A feasibility study to investigate the effectiveness and safety of an intermittent fasting diet for weight reduction in adults with Type 2 Diabetes treated with insulin

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Abstract

Background: Type 2 diabetes (T2DM) is the most common form of diabetes. Obesity is associated with both the development of T2DM and also the development of the complications of diabetes; increasing health care costs and morbidity and mortality. Weight loss and control of blood glucose levels should be managed with a tailored eating plan developed in negotiation between the person with diabetes and their health care team. It is essential that health care professionals are familiar with different strategies that achieve weight reduction, glycaemic and cardiovascular risk reduction goals. One emerging weight reduction strategy is fasting diets. There is currently a gap in the knowledge of whether fasting diets are an effective and safe weight reduction strategy for people with T2DM on insulin.

Aim: To investigate the effectiveness and safety of an intermittent fasting diet (two day per week) as an alternative to standard dietary advice (portion control diet) for weight reduction in obese adults with insulin dependent T2DM attending a 12-week group based intervention at Waitemata District Health Board (DHB).

Methods:

Obese patients with T2DM treated with insulin who were attending Waitemata DHB Diabetes Service were recruited for this two arm open-label design intervention feasibility study. Both dietary strategies were implemented during a 12-week intervention at which participants received monthly dietitian-led group education and support. The intermittent fasting diet (IFD) intervention (n=8) investigated was a two day per week reduced energy intake (550-650kcal / 2300-2700kJ per day) and five days' usual intake making low fat choices. The portion control diet (PCD) was the comparison group (n=7) and focused on daily energy restriction through reduction in portion sizes and low fat food choices in line with current New Zealand dietary recommendations for management of T2DM.

Results: Similar weight loss was achieved in both groups (IFD: 2.7 ± 3.0 kg, PCD: 1.7 ± 2.5 kg). This reduction was not significant between groups. There was a significant difference between groups in reduction in HbA1c. (P=0.003) (IFD: -11 mmol/mol, PCD: -3 mmol/mol). This decrease was significant in the IFD group only (P=0.018). Reported hypoglycaemic events were low in both groups (8 events in IFD; 21 events in PCD). Non-significant between group reductions in waist circumference (P=0.402), waist: height ratio (P=0.455), diastolic (P=0.189) and systolic blood pressure (P=0.443) were observed. Lipid profile remained stable in both groups.

Conclusion: This feasibility study showed that an intermittent fasting diet can achieve similar weight loss to current standard practice dietary advice in people with T2DM. However, it is the significant reductions in HbA1c compared to a daily energy restriction diet over a three-month period seen in this study that warrant further investigation. With education from health care professionals and modification of insulin on pre-fasting and fasting day this diet may be followed safely and hypoglycaemia avoided or managed appropriately.

Acknowledgements

There is a story behind this thesis which may help to put in to context the practical nature of this research. Bear with me. Thirty years ago this year (2016) I was diagnosed with Type 1 Diabetes. Aged 13 and within five days of my diagnosis I had mapped out my career as a Dietitian. This year is also the 22nd anniversary of graduating from Queen Margaret College (now University), Edinburgh with a Bachelor of Science degree in Dietetics. When I was diagnosed with diabetes I was fortunate that neither my parents nor health care team put restrictions on what I could or could not achieve. I feel fortunate that I have travelled the world, had many adventures, run many half-marathons, and have two wonderful daughters, a husband and my health. So, when faced with people who try and tell me that I can't do something just because I have diabetes I don't often believe them. And this is the case with this research. I still have the original Radio Times magazine article about a Horizon documentary that my mother sent me from Scotland. The documentary was about a Doctor, a health journalist, who investigated intermittent fasting because he had been diagnosed with pre-diabetes. Mum wanted to know my opinion. In my investigations I came across many people telling me that people with diabetes on insulin shouldn't fast. Yet I knew that personally I had fasted safely, and professionally I had worked with people who had fasted. Meanwhile, in an office at the hospital I worked at, Dr Catherine McNamara, Consultant Endocrinologist had also heard about intermittent fasting. More than that, she had read the book and the research and was intrigued as to whether it would be of benefit to her patients with Type 2 Diabetes who needed to lose weight. People were asking about this diet in clinics. Together we came up with the research study that is presented here as my MSc thesis. Living and working with diabetes there is one thing that has come up time and time again, and that is there are no set rules when it comes to diabetes. Trying to fit the condition(s) that are labelled as diabetes in to neat boxes does not work, because blood glucose is affected by so many things. People with diabetes tend to have multiple diagnoses and multiple stresses. It was important to keep this research as practical and "real life" as possible, whilst making sure that the results were still meaningful. It seems fitting

that my dietetic career started with a diagnosis of diabetes, and here I am concluding my academic studies with research to help people with diabetes.

I would particularly like to thank the participants of this study. Without you we wouldn't have the knowledge that we now have about this type of dietary intervention. We recognised that diabetes is a condition that takes up a lot of time, effort, brain-power and emotion. Adding a dietary intervention that is slightly out of the box on top of that, I am very grateful for you for spending that extra time and effort to take part in this dietary intervention. Thank you to the staff at the Diabetes Service, Waitemata District Health Board for your support, advice and enthusiasm in helping to recruit and run this study. Especially Eirean Gamble, Diabetes Dietitian Team Leader whose feedback and support was invaluable, and Dr Catherine McNamara, Consultant Endocrinologist who identified the need for this study and provided medical support and input to the study.

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Finally, thanks to my husband, my daughters and my friends and family. It was your support and encouragement along with prayer (and fasting) that kept things running smoothly. However, the only thing that really matters is Acts 2:37-38, and Mark 16: 15-20.

Table of Contents

List of Figures

List of Tables

List of Abbreviations

ADF	Alternate day fasting
BP	Blood pressure
DSME	Diabetes self-management education
GP	General Practitioner
IF	Intermittent fasting
IFD	Intermittent fasting diet
OHA	Oral hypoglycaemic agent
PCD	Portion control diet
SMBG	Self-monitored blood glucose
T2DM	Type 2 Diabetes

CHAPTER 1 INTRODUCTION

Diabetes Mellitus is a group of chronic and progressive metabolic disorders that are characterised by a deficiency in insulin production or decreased sensitivity to insulin. Without sufficient insulin glucose remains in the blood rather than moving in to the cells to provide energy for cellular functions. This results in blood glucose levels rising above the normal or ideal range (American Diabetes Association, 2016b, Scottish Intercollegiate Guidelines Network, 2010, National Institute for Health and Clinical Excellence, 2015). High levels of glucose in the blood (hyperglycaemia) increases the risk of developing the medical complications of diabetes: micro- and macro-vascular diseases such as cardiovascular disease, peripheral and autonomic neuropathies, nephropathy and retinal damage (American Diabetes Association, 2016b, Scottish Intercollegiate Guidelines Network, 2010).

Type 2 diabetes (T2DM) is the most common form of diabetes. Type 2 diabetes is predominantly a disease of insulin resistance however there can be some degree of insulin deficiency (American Diabetes Association, 2016a). Genetic predisposition, obesity, increased waist circumference and reduced physical activity all increase the risk of developing T2DM (American Diabetes Association, 2016a). Coppell *et al.* (2013) using data from the New Zealand Adult Nutrition Survey (University of Otago and Ministry of Health, 2011) found that 4.6% of New Zealand adults who were overweight and 9.8% of those who were obese had diabetes.

Normalising blood glucose levels whilst minimising low blood glucose levels (hypoglycaemia) and hyperglycaemia (American Diabetes Association, 2016b) is the main focus of care for those with T2DM. Diminishing the complications of T2DM by achieving blood glucose goals is best achieved by diet and lifestyle counselling, medication and self-monitoring of blood glucose levels (Daousi *et al.*, 2006).

Not only is obesity associated with the development of T2DM but it is also a risk factor for the advancement of the complications of diabetes; increasing health care costs and the risk of morbidity and mortality (Smith and Singleton, 2013, De Block *et al.*, 2005). Weight reduction through diet and lifestyle changes, surgery or medication is one of the cornerstones of ensuring good outcomes for people with T2DM; reducing microvascular disease and cardiovascular diseases (Dyson *et al.*, 2011, Henry *et al.*, 2013, Evert *et al.*, 2014). There is also the added burden of the obesogenic effects of insulin and certain oral hypoglycaemic agents used in the treatment of T2DM which must be considered when setting glycaemic and weight loss goals (Van Gaal and Scheen, 2015).

It has been acknowledged by the American Diabetes Association (Evert 2014) that there is no single best way of eating that is recommended for people with diabetes. A tailored eating plan should be developed in negotiation between the person with diabetes and their health care team. It is therefore essential that health care professionals should be aware of and familiar with different strategies that achieve weight reduction, glycaemic and cardiovascular risk reduction goals (Evert 2014).

A variety of different weight reduction strategies have been investigated for use in people with T2DM. Weight reduction strategies recommend an overall reduction in energy intake which can be achieved by modifying dietary intakes or eating behaviours and patterns (Dyson *et al.*, 2011). A healthy eating, low energy diet is usually the first type of dietary recommendation used to promote normoglycaemia and weight loss in people with T2DM (Diabetes New Zealand, 2014, Dietitians New Zealand Diabetes Special Interest Group, 2014, Dyson *et al.*, 2011, Scottish Intercollegiate Guidelines Network, 2010). In recent years novel weight loss strategies including low carbohydrate, high protein, very low calorie and low glycaemic index diets have also been investigated in people with T2DM (Castaneda-Gonzalez *et al.*, 2011, Larsen *et al.*, 2011, Tay *et al.*, 2015, Dong *et al.*, 2013, Krebs *et al.*, 2012, Steven and Taylor, 2015, Snel *et al.*, 2012, Chiavaroli *et al.*, 2016, Jenkins *et al.*, 2012). Krebs and Parry-Strong (2013) in a review of these diets for weight reduction in people with T2DM concluded that the strategy that works is the

strategy that works best for the individual. This is aligned with the American Diabetes Association recommendations (Evert *et al.*, 2014) that there is no single diet which works for all people with T2DM. Therefore, health care professionals working with people with T2DM need to be familiar with a range of weight reduction strategies and be able to give appropriate evidence based advice regarding new weight reduction strategies.

1.1 Justification of the study

It has already been stated that the most successful weight reduction strategies are ones that the patient is able to adhere to (Krebs and Parry-Strong, 2013). There is the need to investigate the effectiveness and safety of emerging weight reduction strategies for people with T2DM which may help individuals achieve weight loss goals. One emerging weight reduction strategy is fasting diets (Collier, 2013). Fasting diets involve a severe energy restricted intake on between two and four days of the week with an unrestricted energy intake on the remainder of the week. Two types of fasting diets are commonly used: alternate day fasting (ADF) where participants consume approximately 25% of energy requirements on alternating days to normal energy intake, and intermittent fasting (IF) where 25% of energy intake is consumed on only one or two days each week and unrestricted energy intake on the other days (Varady and Hellerstein, 2007) (Brown *et al.*, 2013). Research has shown that fasting diets achieve success due to severe energy restriction for a few days each week being more able to be adhered to consistently than a daily energy restriction, whilst achieving similar weekly energy intakes (Harvie *et al.*, 2013, Varady *et al.*, 2009, Harvie *et al.*, 2011). However, there are indications that fasting diets also improve insulin sensitivity and reduce inflammation and oxidative stress more effectively than other weight reduction strategies (Trepanowski *et al.*, 2011). The results of studies investigating the use of fasting diets in healthy obese and overweight adults show that these diets can result in weight loss of approximately 0.5kg per week, a similar amount seen in other types of weight reduction strategies.

To date there has been one published study looking at a fasting diet in people with T2DM (Williams *et al.*, 1998). These participants were not taking insulin injections and had their oral hypoglycaemic agents (OHA) discontinued at the beginning of the study. For those people with T2DM who take certain types of OHA or insulin the use of fasting diets may increase the risk of hypoglycaemia caused by a reduction in carbohydrate intake if medication is not adjusted accordingly. There is data from research on people with T2DM who fast during the religious festival of Ramadan that can be applied when considering fasting diets for people with T2DM. Results from the Ramadan studies suggest that the key to safe fasting is education and appropriate medication adjustment (Aldasouqi *et al.*, 2013, Reiter *et al.*, 2007, Loke *et al.*, 2010, Ahmed and Abdu, 2011, Salti *et al.*, 2004). Also, in recent years the mode of action of modern insulin has enabled the development of strategies to teach people with T2DM how to change their own insulin doses depending on dietary intake, activity and illness (DAFNE study group, 2002). Therefore, in theory, it should be possible for people with T2DM who are treated using OHA and insulin to follow a fasting diet under supervision.

1.2 Statement of the research problem

There is currently a gap in the knowledge of whether fasting diets are an effective and safe weight reduction strategy for people with T2DM on insulin who may also be taking OHA. It is not known whether the obesogenic effect of insulin and certain types of OHA will result in similar rates of weight loss seen in studies on fasting diets in overweight or obese people without diabetes. It is not known whether fasting diets will result in increased rates of hypoglycaemia or hyperglycaemia in those on insulin.

Anecdotal evidence from diabetes health care professionals at Waitemata District Health Board (DHB) indicated that in 2013/2014 patients who were attending the Waitemata DHB Diabetes Service were requesting information on fasting diets and whether it was safe for them to follow such a diet. There was a lack of research evidence available to guide the advice that health care professionals were able to offer.

1.3 Purpose of the feasibility study

1.3.1 Aim

The aim of this feasibility study was to investigate the effectiveness and safety of an intermittent fasting diet (two days per week) as an alternative to standard dietary advice (daily energy restriction) for weight reduction in obese adults with insulin dependent Type 2 Diabetes attending a 12-week group based intervention through the Waitemata DHB Diabetes service.

1.3.2 Objectives

The primary objective was to investigate weight change during a 12-week group-based education programme, delivering an intermittent fasting diet compared to current standard practice (portion control) dietary advice in obese adults with T2DM treated using insulin.

The secondary objectives were:

1. To examine the effect of a 12-week intermittent fasting diet against standard practice dietary advice on hypoglycaemia events and glycaemic control (HbA1c).
2. To investigate cardiovascular disease risk measures (waist circumference, waist: height ratio, blood pressure and serum lipids) when following a 12-week intermittent fasting diet compared with standard practice dietary advice.
3. To examine participants acceptance of the dietary interventions advised during the study.

1.3.3 Hypothesis

It is hypothesised that for adults with T2DM using insulin, following an intermittent fasting diet will result in similar weight loss and change in glycaemic and cardiovascular markers than when following standard treatment for weight loss, and that this diet will not significantly increase the risk of hypoglycaemia.

1.4 Structure of the thesis

A review of current literature is presented in Chapter Two. This includes a background to diabetes care and the challenges of weight reduction for people with T2DM. A variety of weight loss strategies are discussed and the rationale for intermittent fasting as an emerging weight loss strategy is presented. In Chapter Three the methodologies used in the study are described including the development of the dietary interventions and education sessions used to present the interventions. In Chapter Four the results of the dietary strategies on weight loss, blood glucose control, cardiovascular risk measures and acceptability of the dietary interventions to the participants are presented. These results are discussed in Chapter Five. In Chapter Six the strengths and limitations of the feasibility study are critically discussed, final conclusions are drawn and recommendations for further research are given.

CHAPTER 2 LITERATURE REVIEW

2.1 An overview of diabetes

2.1.1 Definition of diabetes

Diabetes Mellitus is a group of chronic and progressive metabolic disorders characterised by deficiencies in insulin secretion, insulin action or both (American Diabetes Association, 2016a, Scottish Intercollegiate Guidelines Network, 2010). Insulin is a hormone that helps regulate levels of glucose in the blood. Insulin allows the glucose to enter cells where it is used as energy. Lack of insulin results in glucose remaining in the blood stream, with a subsequent lack of energy available for cellular functions. Consistently high levels of glucose in the blood causes damage to the kidneys (nephropathy), the autonomic and peripheral nervous systems (neuropathy), eyes (retinopathy) and cardiovascular system.

The American Diabetes Association (2016a) defined four clinical classes of Diabetes Mellitus. Type 1 Diabetes accounts for approximately 5-10% of total diabetes diagnoses. It is the result of either an immune-mediated or a detruction by an as yet unknown cause, of ß-cells in the pancreas resulting in total insulin deficiency. Type 2 Diabetes is the most common form of diabetes, accounting for approximately 90-95% of total diagnoses. Insulin resistance is the predominant feature along with some degree of insulin deficiency. Gestational diabetes occurs only during pregnancy and resolves after birth, although can predispose to an increased risk of developing Type 2 Diabetes later in life. The fourth class of diabetes includes other causes such as: diseases of the pancreas, chemical or drug induced pancreatic damage or other genetic defects resulting in insulin resistance, insulin deficiency and increased blood glucose levels. As the topic of this research thesis focuses on people with Type 2 Diabetes, the remainder of this literature review will concentrate on Type 2 Diabetes.

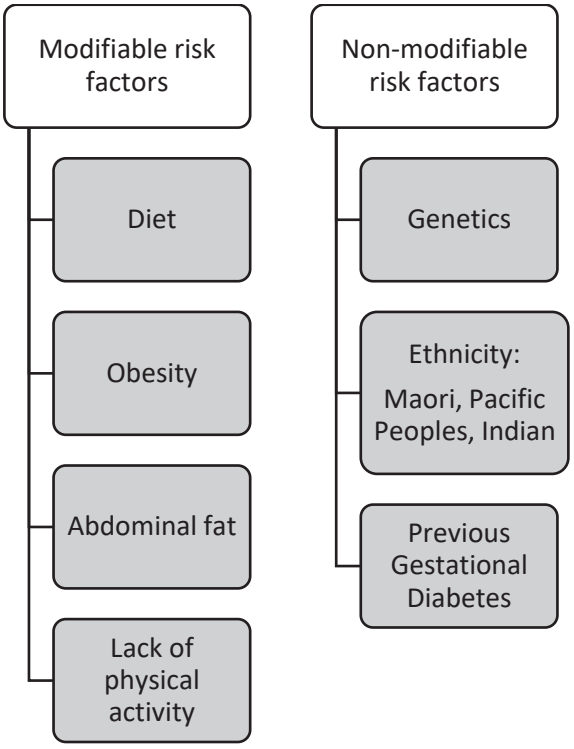
2.1.2 Diagnosis of Type 2 Diabetes

Two blood tests are used in the diagnosis of Type 2 Diabetes (T2DM) – a blood glucose test indicating current blood glucose levels, or glycosylated haemoglobin A1c (New Zealand Guidelines Group, 2012). The test for glycosylated haemoglobin A1c (HbA1c) measures the amount of glucose bound to red blood cells. The binding of a molecule of glucose to haemoglobin occurs depending on surrounding glucose concentrations, age of the red blood cells and rate of glycation (Hare *et al.*, 2012). Glycosylated haemoglobin A1c provides a measure of glucose concentrations over a two to three months period (American Diabetes Association, 2016a, New Zealand Society for the Study of Diabetes, 2011). In New Zealand a diagnosis of T2DM is made with an HbA1c of ≥50 mmol/mol, a fasting blood glucose level of ≥7.0 mmol/L or a non-fasting blood glucose level of ≥11.1 mmol/L (New Zealand Society for the Study of Diabetes, 2011).

The symptoms of diabetes occur as the body tries to manage increasing levels of glucose in the blood (hyperglycaemia). Symptoms of poorly managed or undiagnosed T2DM include excessive thirst (polydipsia), frequent urination (polyuria) , blurred vision, non-healing wounds, frequent infections and lack of energy (American Diabetes Association, 2016a). Routine screening for T2DM is recommended alongside cardiovascular screening in primary care (New Zealand Society for the Study of Diabetes, 2011), and in people at high risk of developing T2DM (New Zealand Guidelines Group, 2012).

2.1.3 Risk factors for developing Type 2 Diabetes

Type 2 Diabetes is caused by both modifiable and non-modifiable risk factors. Although there is a genetic component to T2DM the full mechanisms are not yet fully understood (American Diabetes Association, 2016a). Figure 1 shows the modifiable and non-modifiable risk factors that contribute to the development of T2DM.



(American Diabetes Association, 2016a, Ministry of Health, 2015c)

Figure 1 Risk factors for the development of type 2 diabetes

Diet increases the risk of developing T2DM by influencing obesity and abdominal fat (Evert *et al.*, 2014, American Diabetes Association, 2016b). High fat diets have been linked to increased insulin resistance (Lazarou *et al.*, 2012). Obesity has been linked to the development of 60-90% of all cases of T2DM (Aucott *et al.*, 2004). The results of a meta-analysis of 18 cohort studies (Abdullah *et al.*, 2010) indicated that the relative risk of developing T2DM in obese men was six times higher and in obese women was eight times higher risk than normal weight individuals. The Asia Pacific Cohort Studies Collaboration (2006) reported that every 2 kg/m^2 reduction in body mass index resulted in a 27% reduction in the risk of developing T2DM.

