set of data to evaluate. Nevertheless, the limitations of the diet history interview were recognised, such as its reliance on memory (Rutishauser 1997, Nelson and Bingham 1997) and labour intensiveness for both parties within the interview (Rutishauser 1997). As supported by this thesis and concluded by Krebs-Smith *et al* (2000) further methodological work is warranted in the area of reporting, with a need to

reduce the chance of neglecting to report foods and underestimating portion sizes (Krebs-Smith, Graubard, Kahle, Subar, Cleveland and Ballard-Barbash 2000). For these reasons, and to enhance accuracy of reporting that is a constant phenomenon among all methods, the method development work on this tool was valuable.

Targeting the actual food items in the interview may be the best approach to ensuring accurate reporting. That is, knowing which foods are likely to be misreported, and explicitly addressing these items in a food frequency checklist at the end of the diet history interview. In addition, encouragement to report sensitive foods without reluctance, is desirable. In this thesis, preliminary work was completed on the diet history interview to foster accurate reporting of usual dietary intake (see for example, Tapsell, Brenninger and Barnard 2000, Brenninger 1998). In the methods development component of this thesis, there were a number of energy dense foods that appeared to be problematic to report.

5.2.1 The diet history interview in clinical research

An appraisal of diet history interviews using conversation analysis was pioneered by Tapsell in 1992 (Tapsell 1995, 2000), and was timely considering the deficient link between the body of physiological studies and lack of improvements in population health outcomes. Comprehending psychosocial factors that may impact on a treatment's success is an important target (Anderson, Goddard, Vazquez, Garcia, Guzman and Fitzgerald 1998) though we remain unsure if we are achieving the dietary changes. The diet history would help expose this.

The diet history is a form of client-provider interview. In this setting, however, each person has a very different set of circumstances that the interviewer needs to take time to discover, and process accordingly (Anderson and Robins 1998). In doctor-patient encounters, the way in which information is elicited and received by the doctor, and how the patient transforms their reason for visiting into medically relevant descriptions, have been suggested to influence diagnosis and treatment of the patient (Ruusuvuori 2001). Likewise, we need to ask the most appropriate questions in the assessment of their dietary intakes (Tapsell, Brenninger and Barnard 1999) to obtain accurate records, assessment and therapy.

Analysis of interview data demonstrated that the confidence of reporting dietary intake seemed to dissipate when qualifying dinner foods. There were however limitations with this preliminary study, namely that appropriately sized food models were not available for meals including plated mixed vegetables, rice, pasta, pizza, breakfast cereal, nor for most fluids, such as milk in coffee, wine glasses and various spoon measures. Nevertheless, recognising that the report on dinner is an inherent source of inaccuracy proved to be helpful by fostering the use of food photographs which depicted larger sizes, provision of adequate time and directed attention by the interviewer to verbal cues of uncertainty.

In terms of the resultant accuracy of reporting during the RCT from these targeted interview techniques, only nine of the twenty-three subjects were inaccurate reporters of energy intake at baseline. With regard to the specific nutrients, there appeared to be some shift in nutrient amounts or percent contribution to energy over time. Variation

occurred in the percentage of energy derived from MUFA and SFA, though not apparent in reference to their absolute amounts. Conversely, the absolute amount of PUFA appeared to vary over time, though not with respect to its proportional energy contribution. This was notable, considering that the variation was not reflected in total fat or total energy intake during the course of the trial. The lack of congruence suggests that this was not a significant confounder on the results from this study. However, dietary fibre intake, a close relation to RS intake, was significantly different between groups for the intervention period overall, with the RS group displaying significantly higher intakes. This finding may be interpreted as evidence supporting dietary compliance and feasibility within intervention groups. Last, the amounts of calcium and phosphorus varied between measures. If we return to what this may indicate in food forms, this suggests variation in dairy foods, meat, fish and poultry occurs over time, though attending the accuracy of reporting dietary intakes overall remains crucial to the interpretation of the diet-disease relationship and requires further work.

Whilst the small degree of under-reporting of energy intake in the RCT presented here is of concern, it is unlikely to weaken the intervention trial findings since under-reporting is more likely to be related to fat intake (Heitmann *et al* 2000). Furthermore, in the carbohydrate fraction**,** under-reporting is more likely to be associated with sugary snack foods, rather than core foods (Poppitt *et al* 1998). Similarly, the foods high in sugar and fat appeared more problematic to report in the preliminary work performed on the diet history interview discussed in this thesis. Energy dense foods appeared more sensitive to report, whereas the foods provided for the intervention were not commonly

considered problematic to report. Thus, the variable of interest – resistant starch – was unlikely to be affected by under-reporting.

5.2.2 Achieving dietary targets with enriched food products

Human research for health encompasses social aspects such as cultural, environmental, food patterns and a person's lifestyle. Some studies (Williams *et al* 2000, Huijbregts, Feskens and Kromhout 1995, Kant *et al* 1995, Whichelow and Prevost 1996, Gittelsohn, Wolever, Harris, Harris-Giraldo, Hanley and Zinman 1998) have shifted their focus to the association between food patterns and disease status rather than individual nutrients. Using evidence derived from studies of dietary patterns on disease which can be readily translated to public health recommendations (Williams *et al* 2000).

The use of actual foods was successfully implemented in the current study. However, the incorporation of a food has the potential to disrupt usual food consumption, leading to nutrient displacement and consequently, complicate our understanding a specific diet-disease relationship. For example, on an acute basis, if fat replaces CHO in a meal, oxidation of fat may increase slightly as the trigger for respiratory quotient at an acute level is primarily dependant on CHO consumption (Flatt 1995). In addition, fat has a major impact on energy density which has been implicated in weight management (Yao and Roberts 2001). It was important then to exchange CHO foods for CHO foods, rather than CHO foods for high-fat, low-CHO foods. The foods provided in the intervention trial appeared to suit and interchange easily with the usual dietary patterns of the participants, with the exception of some difficulties meeting 4 slices of bread or more

each day for 12 weeks. Overall, the checklists indicated compliance, suggesting easy application in similar populations in the 'real world'.

5.3 The social context of dietary intake

Modernisation of society, having encouraged high-fat, energy-dense intake and less physical activity is the prevailing explanation for the obesity epidemic (World Health Organisation 1997). However, it has "been difficult to show that differences between individuals in dietary and physical activity habits influence the subsequent risk of developing obesity." (Sørensen 2000:B3). Thus a consideration of the social context was useful. Furthermore, a review derived from the National Institute of Diabetes and Digestive and Kidney Diseases declared four priority areas for future obesity and physical activity research (Wing *et al* 2001) indicating a strong move towards lifestyle related aspects. The four primary areas included: environmental factors related to obesity, eating and physical activity, adoption and maintenance of healthful eating, physical activity and weight, aetiology of eating and physical activity, and multiple behaviour change.

In this thesis, lifestyle factors were collected as part of the baseline ethnographic description of study participants. "It is not enough to simply collect facts. Nor is it sufficient simply to develop explanations without testing them against facts." (de Vaus 1995:10). Surveys are one method used to collect facts, organise and analyse data. It may be suitable for studies to utilise a variety of such research methods to obtain an accurate description by utilising methods and techniques which enhance understanding (de Vaus 1995).

The lifestyle history questionnaire displayed observational data on weight history, exercise patterns, eating patterns and food knowledge. This survey provided evidence of variation in a number of areas which may help explain the findings from the RCT. Weight history, that lead to their current overweight or obese status was believed to be a consequence of increasing age, or steady increase in weight beginning post pregnancy, or in their mid-thirties or forties. Other factors reported to impact on their weight were weight cycling, dieting or exercise shifts, sedentary behaviour in general and the type of food eaten or control issues with food intake. In addition, in 65% of cases, at least one of the immediate family members of the participant was substantially overweight. All of these reasons could contribute to the inconsistency seen in animal experiments compared to human trials. Animal models used to measure the metabolic outcomes from intake of RS have not always simulated the effect produced in humans (Baghurst *et al* 1996). The reverse is also supported, whereby the beneficial link between dietary fibre intake and cholesterol metabolism in humans have not been replicated in rats (Baghurst *et al* 1996).

Another important point to draw from these observations is the issue of dieting shifts. As previously mentioned, we have greater acute fuel oxidation responsiveness to changes in CHO than when fat intake is altered, a compensatory response that may take up to 7 days for the latter (Schrauwen *et al* 1997). In addition, more recent research (Tucker and Peterson 2000) suggests that people who consume an unstable energy intake and food intake in general are less able to adjust their metabolisms accordingly and tend to be more overweight. Except in cases where an increase in energy expenditure through physical activity provides some protection against weight gain. On

average though, the study sample had been within the healthy weight category until their mid-thirties or forties and/or before pregnancy. Environmental factors appeared to be largely related to excess body weight, which supported the need for addressing physical activity and energy intakes. The participants in this trial tended to have variable self-reported physical activity levels, whereby exercise patterns varied between and within subjects, another aspect that may have influenced the results of the study. However, the physical activity levels overall were relatively low and participants reported that many barriers inhibited their achieving regular activity, especially insufficient time, injury or disability and lack of motivation.

Although all participants had a body mass index greater than 25kg/m^2, they reported knowledge gained through a variety of mediums, targeting weight loss. It appears that regular eating patterns are associated with weight control, more successful weight loss and better dietary profiles (Tucker and Peterson 2000, Shigeta, Shigeta, Nakazawa, Nakamura and Yoshikawa 2001). Variable food intake is believed to have a significant impact on appetite regulation also, whereby erratic consumption patterns appear to disrupt this system. The study by Shigeta *et al* (2001) added that in addition to erratic eating and eating between meals, other lifestyle factors including, skipping breakfast and insufficient sleep (<6 hours) were associated with obesity and insulin resistance. In their study, insulin resistance was assessed by the HOMA (Mathews, Hosker, Rudenski, Naylor, Treacher and Turner 1985 cited in Shigeta *et al* 2001) a less reliable measure of insulin action than the 'clamp' method, however commonly used and accepted.

Regularity of consumption may be more important than actual food intake (Mela 2002). One investigation discovered that the frequency of eating is consistently and negatively associated with total and LDL cholesterol concentrations (Titan, Bingham, Welsch, Luben, Oakes, Day and Khaw 2001). Research concentrating on the impact of snacking on an increase in energy intake increases have been contradictory (Havenman-Nies, de Groot and van Staveren 1998). Yet, there is concern that the shift towards greater snacking rather than the traditional three meals per day contributes to augmenting sugar consumption (Summerbell, Moody, Shanks, Stock and Geissler 1994).

The subjects in the current trial consumed three meals on average per day and for most, there was no particular pattern for snacking. Most subjects felt that they ate regular meals and though some ate meals in no particular pattern. The alternate was found with reference to the pattern of snacking, though 5 stated that they rarely consumed snacks. These patterns were believed to fluctuate with workload, work shifts, exercise patterns or other activities. For meals, the numbers of times each were considered a takeaway food or eaten out of home was very rare for breakfast (mean = 0.01/week). The mean number of occasions for lunch and dinner were 1.4/week and 3.3/week respectively. If meals as opposed to food items had been provided to participants, there would have been a downward shift in the number of take away meals and possibly a significant shift in nutrient profile. These results are important considering the way researchers and clinicians need to manipulate dietary composition and also with regards to the evidence building on the impact of dietary and snacking variability on weight control (Mela 2002, Shigeta *et al* 2001).

Last, the survey demonstrated that to ensure accuracy of dietary accounts and hence better understanding of obesity and insulin resistance, the communication between the dietitian and the participant would need facilitation by portion size photographs, food models and a number of cups, spoons and example food packages. The recognition of portion sizes, in particular amorphous foods such as rice, was reasonably well answered, which is reassuring for the measurement of dietary intake in this trial.

In addition to the lifestyle survey, a questionnaire on the feasibility of dietary changes was administered. Following the initial closed-ended questions, social support was addressed with some open and closed-ended questions. Participant's responses concerning how often they should see the dietitian or health professional varied, reiterating the perceived importance of providing individualised treatment strategies. Despite the achievement of dietary goals, there were some barriers suggested and again an increased need to assess each subject on an individual level. However, families were considered to be supportive in general and participants felt that the strongest influence on their ability to adhere to the dietary intervention were the participants themselves.

Most people volunteered for the trial as a means to help others by furthering research into diabetes. Other reasons were to help promote the subject's knowledge of management of lifestyle related chronic diseases or simply to know what to eat. They believed that monitoring, the support from others (including the dietitian) and an increase in awareness regarding diet were the best features of the trial. A few subjects, when asked to comment about the worst feature of the trial responded with the time required for visitation to the University for appointments.

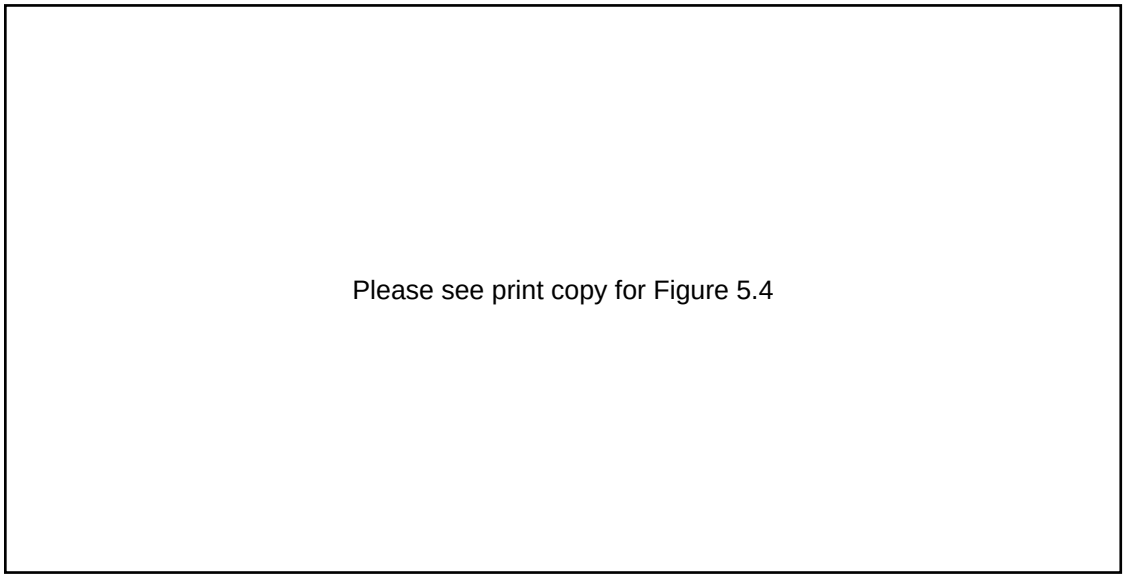
One of the limitations in applying the outcomes from the observational studies however is the chance of observer bias. A single researcher (Brenninger V) who interpreted responses at 'face value' as required, conducted content analysis of the two surveys. However attempts were made to reduce the potential of observer bias though the provision of close-ended responses in addition to the content analysable open-ended responses.

Choosing the study population for this type of research produced a number of issues for discussion, namely, the use of a representative sample, the inclusion of females or only males, and who in the population would benefit most from intervention. In addition, there were and will continue to be metabolic and dietary measurement issues. The use of metabolically fit males for intervention is perhaps an easier option for researchers, considering that the menstrual cycle and higher percentage of fat mass in women tend to add "noise" to the data collected. Overweight and obese people may also limit the effectiveness of dietary treatments due to the belief that weight cycling may decrease a person's homeostatic sensitivity and possibly sensitivity to treatments.

5.4 Providing evidence for the dietary management of disease

Establishing evidence based practice for the dietary management of disease requires many lines of research. Research into human health progresses from laboratory studies at the biochemical and cellular level to generate hypothesises which can be trialled on the individual in the free living environment. Further, often heterogeneous results in clinical trials may then initiate research in the laboratory at a mechanistic level. Figure 5.4 displays the types of studies that may be used, including their respective constraints.

Figure 5.4 Constraints and limitations that the experimental environment places on studies of human feeding



Quality evidence based research is of utmost importance in fields such as obesity (Egger *et al* 1999). The natural environment is important to assess the feasibility of research in an applied situation, though the lack of control promotes ambiguity with data interpretation (Figure 5.4). A number of Government-funded organisations, such as the NHMRC, the Cochrane collaboration, the ANZFA and the National Heart Foundation, currently rate RCTs as providing the highest form of evidence for diet-disease relationships (Truswell 2002). The NHMRC alone accounts for 25 per cent of the funding supplied for health research in Australia (Anderson 1997), this represents a substantial influence on publications which shape evidence based practice.

This hierarchy of evidence is problematic for dietary trials, as they involve complex systems of food intake (Truswell 2002) influenced by lifestyle factors. Drawing upon their definition, higher levels of evidence do not easily assess these. To illustrate, in 1998, the journal 'Diabetes Care' published an editorial on the pedagogical approach to

diabetes management. This editorial pinpointed a critical and universal issue in clinical praxis, the noticeable incongruence between the providers and patient's diabetes management expectations (Anderson and Robins 1998). With reference to key studies (Anderson *et al* 1998; Larme and Pugh 1998) this standpoint promoted the term 'non-compliance' to be redefined, while paving the way to support further studies that combine qualitative with quantitative research, such as the one described in this thesis. Furthermore, it has been documented that behavioural aspects, promoted through intensive therapy may aid dietary management (Ash 2002).

Generating evidence for healthful dietary patterns or 'evidence-based nutrition' requires an understanding of the limitations of this research. There needs to be reflection on the value of the study's findings (Truswell 2002) and an improvement upon nutrition intervention research that is difficult to mould into the RCT. Nevertheless, in today's climate the accepted form of best evidence for practice lies in this approach. One of the major problems in establishing this form of evidence is variation in response within the study population due to genetic and environmental factors (Simopoulos 1995) or simply differences in food intake, which are often correlated with lifestyle factors (Margetts and Jackson 1993). The RCT that adds a sociology component will thereby attend to the clinical application of successful results and provide some theoretical evidence for the discussion on variation in human metabolic responses, such as in the research presented here.

The differences in assumptions attached to the associated methodologies provided a challenge in combining research approaches. A brief outline of the methodological

characteristics that lend themselves to quantitative, experimental (positivist) and qualitative, sociological (naturalist) research is outlined in table 5.4 below.