The results of systematic reviews and meta-analysis (Freemantle *et al.*, 2008, Kodama *et al.*, 2012) indicate that central obesity increased the risk of developing T2DM by one and a half to two times. Freemantle *et al.* (2008) reported that using either waist circumference measurement or waist hip ratio calculation was an appropriate method for estimating central obesity. In a further study, a reduction

in waist circumference of ≥3 cm was found to double the likelihood of impaired glucose tolerance returning to normoglycaemia (Bodicoat *et al.*, 2016).

Exercise and physical activity have been shown to prevent or delay the onset of diabetes when recommended as part of lifestyle modifications (American Diabetes Association, 2016b). These effects have been found to be independent of weight loss (American Diabetes Association, 2016b). One hundred and fifty minutes of exercise a week, as part of lifestyle modifications, has been shown to reduce by half the risk of developing T2DM (Hordern *et al.*, 2012).

2.1.4 The scale of diabetes

Globally the incidence of T2DM is increasing. The World Health Organization (2016) estimated the number of adults worldwide who are living with some form of diabetes at 422 million compared to 108 million in 1980. This is predicted to rise to 642 million by 2040 (International Diabetes Federation, 2015). The regions in the world with the highest number of people living with diabetes are the Western Pacific Region (131 million people) and the South-East Asia Region (96 million people) (World Health Organization, 2016). The prevalence of diabetes in the Western Pacific Region is estimated to be 8.4% (World Health Organization, 2016). Not only does New Zealand fall within the geographical area of the Western Pacific Region, but it has many immigrants from other areas in the Western Pacific and South-East Asian Regions. The International Diabetes Federation (2015) estimate that 320.5 million people aged between 20 and 64 years old, and 94.2 million people aged 65 to 79 years old live with diabetes. There is a very similar distribution between genders for those diagnosed with diabetes (International Diabetes Federation, 2015). For New Zealand the International Diabetes Federation (2015) estimate the age adjusted prevalence of diabetes in adults aged 20 to79 years to be 7 - 9%. This is higher than prevalence in Australia and the United Kingdom, but lower than prevalence in the United States of America, the Middle East, Papua New Guinea and some South American countries (International Diabetes Federation, 2015, World Health Organization, 2016).

In New Zealand diabetes is one of the most common chronic medical conditions and is a cause of considerable morbidity and premature mortality. It is estimated that approximately 260,000 adult New Zealanders have been diagnosed with some form of diabetes (Ministry of Health, 2012), indicating a prevalence of 7% (Coppell *et al.*, 2013). These numbers are reflected locally in the Auckland Region, with data from 2011 indicating an age-standardised prevalence of 7.5% (Warin *et al.*, 2016). Approximately 90% of people diagnosed with diabetes in New Zealand are diagnosed with T2DM (Diabetes Care Workforce Service Review Team, 2011). The prevalence of New Zealanders with diabetes is rising, with an estimated 7% increase each year since 2008 (Ministry of Health, 2015a). The report by the Ministry of Health (2015c) 'Living well with Diabetes' states that diabetes is on the rise across all ethnic and age groups, however the largest increase is seen in adults aged 25 to 44 years.

With an increase in diagnosis comes a rise in disease-related costs. All types of diabetes are estimated to cost the world US$ 827 billion each year (World Health Organization, 2016). In the ten years between 2003 and 2013 the International Diabetes Federation (2015) estimated that the health care spending on diabetes related illnesses more than tripled. It is predicted that in New Zealand government spending on treating T2DM could rise from NZ$600 million (National Party Question 2012) to NZ$1,600 – NZ$1,800 million by 2020 (Diabetes Care Workforce Service Review Team, 2011). Costs incurred can be attributed to medications and equipment used to treat diabetes, hospital visits and admissions with complications of diabetes (Collins and Anderson, 1995, Diabetes Care Workforce Service Review Team, 2011).

2.2 Management of Type 2 Diabetes

Normalising blood glucose levels whilst minimising low or high blood glucose levels (hypoglycaemia or hyperglycaemia respectively), is the main focus of care for those with T2DM. (American Diabetes Association, 2016b). Blood glucose levels can be monitored daily by people with diabetes using self-monitored blood glucose (SMBG) readings. SMBG is not a general recommendation for people with T2DM, however it is recommended when insulin therapy is commenced. Glycosylated haemoglobin A1c (HbA1c) is the primary marker used internationally and in New Zealand to determine long term blood glucose control in people with diabetes (Daousi *et al.*, 2006, New Zealand Guidelines Group, 2012). An HbA1c of ≤50 mmol/mol is associated with lower risk of developing cardiovascular, microvascular and neuropathic disease related to poor glucose control (Daousi *et al.*, 2006). An HbA1c ≥55 mmol/mol is associated with a higher risk of developing complications of diabetes and the risk of developing complications increases as HbA1c increases (New Zealand Guidelines Group, 2012).

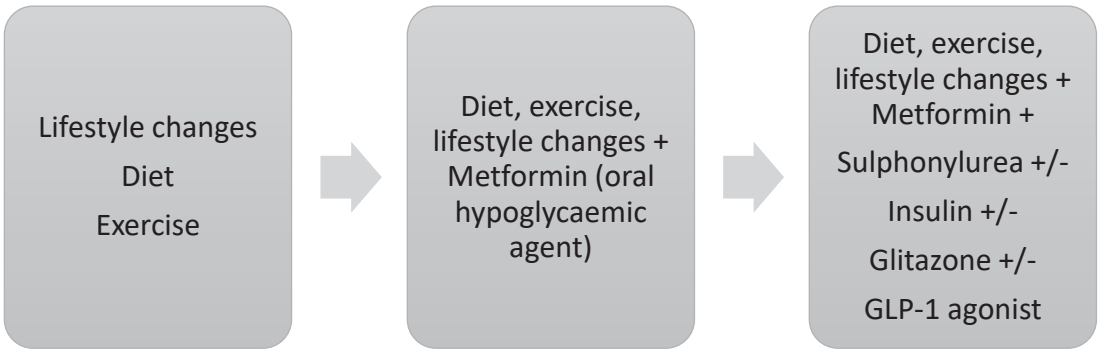
Targets for glycaemic control, weight management, cardiovascular risk and physical activity levels have been recommended for adults with T2DM (American Diabetes Association, 2016b, New Zealand Guidelines Group, 2012, Dietitians New Zealand Diabetes Special Interest Group, 2014) to reduce morbidity and mortality associated with this condition. These goals are summarised in Table 1.

Table 1 Treatment goals for people with Type 2 Diabetes

Area	Goal
HbA1c	• <50-55 mmol/mol
Glucose	• Pre-prandial 4.4-7.2 mmol/L • Peak postprandial 10.0 mmol/L
Weight / BMI	• BMI 18.5-24.9 kg/m^2('normal range') • 5% weight loss for those with BMI ≥25.0 kg/m^2
Blood pressure	• Systolic blood pressure <130 mmHg • Diastolic blood pressure ≤80 mmHg
Serum lipid levels	• Triglyceride <1.7 mmol/L • HDL >1.0mmol/L men, >1.3 mmol/L women • Total cholesterol <4 mmol/L
Activity	• 150 min/week moderate intensity aerobic activity over at least 3 days per week. No more than 2 consecutive days without exercise • Resistance training twice weekly • Aim for 60 minutes daily exercise

(American Diabetes Association, 2016b, New Zealand Guidelines Group, 2012, Dietitians New Zealand Diabetes Special Interest Group, 2014)

Diminishing the complications of T2DM by achieving blood glucose goals and weight loss are best achieved by diet and lifestyle counselling, medication and self-monitoring of blood glucose levels (Daousi *et al.*, 2006). Lifestyle changes including diet and exercise is the cornerstone of treatments for those diagnosed with T2DM. If the treatment targets outlined in Table 1 are not met using lifestyle changes alone then medications to help control blood glucose levels, blood lipid levels and blood pressure are introduced. The progression of introducing medications to assist in achieving normoglycaemia in the treatment of T2DM is shown in Figure 2.



Modified from Inzucchi *et al.* (2015)

Figure 2 Progression through glycaemic treatment options

2.2.1 Lifestyle interventions

Lifestyle interventions recommended for the treatment of T2DM address dietary intake, alcohol intake, physical activity, and smoking cessation (Scottish Intercollegiate Guidelines Network, 2010). In combination, these interventions generally reduce HbA1c by 3-11 mmol/mol (Scottish Intercollegiate Guidelines Network, 2010).

The goals of dietary advice for those with T2DM are to provide a nutrient dense, healthy eating plan. This should be made up of appropriate foods in appropriate portion sizes to help normalise blood glucose control, lipid profile, blood pressure, achieve and maintain weight goals and reduce risk of complications (Evert *et al.*, 2014). Dietary advice (not specifically weight reduction advice) for T2DM has been shown to reduce HbA1c. In a systematic review by Huang *et al.* (2016) nutritional lifestyle changes showed a change in HbA1c of 3.3 mmol/mol standardised difference in means.

Current best practice dietary advice as advocated by the American Diabetes Association (2016b) puts an emphasis on individually negotiated goals which meet the needs of the person with diabetes. Collaboration, education and self-management are key to this updated concept that concentrates more on supporting people with the nutrition choices they make rather than what people with T2DM should be eating to maximise health and wellbeing. Health care professionals are encouraged to be knowledgeable and informed about dietary interventions so as to be supportive of patient choices (American Diabetes Association, 2016b). Dietary advice should be tailored to the needs of the individual, taking in to account culture, health literacy, individual preferences and nutritional needs, and be practical and support self-management (Evert *et al.*, 2014, Dyson *et al.*, 2011).

In New Zealand dietary recommendations have been made by Dietitians New Zealand, Diabetes Special Interest Group (Dietitians New Zealand Diabetes Special Interest Group, 2014). These New Zealand recommendations for all people (normal weight, overweight and obese) are summarised in Table 2.

Table 2 New Zealand dietary guidelines for people with Type 2 Diabetes

	Recommendations
Plate model	• ½ plate non-starchy vegetables, ¼ plate protein, ¼ plate carbohydrate
Cooking methods	• Healthy (low fat) cooking methods
Carbohydrate	• Total intake should be appropriate to encourage weight loss where required • Approximately 45-60% energy intake • Carbohydrate should be eaten at each meal, with similar grams of carbohydrate consumed at each meal • Carbohydrate counting (simple or advanced) should be taught • Limit added sugar • 3-4 serves whole fruit per day, spread out over the day • Glycaemic index and glycaemic load should only be taught when appropriate
Fat	• Total intake should be appropriate to encourage weight loss where required • Approximately 30% total energy from fat
Protein	• Total intake should be appropriate to encourage weight loss where required • Approximately 15-20% total energy from protein • Extreme intake should be avoided as it may influence development of kidney disease
Sodium	• Reduce overall intake. Target less than 2300mg total sodium per day (1 tsp table salt)
Fibre	• Choose wholegrain foods that are high in fibre • Aim for 30-40 g fibre daily, of which half should be soluble fibre • Emphasis should be on wholegrains, vegetables and fruits and high fibre cereals
Alcohol	• Alcohol in moderation • 2-3 standard drinks for men and 1-2 standard drinks for women per day, with some alcohol-free days each week

(Dietitians New Zealand Diabetes Special Interest Group, 2014, Diabetes New Zealand, 2014)

Dietary advice for those with T2DM encourages regular high fibre carbohydrate, minimal refined sugars and a reduction in total fat and saturated fat (Evert *et al.*, 2014, New Zealand Guidelines Group, 2012, American Diabetes Association, 2016b). Carbohydrates are broken down in the body to produce glucose which the body uses for energy. As carbohydrates are an important source of energy for the body it is considered ideal to eat carbohydrates from a variety of sources (vegetable, fruit, whole grains and pulses) at regular meals during the day (Evert *et al.*, 2014). Carbohydrate eaten at each meal in similar quantities can help to stabilise daily blood glucose control and reduce the risk of hypoglycaemia, especially in those on fixed doses of daily insulin (Dietitians New Zealand Diabetes Special Interest Group, 2014, Evert *et al.*, 2014). After carbohydrates are eaten, blood glucose levels increase to reach a peak at approximately two to three hours after ingestion. Some carbohydrates produce sharp, high rises in blood glucose levels after meals and some produce more gradual and lower rises. The increase in blood glucose produced by different foods is often referred to as their "glycaemic index" or "glycaemic load"(Brand-Miller *et al.*, 2003). Foods that contain high fibre carbohydrate (from whole grains, fruit, vegetables and legumes) tend to produce more gradual and lower rises in blood glucose levels (low glycaemic index). High fibre or low glycaemic index carbohydrates are recommended because of this lower glycaemic peak after meals (Evert *et al.*, 2014, Dyson *et al.*, 2011).

The total amount of daily carbohydrate should be individually negotiated as there is no conclusive recommended daily intake for people with diabetes, although an intake of 40-60% of daily energy requirements has been suggested (Dietitians New Zealand Diabetes Special Interest Group, 2014). Recommendations for total carbohydrate intake are in line with dietary advice for healthy adults in New Zealand, i.e. at least six servings of grain foods daily (wholegrain breads, cereal, pasta, rice) (Ministry of Health, 2015b). Individuals may be advised to reduce their carbohydrate as part of an overall reduction in energy intake for weight reduction (Scottish Intercollegiate Guidelines Network, 2010, American Diabetes Association, 2016b).

A reduction in total and saturated fat intake is recommended to both reduce energy intake thus encouraging weight reduction, and to manage serum lipid levels which may increase cardiovascular risk (Dyson *et al.*, 2011, Evert *et al.*, 2014, Scottish Intercollegiate Guidelines Network, 2010). As with carbohydrates, research in to the optimal macronutrient balance of healthy eating diets for people with T2DM has not shown an ideal level of fat in the diet. Therefore recommended daily intakes should be in line with healthy eating recommendations for healthy adults (Ministry of Health, 2015b) for approximately 30% of daily energy intake from fat (Dietitians New Zealand Diabetes Special Interest Group, 2014). Individual advice on total dietary fat intake should be in line with weight loss goals (Evert *et al.*, 2014). People with T2DM should be encouraged to choose monounsaturated or polyunsaturated fats, consistent with a Mediterranean-style diet to help reduce cardiovascular disease risk factors and assist in glycaemic control (Evert *et al.*, 2014).

Protein intake for people with T2DM should be in line with current healthy eating recommendations for healthy adults (Ministry of Health, 2015b), 15-20% of total energy intake or 0.8 - 1.0 g/kg/day (Dietitians New Zealand Diabetes Special Interest Group, 2014). As with other macronutrients, actual quantities of protein should be adjusted according to energy restrictions for weight loss or maintenance (Dietitians New Zealand Diabetes Special Interest Group, 2014). Additional care may need to be taken when advising protein intake in people with T2DM if kidney disease is present. In people with T2DM protein intake does not seem to have a significant effect on blood glucose levels through gluconeogenesis. However protein can increase the insulin response in people with T2DM and therefore protein foods should not be used to treat hypoglycaemia (Evert *et al.*, 2014).

As people with T2DM are at higher risk of cardiovascular disease there is a recommendation that sodium intake be limited to ≤ 2300mg per day (Dietitians New Zealand Diabetes Special Interest Group, 2014, Evert *et al.*, 2014, American Diabetes Association, 2016b). Reducing the dietary intake of sodium in people with T2DM has been shown to improve blood pressure (Suckling *et al.*, 2010). Having

high blood pressure (hypertension) is an important risk factor in the development of cardiovascular disease (Fox *et al.*, 2015).

For people wishing to lose weight reducing alcohol can help to reduce total energy intake. Alcohol also increases the risk of hypoglycaemia in people with T2DM who are taking insulin or certain oral hypoglycaemic agents (OHA) (Evert *et al.*, 2014). For those people with T2DM who consume alcohol within the recommended levels, little or no effect is seen on glucose control (Evert *et al.*, 2014). A moderate intake of alcohol may be linked to improved glycaemic control and can benefit cardiovascular disease risk (Dyson *et al.*, 2011). Alcohol intake should be the same as is recommended for healthy adult New Zealanders: limited to one to two standard units per day for women or three to four standard units per day for men, with some alcohol free days each week (Dietitians New Zealand Diabetes Special Interest Group, 2014).

Physical activity is another aspect of lifestyle changes that are recommended for people with T2DM. Regular structured physical activity over an eight week period has been shown to reduce HbA1c by approximately 6 mmol/mol independent of weight loss (American Diabetes Association, 2016b). The results of a systematic review by Huang *et al.* (2016) indicated that physical activity may change HbA1c by a standardised difference in means of -11 mmol/mol. Regular physical activity has been shown to assist in non-insulin mediated blood glucose uptake, improve glycaemic control for up to 72 hours post activity, reduce all cause and cardiovascular mortality and reduce depression (Colberg *et al.*, 2010). The 2016 standards of diabetes care (American Diabetes Association, 2016b) recommend that adults should participate in at least 150 minutes per week of moderate intensity aerobic activity, spread over at least three days and that two consecutive days should not go by without activity. They also recommend that adults with T2DM should participate in resistance training twice a week.

Smoking cigarettes and being exposed to second hand smoke increases the risk of cardiovascular and microvascular disease (American Diabetes Association, 2016b).

Smoking has been implicated as a risk factor for the development of T2DM in smokers over the age of 35 (Jankowich *et al.*, 2011). Type 2 Diabetes and smoking more than doubles the risk of developing cardiovascular disease (Scottish Intercollegiate Guidelines Network, 2010). Lifestyle interventions for T2DM therefore include recommendations to stop smoking using a combination of motivational and behavioural interventions and pharmacological support as required (Scottish Intercollegiate Guidelines Network, 2010, American Diabetes Association, 2016b).

2.2.2 Diabetes self-management groups

Diabetes Self-Management Education (DSME) programmes are now a main-stay of teaching lifestyle changes and self-management of diabetes (Evert *et al.*, 2014, Haas *et al.*, 2014, American Diabetes Association, 2016b). The American Diabetes Association (2016b) list self-management support as one of the six key elements of their chronic care model to improve diabetes care. DSME sit within this element and have been shown to improve self-management and glucose control (American Diabetes Association, 2016b). In a systematic review and meta-analysis of 26 studies of 2833 participants, Steinsbekk *et al.* (2012) reported that group based DSME significantly improved HbA1c as well as diabetes knowledge, self-management skills and empowerment. These results have been replicated in New Zealand in a local study by Krebs *et al.* (2013) where attending a DSME improved HbA1c. Strategies that should be included within good quality DSME are clinical content and skills, behavioural strategies (goal setting and problem solving) and engagement with psychosocial concerns (American Diabetes Association, 2016b). Diabetic Self-Management Education programmes such as Dose Adjustment for Normal Eating (DAFNE) in people with Type 1 Diabetes have been shown to successfully educate participants in medication adjustment and blood sugar pattern management to allow for variable carbohydrate intakes and hypoglycaemia management (DAFNE study group, 2002). Medication dose adjustment based on carbohydrate amounts have also been successfully taught to people with Type 2 Diabetes (Bergenstal *et al.*, 2008, Lowe *et al.*, 2008).

2.2.3 Medications for the management of Type 2 Diabetes

Medications are used in the treatment of T2DM to help bring blood glucose levels to within normal or goal ranges, or are related to management / reduction in complications i.e. control of hypertension and lipid levels. If lifestyle changes including diet and activity do not manage to achieve blood glucose levels then initial drug treatment starts with metformin, before addition of sulfonylureas, glitazones, GLP-1 agonists and / or insulin as required (Inzucchi *et al.*, 2015). The details of the most common medications used to achieve normoglycaemia are presented in Table 3.

Table 3 Medications used in New Zealand to achieve normoglycaemia

Medication	Type	Action
Metformin	Oral hypoglycaemic agent (OHA)	• Increases the effectiveness of remaining insulin • Allows insulin to be taken up from the blood in to the cells • Requires insulin to be present in the body to work • Does not increase the risk of hypoglycaemia
Sulfonylureas E.g. Gliclazide, Glipizide, Glibenclamide, Tolbutamide	Oral hypoglycaemic agent (OHA)	• Increase the production of insulin by the pancreas. • Requires insulin to be present in the body to work • Have the potential to cause hypoglycaemia if not administered correctly or if it is taken and no food consumed
Glitazones or GLP-1 agonists E.g. Pioglitazone	Oral hypoglycaemic agent (OHA)	• Increases insulin sensitivity • Use is limited due to side effects such as weight gain, fluid retention, increased risk of bladder cancer and increased risk of bone fractures
Insulin	Sub-cutaneous injection	• Types of insulin can be grouped according to the length of time that they act in the bloodstream. • Rapid, quick, intermediate or long acting • Insulin doses are calculated on weight and carbohydrate intake. • Incorrect administration of insulin may lead to hypoglycaemia

2.2.4 Complications of Type 2 Diabetes

Achieving normoglycaemia using diet, lifestyle and medication can help to reduce health complications that might occur due to poor blood glucose control (Daousi *et al.*, 2006). People with T2DM are at higher risk of micro- and macrovascular diseases, such as cardiovascular disease, neuropathy, nephropathy and retinal damage (American Diabetes Association, 2016b, Scottish Intercollegiate Guidelines Network, 2010).

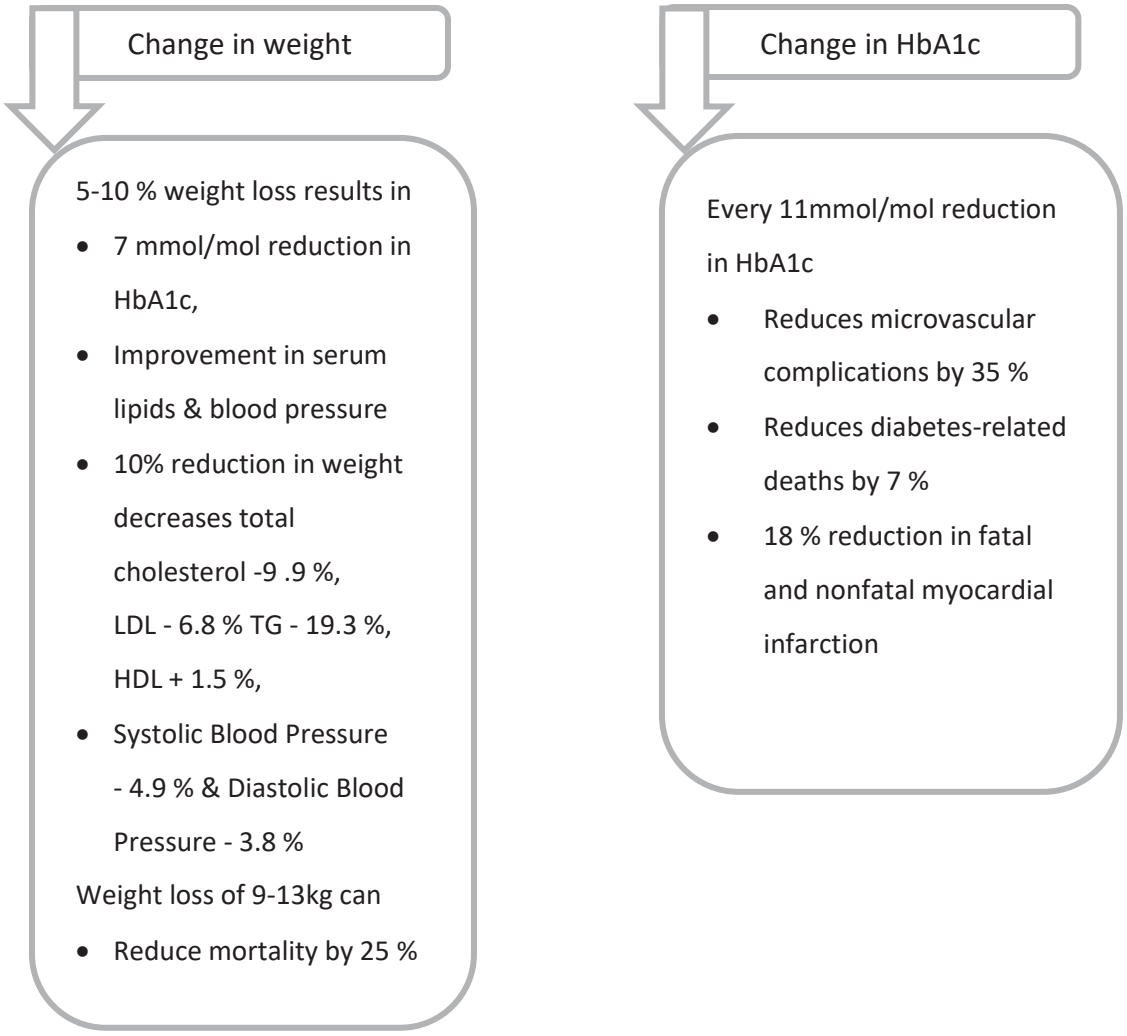
Cardiovascular disease (CVD), including myocardial infarct, acute coronary syndromes, atherosclerosis and stroke are all leading causes of morbidity and mortality in people with diabetes. Diabetes is an independent risk factor for the development of CVD (American Diabetes Association, 2016b, Fox *et al.*, 2015, Anderson *et al.*, 2003), and even an increase in HbA1c which is under the level for diagnosis of diabetes (prediabetes) can increase CVD risk (Fox *et al.*, 2015). Management of blood pressure and serum lipid levels are key to reducing CVD complications in T2DM. Cardiovascular disease management in T2DM focuses on weight management, antihypertensive medications and statins. The American Diabetes Association (2016b) advise that lifestyle interventions be recommended for people with T2DM who have a blood pressure greater than 120/80 mmHg and that medication be started for those who have a blood pressure greater than 140/90 mmHg. Lifestyle changes that support a reduction in blood pressure include weight loss if overweight or obese, a reduction in dietary sodium and an increase in dietary potassium, reducing alcohol intake and commencing regular physical activity (American Diabetes Association, 2016b, New Zealand Guidelines Group, 2012). Dietary changes are also recommended for the reduction of serum cholesterol and triglycerides: weight loss if required, reduction in saturated and trans fats and cholesterol, an increase in omega 3 fatty acids, fibre and plant stanol/sterols (New Zealand Guidelines Group, 2012, American Diabetes Association, 2016b).

An updated review of recent studies including the Look AHEAD (Action for Health in Diabetes) and PREDIMED (Prevention with Mediterranean Diet) studies by the American Heart Association and the American Diabetes Association (Fox *et al.*, 2015) supports recommendations for the importance of weight reduction in those who are overweight, a Mediterranean style diet with a focus on fruit, vegetables, whole grain and dairy over other carbohydrates and reduction in sodium intake in the prevention of cardiovascular disease in those with T2DM.

Microvascular complications of T2DM include damage to the small blood vessels of the eyes, kidneys and limbs (retinopathy, nephropathy and neuropathy). The damage to these blood vessels occurs as a direct result of increased circulating glucose in the body. It has been estimated that 40% of people with T2DM go on to develop nephropathy (He *et al.*, 2013). This complication of diabetes is now thought to account for the majority of cases of end-stage renal failure in developed countries (He *et al.*, 2013). Prevalence of retinopathy has been estimated at 22 – 37 % in people with diagnosed T2DM (Ruta *et al.*, 2013). The results of a Post Hoc analysis of a section of the PREDIMED study participants indicated that a Mediterranean diet supplemented with 50 ml extra virgin olive oil reduced incidence of retinopathy but not nephropathy (Diaz-Lopez *et al.*, 2015). Lifestyle and medication treatments that reduce weight and HbA1c also reduce the risk of developing these microvascular complications. As HbA1c increases, the risk of microvascular complications increases (Genuth *et al.*, 2003).

2.2.5 Summary

The two main goals in the management of T2DM are achieving normoglycaemia (or as near as safely possible) and weight loss. These goals can be met by lifestyle changes including diet, activity and smoking cessation, and medication for the treatment of hyperglycaemia, hypertension and hyperlipidaemia. Achievement of these goals results in a reduced risk of developing medical complications of diabetes. A summary of the clinical impact seen with a reduction in HbA1c and weight is shown in Figure 3.



(Genuth *et al.*, 2003, Anderson *et al.*, 2003, Aucott *et al.*, 2004)

Figure 3 Clinically significant results of reducing HbA1c and weight

2.3 Obesity and Type 2 Diabetes

Weight loss or prevention of weight gain is advocated as an important treatment goal in overweight and obese adults with diabetes (Dyson *et al.*, 2011, Henry *et al.*, 2013, Evert *et al.*, 2014, American Diabetes Association, 2016b). Obesity has been linked to the development of microvascular and cardiovascular complications related to diabetes (Smith and Singleton, 2013, De Block *et al.*, 2005). Coppell *et al.* (2013) using data from the New Zealand Adult Nutrition Survey (University of Otago and Ministry of Health, 2011), found that 4.6% of New Zealand adults who were overweight and 9.8% of those who were obese, had diabetes.

Weight reduction should be recommended for people with T2DM who have a body mass index (BMI) ≥25 kg/m^2 (ideal adult BMI range 18.5-24.9 kg/m^2) (American Diabetes Association, 2016b). Weight loss of 5-10 % is known to improve the long term measure of glucose control, HbA1c, and cardiovascular profiles of obese people with T2DM (American Diabetes Association, 2012, Anderson *et al.*, 2003, Look AHEAD Research Group, 2013, Aucott *et al.*, 2004). In a systematic review Aucott *et al.* (2004) examined the long term effects of weight loss on diabetes outcomes in obese people with and without diabetes. Studies of longer than two years were included in the systematic review which found that intentional weight loss in those with diabetes reduced the relative risk of all-cause mortality by up to 25 %.

In an earlier prospective analysis over a 12 year follow up period of nearly 5000 overweight Americans (Williamson *et al.*, 2000) it was found that weight loss of 9-13 kg was associated with greatest protection from mortality, with over 33 % reduction in mortality. It was noted that these subjects had often lost weight within a 12-month timeframe. Relative risk reduction of death from cardiovascular disease was 0.79 for those with intentional weight loss. Anderson *et al.* (2003) reported in a meta-analysis of weight management and T2DM, that 10 kg weight loss would result in a 9.9 % reduction in fasting serum cholesterol, a 6.8 % reduction in fasting serum LDL cholesterol, 19.3 % reduction in fasting

triglycerides, 1.3% increase in HDL cholesterol, and a reduction of 4.9 % and 3.8 % in systolic and diastolic blood pressure respectively. In a meta-analysis of weight management and T2DM, Anderson *et al.* (2003) estimated that a 5kg weight gain in men would increase CVD risk by 30%, and the effect of this weight gain on blood pressure and serum lipid levels could increase CVD risk by a further 20%.

Lifestyle interventions for weight loss have been shown to result in a reduction in HbA1c of approximately 3 mmol/mol for studies over 12 weeks duration (Terranova *et al.*, 2015), however more intensive dietary interventions can result in a significant reduction in HbA1c of up to 22 mol/mol (Evert *et al.*, 2014).

Minimising complications of T2DM by achieving blood glucose goals and weight loss are best achieved by diet and lifestyle counselling, medication and self-monitoring of blood glucose (SMBG) levels (Daousi *et al.*, 2006). A short term weight loss of 5 % is recommended however 7 % or more is considered ideal (American Diabetes Association, 2016b). A guideline for the best treatment of overweight and obesity in T2DM, as recommended by the American Diabetes Association (2016b) is shown in Table 4.

Table 4 American Diabetes Association recommendations for weight reduction strategies

	BMI category (kg/m^2)				
Treatment	**25.0-26.9**	**27.0-29.9**	**30.0-34.9**	**35.0-39.9**	**≥40**
Diet, physical activity and behavioural therapy	✓	✓	✓	✓	✓
Pharmacotherapy		✓	✓	✓	✓
Bariatric surgery				✓	✓

(American Diabetes Association, 2016b)

2.3.1 Dietary treatment of obesity in Type 2 Diabetes

Long term studies on weight loss diets in people with T2DM show that most weight loss is seen within the first 3-6 months (Hensrud, 2001). Weight regain of 30-50 % is often seen within the first year of treatment resulting in an overall loss from baseline weight of often only 5 kg (Hensrud, 2001). The results of a Cochrane review investigating long term weight loss in people with T2DM (Norris *et al.*, 2009) indicated that lifestyle interventions result in a pooled weight loss of 1.7 kg in studies between one and two years duration. Often both control and intervention groups in the studies reviewed experienced weight loss. Terranova *et al.* (2015) reported that from weight loss studies of over 12 weeks in duration a pooled weight loss of 3.3 % was seen. This was a significantly greater reduction than from usual or minimum care.

A variety of dietary strategies have been studied in the quest to find the best diet to assist with weight reduction in people with diabetes (Krebs and Parry-Strong, 2013, Ajala *et al.*, 2013, Dyson *et al.*, 2011). The aim of weight reduction strategies is to achieve a 500-750 kcal (2000-3100 kJ) daily energy deficit (American Diabetes Association, 2016b). This level of energy deficit can result in a weight loss of 0.5 – 1 kg per week for people with T2DM (American Diabetes Association, 2016b, Klein *et al.*, 2004). Typically healthy eating, low energy diets as recommended by the New Zealand Ministry of Health (Ministry of Health, 2015b) for weight loss in healthy adults provide an energy intake of approximately 1200-1600 kcal (5000-6700 kJ) per day (Ministry of Health, 2009, American Diabetes Association, 2016b). Healthy eating diets are often advised alongside other lifestyle interventions such as physical activity or intensive support programmes. In this context decreases in weight of 0.2 – 6.0 kg (Norris *et al.*, 2005, Wolf *et al.*, 2004, Manning *et al.*, 1998, Franz *et al.*, 2007), and reductions in HbA1c of 2 mmol/mol have been reported (Norris *et al.*, 2005, Wolf *et al.*, 2004).

Mediterranean, low glycaemic index, high protein and low carbohydrate versions of healthy eating have all been investigated in the treatment of obesity in people with T2DM (Krebs and Parry-Strong, 2013, Ajala *et al.*, 2013, Esposito *et al.*, 2010). Other interventions have explored the use of severe energy restrictions such as very low calorie diets (VLCD) (Day and Bailey, 2012) and fasting diets (Barnosky *et al.*, 2014).

The "Mediterranean" diet is characterised by being high in fruits, vegetables, legumes, nuts and whole grains (Panagiotakos *et al.*, 2005, Trichopoulou *et al.*, 2003). Protein is mainly from fish and poultry and there is a low intake of red meat and dairy products. Fat is obtained mainly from mono unsaturated fats, especially olive oil. Trichopoulou *et al.* (2003) investigated what constitutes a Mediterranean diet and they reported a scale to show adherence to a Mediterranean (Greek) diet that showed beneficial health outcomes. A similar scale was published by Panagiotakos *et al.* (2005). This more specifically described the Mediterranean diet as daily consumption of wholegrain carbohydrates; four to six servings of vegetables daily; two to three servings of fruit daily; olive oil, low fat products once or twice daily; consumption of fish, poultry, potatoes, olives, pulses and nuts (four to six servings weekly); eggs and sweets one to three times weekly; red meat products four to five servings a month; and a high monounsaturated to saturated fat ratio. Esposito *et al.* (2010) conducted a systematic review of the Mediterranean diet and glycaemic control in people with T2DM. Six studies reported glycaemic control and the results showed that following a Mediterranean diet decreased HbA1c by 1-6 mmol/mol. In a systematic review by Ajala *et al.* (2013) three studies on Mediterranean diet showed a reduction in HbA1c of 5 mmol/mol. The same systematic review also showed a weighted mean difference in weight loss of -1.84kg.

The glycaemic index (GI) of foods is the measure of changes in glucose levels after eating (Fleming and Godwin, 2013). A high GI score indicates that the food is rapidly absorbed and causes blood glucose levels to rise quickly and often to a high level. A low GI score shows the food is slowly absorbed. Typically foods low in GI are high in fibre, however high fat foods also lower the GI response due to a delay

in carbohydrate absorption. The results of a systematic review and meta-analysis of diets for managing T2DM (Ajala *et al.*, 2013) showed pooled results from three studies that examined the effect of low GI diets. A low GI diet was found to reduce HbA1c by approximately 2 mmol/mol. Weight loss did not occur with a low GI diet; a 1.39kg weight gain was observed. In a second meta-analysis (Brand-Miller *et al.*, 2003) of eight studies, HbA1c was reduced by approximately 4 mmol/mol when participants followed low GI diets for approximately 10 weeks.

High protein diets typically are made up of more than 20-25% of daily energy from protein. A high protein diet is thought to help with weight loss due to the increased satiety value of protein, preserving lean muscle mass and increasing diet induced thermogenesis (Krebs and Parry-Strong, 2013, Dong *et al.*, 2013). In a meta-analysis of randomised controlled trials Dong *et al.* (2013) summarised that following a high protein diet can result in weight loss of approximately 2kg and a change in HbA1c of 5 mmol/mol over three months. However, Krebs *et al.* (2012) concluded that results of changes to HbA1c on a high protein diet are variable and often due to the macronutrient composition of the remainder of the diet. Ajala *et al.* (2013) in a meta-analysis showed high protein diets had a weighted mean difference of a 2 mmol/mol decrease in HbA1c, however weight loss was not achieved.

The traditionally recommended intake of carbohydrate for people with T2DM is between 40-60% of total daily energy intake (Dyson *et al.*, 2011). There are a variety of definitions for what constitutes a 'low carbohydrate diet' (Castaneda-Gonzalez *et al.*, 2011, Dyson, 2015). Twenty grams per day seems to be the lower daily limit up to 40% of total daily energy intake (Evert *et al.*, 2014). Low carbohydrate diets, below 130 g daily, have been suggested to reduce both total energy intake and glycaemic rises after eating (Castaneda-Gonzalez *et al.*, 2011). The results of a systematic review of low carbohydrate diets in people with T2DM (Castaneda-Gonzalez *et al.*, 2011), based on eight studies showed that a low carbohydrate diets resulted in weight loss of between 3-11 kg. In a systematic review and meta-analysis Ajala *et al.* (2013) reported that following a low

carbohydrate diet had a significant improvement on HbA1c (2 mmol/mol reduction) and a similar weight loss to higher carbohydrate diets: a weighted mean difference of -0.69kg. A similar rate of weight loss was observed in a systematic review and meta-analysis undertaken by Naude *et al.* (2014) when reviewing data from people with T2DM following low carbohydrate diets (2.79 - 5.5 kg in 3-6 months), and balanced diets (3.08 - 5.4 kg). No difference in change to HbA1c was found when comparing results from low carbohydrate diet studies and balanced diets.

Very low calorie diets (VLCD) provide generally less than 800 kcal (3400 kJ) of energy daily (Klein *et al.*, 2004). Studies of less than six months in people with T2DM have shown successful weight loss, improvement in glycaemic control and reduction in cardiovascular risk (Capstick *et al.*, 1997, Berk *et al.*, 2012, Jazet *et al.*, 2005, Jackness *et al.*, 2013) and mimics the effect of bariatric surgery (Jackness *et al.*, 2013). The results from a recent study by Steven and Taylor (2015) showed that after an 8 week liquid VLCD mean HbA1c decreased by 6 -11 mmol/mol, and weight by 14%. A 12-week study of a 425 kcal (1800 kJ) daily VLCD (Capstick *et al.*, 1997) resulted in a weight loss of 3.2 kg and decrease in HbA1c of 2 mmol/mol. The American Diabetes Association (2016b) report that short term (3 month) treatments with VLCD can result in weight loss of 10 - 15%, however weight regain following a VLCD may be more than with other diets. This highlights the importance of maintenance diets following VLCD treatment.

Many reviews have concluded that there is often inconsistency between studies in the amount of weight loss experienced after following different diets (Castaneda-Gonzalez *et al.*, 2011, Krebs and Parry-Strong, 2013). All the diets discussed in this section result in similar weight loss, except for VLCD. Five percent weight loss can be expected from most dietary interventions that achieved a 500-750 kcal (2000-3100 kJ) per day energy deficit regardless of macronutrient content. However a 10-15% weight loss can be experienced with a short term VLCD that can also result in significant reductions in HbA1c (American Diabetes Association, 2016b, Steven and Taylor, 2015). It is acknowledged that the most successful long term weight loss strategies are those which are most acceptable to the individual patient (Makris

and Foster, 2011, Evert *et al.*, 2014, Krebs and Parry-Strong, 2013, Dansinger *et al.*, 2005). With this in mind it becomes important to investigate new weight loss strategies and determine their effectiveness and safety for use in people with T2DM.

2.4 Fasting as a weight loss strategy

The effects of food restriction on the body and its therapeutic uses have been investigated for over a century (Geyelin, 1921, Paton and Stockman, 1890). Whilst the majority of research has been on cellular and animal models (Trepanowski *et al.*, 2011, Varady and Hellerstein, 2007) in recent years there has been an increase in human studies investigating the effects of food restriction on chronic disease, longevity and metabolism (Patterson *et al.*, 2015, Azevedo *et al.*, 2013, Barnosky *et al.*, 2014). Periods of deliberate food restriction are referred to as 'fasting'. In the public arena fasting diets are increasingly talked about following publications of books such as "The Fast Diet" (Mosley and Spencer, 2014) and "The 2 Day Diet" (Harvie and Howell, 2013). Table 5 summarises the key definitions used when discussing food restriction.