Table 5.4 Positivist (scientist) verses Naturalistic paradigm – methodological characteristics

Please see print copy for Table 5.4

Although a focus on the dichotomies in research extends beyond quantitative and qualitative or positivist and naturalist, the 'real life' context of dietary intervention support that combined methods are needed. Objectivity is supported by the RCT, while ethnographic approaches (the study of the human experience) are able to follow the variable nature of consumption patterns, lifestyle impacts and other factors that influence the feasibility and efficacy of dietary recommendations as shown in this thesis.

Chronic disease is the product of the interaction between individual's genes, their environment, personal life history and medical technology. Such complex interactions are problematical in establishing dietary roles in the prevention and management of these diseases. The outcomes from the lifestyle related evidence provide a number of areas for comparison with the intervention trial, and agree in part with previous studies investigating the intensity of treatment. The qualitative research conducted on the diet history interview appeared to promote valid reporting if sufficient time was allowed. In addition the current study reinforced that providing study foods is desirable, contact with the dietitian or health professional should be regular, though individualised and personal commitment to adhering to the study requirements needs to be fostered. Together with evidence from previous large-scale dietary trials, individualised approaches are considered to be more effective than general advice (Tuomilehto *et al* 2001, DPP 2002). This thesis demonstrates that the RCT when used to establish medical nutrition therapy alone also requires an understanding of lifestyle variables to inform the clinician drawing upon evidence based practice.

6. Conclusion

Evidence for the effectiveness of dietary management of disease: lessons from a case study of the impact of a resistant starch enriched diet on indicators of the insulin resistance syndrome.

This thesis has addressed a number of hypotheses regarding the establishment of evidence for practice from dietary intervention trials. It has been demonstrated here that for evidence based practice to be most relevant, collecting this evidence from both qualitative and quantitative research methodologies is warranted. Specifically:

1. The study of diet history interviews demonstrated that patients will show evidence of variation in reporting dietary patterns;
2. The lifestyle history questionnaire exposed a range of lifestyle factors likely to impact on compliance and responsiveness, and a post-intervention survey found individual barriers to dietary compliance;
3. The results of an intervention trial comparing the chronic effectiveness of a high RS versus low RS dietary protocol found no significant differences in metabolic effects over 12 weeks;
4. The results of an end of trial meal study found that chronic RS intake lowered the glycaemic response to both types of acute meal challenge at breakfast, though not over the entire meal challenge study. There was a small but significant effect of acute RS meals to reduce post-prandial insulin levels that did not translate into a chronic benefit;

5. The dietary data from the trial were found to be not significantly different between groups, except for dietary fibre, confirming compliance with test foods enriched with RS;
6. The dietary data from the trial found under-reporting only at the week 12 time point and valid reporting for all other four time points.

6.1 Implications for evidence based practice and future research

In studies linking nutrition and disease in Westernised countries, the role of macronutrients is difficult to assess due to poor adherence, high attrition rates, the lack of or contradictory evidence and the validity of the data. The data collected must also be applicable and show efficacy in clinical practice. Here you would want to see effects in the greater proportion of patients, that is, effects should be demonstrable in relatively small intervention studies. However, many factors influence food consumption patterns, and each patient presents their own set of disease manifestations and lifestyle variables that will impact on their management and outcomes. The challenges raised formed the ambiance for this thesis, taking the theoretical position that establishing the evidence to base dietetic practice upon must draw on the scientific and naturalist dichotomies in the research context. This thesis therefore links physiology to sociology using a dietetic perspective.

This thesis hypothesised that evidence based practice needs to draw on naturalistic evidence in a complimentary fashion with research using more widely accepted scientific (positivist) high-level evidence such as the RCT. This hypothesis was tested through an RCT complemented by observational naturalistic research. The diet-disease

relationship chosen for this comparison was addressed through the use of resistant starch in the treatment of an overweight insulin resistant clinical group. The RCT did not show definitive evidence for the inclusion of RS in the diet, but the analysis of qualitative data provided additional information that could be applied to practice.

The evidence presented here demonstrated that the RCT, the accepted design for establishing evidence based practice, is of limited value on its own. This is because the extent of human variability, from both biological and social influences, makes it difficult for studies of a size feasible in practice to produce definitive results where biological outcomes are tested. Evidence based practice would benefit from further research that includes both qualitative and quantitative research so that practitioners have a range of information on which to base their decisions.

6.2 Recommendations for further research

Some authors believe that nutrition research has customarily targeted single issues in 'at risk' individuals, "whereas what we need to address is the question of all the possible effects of specific food components in a genetically heterogeneous population. This is especially important for determining unintended risk as well as intended benefit" (Elliott and Ong 2002: 1438-1439). This research is perhaps one of the first to rise to this challenge and practice the use of combined methods to understand the outcomes.

A heterogeneous group contributes to variation in response and consequently produces results that do not achieve statistical significance. In humans, even when animal based research may provide a sufficient reason to anticipate an effect, the interaction of

lifestyle and cuisine complicate any seemingly straightforward diet-disease investigation.

The sample of overweight insulin resistant people recruited for the RCT showed variation in response in terms of their metabolic changes to chronic acute exposure to RS. It is possible that greater doses of RS may have been need, possibly to overcome the potentially greater impact of other dietary components, including readily available carbohydrates or saturated fats. In addition, dropouts substantially reduced the power of the RCT and future studies of this type would need an increase in recruitment. Nevertheless, the RS diet using currently available commercial foods was well tolerated by the subjects in the study. The results obtained showed that no substantial effects of the chronic RS treatment on metabolic variables could be detected. Body mass index values correlated with this group's insulin resistance, so, rather than attempt to work at fuel quality, caloric reduction may achieve the fundamental manipulation of metabolism required. Reducing energy intake can be achieved by displacing energy dense foods with a more pronounced amount of RS alternatives. A more precise measure of abdominal visceral fat would aid the discovery of any fat utilisation shifts and may have been useful for detecting more subtle changes.

The accuracy of the diet history interview is an important target to adequately question the diet-disease relationship. For future research involving the collection of dietary intake data, the use of food models and food portion photographs are likely to lessen the need for verbal cues such as 'probably' to be displayed. Addressing the variable nature of responses to questions on dinner may be reduced by facilitating recall with cues such

as keeping brief records of what was eaten for dinner during an intervention trial. Verbal cues such as use of "probably" and "[it] depends" may emerge in the interview. Without recognising their use, a dietitian may not offer help or know to probe further. This thesis has shown that in a research setting, a dietitian measuring food intake using the diet history interview, should try to develop rapport and foster accurate reporting by encouraging the use of resources and responding to verbal cues of uncertainty. How we may improve the accuracy of the diet history for research is not completed from this preliminary study alone, however at least we can begin by addressing our approach to 'dinner' meals with more discussion and more appropriate visual aids.

Utilising methods, such as surveys that examine lifestyle variables is recommended for future studies based in the 'free living' environment. These forms of data provided evidence to complete the discussion on evidence based research by emphasing the base from which the clinician attempts to manipulate lifestyle changes.

6.3 Conclusions

A common health problem in Westernised societies is that of insulin resistance and its related complications; diabetes, obesity and elevated cholesterol levels. There are currently two methods of management of insulin resistance namely through diet and lifestyle prescription and secondly if required, through medication. The increasing rates of obesity and diabetes in our society imply limited success of currently recommended lifestyle modifications to the general population. Humans consume a wide variety of foods and whilst small changes to a diet are possible, significant multidimensional changes may be required to have a health benefit.

Levels of evidence have been established for use in forming guidelines for clinicians to base practice upon. The social context within which lifestyle modifications are recommended to an individual is not captured within the randomised controlled trial, an accepted cornerstone of evidence based practice. This thesis has looked closely at the RCT as the main type of research believed necessary for evidence and considered instead the nature of human variability and lifestyle factors in health-related research. Combining an RCT with naturalistic or observational type research has allowed for a well-rounded, holistic discussion on the complex nature of treating lifestyle disease.

The example used in this thesis, using an RCT as its basis, showed that the effects of RS on the insulin resistance syndrome were equivocal. The reasons for this were explained in the way in which outcomes are assessed and measured. There were a number of potential areas for variability to infiltrate. These included the measurement or instrumentation, socially relevant aspects, physiological differences and the environmental foundation in which the changes were established. There is also diversity among humans in their genetic predisposition to disease.

Therefore if we hope to gain more insightful evidence into the management and prevention of chronic disease with dietary manipulation, greater effort into trials that take a more holistic approach are needed. Research needs to address aspects of social and environmental influences in human trials that manipulate dietary intake. This will facilitate the construction of evidence based practice guidelines which have been tested

against the ‘free living’ condition for the clinician and actually apply to the individual requiring treatment.

This thesis has involved examining the literature, developing methods, conducting an RCT and applying observational methods, and has shown that converting what we understand into a straightforward approach for optimising dietary intake in individuals at risk of the metabolic syndrome remains a profound challenge. The ongoing development of new methods of assessment is a confirmation of this demanding climate. It is problematic that need large numbers of patients are needed to gain less ambiguous results. Ideally to expose clinically relevant associations between nutrition therapy and disease biomarkers, we need to be able to prove this in small number of participants.

It is well known that positivists and naturalists do not readily appreciate each other’s work. However, many experienced researchers and rigorous methods are available for both. Most importantly, diet-disease studies need to use sound methods to collect dietary data. The compilation of these methodologies led to in-depth findings that more appropriately translate into clinical practice. The diet history interview is appropriate for use in free-living intervention trials.

The thesis hypothesised and demonstrated that a reductionist approach enforced by a RCT alone lacked the additional information required for the implication of findings where lifestyle changes form a ubiquitous attribute. However, non-RCT forms of research are best implemented in research where accepted higher levels of evidence are

available so that they may be used to explain these results, as qualitative measures are intended to do. Standards for research and clinical practice are continually evolving and now require inclusion of qualitative research to complement diet-disease relationships explored using the RCT. This is to ensure that it remains relevant to the individual and applicable to the clinician in the 'real world'.

THE END

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8. Appendices

Appendix 1. Screening form.

This tool was an interview-administered survey, either completed in person or via the telephone.

Subject Information

Mr / Mrs / Ms / Miss ……

Address: ……

Phone No.:……DOB: ……

SCREENING CRITERIA FOR ELIGIBILITY

Medical history: *Volunteer is not eligible if they have any of the following eleven criteria:*

1. Life threatening or serious illness: Y / N
2. Crohns disease, ulcerative colitis, or coeliac disease: Y / N
3. Any other major bowel disorders or gall bladder disease within the past 6 months: Y/N
4. Glucose intolerance: Y / N
5. Diabetes mellitus: Y / N
6. Kidney disease: Y / N
7. Pregnant: Y / N
8. Medication for high blood cholesterol or lipids: Y / N
9. Antibiotics within the last 3 weeks: Y/N
10. Smoke: Y/N Special diet: Y/N

11. Please note any other medication, (prescribed e.g. laxatives, herbal or supplements e.g. Fish oil capsules) ……..(NB. These may alter metabolism and subjects may not wish to discontinue their use if suitable for the project).
12. Has your weight been much the same for the past six months? Y / N

    ↳ If 'no' … volunteer is not eligible for the study.

    ↳ If 'yes' … what is your approximate weight? ……

    … what is your approximate height? ……

    BMI = _____ $kg.m^2$

❑ Sent info sheet _____(date)

❑ Sent consent forms_____(date)

Appendix 2. Focus Group Outline

Introductory question: Briefly tell us about your diabetes. Cues – how long have you had diabetes? How do you manage your diabetes? Why did you join the study? And which dietary group were you placed in?

1. What aspects of having diabetes concern you the most? How have these concerns impacted/effected you?
2. What changes do you expect you will be making to your usual diet to meet the requirements of the study diet? How do you feel about trying new foods? For example Asian, Mediterranean, low fat foods. Cue – taste of new foods.
3. With regard to the study diet, how do you feel about trying any new cooking methods? For example, Asian/Mediterranean. Cues – time it takes to prepare new foods; skills required for new cooking techniques; any new equipment purchased.
4. How do you think your usual family meal patterns and family food preferences will affect your ability to follow the study diet? Cue – will the person in charge of cooking need to prepare separate dishes for you or the rest of the family?
5. Thinking of the way in which you usually shop for food, how do you think it will change with the study diet? Cues – type of food brought; time taken to do the grocery shopping; reading of nutrition food labels; availability for appropriate foods; amount of money spent on food.
6. How do you think the diet will affect your ability to eat out socially? For example, your ability to eat away from home in restaurants or at friends?
7. What kinds of support do you think you will receive from family and friends to help you stick to the study diet?
8. Which of the changes, that we have discussed do you think will be easiest to maintain and which will be the most difficult?
9. How confident are you about being able to follow the diet? What makes you feel this way? Why?
10. Are there any other issues anyone feels are worthwhile to discuss with the rest of the group?

Discuss them over some light refreshments? Thank you for your time.

Appendix 3. Intervention trial survey

Dear participant,

Thank you for being involved in the dietary intervention trial, the most important step to developing health promoting diets. Your efforts were greatly appreciated by the University of Wollongong and in particular the coordinators of the project.

To finish this project we would like you to answer this survey which raises a number of issues that many of you expressed throughout the trial and some additional questions that are very relevant to the health professionals. We have also left a space at the end of the survey for any further comments that you feel are important, such as your general opinion on the trial or a personal change that you noticed. The survey is anonymous and will take approximately 15 minutes to complete.

Please return the survey in the envelope provided to:

Vanessa Brenninger –
Department of Biomedical Science
University of Wollongong, NSW 2522.

Dietary Intervention Trial Survey

Glossary

Food goals: the specified foods you were asked to eat certain quantities of for the study.

Diet requirements: the targets you were asked to meet for the foods used in the study.

For the following survey, please answer in the space provided or tick ☑ the most appropriate response where boxes (❒) are given.

1) What foods were listed in your dietary goal sheets? **(please answer in the space provided)**

_____

_____

_____

For the following questions (2 and 3) please tick only <u>one</u> box.

2) Did you have any reservations / concerns about being in this trial?

❒ No

❒ Yes. If yes, please state what these were **(answer in the space provided)**

_____

3) Did you continue doing the same level of exercise as at the beginning of the study?

❒ Yes ❒ No, I did less ❒ No, I did more ❒ Unsure

❒ It varied (sometimes more, sometimes less)

Social Support

4) How often do you need to see the dietitian or health professional for dietary assistance **(answer in the space provided)**?

_____

For the following questions (5 to 8) please tick only one box.

5) In your opinion, what level of assistance is needed to help you adhere to the diet?

❒ Regular contact with the same health professional

❒ Regular contact with a range of health professionals

❒ Regular contact with people who need to adhere to a similar diet

❒ Assistance by a health professional at the beginning only

❒ I do not require any assistance with health professionals or similar groups

6) How difficult do you feel it was to adhere to the requirements of the diet intervention?

❒ Very difficult ❒ Difficult ❒ Acceptable ❒ Easy ❒ Very easy

❒ It depends (please comment)

_____

7) Has being in a program / University study helped you maintain adherence to the diet?

❒ Yes ❒ No ❒ Unsure

8) Was having a meal plan or goals in this study important for you?

❒ Yes ❒ No ❒ Unsure

9) What helped you keep within the requirements of the study? **(Please answer in the space provided)**

_____

_____

_____

Eating Out

For the following questions (10 and 11) please tick only <u>one</u> box.

10) How often do you eat out (e.g. restaurants or takeaway)?

❒ Never (go to question 12)

❒ Once a month

❒ Once a fortnight

❒ Once a week

❒ More than once a week (please specify)

_____

11) When eating out, have you felt that it is usually:

❒ Easy to stick to the diet

❒ Sometimes easy to stick to the diet

❒ It depends (please comment)

_____

❒ Difficult to stick to the diet, but I try

❒ I am not able to stick to the diet

12) When was it most difficult to keep to requirements **(please answer in the space provided)**?

_____

_____

Dietary Changes

For the following questions (13 to 15) please tick only <u>one</u> box.

13) How would you rate the food goals provided for you to meet the study requirements?

❒ Too difficult ❒ Difficult ❒ Reasonable ❒ Easy ❒ Too easy

14) How long did you need to adjust to the intervention regimen?

❒ Instantly ❒ 1 week ❒ 1 month ❒ 6 months ❒ I didn't adjust

15) Were the dietary requirements significantly different to what you normally do?

❒ Yes ❒ No ❒ Unsure

If **yes**, how were they different? **(Please answer in the space provided)**

_____

_____

16) What were the main problem areas (if any) in meeting the diet requirements? **(Please answer in the space provided)**

_____

_____

_____

Personal Food Preferences

For the following question please answer in the space provided.

17) With respect to the dietary requirements/ food goal:

a) Which foods did you dislike most?

_____

_____

b) Which foods did you like most?

_____

_____

c) Which foods did you eat most regularly?

_____

_____

Family Meal Patterns and Food Preferences

For the following questions (18 and 19) please tick only one box.

18) Do you feel your family was supportive in meeting the intervention requirements?

❒ Yes ❒ No ❒ Unsure

19) Who had the most influence on your ability to adhere to the dietary intervention? (Place a score in the following boxes from 1 to 5, where 1 is most influencing and 5 is least)

❒ Your self ❒ Family ❒ Friends ❒ Researchers ❒ The dietitian

❒ Other **(please specify)**

_____

Food Preparation, Meal Planning, Cooking Methods and Shopping

20) How did you adapt some of your favorite or regular meals to meet the study requirements? **(Please answer in the space provided)**

_____

_____

_____

21) Compared to before the study, please tick the most appropriate response for each of the following with regard to preparing the diet **(tick one box for each (a) to (e))**:

a) Time required to prepare meals: ❒ More ❒ Less ❒ No difference
b) Expense required to shop for foods: ❒ More ❒ Less ❒ No difference
c) Time required to shop for foods: ❒ More ❒ Less ❒ No difference
d) Planning meals: ❒ More ❒ Less ❒ No difference
e) Amount of food you had to eat: ❒ More ❒ Less ❒ No difference

For the following questions (22 to 25) please answer in the space provided.

22) What was the main reason you volunteered for the trial?

_____

_____

23) What was the best thing about being in the study?

_____

_____

24) What was the worst thing about being in the study?

_____

_____

25) The following space is for you to make any other suggestions or comments …

_____

_____

_____

_____

THE END

Thank you for your time, please check that you have completed all the questions and return the survey to Vanessa Brenninger. Please phone 02 4221 4232 if you have any questions.

Appendix 4: Lifestyle history questionnaire

Lifestyle History Questionnaire Name: _____

PART A: Weight History

For questions 1-4, please give an answer in kilograms **OR** stones and pounds for weight, and in centimetres **OR** feet and inches for height.