Table 5 Definitions of types of fasting diets

Type of fasting diet	Description
Calorie restriction	• Daily restriction of 20-50% of daily energy requirements
Alternate day fasting	• Alternating one day fasting followed by one day normal food intake (total 3-4 fasting days per week) • Fasting day can provide no energy intake through to a restriction of 60-80% of daily energy requirements • Often energy intake only provided at one meal time on the fasting day • Non-fasting day may provide no restriction on energy intake (ad libitum intake), healthy eating recommendations or eat to 100% of requirements recommendation
Intermittent fasting	• Fasting on 1-3 days per week • Fasting day restriction of 60-80% of daily energy requirements • Energy intake may be provided at one meal time on the fasting day or several smaller meals • Non-fasting day may provide no restriction on energy intake (ad libitum intake), healthy eating recommendations or eating to 100% of requirements recommendation
Food restriction	• Food is restricted for extended periods during the day • Normal energy intake is eaten during a short 1-2 hour non-fasting period
Religious fasting	• Ramadan: no food is consumed between sunrise and sunset for one lunar month prior to Eid (New Year). Fasting is broken at sunset • Christian: including Nativity fast, Lent, Assumption, Daniel fast where no food may be consumed or food restrictions may apply • Buddhist, Hindu fasting periods

(Trepanowski *et al.*, 2011, Barnosky *et al.*, 2014)

Calorie restriction (CR) diets which reduce daily energy intake by 25% of requirements are commonly used as weight loss diets. Calorie restriction diets that restrict daily intake to 60-80% of requirements are considered to conform to a fasting diet and are likely to result in similar outcomes as other fasting diets. Alternate day fasting (ADF) and intermittent fasting (IF) vary mainly in the number of fasting days per week. ADF in research studies have investigated both a total exclusion of energy containing foods on fasting days (Heilbronn *et al.*, 2005a, Halberg *et al.*, 2005) and a 60-80%% energy restriction on fasting days (Hill *et al.*, 1989, Johnson *et al.*, 2007, Varady *et al.*, 2009, Varady *et al.*, 2013). IF diets generally provide a 70-75% energy restriction on fasting days (Harvie *et al.*, 2013, Harvie *et al.*, 2011, Williams *et al.*, 1998). The 70-75% energy restriction on fasting

days is designed to provide a similar weekly energy intake as experienced when following a healthy eating weight loss diet based on a 500-750 kcal (2000-3100 kJ), approximately 25%, daily energy restriction.

Food restriction (FR) focuses on restricting the times of the day when food is consumed. Food may be restricted between early evening and breakfast (LeCheminant *et al.*, 2013) or as part of ADF or IF where daily nutrient intake is provided as one meal or eaten within a certain time period (Hoddy *et al.*, 2014). Fasting is undertaken by several religious groups, most notable are the month of Ramadan for Muslims and for Orthodox Christian groups at Lent (Easter). In these cases, fasting is not done for the purpose of energy limitation or longevity but as part of religious doctrine.

To understand the rationale behind the use of fasting as a weight reduction strategy, in disease risk reduction and metabolic health it is important to understand the mechanisms by which fasting affects the body.

2.4.1 Psychological mechanisms of fasting

It has been suggested that fasting may be a successful weight reduction strategy because it does not require those following the diet to follow a daily modified eating pattern (Harvie *et al.*, 2011). Daily energy restriction for weight loss requires constant attention to food choices and eating behaviours which may be linked to increased stress, poor work performance and impaired decision making (Appleton and Baker, 2015). However, the impact of severe energy restriction on hunger and mood may also be one reason why people may not wish to follow an ADF or IF fasting diet (Johnstone, 2014). Studies in overweight or obese populations indicate that satisfaction and fullness increased over time and over eating on non-fasting days did not occur (Harvie *et al.*, 2013, Varady *et al.*, 2013).

2.4.2 Physiological mechanisms of fasting

The aim of fasting may not be to only achieve energy deficit but to also put the body under mild stress (Kouda and Iki, 2010). Hormesis is defined as a phenomenon that occurs when a beneficial effect occurs after a low level stress or harmful condition (Kouda and Iki, 2010). In the case of fasting the stress to the body is a restriction on available energy to the body. Whilst the majority of research investigating the role of hormesis as a mechanism of action to explain the effects of fasting has been conducted on animal models, some of these actions have now been replicated in human subjects (Allard *et al.*, 2008, Heilbronn *et al.*, 2005a). One mechanism by which fasting and the resulting low-dose stress has been shown in both animal and human models to influence cell survival and increase cell tolerance to oxidative and heat stress is by causing an increase in SIRT1 mRNA expression in muscle tissue (Kouda and Iki, 2010, Allard *et al.*, 2008, Heilbronn *et al.*, 2005a). This gene is also integral in the regulation of food intake and fat metabolism (Azevedo *et al.*, 2013). Alternate day fasting (ADF) has been shown in human studies to be more successful than daily calorie restriction (CR) at increasing skeletal muscle expression of SIRT1 mRNA (Allard *et al.*, 2008).

Another mechanism through which fasting is thought to affect the body is the changes in hormones and nutrients that are available to the body during times of restricted food intake. In both animal and human models fasting has been shown to reduce serum glucose and diminish glycogen stored in the liver (Brown *et al.*, 2013, Barnosky *et al.*, 2014, Trepanowski *et al.*, 2011). This results in ketone bodies and free fatty acids being used as energy sources for the body and brain instead of glucose (Longo and Mattson, 2014, Azevedo *et al.*, 2013). This change in the hormones and nutrients available have been shown to change gene expression involved in stress response and disease resistance (Allard *et al.*, 2008). ADF diets in animal models have been shown to improve insulin sensitivity and reduce fasting insulin levels (Longo and Mattson, 2014). The effect of fasting on the body has been summarised by Azevedo *et al.* (2013). This is illustrated in Figure 4.

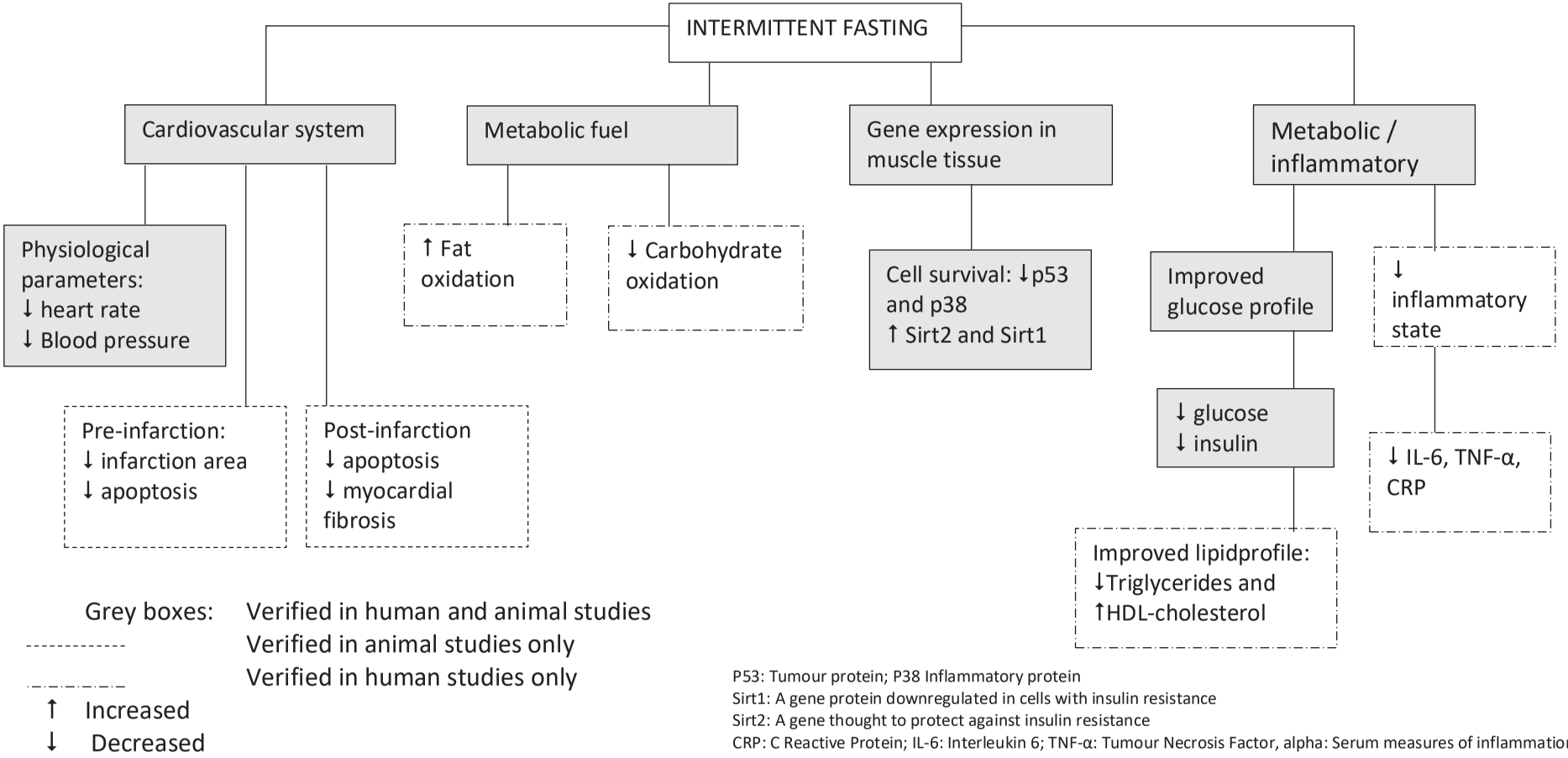


Figure 4 Potential targets for interventions using intermittent fasting

(Azevedo et al., 2013)

2.4.3 Human studies on fasting

The majority of research on the effects that fasting has on human health has been on the effects of fasting for Ramadan, the Muslim religious festival. The regularity of fasting for the month of Ramadan has provided researchers with an ideal platform to examine the effects of fasting on many aspects of health. Ramadan is a 29-30 day period during which Islamic laws require healthy, adult Muslims to fast between sunrise and sunset and abstain from smoking (Rouhani and Azadbakht, 2014). After sunset food can be consumed freely and often traditional foods are chosen (Shadman *et al.*, 2014). A reduction in nutrient or energy intake is not the aim of fasting during Ramadan, however because of the limited time to consume food prior to and following sleep a decrease in nutrient intake may occur during Ramadan (Shadman *et al.*, 2014, Sadeghirad *et al.*, 2014). If more traditional foods (such as dates, honey and sweets) are consumed at the end of fasting times there may also be a change in overall nutrient intake, for example more carbohydrates and less calcium (Shadman *et al.*, 2014).

Rouhani and Azadbakht (2014) reported the results of a systematic review on health outcomes during Ramadan. Weight loss was greater in men compared with women during this fasting time, however weight returned to usual after fasting concluded, for both genders. Another systematic review (Sadeghirad *et al.*, 2014) indicated that whilst fasting resulted in mean weight loss of 1.24 kg, weight returned to normal after two weeks post-fasting. The results of systematic reviews have reported that lipid profile can also change during fasting with decreased total cholesterol and triglycerides seen in men and an increase in HDL seen in women (Rouhani and Azadbakht, 2014, Mazidi *et al.*, 2015, Akrami Mohajeri *et al.*, 2013). Rouhani and Azadbakht (2014) noted that measurements taken 30 days after fasting had ceased showed increases above pre-fasting levels of abdominal fat and triglycerides in women. Inflammatory markers were reduced during the fasting month (Akrami Mohajeri *et al.*, 2013, Faris *et al.*, 2012) as were fasting blood sugars (Akrami Mohajeri *et al.*, 2013, Gnanou *et al.*, 2015).

Results from studies during fasting as part of the month of Ramadan support both animal and human studies on other forms of non-religious fasting. Due to the short period of

fasting (29-30 days) and the significant changes made to lifestyle and medication administration during Ramadan there is still the need to observe the effects of longer term fasting in human participants.

Bloomer *et al.* (2011) investigated the effects of a 21 day Daniel Fast on markers of antioxidant status and oxidative stress in adults. The Daniel Fast is based on reports of fasting from the book of Daniel, Chapter 10 verses 2-3 and is a form of fasting in which food selection is restricted rather than total quantities of food or timings of meals. Foods to be avoided are animal products, processed foods, caffeine and alcohol, sweeteners, flavourings and preservatives (Bloomer *et al.*, 2011). Food choices are made from whole grains, fruits, vegetables, nuts, seeds and oils. Results showed that weight reduced by an average of 2.8 kg over the 21 days, even though a restriction in energy intake was not a requirement of the diet. Significant decreases in energy, protein and fat and an increase in percentage carbohydrate and vitamin C intake were observed. Measures of antioxidant status improved and oxidative stress decreased after the fasting period.

Recently the effect of fasting diets on body composition and metabolism has been investigated for conditions such as asthma and cardiovascular disease (Heilbronn *et al.*, 2005a, Heilbronn *et al.*, 2005b, LeCheminant *et al.*, 2013) and as a novel weight loss solution in people who are overweight (Harvie *et al.*, 2011, Harvie *et al.*, 2013, Bhutani *et al.*, 2013b, Eshghinia and Mohammadzadeh, 2013, Hill *et al.*, 1989, Klempel *et al.*, 2012, Varady *et al.*, 2013).

A focused literature search was conducted to identify research on ADF and IF in overweight or obese human participants. Inclusion criteria were that the diet had to meet the definitions for ADF or IF as listed in Table 5, the energy intake on fasting days was lower than for non-fasting days, and either food or replacement drinks could be used. Studies needed to report on weight loss and glucose or cardiovascular outcomes. Only studies published in English were reviewed. Details of these studies are shown in Table 6. Where two or more papers were published from the same study these results have been presented together and references for all papers provided.

Table 6 Studies investigating the effect of ADF and IF diets on overweight or obese adults

Study	Sample size and characteristics	Type of fasting	Intervention details	Length of intervention	Outcomes (between group where applicable)		
					Weight	Glucose	Cardiovascular
Williams *et al.* (1998)	• 23 men, 31 women • Type 2 diabetes: medications discontinued • Mean age group 1: 51.4 ±7.9 years; group 2: 50.3 ± 8.6 years; group 3: 54.1 ± 7.0 years • Mean BMI (kg/m^2) group 1: 35.4 ± 5.4; group 2: 37.3 ± 4.8; group 3: 35.0 ± 5.2 • 13% non-completer rate	IF (6:1)	• Fasting day: 4-600kcal per day (normal food) • Non-fasting day:1500-1800kcal per day • Group 1: fasting day five days in week one then one day a week for 15 weeks • Group 2: fasting day five day block every five weeks • Group 3: 1500-1800kcal/day standard treatment group • Weekly group behavioural, nutrition and exercise education	15 weeks	Group 1: ↓9.6 ± 5.7 kg Group 2: ↓10.4 ±5.4 kg Group 3: ↓5.4 ±5.9kg (P=0.04)	**HbA1c** Group 1: ↓- 8 mmol/mol ±17 mmol/mol; Group 2: ↓11 mmol/mol ±19 mmol/mol Group 3: ↓0 mmol/mol ±11 mmol/mol (not significant)	**Total cholesterol** All groups decreased. Not significant **LDL cholesterol** All groups decreased. Not significant **HDL cholesterol** No changes. Not significant **Triglycerides** All groups deceased. Not significant
Johnson *et al.* (2007)	• 2 men, 8 women • Stable moderate asthma • Mean age not provided. • Mean BMI not provided, but BMI>30 kg/m^2 recruited • 10 % non-completer rate	ADF	• Fasting day: 380kcal men, 320kcal women (meal replacement drink) • Non-fasting day: ad libitum diet • No control group • Weekly group support session, no education	8 weeks	↓8.5 ±1.7kg (P=0.001)	**Fasting glucose** ↑5.1 ± 4.3 (not significant)	**Total cholesterol** ↓9.3 ±4.0% (P0.04) **LDL cholesterol** ↓10.5 ±8.9 (not significant) **HDL cholesterol** ↑4.1 ±1.3 (P0.01) **Triglycerides** ↓118.3 ±66.8 (P=0.03)

Study	Sample size and characteristics	Type of fasting	Intervention details	Length of intervention	Outcomes		
					Weight	Glucose	Cardiovascular
Varady *et al.* (2009) Bhutani *et al.* (2010) Klempel *et al.* (2010)	• 4 men, 12 women • Healthy • Mean age 46 ± 2.4 years • Mean BMI (kg/m^2) 33.8 ± 1 • 20% non-completer rate	ADF	• Fasting day: 25% of energy requirements (food). One meal consumed between 12 – 2pm • Non-fasting day: ad libitum • No control group • 4 weeks fasting meal provided by researchers. Next 4 weeks' food selected at home • Weekly individual meetings on final 4 weeks to develop meal plan and healthy food choices on ad libitum days	8 weeks	↓5.6 ±1.1kg (P=0.001)	Not reported	**Total cholesterol** ↓21.2 ±4.3% (P=0.001) **LDL cholesterol** ↓24.8 ±9.6% (P=0.008) **HDL cholesterol** No change **Triglycerides** ↓32.2 ±6.4% (P=0.01)
Harvie *et al.* (2011)	• 107 women • Healthy • Mean age group 1: 40.1 ± 4.1 years; group 2: 40.0 ± 3.9 years • Mean BMI (kg/m^2) group 1: 30.7 ±5.0; group 2: 30.5 ± 5.2 • 17% non-completer rate	IF (5:2)	• Fasting day: 25% of energy requirements (food) • Non-fasting day: 100% energy requirements • Group 1: Fasting two consecutive days, non-fasting five days each week • Group 2: 75% of energy requirements Mediterranean-type diet • Fortnightly phone calls and monthly appointments: motivation, anthropometry, cognitive behavioural therapy techniques	6 months	Group 1: mean ↓81.5 kg (95% CI 77-85.4) to 75 kg (95% CI 71.2-78.8) Group 2: mean ↓84.4 kg (95% CI 79.7-89.1) to 78.7 kg (95% CI 74.2-83.2) (not significant)	**Fasting glucose** Group 1: No change Group 2: No change	**Total cholesterol** All groups decreased. Not significant **LDL cholesterol** All groups decreased. Not significant **HDL cholesterol** No changes. **Triglycerides** All groups deceased. Not significant

Study	Sample size and characteristics	Type of fasting	Intervention details	Length of intervention	Outcomes		
					Weight	Glucose	Cardiovascular
Eshghinia and Gapparov (2011)	• 26 women • Healthy • Mean age not reported • Mean BMI (kg/m^2) 37.38 ± 7.35 • 0% non-completer rate	ADF	• Fasting day: 25-40% energy requirements • Non-fasting day: 1600-1700kcal healthy eating • No control group • Women resident in inpatient facility	4 weeks	↓96.87 ± 21.34 to 92.16 ±19.85 (P=0.0001)	**Fasting glucose** ↓5.9 ±1.05 to 5.23 ±0.92 mmol/L (P=<0.0001)	**Total cholesterol** mmol/mol ↓6.12 ±1.1 to 5.42 ± 1 (P=0.0001) **LDL cholesterol** **m**mol/L ↓3.99 ± 0.96 to 3.34 ±0.87 (P=0.0001) **HDL cholesterol** ↓1.43 ± 0.38 to 1.30 ± 0.31 (P=0.005) **Triglycerides** ↑1.59 ± 0.6 to 1.69 ±0.7 (not significant)
Arguin *et al.* (2012)	• 25 women • Healthy postmenopausal • Mean age 60.5 ± 6.0 Years • Mean BMI not reported (“obese”) • Mean % fat mass 47.2 ± 5.3% • 0% non-completer rate	IF	• Group 1: 5 weeks energy restriction followed by 5 weeks weight maintenance, repeated over 25 weeks • Group 2: daily energy restriction for 15 weeks • Nutrient intake deficit to produced 1% weight loss per week • Weekly group education on nutrition, health and lifestyle habits	15 weeks	Group 1: ↓ 10.7 ±3kg Group 2: ↓ 9.5 ±2.1kg (not significant between groups)	**Fasting glucose** mmol/L change Group 1: ↓0.29 ±0.43 Group 2: ↓0.27 ±0.68 (not significant between groups)	**Total cholesterol** not significant decrease **LDL cholesterol** not significant decrease **HDL cholesterol** No change **Triglycerides** not significant decrease

Study	Sample size and characteristics	Type of fasting	Intervention details	Length of intervention	Outcomes		
					Weight	**Glucose**	**Cardiovascular**
Bhutani *et al.* (2013b)	• 83 women • Healthy • Mean age group 1: 45 ± 5 years; group 2: 42 ± 2 years; group 3: 42 ± 2 years; group 4: 49 ± 2 years • Mean BMI (kg/m^2) all groups 35 ± 1 • 23% non-completer rate	ADF	• Fasting day: 25% of energy requirements (food). One meal consumed between 12 – 2pm • Non-fasting day: ad libitum healthy eating choices • 4 weeks fasting meal provided by researchers. Next 4 weeks food selected at home • Weekly individual meetings on final 4 weeks to develop meal plan and healthy food choices on ad libitum days • Group 1: ADF + exercise • Group 2: ADF only • Group 3: Exercise only • Group 4: Maintain regular intake and exercise	12 weeks	Group 1: ↓6 ±4kg Group 2: ↓3 ± 1kg Group 3: ↓1 ± 0kg (P=<0.001)	**Fasting glucose** No change	**Total cholesterol** % change No change **LDL cholesterol** % change Group 1: ↓12 ±5% Group 2: ↓1 ±6% Group 3: ↓ 0 ±5% Group 4: ↑3 ±5% (not significant between groups) **HDL cholesterol** %change Group 1: ↑18 ± 9% Group 2: 0 ±4% Group 3: ↑2 ± 3% Group 4: ↑ 8 ± 5% (P=0.016) **Triglycerides** No change

Study	Sample size and characteristics	Type of fasting	Intervention details	Length of intervention	Outcomes		
					Weight	Glucose	Cardiovascular
Eshghinia and Mohammadzadeh (2013)	• 15 women • Healthy • Mean age 33.4 ±5.9 years • Mean BMI (kg/m^2) 33.16 ± 5.02 • 50% non-completer rate	ADF	• Fasting day: 25-30% of energy requirements • Non-fasting day: 1700-1800kcal healthy eating diet • No control group	6 weeks	↓ 6 ±1.2kg (P=<0.001)	**Fasting glucose** mg/dl ↓102 ± 14.7 to 96 ±11.79 (not significant)	**Total cholesterol** not significant decrease **LDL cholesterol** not significant decrease **HDL cholesterol** not significant increase **Triglycerides** not significant decrease

Study	Sample size and characteristics	Type of fasting	Intervention details	Length of intervention	Outcomes		
					Weight	**Glucose**	**Cardiovascular**
Harvie *et al.* (2013)	• 115 women • Healthy • Mean age group 1: 45.6 ± 8.3 years; group 2: 48.6 ± 7.3 years; group 3: 47.9 ± 7.7 years • Mean BMI (kg/m^2) group 1: 29.6 ±4.1; group 2: 31.0 ±5.7; group 3: 32.2 ± 5.6 • 23% non-completer rate	IF (5:2)	• Fasting day: 30% of energy requirements • Non-fasting day: 100% requirements Mediterranean-style diet • Group 1: Fasting two consecutive days each week • Group 2: Fasting two consecutive days each week plus free protein intake on fasting days • Group 3:75% of energy requirements daily, Mediterranean-style diet • 5 x 45minutes exercise per week • Fortnightly phone calls and monthly appointments: motivation, anthropometry, cognitive behavioural therapy techniques	3 months	Group 1: ↓ 79.4 (95% CI 74.6-8 – 84.1) to 74.4 (95% CI 70-78.9) Group 2: ↓82.4 (95% CI 77.2-87.6) to 77.6 (95% CI 72.9-82.4) Group 3: 86.0 (95% CI 80.6-91.3) to 82.3 (95% CI 77.1-87.5) (not significant)	**Fasting glucose** No change **HbA1c** No change	**Total cholesterol** not significant decrease **LDL cholesterol** not significant decrease **HDL cholesterol** No change **Triglycerides** not significant decrease

Study	Sample size and characteristics	Type of fasting	Intervention details	Length of intervention	Outcomes		
					Weight	**Glucose**	**Cardiovascular**
Varady *et al.* (2013)	• 8 men, 22 women • Healthy • Mean age group 1: 47 ± 3 years; group 2: 48 ± 2 years • Mean BMI (kg/m^2) group 1: 26 ±1 group 2: 26 ± 1 • 6% non-completer rate	ADF	• Fasting day: 25% of energy requirements (food). One meal consumed between 12 – 2pm • Non-fasting day: ad libitum healthy eating choices • Group 1: ADF • Group 2: No dietary changes	12 weeks	Group 1: ↓5.2 ±0.9kg (p=<0.001) Group 2: weight change not reported in kg	Not reported	**Total cholesterol** Not significant decrease **LDL cholesterol** Not significant decrease **HDL cholesterol** No change **Triglycerides** Not significant decrease
Klempel *et al.* (2013a) Klempel *et al.* (2013c) Varady *et al.* (2015)	• 35 women • Healthy • Mean age group 1: 42.4 ± 3 years; group 2: 43.2 ± 2.3 years • Mean BMI (kg/m^2) group 1: 35.3 ± 0.7; group 2: 35.5 ± 0.7 • 8% non-completer rate	ADF	• Fasting day: 25% of energy requirements (food). One meal consumed between 12 – 2pm • Non-fasting day: 125% energy requirements over 3 meals daily • Group 1: ADF: High fat (45% fat) • Group 2: ADF: Low fat (25% fat)	8 weeks	Group 1: ↓4.3 ± 1.0kg Group 2: ↓3.7 ±0.7kg (not significant)	**Fasting glucose** No change	**Total cholesterol** Not significant decrease **LDL cholesterol** Not significant decrease **HDL cholesterol** No change **Triglycerides** Not significant decrease

Study	Sample size and characteristics	Type of fasting	Intervention details	Length of intervention	Outcomes		
					Weight	**Glucose**	**Cardiovascular**
Hoddy *et al.* (2014)	• 9 men, 50 women • Healthy • Mean age group 1: 45 ± 3 years; group 2: 45 ±3 years; group 3: 46 ± 2 years • Mean BMI (kg/m^2) group 1: 35 ±1; group 2: 34 ±1, group 3 34 ± 1 • 20% non-completer rate	ADF	• Fasting day: 25% of energy requirements (food). • Non-fasting day: Ad libitum intake • Group 1: ADF meal at lunch • Group 2: ADF meal at dinner • Group 3: ADF small meals	8 week	Group 1: ↓ 3.5 ± 0.4kg Group 2: ↓ 4.1 ±0.5kg Group 3: ↓ 4.0 ±0.5kg (not significant)	**Fasting glucose** No change	**Total cholesterol** No change **LDL cholesterol** No change **HDL cholesterol** No change **Triglycerides** Not significant decrease

In total 16 published research papers from 12 clinical trials were found that met the literature review inclusion criteria. One trial was performed in Russia, one in Iran, two in the United Kingdom and 12 in the United States of America.

One of the complicating factors when reviewing studies on fasting diets is that there is considerable discrepancy between dietary interventions. Table 7 summarises the differences between prescribed diets on fasting and non-fasting days in ADF and IF studies.

Table 7 Differences between fasting and non-fasting day intake fasting studies

Study	ADF / IF	Fasting day intake	Non-fasting day intake
Varady *et al.* (2009) Bhutani *et al.* (2010) Klempel *et al.* (2010)	ADF	25% of energy requirements based on Miflin equation (? Ref) Food provided at study / by participant	Free choice Provided by participant
Bhutani *et al.* (2013b) Varady *et al.* (2013)	ADF	25% of energy requirements based on Miflin equation Food provided at study	Free choice: healthy eating Provided by participant
Klempel *et al.* (2013a) Klempel *et al.* (2013c) Varady *et al.* (2015)	ADF	25% of energy requirements based on Miflin equation Food provided at study	Prescribed 125% of energy requirements Provided by participant
Eshghinia and Gapparov (2011)	ADF	25-40% of energy requirements Food provided at study	1700-1800 kcal (7000-7500 kJ) per day intake based on healthy eating recommendations Food provided during study
Eshghinia and Mohammadzadeh (2013)	ADF	25-30% of energy requirements Food provided by participant	1700-1800 kcal (7000-7500 kJ) per day intake based on healthy eating recommendations One day per week free choice Provided by participant
Johnson *et al.* (2007)	ADF	320 – 380 kcal (1400-1600 kJ) Liquid provided by study	Free choice provided by participant
Hoddy *et al.* (2014)		25% of energy requirements based on Miflin equation Food provided at study	Free choice provided by participant
Harvie *et al.* (2011)	IF 5:2	25-30% of energy requirements based on Schofield's equation Food provided by participant	100% energy requirements provided by participant
Harvie *et al.* (2013)	IF 5:2	25-30% of energy requirements based on Schofield's equation Food provided by participant	100% energy requirements provided by participant
Williams *et al.* (1998)	IF 1:6	400-600 kcal (1700-2500 kJ) per day Food provided by study	1500-1800 kcal (6200-7500 kJ) per day
Arguin *et al.* (2012)	IF	Details not provided	Details not provided

Food intake on the fasting days in the ADF groups was limited to one meal per day, except in the study by Hoddy *et al.* (2014) where timing and number of the fasting day meals during the day was investigated. Neither study (Harvie *et al.*, 2013, Harvie *et al.*, 2011) specified meal timings, however, in the book that was published following this research (Harvie and Howell, 2013) three mini meals a day were recommended. Neither Williams *et al.* (1998) nor Arguin *et al.* (2012) specified the number of meals that participants were recommended to eat on fasting days. Therefore, discrepancies in results between studies may be attributed in part to differences in what fasting diet was used (ADF or IF), how the fasting day diet energy requirements were calculated and what dietary intake was prescribed on non-fasting days.

Only one diet has investigated the effect of fasting in overweight and obese people with T2DM: Williams *et al.* (1998). This study mimicked what is now called an intermittent fasting diet by using a VLCD one day a week for 15 weeks after an initial five day VLCD diet. The comparison groups were a 1500-1800 kcal (6200-7500 kJ) healthy eating diet (control group) and a five day VLCD once every five weeks. The results of the five day VLCD group will not be discussed here. Fifty four people with T2DM completed the clinical trial. All had their oral hypoglycaemic agents discontinued at the start of the trial, and none were taking insulin at the start of the trial. Seven participants had their OHA restarted again during the trial due to increased fasting blood glucose levels. Data past the point of resuming OHA in these participants was excluded. Dietary intervention was a 400-600 kcal (1700-2500kJ) per fasting day food-based diet provided by the research centre. Non-fasting days were chosen and food was prepared by the participants in their own homes after receiving education on healthy food choices from a dietitian. Participants were taught how to self-monitor their fasting blood glucose levels twice weekly and were given an action plan of when to contact the research team if blood glucose levels were increased.

The IF group lost a mean of 9.6 ± 5.7 kg compared to the control group who lost 5.4 ± 5.9 kg (P= 0.04). The study also found that men in the IF group lost more weight

than the men in the control group, however women lost similar weight regardless of intervention group. Sixty nine percent of participants in the IF group compared to 50% of participants in the control group achieved over 5% weight loss in 15 weeks, however this was not statistically significant. HbA1c was reduced by a mean (± standard deviation) of 8 ±17 mmol/mol compared to 0 ±11 mmol/mol in the control group. Lipid results indicated that total cholesterol, LDL cholesterol and triglyceride decreased but the results were not statistically significant when compared to the control group. There was no change in HDL cholesterol levels. All groups had a lower fasting insulin level at the end of the trial, however the differences were not statistically significant. Weight change over the whole trial was significantly associated with improvements in fasting blood glucose levels and HbA1c. No hypoglycaemic events were noted as an outcome of this trial.

This is the only study that reports an intermittent fasting style of dietary intervention in people with T2DM. Results seen within this group of participants is similar to results observed in fasting diets in the general overweight and obese population, and indicate that this type of diet could be a successful weight loss strategy for obese people with T2DM. However, there is still a gap in knowledge as to the safety of undertaking fasting diets with people with T2DM who are taking insulin and OHA during the dietary intervention.

Weight loss (statistically significant or not) was seen in all fasting diet groups. When the results from the ADF studies on overweight or obese participants reviewed above were pooled a mean weight loss of 0.69 kg (range 0.25-1.17 kg) per week. Pooled results from the IF studies indicate a mean weight loss of 0.49kg (range 0.27-0.64 kg) per week. This compares to the pooled results from the four control groups in these studies where participants were advised on a daily calorie restriction of a mean weight loss of 0.38 kg (range 0.24-0.63 kg) per week. From these studies it indicates that ADF diets result in slightly more weight loss per week than IF diets, which could be nearly double the weight loss seen in the daily calorie reduction control groups. Lifestyle changes to lose weight including a low energy

diet have been reported to result in weight loss of approximately 0.25 kg per week for interventions over 6-12 months (Makris and Foster, 2011).

Changes in fat mass and fat free mass was also reported in nine ADF studies and is shown in Table 6 (Arguin *et al.*, 2012, Harvie *et al.*, 2011, Harvie *et al.*, 2013, Varady *et al.*, 2009, Varady *et al.*, 2013, Klempel *et al.*, 2013a, Bhutani *et al.*, 2013b, Klempel *et al.*, 2013c, Varady *et al.*, 2015). Arguin *et al.* (2012) reported that there were no statistically significant differences between the groups in decrease in fat mass, however women following the intermittent diet experienced a statistically significant reduction in fat free mass (P=0.03) when compared to a daily energy restriction control group. Harvie *et al.* (2011)and Harvie *et al.* (2013) reported that both the IF and control groups lost similar amounts of fat mass and fat free mass over both a six month and a three month intervention trial. The trial conducted by the Chicago group (Bhutani *et al.*, 2010, Varady *et al.*, 2009, Klempel *et al.*, 2010) reported a significant decrease in fat mass of 5.4 ± 0.8 kg (P=<0.05) during the 8 week ADF intervention however no change was found in fat free mass. Similar results of a significant reduction in fat mass but not fat free mass were seen in the studies by Varady *et al.* (2013), Klempel *et al.* (2013a), Klempel *et al.* (2013c), Bhutani *et al.* (2013b) and Varady *et al.* (2015). Investigating different timings of meal intake on an ADF revealed that fat and fat free mass were reduced by similar amounts in the three intervention groups. From this data the only conclusions that can be drawn is that fat mass is reduced during fasting diets, however it might not be any more than would be expected from a control diet, and that there are indications that fat free mass may be preserved during alternate day fasting but not intermittent fasting.

Clinical outcomes for cardiovascular disease risk (blood pressure and serum lipid levels) were reported in all studies, however, the results again were inconsistent. Results from ADF interventions show that total cholesterol and LDL cholesterol levels were significantly reduced in some studies (Johnson *et al.*, 2007, Varady *et al.*, 2009, Eshghinia and Gapparov, 2011), but that reductions in these serum lipid

levels were not significant in the other ADF studies. A significant reduction in triglyceride levels was reported by Johnson *et al.* (2007) and Varady *et al.* (2009) but other studies found either no change or a non-significant decrease. Eshghinia and Mohammadzadeh (2013) found no significant changes in lipid levels. Varady *et al.* (2013) reported that the reduction in blood pressure was not significant however Bhutani *et al.* (2013b), Eshghinia and Gapparov (2011) and Eshghinia and Mohammadzadeh (2013) found a significant reduction in both systolic and diastolic blood pressure in obese subjects following an ADF. It was observed by Hoddy *et al.* (2014) that there was a significant within-group decrease in systolic blood pressure in ADF groups where three meals on fasting days were provided (P=0.04) but no change in the groups where one meal a day was provided. No changes in diastolic blood pressure were seen.

Results from IF studies have been similarly varied with Harvie *et al.* (2011) and Harvie *et al.* (2013) reporting a small, non-significant decrease in total and LDL cholesterol in all groups, including the control group and no change in HDL cholesterol. Blood pressure was reduced, but not significantly in both groups. Arguin *et al.* (2012) found a non-significant decrease in serum lipids and no change in HDL levels, but blood pressure was not reported. Harvie *et al.* (2013) reported participants who were taking statin and "CVD medication", although did not discuss what "CVD medication" was. It could be assumed that these medications would include antihypertensives for the treatment of blood pressure. Medication use was not reported by Johnson *et al.* (2007). The remainder of studies reported that participants who had evidence of cardiovascular disease or hypertension were excluded from the study.

Klempel *et al.* (2013b) and Bhutani *et al.* (2013a) specifically investigated the effect of ADF diets on vascular health. Results indicated that brachial artery flow-mediated dilation (FMD) significantly decreased (P=<0.05) in the high fat ADF diet compared to baseline measurements, but in the low fat ADF diet dilation increased (P=<0.05) (Klempel *et al.*, 2013a). Results indicated that this improvement in

dilation was not governed by adipokines (a hormone derived from fat cells that protects the endothelium by reducing oxidative stress). Bhutani *et al.* (2013a) reported an increase in FMD (P=0.05) in a group following an ADF diet who also experienced a reduction in blood pressure. The trial by Klempel *et al.* (2013a) also reported LDL particle size and showed that LDL particle size increased in both groups (P=<0.005) and the proportion of small particle sized LDL cholesterol decreased. An increase in LDL particle size was also reported by Hoddy *et al.* (2014) in all ADF treatment groups. Small particle sized LDL is more harmful to vascular health. Medication use could provide some explanation for the discrepancies seen between trials in cardiovascular results, as could differences in dietary intervention. However further investigation of the effect of fasting diets on the intricacies of LDL particle size and dilation of blood vessels may also explain why crude measures of cardiovascular risk yield varying results.

Johnson *et al.* (2007) reported a non-significant increase in fasting blood glucose after eight weeks of ADF, however all other ADF groups either reported no change or a non-significant decrease in fasting blood glucose levels. Changes in fasting blood glucose were reported in 10 of the 12 clinical trials and HbA1c changes in two trials (Williams *et al.*, 1998, Harvie *et al.*, 2013). Williams *et al.* (1998) investigated a 15 week intermittent fasting diet in people withT2DM who were taken off oral hypoglycaemic agents and reported a reduction in HbA1c of 8 ± 17 mmol/mol. Harvie *et al.* (2013) reported no change in HbA1c over a 3 month period, however participants did not have diabetes.

Bhutani *et al.* (2010), Johnson *et al.* (2007) and Hoddy *et al.* (2014) found no significant or clinical effect on insulin sensitivity or insulin resistance in participants following an ADF. Harvie *et al.* (2011) reported no significant improvement but a small clinical improvement that was greater in the IF group to insulin sensitivity and insulin resistance in a group of overweight women following a 5:2 IF diet compared to a control group. In a later study using a protein restricted 5:2 IF diet (Harvie *et al.*, 2013) a significant reduction in fasting insulin (P=0.014) and insulin resistance

(P=0.02) using HOMA-IR (homeostatic model assessment of insulin resistance) was found.

The results of these studies suggest that there may be more of an effect on insulin resistance and insulin sensitivity when following a 5:2 pattern IF diet than an ADF diet, and that the effect may be greater when following a restricted protein IF diet. However, the effect seems to be small and certainly no conclusions can be reached with such a small number of studies. As the participants in these studies did not show signs of insulin resistance or reduced insulin sensitivity at the outset of the study it may be that changes in these markers would not be expected unless insulin resistance was present or insulin sensitivity impaired.

In animal models it has been found that metabolic hormones ghrelin, adiponectin and leptin change during fasting. Ghrelin levels usually increase during fasting and stimulate appetite whilst leptin suppresses appetite and levels fall during fasting (Longo and Mattson, 2014). Raised levels of leptin are often associated with inflammation. Adiponectin and ghrelin may reduce inflammation and improve insulin sensitivity (Longo and Mattson, 2014). Human studies have investigated the impact of fasting on metabolic hormones. Johnson *et al.* (2007) found that leptin levels were lower on fasting days and that leptin levels on non-fasting days progressively decreased over an eight week study, however, ghrelin was not affected by fasting or non-fasting days. Bhutani *et al.* (2010), Varady *et al.* (2013) and Klempel *et al.* (2013a) all reported statistically significant reductions in leptin and an increase in adiponectin on fasting days.

Insulin like growth factor (IGF) improves insulin sensitivity (Clemmons, 2004). Harvie *et al.* (2011) reported comparable increases between IF and the control diet in insulin like growth factor binding protein-1 and -2 (IGFBP-1 and IGFBP-2) during a six month diet, however, total and free IGF remained stable. Both groups showed a slight decrease in C-reactive protein and oxidative stress markers. In a later study (Harvie *et al.*, 2013) after a three month IF intervention found low protein, high

protein IF diets and a control group all had similar reductions in leptin and inflammatory marker IL-6, and no change in adiponectin, IGF-1, TNF α or measures of oxidative stress. Johnson *et al.* (2007) found that inflammatory and oxidation markers were reduced after an eight week ADF diet in obese people with moderate asthma. These human studies seem to concur with animal studies that fasting reduces inflammation and oxidative stress. As obesity and T2DM are conditions where inflammation and oxidative stress is raised (Ota and Das, 2015) following an IF or ADF may have additional benefits over and above those seen by achieving weight loss alone.