1. What is your current weight?……. ___ kg **OR** ___st ___ lbs

2. What is your current height?……..…. ___ cm **OR** ___ft ___ ins

3. What is the least you have weighed as an adult?…. ___ kg **OR** ___st ___ lbs

4. What is the most you have weighed as an adult (excluding pregnancy and 6 months post-pregnancy)?…….. ___ kg **OR** ___st ___ lbs

5. Were you ever substantially overweight as a child or adolescent? (circle yes **OR** no **OR** don't know) …… yes/no/don't know

6. Please describe your experiences in regard to gaining/losing weight as an adult.

_____

_____

_____

7. Please comment on any weight changes you have experienced in the last 3 months.

_____

_____

_____

8. Do you go through phases of losing and regaining weight that are not associated with your menstrual cycle? (circle yes **OR** no) …… yes/no

   If yes,

   a) What is the most weight you have ever lost? (please answer in kilograms **OR** stones and pounds)…… ___ kg **OR** ___st ___ lbs

   b) What is the most weight you have ever regained? (please answer in kilograms **OR** stones and pounds)……. ___ kg **OR** ___st ___ lbs

9. Not including adoptive family, has anyone in your immediate family (parent, brother or sister) ever been substantially overweight? (circle yes **OR** no **OR** don't know) ….……..…… yes/no/don't know

10. If a person were trying to lose weight, do you think there are some foods better avoided than others? (circle yes **OR** no)……... …… yes/no

    If yes, which foods? _____

    _____

PART B: Exercise Patterns

11. Would you describe your usual exercising pattern as (please tick **ONE** box only):-

☐ non-existent (sedentary) (go to **question 14**)

OR

☐ much the same from week to week

☐ variable (please comment on the pattern of variation): _____

_____

_____

_____

12. Including walking, how often do you exercise continuously for 20 minutes or more at **EACH** of the following effort levels (please give an answer for **EACH** effort level):-

a) I exercise for 20 minutes at **light** effort (e.g. strolling on level ground)
_____ times per week.

b) I exercise for 20 minutes at **light to moderate** effort (e.g. gardening – weeding, trimming)
_____ times per week.

c) I exercise for 20 minutes at **moderate** effort (e.g. slow cycling, slow jogging, walking uphill)
_____ times per week.

d) I exercise for 20 minutes at **moderate to hard** effort (e.g. swimming laps, running cross country)
_____ times per week.

e) I exercise for 20 minutes at **hard or very hard** effort (e.g. competitive cycling or rowing, fast running)
_____ times per week.

13. Is any of the exercise that you have participated in during the last 3 months different to what you would usually do in type, time spent, or effort? (circle yes **OR** no) …… yes/no

If yes, how has it changed?

_____

_____

_____

14. How important do you feel exercise is in weight loss? (please tick **ONE** box only)

- ☐ very important
- ☐ important
- ☐ kind of important
- ☐ not important
- ☐ not sure

15. Which, if any, of the following reasons have consistently stopped you from exercising regularly in the past? (please tick **ONE OR MORE** boxes)*

- ☐ nothing has consistently stopped me from exercising regularly **(go to question 16)**

OR

- ☐ I haven't had enough time
- ☐ my health hasn't been good enough
- ☐ there's been no-one to do it with
- ☐ I haven't been able to afford it
- ☐ I've had an injury or a disability that has stopped me
- ☐ I've been too shy or embarrassed
- ☐ I'm not the sporty type
- ☐ there have been no suitable facilities nearby
- ☐ I have needed to rest and relax in my spare time
- ☐ I've had young children to look after
- ☐ I've been too lazy/haven't been motivated/haven't been able to get started
- ☐ I've been afraid that I might get injured or damage my health
- ☐ I don't enjoy physical activity
- ☐ I haven't had the right clothes or equipment
- ☐ I'd never keep it up
- ☐ I'm too fat
- ☐ I haven't had the energy
- ☐ other (please describe the reason):_____

_____

_____

PART C: Eating Patterns

For questions 16-18, please indicate whether your consumption pattern for the meal varies **OR** indicate the number of times per week you eat the meal.

16. On average, how many times a week do you eat breakfast?:-

☐ it varies (please comment on the pattern of variation): _____

_____

OR

I eat breakfast_____ times per week (please indicate number of times)

17. On average, how many times a week do you eat lunch?

☐ it varies (please comment on the pattern of variation): _____

_____

OR

I eat lunch _____ times per week (please indicate number of times)

18. On average, how many times a week do you eat tea/dinner?

☐ it varies (please comment on the pattern of variation): _____

_____

OR

I eat tea/dinner_____ times per week (please indicate number of times)
week)

19. On average, how often would you buy takeaway food or eat out? (please indicate number of times per week for **EACH** meal)

a) I buy takeaway food or eat out for breakfast

_____ times per week (please indicate number of times)

b) I buy takeaway food or eat out for lunch

_____ times per week (please indicate number of times)

c) I buy takeaway food or eat out for tea/dinner

_____ times per week (please indicate number of times)

Do you have any additional comments about this pattern?

_____

_____

20. How would you best describe your meal pattern (please tick **ONE** box only):-

- ☐ I eat regular meals
- ☐ I eat meals in no particular pattern

OR

- ☐ I rarely eat meals

21. How would you best describe your snacking pattern (please tick **ONE** box only):-

- ☐ I eat regular snacks
- ☐ I eat snacks in no particular pattern

OR

- ☐ I rarely eat snacks

22. Do fluctuations in your workload, work shifts, exercise patterns, or other activities cause you to change your pattern of eating (please tick **ONE** box only):-

- ☐ often
- ☐ sometimes
- ☐ rarely

PART D: Food Preparation and Familiarity

23. On average, how often would you prepare your own meals? (please indicate number of times per week for EACH meal)

    a) I prepare my breakfast

       _____ times per week (please indicate number of times)

    b) I prepare my lunch

       _____ times per week (please indicate number of times)

    c) I prepare my tea/dinner

       _____ times per week (please indicate number of times)

    Do you have any additional comments about this pattern?

    _____

    _____

24. On average, how often would you shop for food for the household (not including take-away meals/snacks)? (please tick ONE box only)

    ☐ always (I do all the shopping for my household)

    ☐ regularly (I share shopping with others in my household)

    ☐ occasionally (others in my household usually do the shopping)

    ☐ never

25. Have you tried any new or unfamiliar food products recently (e.g. a new bread or margarine? (please circle yes OR no)..…… yes/no

    If yes, which ones?

    _____

26. In general, which foods would you prefer to eat on a day-to-day basis?

Why?

---

27. In general, which foods would you prefer to avoid eating on a day-to-day basis?

Why?

---

28. In general, which foods do you think are good for you?

Why?

---

29. In general, which foods do you think are not good for you?

Why?

---

30. On average, how often would you eat the following foods? (please indicate how often OR place a tick in ONE box only)

a) pasta

_____ (please indicate how often) OR ☐ too difficult to judge
☐ I don't eat or rarely eat it

b) Rice

_____ (please indicate how often) OR ☐ too difficult to judge
☐ I don't eat or rarely eat it

c) Bread

_____ (please indicate how often) OR ☐ too difficult to judge
☐ I don't eat or rarely eat it

d) margarine/butter

_____ (please indicate how often) OR ☐ too difficult to judge
☐ I don't eat or rarely eat it

e) Alcohol

_____ (please indicate how often) OR ☐ too difficult to judge
☐ I don't eat or rarely eat it

f) milk in cereal

_____ (please indicate how often) OR ☐ too difficult to judge
☐ I don't eat or rarely eat it

g) Vegetables

_____ (please indicate how often) OR ☐ too difficult to judge
☐ I don't eat or rarely eat it

h) Fruit

_____ (please indicate how often) OR ☐ too difficult to judge
☐ I don't eat or rarely eat it

31. When you eat each of these foods, how much would you normally eat on each occasion? (please indicate amount OR place a tick in ONE box only)

a) pasta

_____ (please indicate amount) OR ☐ too difficult to judge
☐ I don't eat or rarely eat it

b) rice

_____ (please indicate amount) OR ☐ too difficult to judge
☐ I don't eat or rarely eat it

c) bread

_____ (please indicate amount) OR ☐ too difficult to judge
☐ I don't eat or rarely eat it

d) margarine/butter

_____ (please indicate amount) OR ☐ too difficult to judge
☐ I don't eat or rarely eat it

e) alcohol

_____ (please indicate amount) OR ☐ too difficult to judge
☐ I don't drink or rarely

f) milk in cereal

_____ (please indicate amount) OR ☐ too difficult to judge
☐ I don't eat or rarely eat it

g) vegetables

_____ (please indicate amount) OR ☐ too difficult to judge
☐ I don't eat or rarely eat

h) fruit

_____ (please indicate amount) OR ☐ too difficult to judge
☐ I don't eat or rarely eat it

PART E: Study Expectations

32. Whilst participating in this study, do you expect your weight to change? (circle yes OR no OR don't know) …… yes/no/don't know

33. Do you expect that your eating patterns will change over the course of the study? (circle yes OR no OR don't know) yes/no/don't know

….……..……

34. Do you expect that your exercise patterns will change over the course of the study? (circle yes OR no OR don't know) yes/no/don't know

……...……

35. What do you hope to learn from participating in this study?

_____

_____

_____

☺ Thank you for completing this questionnaire.

Your answers will remain confidential.