Only four trials investigated IF diets, and only one trial included participants who had T2DM. Because of the differences in dietary interventions very few conclusions can be reached about the impact of fasting diets on weight, cardiovascular or blood glucose responses. Fasting diets, either ADF or IF, have been investigated using high protein, high fat or low fat options and with or without the addition of exercise. However, some trends in results have been identified. Pooled results of weight loss from the studies indicate that ADF might perform slightly better than IF for weight loss. However all forms of ADF or IF seem to result in similar weight, glucose or lipid changes whether they are based on healthy eating recommendations, high protein, high fat or low fat diets. The amount of weight loss and favourable changes in lipid levels is comparable to that reported in daily energy restriction diets. Where there is still a gap in knowledge is in how fasting diets affect those with T2DM who are treated using OHA or insulin. It is not known whether the obesogenic effect of insulin and certain types of OHA will result in similar rates weight loss seen in studies on fasting in overweight or obese people without diabetes. Furthermore, it is not known whether fasting diets will result in increased rates of hypoglycaemia or hyperglycaemia in those on insulin.

2.4.4 Hypoglycaemic safety of intermittent fasting

Hypoglycaemia is defined as a blood glucose level of 4 mmol/L or less. Mild hypoglycaemia is able to be appropriately recognised and managed by the person with diabetes. Severe hypoglycaemia is when the assistance of another person is required to administer treatment. Untreated hypoglycaemia can result in coma and death (American Diabetes Association, 2016b).

Hypoglycaemic as a risk to those with T2DM who are treated using insulin or oral hypoglycaemic agents when following a diet that seeks to restrict carbohydrate intake. The safety of fasting for people with diabetes has been studied mainly in populations who fast for religious reasons such as Ramadan (Ahmedani *et al.*, 2012). Unfortunately much of the research on hypoglycaemia when observed during religious fasting cannot be routinely applied to the type of fasting during intermittent fasting for weight loss. Intermittent fasting, as previously discussed, focuses on a severe energy restriction for a 24 hour period several times a week. In Ramadan fasting is undertaken during daylight hours and followed by eating a large meal after sunset and again before sunrise for a 29-30 day period. Foods eaten between sunset and sunrise may differ from usual food choices, and may conform to traditional foods or eating styles (Shadman *et al.*, 2014, Norouzy *et al.*, 2013, Vasan *et al.*, 2012). It is because of the discrepancies in dietary patterns following the fasting daytime period that results of research in to glycaemic responses to Ramadan fasting may not necessarily be appropriate to be extrapolated to IF diets. Energy intakes during Ramadan are not as restricted as during intermittent fasting for weight loss. Studies have detailed nutrient intakes before, after and during Ramadan fasting and indicate that energy intake during Ramadan fasting may be 1600-2000 kcal (6700-8300 kJ) daily with carbohydrate intakes of 250-270 g daily through two meals overnight (Vasan *et al.*, 2012, Norouzy *et al.*, 2013). Typically energy intakes during IF are considerably lower at approximately 500-600kcal (2000-2500kJ) daily, through two to three meals daily (Harvie *et al.*, 2013, Harvie *et al.*, 2011). However, there are some themes that come from the research on people with T2DM during Ramadan that can be applied when considering

intermittent fasting for people with T2DM; these are that the key to safe fasting seems to be education and appropriate medication adjustment (Aldasouqi *et al.*, 2013, Reiter *et al.*, 2007, Loke *et al.*, 2010, Ahmed and Abdu, 2011, Salti *et al.*, 2004).

The other type of eating that mimics intermittent fasting days are very low calorie diets (VLCD). Studies investigating VLCD using meal replacements for weight loss in people with T2DM have excluded participants who are taking insulin or OHA, stopped these medications prior to the study commencing or not reported frequency of hypoglycaemic events (Jazet *et al.*, 2005, Ash *et al.*, 2003, Williams *et al.*, 1998, Kelley *et al.*, 1993, Henry *et al.*, 1985). With insulin and some other OHA's being obesogenic, those who are overweight or obese and taking these medications would potentially benefit most from weight reduction, improved insulin sensitivity and reduced insulin resistance. Therefore it is important to be able to assess the safety of IF diets in people with T2DM who are taking insulin or other OHA.

2.5 Conclusion

Type 2 diabetes and obesity are inextricably linked. Obesity predisposes to the development of T2DM through increased insulin resistance and reduced insulin sensitivity. Obesity has also been implicated in an increased risk of developing complications of diabetes. Weight loss as well as achievement of appropriate blood glucose levels are the two cornerstones of treatment to achieve and maintain good health when living with diabetes. It is the achievement of weight loss that is often a barrier to good health. Many diets have been advocated for those with T2DM to assist with weight loss, and the majority (with the exception of VLCD and bariatric surgery) seem to result in similar amounts of weight loss. However, what has consistently been implied by the findings is that it is the diet that works for the individual which is the diet that works. Enabling health care professionals to be able to give recommendations on an appropriate range of safe weight loss options

is a significant progression in assisting people with T2DM to achieve their health goals.

With this in mind there is some initial evidence that IF may be an effective diet strategy for weight loss in people with T2DM. Intermittent fasting might also have extra benefits such as reducing insulin resistance and inflammation and preserving lean body mass during weight loss. However, research is lacking on IF in people with T2DM, especially with evidence of safety with regards to blood glucose management for those in insulin.

CHAPTER 3 METHODOLOGY

The aim of this feasibility study was to investigate the effectiveness and safety of an intermittent fasting diet (two fasting days per week) as an alternative to standard dietary advice (daily calorie restriction) for weight reduction in obese adults with insulin dependent Type 2 Diabetes (T2DM) attending a 12 week group based intervention at Waitemata District Health Board. This chapter describes the design and methodologies use in the 12 week feasibility study including recruitment, dietary interventions and education, measurements and data analysis.

3.1 Study design

The 'Intermittent fasting for T2DM (IFOOD)' feasibility study was a two arm open-label design 12 week intervention study. Participants were not matched and were randomly assigned to one of two intervention groups. Figure 5 shows the study enrolment process and design.

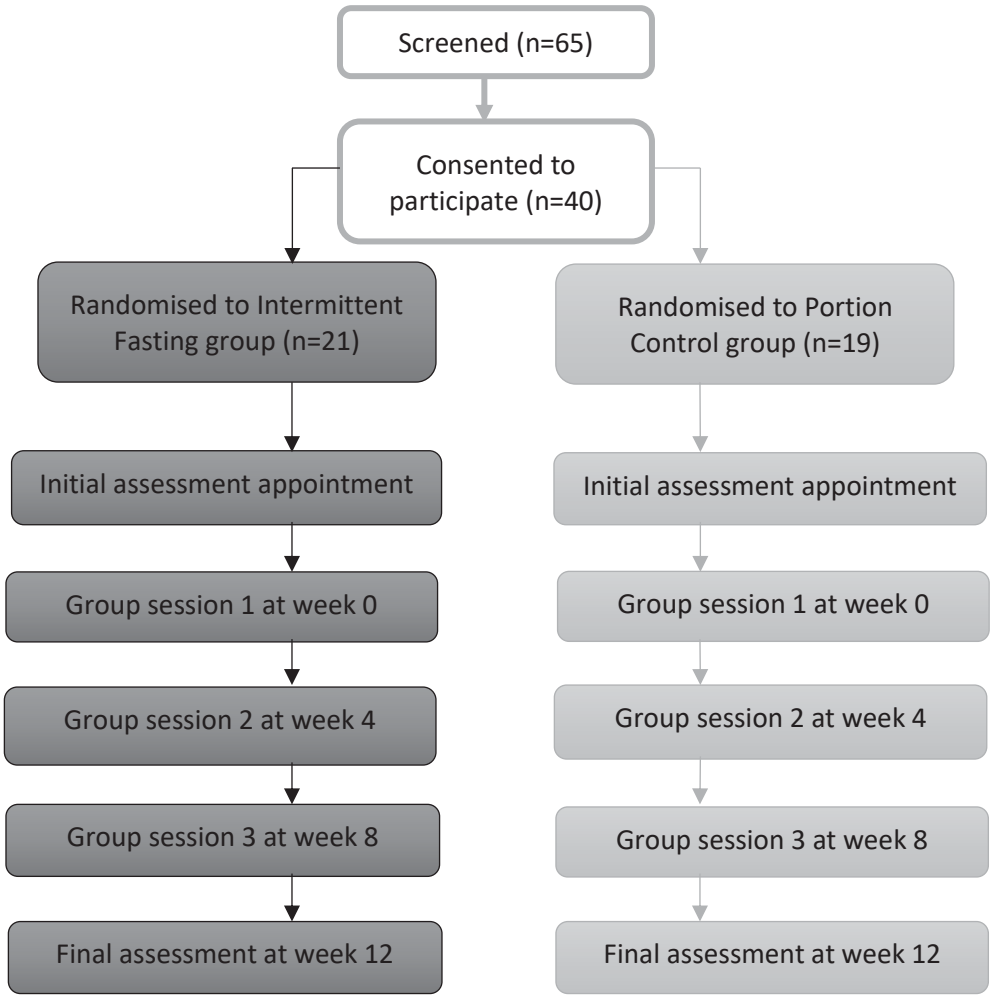


Figure 5 Study enrolment and design

3.2 Permissions and ethical approval

Permission for this feasibility study to be conducted was given by Waitemata District Health Board (DHB). Ethical approval was granted by the New Zealand Health and Disability Ethics Committee Northern B (application 14/NTA/11). In accordance with both these approval bodies the study was also registered with the Australian New Zealand Clinical Trails Registry (Registration number: ACTRN12614000220662).

3.3 Study population and recruitment

This study was carried out at the Diabetes Service, Waitemata (DHB), Auckland, New Zealand. Based on the population treated at the Waitemata DHB Diabetes Centre and predicted enrolment rates in the study forty participants were enrolled. As this was a feasibility study there was no specific sampling of population groups such as Māori.

3.3.1 Inclusion and exclusion criteria

Participants were recruited from the patients who attend the Diabetes Services at Waitemata DHB. Inclusion criteria were people between the ages of 35-65 years who:

- had diagnosed T2DM and were taking insulin as part of the medical treatment of their diabetes
- were obese and had a body mass index (BMI) of 30-49.9 kg/m^2
- had an HbA1c between 55 and 90 mmol/mol
- were screened to show they had hypoglycaemic awareness
- had stable and well controlled other medical conditions
- were willing to undertake a 12 week dietary intervention for weight loss

Exclusion criteria were those who did not meet the inclusion criteria, or:

- had hypoglycaemic unawareness or hospital admission from diabetic ketoacidosis / hyperglycaemia / hypoglycaemia in the previous 12 months
- had renal failure / chronic kidney disease
- had unstable heart disease
- had a history of diagnosed eating disorder
- had a medical condition where sudden weight loss would impact upon either condition or treatment
- were pregnant or breastfeeding women
- required translation of written / spoken English

3.3.2 Recruitment

Participants were recruited and enrolled over a 15 month period between April 2014 and June 2015. Eligible candidates were identified and approached by Waitemata DHB Diabetes Services health care professionals or by participants registering interest from seeing posters advertising the study at the Diabetes Centre at North Shore and Waitakere Hospitals, Waitemata DHB. The primary researcher made contact with the candidates by telephone to ensure they met inclusion criteria and to discuss the study. If verbal consent to enrol in the study was obtained then the participant information sheet, a consent form (see Appendix 1), group session dates, food record diary (see Appendix 2) and a hypoglycaemia awareness questionnaire (see Appendix 3) were posted to the participant by the primary researcher. At this time the first assessment appointment was booked and dates for the group education sessions confirmed. Participants were able to withdraw prior to the study starting or during the study at any time.

3.3.3 Randomisation

Participants were randomised at recruitment when verbal consent had been obtained. A randomisation block of four (ABAB / BABA / AABB / BBAA / ABBA / BAAB), where diet A was intermittent fasting and diet B was portion control diet, was used to allocate the dietary intervention.

3.3.4 Study procedure

All participants attended a total of two individual 45 minute appointments, (at the start of the intervention and at week 12), and three one hour group education sessions (week 0, 4 and 8). The primary researcher made contact with the participants at week 2, 6 and 10 via telephone or email to check hypoglycaemic events, maintain participant motivation and answer any questions arising. The group sessions were held in the evenings at Waitemata DHB sites (North Shore or Waitakere Hospitals). Participants saw their usual diabetes team (Doctor, Diabetes

Specialist Nurse, Dietitian, Podiatrist) as normal during the study period. Medical supervision of participants was undertaken by a Consultant Endocrinologist who worked at the Diabetes Service, Waitemata DHB. Participants did not necessarily have contact with the Consultant Endocrinologist as all information was passed through the primary researcher.

The participant's general practitioner (GP) and diabetes team were notified by letter or email that the participant had been enrolled in the study and which intervention group they were randomised to. After the final assessment appointment at week 12, the participant's GP and the diabetes team received a written confirmation that the participant's involvement in the study had been completed, and whether follow-up by their GP was required. If the participant withdrew or dropped-out of the study, a letter was sent to their GP and diabetes team to notify them. At the final assessment appointment participants were given the choice to continue with the dietary intervention they were following, or to try the other intervention diet, or to return to the dietary recommendations they had been following prior to the study.

3.4 Interventions

3.4.1 Dietary interventions

Both treatment arms were educated on a dietary intervention that should result in weight loss. The portion control diet (PCD) intervention was the standard treatment group and used as the comparison group and the intermittent fasting diet (IFD) the novel treatment group under investigation.

The PCD was developed according to current best practice advice for adults with T2DM (Dietitians New Zealand Diabetes Special Interest Group, 2014). The key points of the dietary approach were to gradually change portion sizes and frequency from the individuals current intake to an intake in line with the recommendations of Diabetes New Zealand (Diabetes New Zealand, 2014), and to

make low fat food and cooking choices. Participants were encouraged to use strategies to help identify where portion sizes were either too large or consumed too frequently, thereby achieving a reduction in energy intake and therefore weight loss. Participants were educated on how to monitor their intake of portions of fruit, vegetables, carbohydrates, protein and fluid. Education was supported with a leaflet that encouraged participants to check-off every time they had eaten a portion. By identifying where they were over or under consuming from specific food groups they were then advised to gradually reduce (or increase) portions every week (See Appendix 4). Specific energy reductions or energy intake goals were not set for either individual participants or for the PCD group as a whole. This was because current dietary standard practice is to achieve weight loss through gradual reduction of portion sizes and frequencies, thereby reducing overall intake. For participant information the PCD was named "Clever Portions".

Resources given to participants in the PCD group were:

- Session workbook and hand-outs
- Diabetes New Zealand dietary recommendations leaflet "Diabetes and healthy food choices"
- "Tick" box tally card that participants were encouraged to complete to show them how much they really were eating
- Fridge poster reminding participants of portion sizes and frequencies, how to make low fat choices and blood glucose test result action points
- Blood glucose monitoring diary

Copies of these resources can be found in Appendix 4.

For the current study the decision was made to use an intermittent fasting style diet based on the type used by Harvie *et al.* (2013), Harvie *et al.* (2011), and in the popular books "The Fast Diet" (Mosley and Spencer, 2014) and "The 2-day diet" by (Harvie and Howell, 2013). These styles of diet promote a 5:2 format of intermittent fasting, i.e. two fasting days and five non-fasting days recommended

each week. It was important to use a style of fasting that was both evidence based and that participants were familiar with from the public arena. At the time the protocol was developed there was a lot of promotion of both of the books mentioned, and patients attending the diabetes centre were asking questions specifically of 5:2 intermittent fasting rather than an alternate day fasting style. Reviewing the information from these two published books available in the public arena it was evident that neither diet would be suitable to use as a basis of an intermittent fasting diet for people with T2DM who were treated using insulin as they included irregular carbohydrate amounts at meals or only two meals per day. The key requirement for a fasting diet for this population group would be a regular consumption of a set amount of carbohydrate at each meal. This would be necessary to enable more accurate dose adjustment of insulin and OHA therefore reducing the risk of hypoglycaemia on fasting days.

The median daily energy intake for adult male New Zealanders is 2500 kcal (10,380 kJ) and for adult women is 1800 kcal (7448 kJ) (University of Otago and Ministry of Health, 2011). From the literature review on intermittent and alternate day fasting an energy intake of approximately 25% of normal is advised on fasting days. Using the median daily energy intake for adult New Zealanders an estimated energy intake on fasting days was predicted to be 450 kcal (1900 kJ) for women and 650 kcal (2700 kJ) for men. This was similar to the level of energy restriction advised by Mosley and Spencer (2014) in the book "The Fast Diet" which proposed a fasting day intake of 500 kcal (2100 kJ) for women and 600 kcal (2500 kJ) for men. As education on the dietary intervention was to be given in a standardised format, in a group education session it was decided that energy intakes should be based on an estimated 25% of requirements rather than individual energy calculations for each participant. The IFD was therefore designed to provide an energy intake of approximately 550-650kcal per fasting day, thus achieving an energy intake of 25% of requirements for the majority of participants. Meal plans were developed based on an intake of 20g carbohydrate per meal at three meals a day (breakfast, lunch and evening meal). Protein intake was approximately 50 g per day as a high protein

diet reduces hunger (Harvie *et al.*, 2013, Dong *et al.*, 2013). The overall diet aimed to provide approximately 40% energy from carbohydrates, 33% energy from protein and 27% energy from fat. This compares to the diet investigated by Harvie *et al.* (2011) which provided 30% energy from protein but did not specify recommended carbohydrate or fat intake on fasting days, and Harvie *et al.* (2013) who recommended 25% energy intake from carbohydrates and less than 10% from saturated fats (other recommended nutrient intakes not specified).

Food was not provided to participants. All food was chosen, bought and prepared by participants according to a "pick and mix" style meal builder (See Appendix 5). The meal builder contained a variety of cultural and ethnic foods common to the population group of Waitemata DHB who have diabetes. This enabled participants to base fasting day meals on normal meal choices and preferences. For participant information the IFD was named "Intermittent Fasting". On non-fasting days participants were encouraged to choose low fat foods (the same as for the portion control group), have carbohydrates at each meal (standard advice for people with type 2 diabetes) and eat the same quantities as they would normally eat.

Resources given to participant in the IFD group were:

- Session workbook and hand-outs
- Fridge poster and handbag / pocket guide to intermittent meal choices and blood glucose test result action points
- Blood glucose and fasting day monitoring diary

Copies of these resources can be found in Appendix 5.

3.4.2 Group education

Education on both diets was delivered during group sessions. These sessions were developed around current diabetes group education provided by the Diabetes Service at Waitemata DHB. Best practice for Diabetes Self-Management Education

(DSME) was incorporated in to the sessions: goal setting, self-management and problem solving. One hour sessions were held at weeks 0, 4, and 8. Teaching plans were written to standardise the information between groups at each session. The only difference between the information given to the intervention groups was the dietary recommendations. A summary of session topics are described in Table 8.

Table 8 Content of group education sessions

Session	Summary of topics covered
1 Week 0	What is diabetes • What is diabetes • Role of insulin • Foods / activities that change blood glucose levels Motivation • Cycle of change • Goal setting • Mindful / awareness of eating behaviours **Dietary intervention (IFD or PCD)** Diabetes management on diet • Blood glucose testing • Actions to take for blood glucose readings
2 Week 4	Group discussion / support Goal setting Identifying blood glucose patterns and insulin adjustment • Foods / activities / medications that change blood glucose levels • How to identify patterns in blood glucose readings • Interpreting patterns and actions to take
3 Week 8	Group discussion / support Goal setting • long and short term Maintaining changes • Label reading • Eating out

Session material was presented as a handbook containing all information discussed at the group sessions. Full teaching plans can be found in Appendix 6.

3.5 Medication changes

As the IFD intervention required participants to eat substantially less carbohydrate than usual on two days a week, modifications to their medications were required. Because of the mode of action, the two groups of medications that required

adjustment were insulins and sulphonylureas. Metformin does not have a risk of hypoglycaemia and so doses did not need to be altered. All medication dose adjustments were calculated for each individual by the Consultant Endocrinologist who supervised the clinical aspects of the research. Dose adjustments for the fasting days were calculated based on the participants' original dose, estimated carbohydrate intake established from baseline food record and carbohydrate intake on fasting days. Participants on long acting insulin (Lantus) were also required to reduce their evening dose of insulin on the night before the fasting day. An example of insulin and medication adjustments is shown in Table 9.