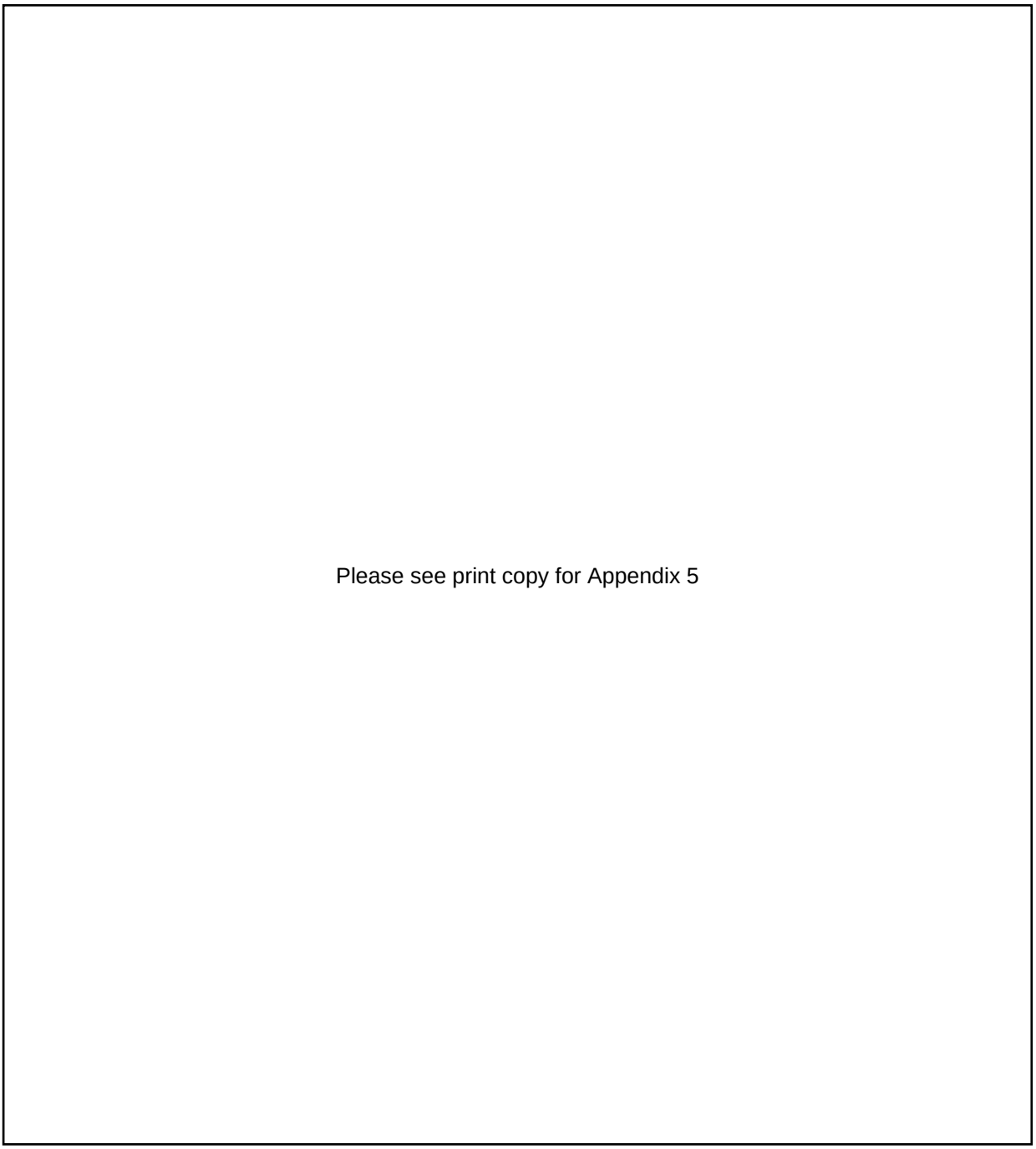
* Barriers to exercise in question 13 taken from Department of the Arts, Sport, the Environment and Territories (1992), *Pilot Survey of the Fitness of Australians*. Australian Government Publishing Service, Canberra.

Appendix 5. Photographic atlas – potion size book.

Please see print copy for Appendix 5

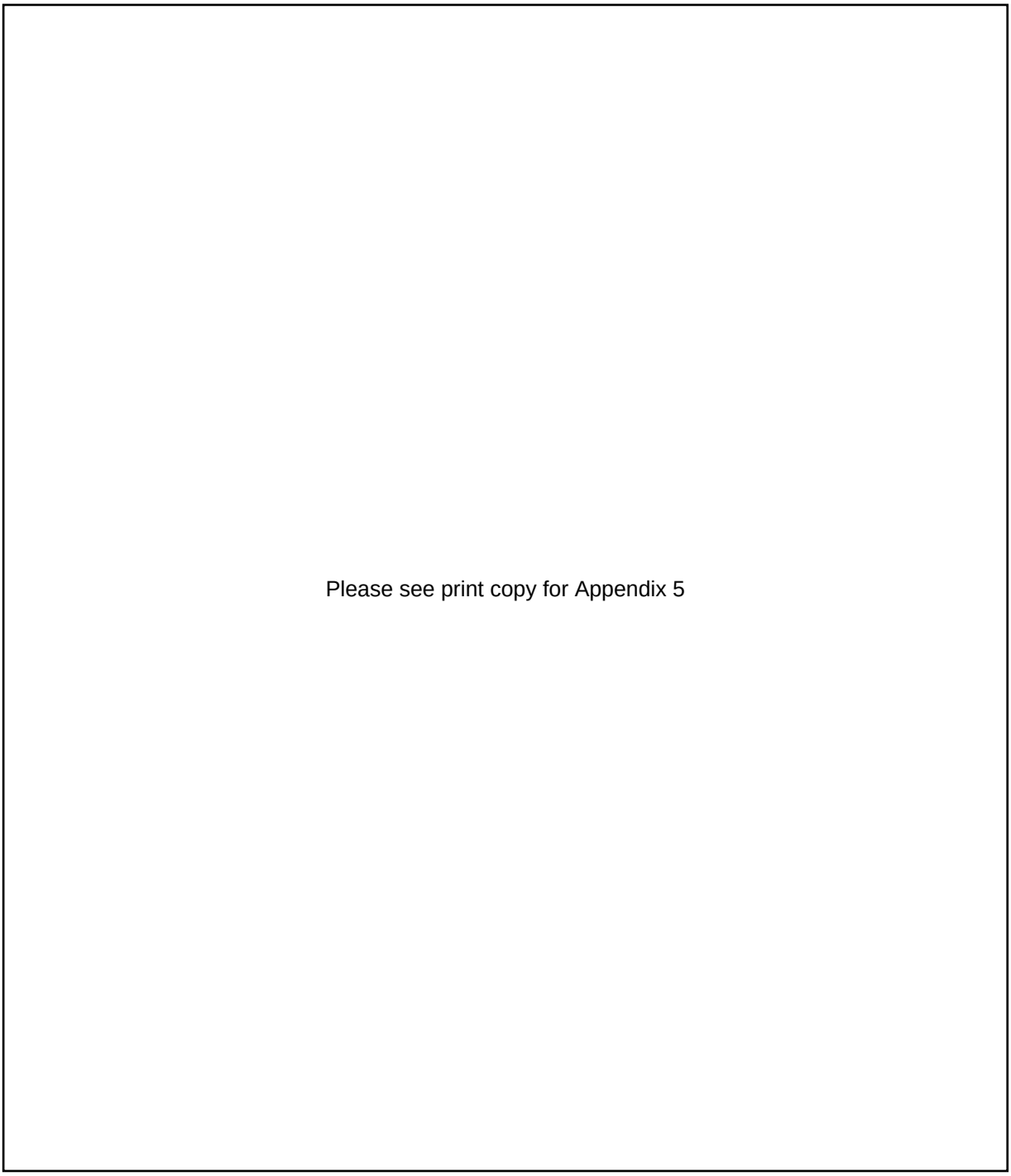
Pasta. Source: Nelson M, Atkinson M and Meyer J (1997) A photographic atlas of food portion sizes. Maff Publications, London.

Photographic atlas – potion size book.



Cheese: Source: Nelson M, Atkinson M and Meyer J (1997) A photographic atlas of food portion sizes. Maff Publications, London.

Photographic atlas – potion size book.



Steak: Source: Nelson M, Atkinson M and Meyer J (1997) A photographic atlas of food portion sizes. Maff Publications, London.

Appendix 6. Nutrient composition of meal challenges

Table 3: Nutrient breakdown for the high resistant starch meal challenge day.

Breakfast	Weight	RS	Energy (kJ)	CHO	Fat	Protein	DF
1 *Wonder White* English muffin	~66g	3.47	633	28.5	1.6	5.2	3.2
Olive Grove margarine	15g	0	417	0	11.1	0	0
Honey – Stringy Bark *Capilano*™	5g	0	18	5	0	0	0
1 banana muffin (sweet cake-like) [1]	~70g	6.06	785.6	39.6	1.8527	2.627	4.9
Total		9.53	1853.6	73.1	14.55	7.827	8.1
Energy (kJ)				1170	538	133	
Percent contribution of energy				63.1%	29%	7.18%	
Lunch	**Weight**	**RS**	**Energy (kJ)**	**CHO**	**Fat**	**Protein**	**DF**
3 slices *Wonder White* bread	~100g	14.4	1201.5	56.4	2.85	8.1	6
Olive Grove margarine	15g	0	417	0	11.1	0	0
2 slices lean ham	32g	0	126	0.2	1.0	6.2	0
Lettuce	15g	0	5	1	0	0	0
High RS lollies (*Greens*)	25g	0.81	332	19.4	0.05	1.2	1.5
Total		15.21	2081.5	77	15	15.5	7.5
Energy (kJ)				1232	555	264	
Percent contribution of energy				59.2%	26.7%	12.7%	

Abbreviations: RS, resistant starch; kJ, kilojoule; CHO, carbohydrate; DF, dietary fibre.