Table 9 Example of medication changes for the IFD intervention group

Medication	Normal dose + time	Pre-fasting day dose + time	Fasting day dose + time
Lantus	70 units at Dinner	30 units at Dinner	30 units at Dinner
Metformin	Metformin 500mg x 3 Breakfast and dinner	Metformin 500mg x 3 Breakfast and dinner	Metformin 500mg x 3 Breakfast and dinner

Those in the PCD group did not require medication changes at the start of the intervention. Participants in both groups were provided with information on when to contact the research team depending on results of self-monitored blood glucose (SMBG) (see Table 10). Medication changes were advised by the Consultant Endocrinologist or the participants own Diabetes Nurse Specialist.

Table 10 Instructions to participants for results of SMBG

If your blood sugar is	This means it is
Over 16	Too high! Call us if it stays this high for 2-3 days.
11-16	Too high! Call us if it stays this high for a week.
9-11	A little high before meals.
4.5-9	The right target for before meals.
Below 4	Too low! Call us if you have more than 2 lows in a week.

At the initial and final assessment appointments participants were asked whether they took antihypertensive and lipid lowering medications. Insulin and oral hypoglycaemic agent (OHA) medications and doses were also recorded. Information from medical electronic records were checked with the participant. Total weekly doses of insulin and OHA were calculated from this data.

3.6 Measurements

Approximately one week before the first group session participants were booked in to a 45 minute individual initial assessment session. Participants were invited to bring a support person, whanau or family member to this session. All information was collected by the primary researcher according to a standardised assessment form (see Appendix 7). Appointments were made by the primary researcher and clinic rooms were booked at the diabetes centre, North Shore Hospital or the outpatient offices at Waitakere Hospital. Measurements were repeated at the week 12 final assessment appointment at the conclusion of the intervention period.

3.6.1 Socio-demographic information

Information on patient's gender (male, female), age, year of diagnosis of diabetes / duration of time with diabetes and ethnicity were collected. If the participant could not recollect when they were diagnosed with T2DM medical records were checked to determine year of diagnosis. Participants were asked which ethnic group they primarily identified with. Ethnic group was recorded using standardised codes defined by New Zealand Statistics (Statistics New Zealand, 2005).

3.6.2 Anthropometric measurements

Participants were clothed in light weight clothing, without shoes. Weight was taken using a SECA stand-on calibrated scale and measured to the nearest 0.1 kg. Height was measured using a calibrated stadiometer to the nearest 0.1 cm. Waist circumference was measured at the mid-point between the iliac crest and the lower

palpable rib, according to World Health Organisation protocol (World Health Organization, 2011) using a measuring tape to the nearest 0.1 cm. Height and waist circumference were measured in triplicate, with the mean taken as the final measurement. Body Mass Index was calculated using weight in kilograms divided by height in metres squared. Waist: height ratio was calculated as waist measurement divided by height measurement in centimetres. All measurements, except height, were repeated by the primary researcher at week 12 assessment appointment. Weight was also measured at group session at weeks four and eight.

3.6.3 Biochemical and clinical measures

To determine changes in blood glucose control and cardiovascular risk the following biochemical and clinical measures were measured: non-fasting HbA1c, total cholesterol, triglycerides, LDL cholesterol, HDL cholesterol, blood pressure and total cholesterol: HDL ratio was calculated. Non-fasting blood samples were taken at the initial and final assessment appointments. If routine blood samples were tested within four weeks of the appointment, these results were used as either baseline or final results instead.

In this study non-fasting serum lipids were analysed. A joint statement from the European Atherosclerosis Society and the European Federation of Clinical Chemistry and Laboratory Medicine (Nordestgaard *et al.*, 2016) recommended that the difference between fasting and non-fasting serum lipids are not clinically significant and that non-fasting blood samples be used for assessing serum lipids. Non-fasting venous blood samples were taken by a registered phlebotomist at Labtests Auckland New Zealand. Verbal consent was received and the procedure explained by the phlebotomist before blood was collected. Blood was taken using a sterile vacutainer flashback needle and needle holder. To reduce participant burden blood samples were taken from the participant who had not fasted and no set time of day for testing was specified. An 8.5ml SST (serum separation tube) was used to collect blood for the lipid profile tests and EDTA

(Ethylenediaminetetraacedtic acid) tube to collect blood for the HbA1c test. HbA1c was tested using the Cobas c™ pack reagent on a Roche Cobas Integra® 800 CTS. Total cholesterol was measured using the CHOL_c method on a Siemens Advia® 2400. The HDL cholesterol was measured using the D-HDL method on a Siemens Advia® 2400. Triglycerides were analysed on the Siemens Advia® 2400 using TRIG_c method. Blood samples were analysed by Labtests Auckland New Zealand, according to local standardised protocols.

A BpTRU-100™ machine was used to measure brachial arterial blood pressure. The participant was in a seated position when blood pressure was taken. Blood pressure was taken on the left arm using either a regular or large sized cuff. Two measurements were taken two minutes apart. The second reading was taken as the final blood pressure measurement.

3.6.4 Glycaemic control and hypoglycaemic awareness

Daily blood glucose readings (SMBG) are part of normal care for people with T2DM who are treated using insulin. All participants used a CareSens™ blood glucose meter with Caresens N™ test strips. Participants were requested to test their blood glucose levels four times daily: before breakfast, lunch, dinner and before bed. Additional tests were advised if participants felt symptoms of hypoglycaemia. Participants were provided with diaries to record daily blood glucose readings. A prescription for extra CareSens N™ test strips was provided by the Consultant Endocrinologist as required. If participants experienced more than two blood glucose levels at 4mmol/l or less per week they were advised to contact the primary researcher. If this occurred the primary researcher contacted the Consultant Endocrinologist or Diabetes Specialist Nurse who advised on an action plan including changes in medications as required.

Awareness of hypoglycaemia can change as blood glucose control improves. Some people with diabetes have diminished awareness of hypoglycaemia because of tight

glycaemic control (Clarke *et al.*, 1995, American Diabetes Association, 2016b). As both dietary interventions could result in improved glycaemic control it was important to establish whether participants were able to appropriately identify hypoglycaemia. Changes in hypoglycaemia awareness were assessed using a validated hypoglycaemic awareness questionnaire (Clarke *et al.*, 1995) (See Appendix 3). Although this questionnaire was developed to identify hypoglycaemic awareness in people with type 1 diabetes (treated using insulin), it was considered appropriate to use this questionnaire on people with T2DM treated using insulin as there was no validated tool to assess hypoglycaemia awareness in people with T2DM. Lack of hypoglycaemic awareness would indicate that the participant would not be safe to be involved in a study that might increase the risk of hypoglycaemia. The hypoglycaemia awareness questionnaire was completed by the participant at the initial assessment appointment and again at the final appointment.

3.7 Measures of dietary intake and adherence

3.7.1 Three-day food record

Dietary intake was estimated from the food record taken at the start of the intervention prior to dietary advice being given and again at week 12. A food record was completed by the participant on the three days prior to attending their assessment appointment. An example of the food diary form is shown in Appendix 2. Written instructions and an example of how to complete the food diary was provided in the food diary. Participants were requested to use household measures to estimate quantities consumed and provide information about brands and preparation methods. At the assessment appointment the primary researcher reviewed the three day food record with the participant to clarify brands, portion sizes and to check for missing foods. Food portion sizes were visually checked against the Carbs and Cals book or app (Cheyette, 2013). If the three-day food record had not been completed or brought to the assessment day the primary researcher interviewed the participant to obtain a three-day food recall of the three days prior to the assessment appointment. At week 12 participants following the

IFD were requested to complete their food record with one fasting day and two non-fasting days.

Analysis of dietary intake was performed using Foodworks 8 (Xyris Software (Australia) Pty Ltd, 2016). Food diaries were entered in to the programme by the primary researcher. If a food was not in the Foodworks 8 database then the most similar food product was used. The mean nutrient intake over the three days was calculated. Mean energy (kcal), protein (g), fat (g) and carbohydrate (g) intake was recorded.

3.7.2 Dietary adherence

Adherence to fasting days was checked verbally at group sessions by the primary researcher. Participants were asked how many days they had fasted, what barriers there were to fasting and what strategies they had found successful. These verbal reports were also compared against the fasting day monitoring record in the participants SMBG monitoring diary. Adherence to portion control strategies (gradual reduction of portion sizes and frequencies) was checked verbally at group sessions by the primary researcher. Participants were asked how they had reduced portion sizes and frequencies, what barriers they had experienced and what strategies they had found successful.

3.7.3 Acceptance of dietary modifications

All participants completed a questionnaire developed by the primary researcher at week 12 to assess how acceptable they found the dietary intervention (see Appendix 8). Questionnaires were completed by the participant whilst in the waiting room before their final appointment. Completed questionnaires were handed back to reception rather than the primary researcher to reduce risk of bias.

3.8 Data handling and analysis

All data was entered in to a Microsoft Excel spreadsheet against a unique participant number. Changes in weight (in kilograms and as a percentage), body mass index, waist circumference, waist: height ratio, OHA and insulin doses and biochemistry were calculated. Changes in mean nutritional intake of energy, protein, fat and carbohydrate were calculated.

3.8.1 Statistical analysis

As this was a feasibility study sample size and effect size calculations were not undertaken. However, other intermittent fasting studies have used sample sizes of 53-54 participants per treatment group (Harvie *et al.*, 2013, Harvie *et al.*, 2011), 23 participants (no control group) (Williams *et al.*, 1998) and 12-13 participants per treatment group (Arguin *et al.*, 2012). Alternate day fasting studies have used sample sizes of 10-83 participants (Hoddy *et al.*, 2014, Klempel *et al.*, 2013c, Eshghinia and Mohammadzadeh, 2013, Eshghinia and Gapparov, 2011, Varady *et al.*, 2013).

Participants who did not complete the study or achieved less than 50% of fasting days during the study were excluded from analysis. Data was analysed using Statistical Package for Social Science (SPSS) for Windows software (version 22, Armonk, NY: IBM Corp). Variables were tested for normality using the Shapiro-Wilk tests and normality plots, and homogeneity of variance using the Levenes test. The data is reported as mean (± standard deviation SD) for normally distributed data and for non-normally distributed data as median (25, 75 percentiles) and categorical data as frequencies. The Independent T-test was used to compare the means at baseline and week 12 of the two treatment groups for normally distributed continuous, independent variables. The Mann Whitney test was used to compare the means of the two treatment groups for non-normally distributed continuous, independent variables. The Dependent T-test was used to compare within group means (eg. change in weight from baseline to end) for normally

distributed continuous, dependent variables. The Wilcoxon Sign Rank test was used to compare within group means for non-normally distributed continuous, independent variables. Two sided tests were used for all variables. Pearson's chi squared test was used to compare the two treatment groups for categorical data. A *P*-value of less than 0.05 was considered statistically significant. Qualitative data obtained from the dietary acceptability questionnaire were grouped by the primary researchers for thematic content analysis. Themes and categories that emerged from the comments made by participants are reported. Individual case results are presented to provide further insight into the use of intermittent fasting diets in people with Type 2 Diabetes (T2DM) who are treated using insulin. This may show independent effects of the different dietary strategies.

CHAPTER 4 RESULTS

This chapter presents the changes in weight, glycaemic control and cardiovascular risk markers measured in obese people with Type 2 Diabetes (T2DM) treated using insulin who followed either a 12 week an intermittent fasting diet (IFD) or portion control diet (PCD). The IFD intervention was structured as two day per week reduced energy intake (550-650kcal / 2300-2700kJ) and five days normal intake making low fat choices. The PCD was used as a comparison group that focused on daily calorie reduction through reduction in portion sizes in line with current New Zealand dietary recommendations for those with T2DM.

It concludes with qualitative data obtained from a dietary acceptability questionnaire given to all participants at the conclusion of the intervention. The results are presented as differences between and within intervention groups. As the numbers of participants who completed the study was small (n=15) the opportunity has been taken to present, where appropriate, individual case results showing the effects of the different dietary strategies. This may provide further insight into the use of intermittent fasting diets in people with T2DM who are treated using insulin.

4.1 Participant characteristics and withdrawal

During the 14-month recruitment period (April 2014 – June 2015) 65 patients were screened to take part in the study. Forty of these patients met the inclusion criteria, agreed to take part in the study and were randomly allocated to either the intermittent fasting diet (IFD) or the portion control diet (PCD) treatment groups. Thirty-two participants attended the initial assessment appointment and first group session. Figure 6 shows the numbers of participants during each stage of the study.

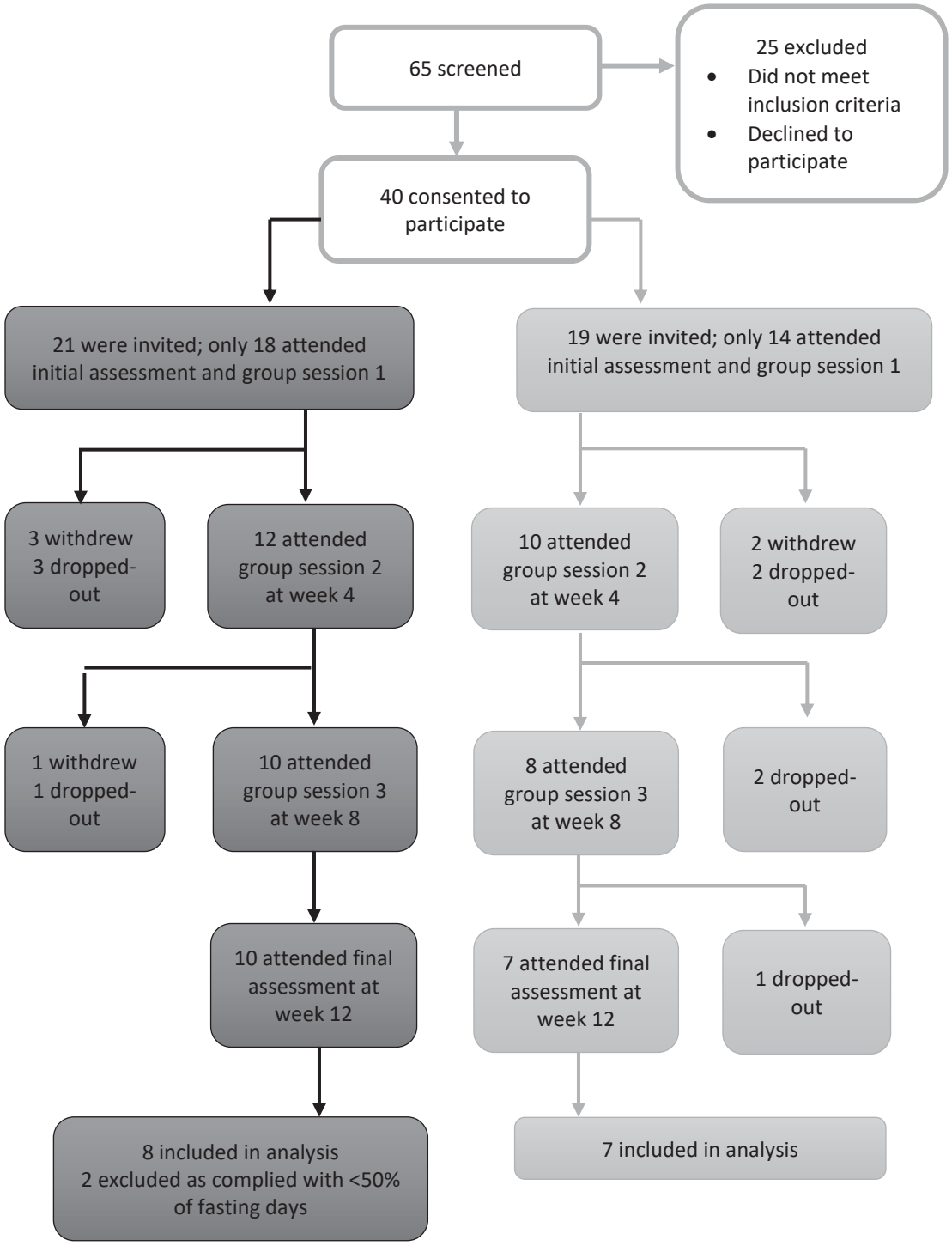


Figure 6 Participant numbers

Five participants allocated to the PCD and three participants allocated to the IFD failed to attend the initial assessment appointment. Total withdrawal / dropout rates for participants who commenced the study were 8 out of 18 (44%) for the IFD group and 7 out of 14 (50%) for the PCD group. Of those who attended the initial assessment and first group session, two participants allocated to the PCD withdrew from the study compared to four allocated to the IFD; reasons for withdrawing included social reasons and on-going illness. Five participants in the PCD and four in the IFD group dropped-out (failed to attend group sessions and did not respond to phone calls). Those who failed to attend their first appointment were contacted by telephone, email or letter to offer another appointment. None of these participants responded, and are considered to have dropped-out.

The IFD protocol required participants to fast for two days each week. Over the 12-week study period this was equivalent to 24 fasting days. Two of the IFD group adhered to less than half the fasting days and were excluded from the final analysis. The mean number (± standard deviation) of fasting days for the remaining eight participants in the IFD group was 21 ± 2.5 days over 12 weeks. Figure 7 shows individual participant compliance with fasting days throughout the 12-week intervention period.

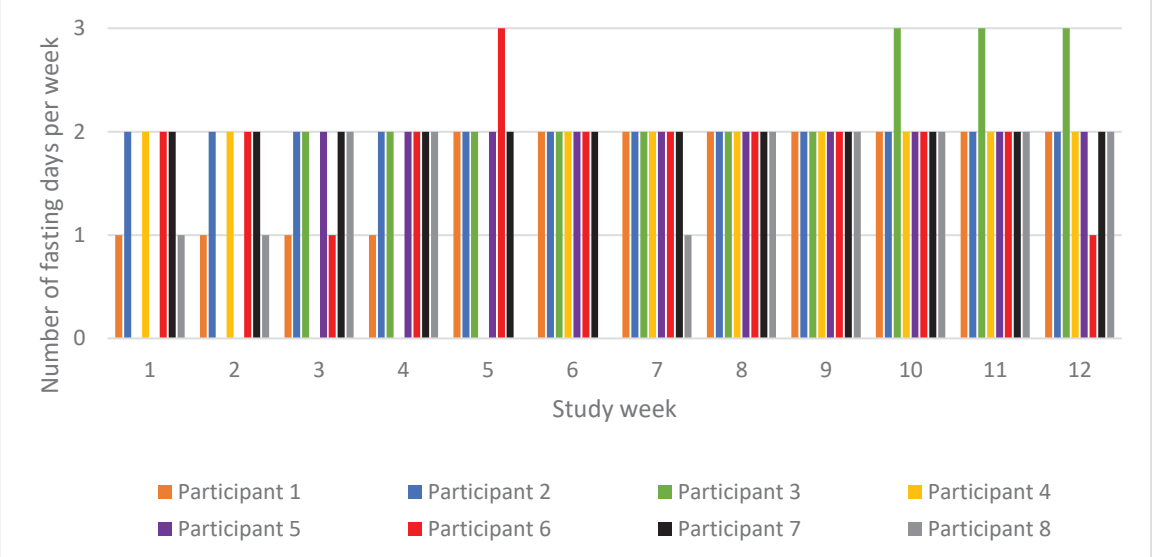


Figure 7 Compliance of participants with fasting days

As is shown in Figure 7, the first three weeks of the intervention had the least consistent fasting days, with more consistent adherence reported in weeks four through 12. The most common self-reported reasons for missing fasting days were being on holiday and not scheduling regular fasting days each week. Table 11 shows the characteristics of participants in the intervention groups at baseline and those who are included in the final analysis.

Table 11 Participant characteristics

Baseline analysis		**PCD (n=14)**	**IFD (n=18)**	**Between group P value**
Gender	Male	8	6	0.178[a]
	Female	6	12	
Age (years)		54.6 ± 6.5 [b]	56.5 ± 7.3 [b]	0.460 [c]
Duration of diabetes (years)		11.5 [d] (8.5-15.0)	13 [d] (9.25-20.25)	0.424 [e]
Ethnicity	NZ European	7	14	0.254[a]
	NZ Maori	3	2	
	Other	4	2	
Final analysis		**PCD (n=7)**	**IFD (n=8)**	**Between group P value**
Gender	Male	3	4	0.782[a]
	Female	4	4	
Age (years)		56.0 (54-57)[c]	60.5 (50-63.25)[c]	0.642[d]
Duration of diabetes (years)		10.7 ± 4.8[a]	17 ± 9.7[a]	0.151[b]
Ethnicity	NZ European	4	6	0.715[a]
	NZ Maori	1	1	
	Other	2	1	

[a] Pearsons Chi-Square P=≤0.05
[b] Mean ± Standard Deviation for normally distributed data
[c] Independent T test P =≤0.05
[d] Median (25^{th}-75^{th} centile) for non-normally distributed data
[e] Mann Whitney U test P =≤0.05
PCD Portion control diet
IFD Intermittent fasting diet

There was no statistical difference between the gender, age, duration of diabetes and ethnicity of participants in the portion control diet (PCD) and those in the IFD intermittent fasting diet (IFD) either at the beginning of the study for those who attended the initial session or for those who were included in the final analysis. There were no significant differences between intervention groups in the number that dropped-out and of those who completed the study. Seven women in the IFD group did not complete the full intervention compared with two women allocated to the PCD group.