[1]Banana muffins were baked in the University of Wollongong, Smart Foods Centre kitchen. The preparation of the muffins were as follows:

Ingredients: 293mL water, 30g 1043 Natural *Hi-Maize*™ powder, 1 x 55g *Veggs* first quality fat modified egg, beaten, *White Wings* 97% Fat Free Banana Muffin Mix.

Directions: 1. Preheat oven to 180°C on fan bake setting. 2. Lightly spray each cup of a 12-cup muffin tray with *Bertolli*® Extra Light Olive Oil spray. 3. Beat egg and water together for approximately 1 minute with a fork. 4. Add muffin mix and 1043 powder. Stir though mixture with a fork for approximately 4 minutes until no flour lumps exist and all powder is evenly throughout the mixture. 5. Spoon mixture evenly into 11 cups of the 12-cup muffin tray. 6. Bake for 20 minutes. 7. Remove tray from oven and allow muffins to cool in pan for 10 mins, then remove from tray and place on a paper towel to cool. 8. Once completely cooled, place each into separate resealable plastic freezer bag, labelled with muffin type, date baked and study name, then frozen at –20°C. 9. Upon re-thawing of muffin, weigh each with electronic weighing scales (*OHAUS*, Model GT410, Florham Park, NJ 07932, made in the USA).

[2]Blueberry muffins for the normal meal challenge were made as follows:
Ingredients: 200mLwater, 1 x 55g *Veggs* first quality fat modified egg, beaten, *Green's* deLites Blueberry 97% Fat Free Muffin Mix.

Directions: 1. Preheat oven to 160°C (325 °F) on fan bake setting. 2. Lightly spray each cup of a 12-cup muffin tray with *Bertolli*® Extra Light Olive Oil spray. 3. Drain and rinse blueberries provided in package, set aside. 4. Beat egg and water together for approximately 1 minute with a fork. 5. Add muffin mix and stir though mixture with a fork for approximately 4 minutes until no flour lumps exist. 6. Stir in drained blueberries into mixture. 7. Spoon mixture evenly into 11 cups of the 12-cup muffin tray. 8. Bake for 20 minutes. 9. Remove tray from oven and allow muffins to cool in pan for 10 mins, then remove from tray and place on a paper towel to cool. 10. Once completely cooled, place each into separate resealable plastic freezer bag, labelled with muffin type, date baked and study name, then frozen at –20°C. 11.

Upon re-thawing of muffin, weigh each with electronic weighing scales (*OHAUS*, Model GT410, Florham Park, NJ 07932, made in the USA).

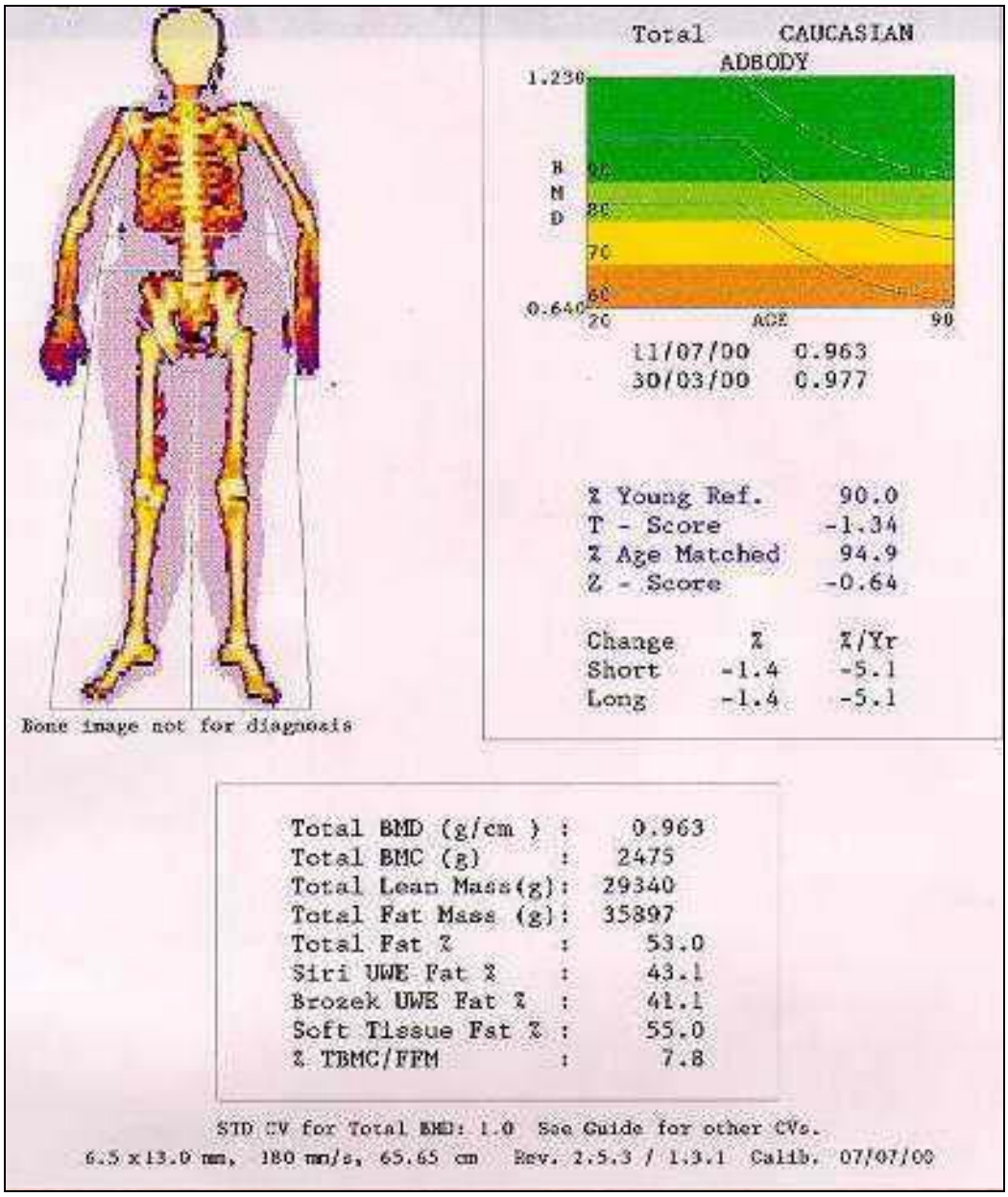
The same method and ingredients were used for muffins distributed to subjects during the 12-week dietary intervention trial. Subjects were blind to what type of muffins they received and both apricot and banana flavours of *White Wings* 97% Fat Free Muffin Mix were used for the high resistant starch group. For the LRS dietary group were given a variety of flavours of Greens muffin mix, such as blueberry, that did not contain any *Hi-Maize*™ powder.

Table 4: Nutrient breakdown for the low resistant starch meal challenge day.

Breakfast	Weight	RS	Energy (kJ)	CHO	Fat	Protein	DF
1 Buttercup English muffin	g	min	633	32.25	0.621	4.585	1.316
Olive Grove margarine	15g	0	417	0	11.1	0	0
Honey – Stringy Bark Capilano™	5g	0	18	5	0	0	0
1 blueberry muffin (cake-like) [2]	71.4g	min	785.6	39.413	1.499	3.427	1.5
Total		min	1853.6	76.663g	13.22g	8.012g	2.816g
Energy (kJ)				1226.61kJ	489.14kJ	136.2kJ	
Percent contribution of energy				66.2%	26.39%	7.35%	
Lunch	**Weight**	**RS**	**Energy (kJ)**	**CHO**	**Fat**	**Protein**	**DF**
3 slices Buttercup sandwich white bread	113.3g	min	1201.5	55.201	2.494	10.201	3.40
Olive Grove margarine	15g	0	417	0	11.1	0	0
2 slices lean ham	32g	0	126	0.2	1.0	6.2	0
Lettuce	15g	0	5	1	0	0	0
Lollies	25g	min	332	18.4	0.217	0.694	0
Total		min	2081.5	74.8g	14.811g	17.095g	3.40g
Energy (kJ)				1196.8kJ	548.01kJ	290.62kJ	
Percent contribution of energy				57.5%	26.3%	14.0%	

Abbreviations: RS, resistant starch; kJ, kilojoule; CHO, carbohydrate; DF, dietary fibre.

Appendix 7. Dual-energy X-ray Absorptimometry (DXA)



DXA scans were completed at the Wollongong Nuclear Medicine premises.

Appendix 8. Hyperinsulinemic: Euglycemic Clamp

Version 3: March 2000

Name: Date: Code:

Weight: Height: SA:

Glucose infusion: Target limit (L): DOB:

Calibration factor (CF) = weight ÷ 70 =

Algorithm: $Ri = [46.8 \times (L - Gi) \times CF] + [70.2 \times (Gi\text{-}1 - Gi) \times CF] + \frac{Ri\text{-}2 + Ri\text{-}1}{2}$

BP: Pulse:

At time 0': start insulin at set rate (change every min for 10 mins) and take 1st blood glucose (BGl).

(**a**) At time 4': start glucose infusion at a rate of (2mg x kg x min)/100 = ☐

(**b**) At time 10': change glucose to a rate of (2.5mg x kg x min)/100

and take 2nd BGl = ☐

(**c**) At time ~12': average rate used is (4mg x kg x min)/100 = ☐

(**d**) 10' Ri = [46.8 x (L – Gi) x CF] + [70.2 x (Gi-1 - Gi) x CF] + [**c**]

(**e**) 15' Ri = [46.8 x (L – Gi) x CF] + [70.2 x (Gi-1 - Gi) x CF] + (**c** + **d**)/2

Time blood taken	Gi	(4.5- Gi) x	(Gi-1 – Gi) x		Ri
0					
4					**a**
10				**c**	**b** **d**
15					**e**

Time blood taken	Gi	(4.5- Gi) x	(Gi-1 - Gi) x	$\frac{Ri-2 + Ri-1}{2}$	Ri	Time rate set		
20								
25								
30								
35								
40								
45								
50							Minutes	Gl infused
55								
60								
65								
70								
75								
80								
85								
90								
95								
100								
105								
110								
115								
120								

Hyperinsulinemic: Euglycemic Clamp Version 3: March 2000

Name: SA:

Priming insulin infusion:

1U = 10ml 1000mU = 10ml 100mU = 1ml 1mU = 0.01ml (10^{-2}ml)

Time	Insulin infusion rate (mU/m^2SA.min)	Insulin infusion rate (ml/m^2SA.hr)	Subject's insulin infusion rate (ml/hr)	
0-1	127.6	76.6		
1-2	113.6	68.2		
2-3	101.2	60.7		
3-4	90.2	54.1		
4-5	80.2	48.1		Gl =
5-6	71.4	42.8		
6-7	63.6	38.2		
7-8	56.8	34.1		
8-9	50.4	30.2		
9-10	45.0	27.0		
10-120	40.0	24.0		Gl =

Appendix 9. Satiety visual analogue scales (not to scale)

Satiety Scales

Code: _____ Interval: _____ Time: _____

Please put an X on the line below that best represents your current feelings about your appetite.

How hungry do you feel RIGHT NOW?

NOT AT ALL HUNGRY — AS HUNGRY AS I HAVE EVER FELT

0 10 20 30 40 50 60 70 80 90 **100**

How full do you feel RIGHT NOW?

NOT AT ALL FULL — EXTREMELY FULL

0 10 20 30 40 50 60 70 80 90 **100**

How strong is your appetite for a meal RIGHT NOW?

WEAK STRONG

0 10 20 30 40 50 60 70 80 90 **100**

How much food could you eat RIGHT NOW?

NOTHING A FULL MEAL

0 10 20 30 40 50 60 70 80 90 **100**

How strong is your desire to eat RIGHT NOW?

WEAK STRONG

0 10 20 30 40 50 60 70 80 90 **100**

Satiety Scale

Extremely Hungry	Hungry	Semi Hungry	No Particular Feeling	Semi Satisfied	Satisfied	Extremely Full

Appendix 10.

Example instruction given and use of daily checklists used by participants

Please write the date in the top square of each column, and then the amount of each of the foods listed that you consumed in the adjacent box. For example, on 21st Feb, you may have eaten 45g of breakfast cereal, 4 slices of bread, 210g of spaghetti, 1 sweet muffin, a tub of yoghurt, a ripe banana, and 140g of potato salad. This would be filled in as follows:

Food / Date:	**21/2/00**						
Bread	4 slices						
English muffin	-						
Sweet muffins	1						
Lollies	-						
Breakfast Cereal	45g						
Spaghetti	210g						
Drink	-						
Yoghurt	1 tub						
Potatoes (hot)	-						
Potatoes (cold)	140g						
Bananas (specify if green)	1 ripe						
Rice (specify type)	-						

PLEASE SPECIFY AMOUNTS, not just a tick.

Appendix 11. Participant information and consent forms

Metabolic Research Centre

PARTICIPANT INFORMATION SHEET

Carbohydrates and their metabolic outcomes

Chief investigators: Vanessa Brenninger, (Ph 4221 4232)
Associate Professor Linda Tapsell (Ph 42213152),
Professor Len Storlien
Professor Denis Calvert

This research study is being conducted by a group of researchers in the Metabolic Research Centre at the University of Wollongong. Vanessa Brenninger is a qualified dietitian, leading the research program, Professors Tapsell and Storlien are nutritionists and scientists who research in diabetes, and Professor Calvert is a physician who researches in diabetes. The aim of the study is to improve our understanding of the benefits of different carbohydrates on metabolism. We will use the results to advance our understanding of the management and treatment of people at risk of developing diabetes and/or diabetic complications. The procedures are quite straightforward, involving measurements of your dietary patterns and the food goals you have been asked to comply with and comparing these with your metabolic response.

Measurements of your metabolic response will involve you spending a number of hours at the university on the first day and final three days of the 3-month study. The first day you will arrive fasted for a spot blood glucose test (finger prick) to test for diabetes, then a dietary interview will take about 1-1¼ hours. The next day, you will arrive fasted and have glucose and insulin infused through a cannula in each arm and blood

taken from time to time (approximately 2 tablespoons in total). The procedure will show how sensitive your body is to insulin over a 4-hour period. Lunch will be provided. You will also begin a 3-day record of what you eat and have a scan for body composition, conducted at Wollongong Nuclear Medicine on commencing the study. This will involve you lying flat for about 20 minutes while a DXA machine does a body scan using an x-ray which delivers the equivalent of one tenth the radiation of a normal chest x-ray. (Pregnant women are excluded from this procedure.) These procedures will all be repeated at the end of the study with a questionnaire on how you felt about your diet over the 3 months. At the end of the study on two days, approximately 1 week apart, we will take a blood sample, through a cannula in a vein in your arm then you will sit and rest all day while we measure your breath carbon dioxide after giving you breakfast and lunch. Any blood taken may cause a small amount of bruising. Other blood samples taken throughout the day, from the cannula, add up to a volume of about 4 tablespoons.

On four more occasions, (at 3-week intervals from when you started) you will have a dietary interview and on two more occasions, you will do a 3-day food record again. You will be given forms to complete for keeping the food record each time. All information will be kept secure and by code rather than by your actual name. Nothing, which identifies individual participants, will be published. Standards of medical confidentiality will apply.

As a result of the study you will be able to gain some basic information about your health status in terms of diet and your body composition. If at any time you have any questions, please do not hesitate to ask. Your involvement in the research is entirely voluntary. You are free to withdraw from the research at anytime without penalty. If you have any enquiries regarding the conduct of the research please contact the Secretary of the University of Wollongong Human Research Ethics Committee on (02) 42214457.

Metabolic Research Centre

CONSENT FORM

Carbohydrates and their metabolic outcomes

Chief investigators: Vanessa Brenninger MSc, APD (Ph 4221 4636)
Associate Professor Linda Tapsell, PhD, APD (Ph 42213152)
Professor Len Storlien, PhD
Professor Denis Calvert, MD

This research study is being conducted by the team listed above. I understand that the data collected will be used to develop the optimal diet for those at risk for diabetes and other metabolic disorders. I consent for the data to be used in that manner. I agree to:

a. Take part in five interviews about my usual dietary intakes and complete three 3-day food records and a basic questionnaire about my exercise, weight patterns and associated information;

b. Eat the diet and food products prescribed, as far as possible for a 3 months period and complete a questionnaire about how I felt about the diet at the end;

c. Have the following procedures done:
   a) an initial fasting finger prick blood test to test for blood glucose level;
   b) height and weight measured (weight measured monthly);
   c) have a session at the beginning and end of the study to measure insulin sensitivity by infusing insulin and glucose into an arm vein (usually the crook of the elbow) and taking blood from a cannula from time to time (cannulas are small soft plastic tubes inserted with a needle that remain in your arm for the session);

d) on two days (at the end of the study) measuring my resting metabolic rate by measuring the carbon dioxide I breath out, eating the breakfast and lunch provided and have small amount of blood taken each hour to see the effects of these meals. Also answer questions on how satiating these meals are;
e) undergoing two DXA scans (a very low dose x-ray).

Your participation in this research is voluntary, you are free to refuse to participate and you are free to withdraw from the research at any time. Your refusal to participate or withdrawal of consent will not affect your treatment or your relationship with the University of Wollongong in any way. If you would like to discuss this research further please contact Vanessa Brenninger on 02 42214636. If you have any enquiries regarding the conduct of the research please contact the Secretary of the University of Wollongong Human Research Ethics Committee on (02) 42214457.

Research Title: Carbohydrate (resistant starch) and metabolic outcomes study.

I have read the participant information sheet and understand what I will be doing. I have been given the opportunity to speak with the researcher, Vanessa Brenninger, about the study and have asked any questions that I wished to ask.

I, ... (Participant's name) consent to participate in the research conducted by Vanessa Brenninger as it has been described to me in the information sheet. I understand that the data collected will be used to develop the optimal diet for those at risk for diabetes and other metabolic disorders and I consent for the data to be used in that manner.

Signed Date

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