4.2 Changes in weight

Weight change for both IFD and PCD groups is shown in Table 12 as changes within and between treatment groups.

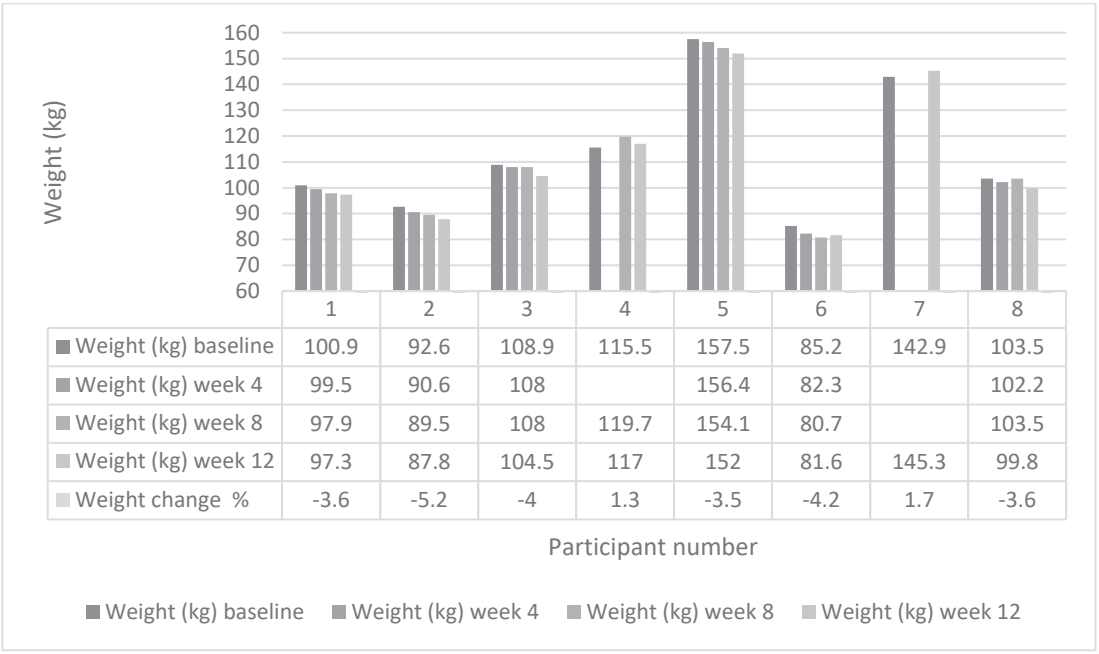
Table 12 Changes in weight and body mass index

	PCD (n=7)	IFD (n=8)	Between group P value
Weight (kg)			
Baseline	111.3 ± 24.8[a]	113.4 ± 24.8 [a]	0.860[c]
Week 12	109.6 ± 19.5 [a]	110.6 ± 25.8[a]	0.492[c]
Change	-1.7 ± 2.5 [a]	-2.7 ± 3.0 [a]	
P value	0.036[d]*	0.125[d]	
Percentage change in weight loss (%)			
Median (25th-75th centile)	-0.8 (-2.8-2.0)[b]	-3.6 (-4.1-0.1)[b]	0.397[e]
Body Mass Index (kg/m^2)			
Baseline	39.9 ± 4.4 [a]	38.4 ± 4.5 [a]	0.520[c]
Week 12	39.3 ± 4.5 [a]	37.4 ± 4.8 [a]	0.480[c]
Change	-0.6 ± 0.9 [a]	-0.96 ± 1.0 [a]	
P value	0.145[d]	0.027[d] *	

*P=≤0.05
[a] Mean ± standard deviation
[b] Median (25th- 75th centile)
[c] Independent T test
[d] Dependent T test
[e] Mann Whitney U test

Participants following both interventions lost weight over the 12-week period. Mean weight change in the PCD group was -1.7 kg (-0.8%) and -2.7 kg (-3.6%) in the

IFD group. The portion control group experienced a significant within-group decrease in body weight (P= 0.036) and the intermittent fasting group a significant within-group decrease in BMI (P= 0.027). The change in weight loss and body mass index (BMI) during the 12-week period was not significant between groups. Figure 8 illustrates the individual weight change for the participants in the IFD group at time points: baseline, weeks 4, 8 and 12 and percentage weight change.



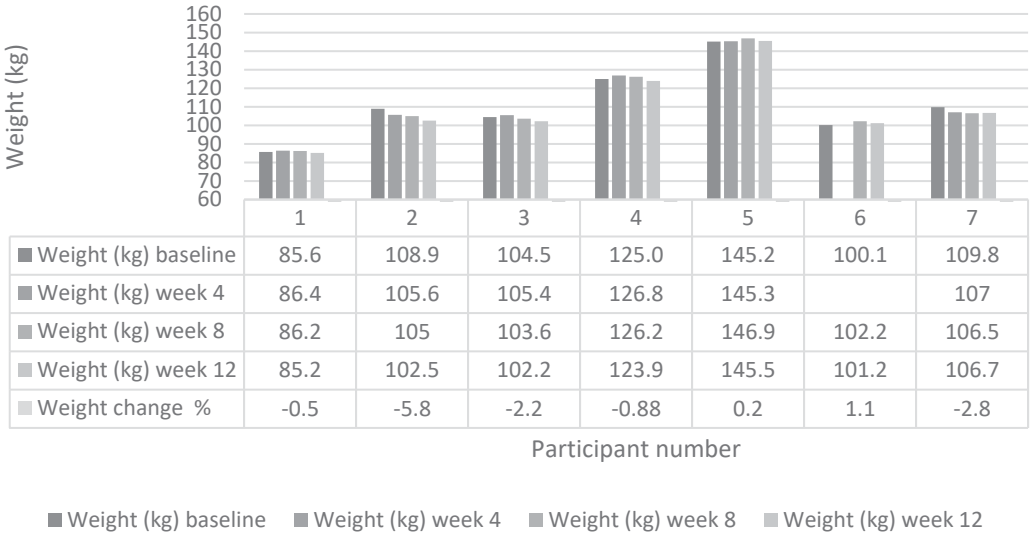
	1	2	3	4	5	6	7	8
Weight (kg) baseline	100.9	92.6	108.9	115.5	157.5	85.2	142.9	103.5
Weight (kg) week 4	99.5	90.6	108		156.4	82.3		102.2
Weight (kg) week 8	97.9	89.5	108	119.7	154.1	80.7		103.5
Weight (kg) week 12	97.3	87.8	104.5	117	152	81.6	145.3	99.8
Weight change %	-3.6	-5.2	-4	1.3	-3.5	-4.2	1.7	-3.6

Empty cell indicates weights that are missing due to participants missing group sessions or equipment not being available.

Figure 8 Individual participant weight change for the IFD group

Six out of the eight participants in the IFD group lost weight during the 12-week intervention. Participant number four gained weight at week 8 due to being away on holiday, however lost weight when she returned from holiday and adhered to the IFD protocol. Monitoring diaries and verbal reporting at support groups indicated that whilst participant number seven was compliant with two days a week fasting throughout the intervention they still gained 2.4 kg. One participant (participant two) attained a clinically significant level of ≥5% weight loss over the 12-week intervention period.

Figure 9 shows the weight change for the participants in the PCD group at time points: baseline, weeks 4, 8 and 12 and percentage weight change.



	1	2	3	4	5	6	7
Weight (kg) baseline	85.6	108.9	104.5	125.0	145.2	100.1	109.8
Weight (kg) week 4	86.4	105.6	105.4	126.8	145.3		107
Weight (kg) week 8	86.2	105	103.6	126.2	146.9	102.2	106.5
Weight (kg) week 12	85.2	102.5	102.2	123.9	145.5	101.2	106.7
Weight change %	-0.5	-5.8	-2.2	-0.88	0.2	1.1	-2.8

Empty cell indicates weights that are missing due to participants missing group sessions or equipment not being available.

Figure 9 Individual participant weight change for the PCD group

Five out of seven of the PCD group lost weight during the 12-week intervention. Two participants gained weight. Participant two attained a clinically significant level of ≥5% weight loss in the 12-week intervention period.

4.3 Dietary intake

To investigate the impact of dietary changes on weight change, the energy, carbohydrate, protein and fat intake of both groups were analysed. Dietary intake was estimated at baseline and week 12 from analysis of a three-day food diary. Daily intake was calculated from the mean of the three-day food diary analysis.

4.3.1 Fasting day intake

The IFD intervention diet was designed to provide approximately 550-650 kcal and 50 g carbohydrate daily on two fasting days per week. This is approximately a 75% reduction in energy intake for these two days. On non-fasting days participants were encouraged to make low fat food choices but not change the quantity of foods eaten from their normal (baseline) dietary intake. Participants following the IFD were required to complete one day of the final three day food record as a fasting day and two days as non-fasting days. Energy, carbohydrate, protein and fat intake on the fasting day for week 12 are shown in Table 13.

Table 13 Energy and macronutrient intake on fasting days

Nutrient	**Intermittent fasting (n=8)**	
	Fasting day	
	Intake	**% of energy intake**
Energy (kcal)	604.7 ± 116.7	
Carbohydrate (g)	57.3 ± 8.9	38%
Protein (g)	51.1 ± 18.6	34%
Total fat (g)	16.1 ± 7.5	24%

The IFD was designed to provide approximately 40% energy from carbohydrates, 33% energy from protein and 27% energy from fat. Actual intakes of energy, carbohydrate and fat showed that participants were meeting these recommendations in week 12.

Analysis of food records showed that one participant in the IFD group achieved a total energy intake of between 550 and 650kcal on the reported week 12 fasting day. Three participants reported consuming under the recommended energy intake, and four participants exceeded the recommended energy intake. Those who over-ate did not exceed 750kcal per fasting day.

The IFD intervention was calculated to provide approximately 60g carbohydrate each day as three meals each providing around 20g carbohydrate. Analysis of

estimated carbohydrate intake on the week 12 fasting day showed that carbohydrate intake ranged from 48 g to 68 g. Six participants out of eight reported carbohydrate intakes that were within 10g of the recommended intake. Two participants consumed only 45 g on the week 12 fasting day.

4.3.2 Fasting day versus non-fasting day dietary intake

The IFD group were advised to eat their usual quantity of food however to make low fat food choices on non-fasting days. As shown in Table 14 dietary analysis of the non-fasting days reported in the three-day food records at weeks 0 and 12 showed that participants did reduce energy intake on non-fasting days (-454.5 kcal per day). However, the decrease was not just from fat restriction (-20.2 g per day) but reductions in carbohydrate and protein intake were also seen. Nutrient and energy reductions between baseline week 0 and week 12 on non-fasting days were not significant.

Table 14 Non-fasting day nutrient intakes

Nutrient	**Intermittent fasting (n=8)**				
	Baseline week 0		**Non fasting day week 12**		
	Intake	**% of energy intake**	**Intake**	**% of energy intake**	P value
Energy (kcal)	1621 ± 761.3[a]		1166.5 ± 330.9[a]		0.089 [c]
Carbohydrate (g)	143.0 (118.5-195.7 [b]	35%	116.3 (93.3-156)[b]	40%	0.069 [d]
Protein (g)	71.7 (52.9-104.7) [b]	18%	67.8 (54.3-73.3)[b]	23%	0.263 [d]
Total fat (g)	56.5 (37.2-74)[b]	31%	36.3 (26.6-53.6)[b]	28%	0.093 [d]

[a] Mean ± standard deviation
[b] Median (25th, 75th centile)
[c] Independent T test
[d] Wilcoxon Sign Rank

4.3.3 Overall dietary intake

Both intervention groups were advised on diets that aimed to achieve weight loss. The PCD group were advised on energy reduction through a decrease in portion sizes and number of portion sizes each day (usual treatment) and the IFD group were advised on energy reduction through two days per week of 75% energy restriction. All groups should therefore show a reduction in energy and macronutrient intake between weeks 0 and 12 if compliant with dietary changes. Table 15 shows the change in energy, carbohydrate, protein and fat intake in both groups from baseline to week 12.

Table 15 Changes in energy and macronutrient intake

Energy (kcal)	**PCD (n=7)** [a]	**IFD (n=8)** [a]	**Between group P value**
Baseline	1872 ± 538.2[a]	1621 ± 761.3 [a]	0.480 [c]
Week 12	1488 ± 301 [a]	952 ± 211.9 [a]	0.001 [c]*
Change kcal	-384 ± 480 [a]	-669 ±707.6 [a]	0.384 [c]
Change %	-15.9 ± 23.9 [a]	-33.2 ± 26.2 [a]	0.206 [c]
P value	0.032 [b]*	0.079 [b]	
Carbohydrate (g)	**PCD (n=7)** [d]	**IFD (n=8)** [d]	**Between group P value**
Baseline	198 (126, 246)[d]	143.0 (118.5-195.7) [d]	0.298 [f]
Week 12	143 (142, 152) [d]	95.5 (78.5-126.0) [d]	0.003 [f]*
Change g	-28 (-105 – 18) [d]	-63.5 (-106.5- -10) [d]	0.298 [f]
Change %	-11.4 (-43.3 – 14.3) [d]	-41.9 (-59 –8.6) [d]	0.203 [f]
P value	0.128 [e]	0.025 [e]*	
Protein (g)	**PCD (n=7)**	**IFD (n=8)**	**Between group P value**
Baseline	104 (74.3-108.6) [d]	71.7 (52.9-104.7) [d]	0.247
Week 12	81 (69.0-90.8) [d]	59.5 (52.1-63.7) [d]	0.011*
Change g	-16 (-27.6-11) [d]	-18.9 (-41.5-3.9) [d]	0.643
Change %	-15 (-25.4-19) [d]	-25.9 (-36.6-9.2) [d]	0.355
P value	0.128 [e]	0.025 [e]*	
Fat (g)	**PCD (n=7)**	**IFD (n=8)**	**Between group P value**
Baseline	65 (63.3-79.7) [d]	56.5 (37.2-74) [d]	0.598 [c]
Week 12	48 (41-82) [d]	30.5 (18.3-40.3) [d]	0.005 [f]*
Change g	-14.2 (-24-8) [d]	-23.8 (-51.2- -5.75) [d]	0.153 [c]
Change %	-22.3 (-36.9-26.7) [d]	-47.1 (-72- -15.1) [d]	0.076 [c]
P value	0.310 [e]	0.024 [b]*	

Where non-parametric data exists, all results for that group are presented as median (25^{th}, 75^{th} centile) to assist in reading the table, however appropriate parametric or non-parametric tests were performed.

* P ≤0.05

[a] Mean ± standard deviation

[b] Paired T test

[c] Independent T test

[d] Median (25^{th}, 75^{th} centiles)

[e] Wilcoxon Sign Rank

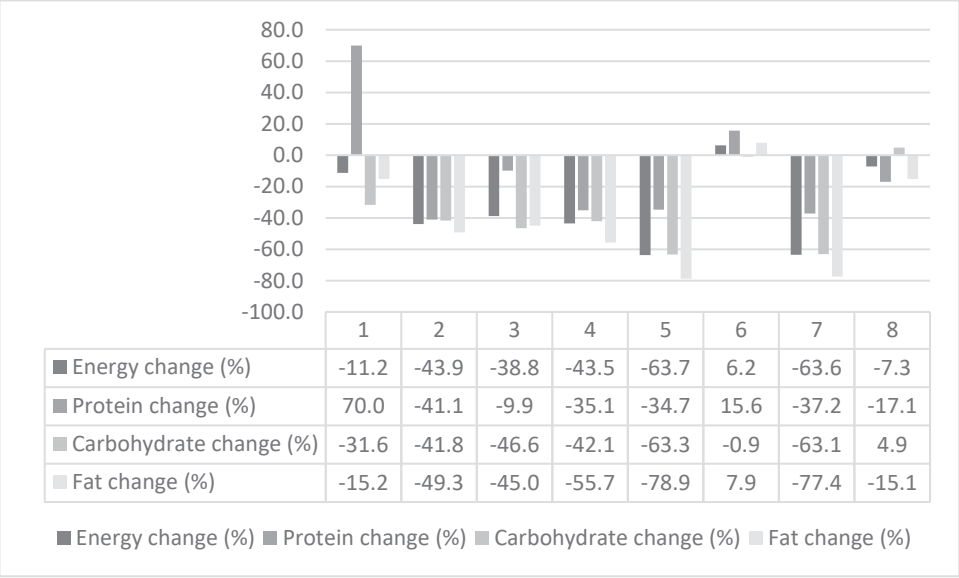
[f] Mann Whitney U test

Both groups reduced their energy, carbohydrate, protein and fat intake between week 0 and week 12. At week 12 the IFD group had significantly lower intakes of energy (P =0.001), carbohydrate (P= 0.003), protein (P= 0.011) and fat (P= 0.005)

than the PCD group. However, the change in intake between groups for energy, carbohydrate, protein and fat intake during the study was not significant.

There was a significant reduction in within group energy intake in the PCD group (P=0.032). Daily energy intake between week 0 and week 12 indicates that participants in the PCD group reduced their energy intake by -384 kcal. Carbohydrate, protein and fat intake all reduced in the PCD between baseline and week 12, however decreases were not significant. Decreases in carbohydrate (P =0.025), protein (P= 0.025) and fat (P=0.024) intake were significant in the IFD group between baseline and end.

Individual results for the IFD participants for percentage change in energy and macronutrient intakes between week 0 and week 12 are shown in Figure 10.



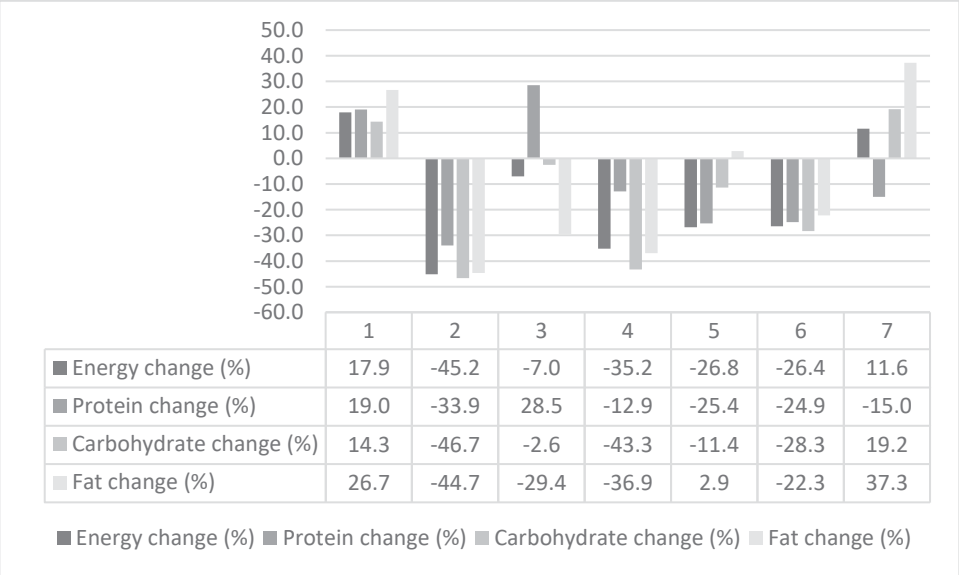
	1	2	3	4	5	6	7	8
Energy change (%)	-11.2	-43.9	-38.8	-43.5	-63.7	6.2	-63.6	-7.3
Protein change (%)	70.0	-41.1	-9.9	-35.1	-34.7	15.6	-37.2	-17.1
Carbohydrate change (%)	-31.6	-41.8	-46.6	-42.1	-63.3	-0.9	-63.1	4.9
Fat change (%)	-15.2	-49.3	-45.0	-55.7	-78.9	7.9	-77.4	-15.1

Figure 10 IFD Changes in individual energy and macronutrient intakes

Individual results showed that six participants in the IFD group had a reduction in energy intake from baseline to week 12. Two participants maintained their estimated energy intake. In the IFD group two participants maintained their carbohydrate intake whilst all other participants reduced their carbohydrate intake.

Participant six had minimal changes in dietary intake, and as was shown in Figure 8 experienced a weight gain of 1.1% between week 0 and 12.

Individual results for the PCD participants for percentage change in dietary intake of energy and macronutrients between week 0 and week 12 are shown in Figure 11.



	1	2	3	4	5	6	7
Energy change (%)	17.9	-45.2	-7.0	-35.2	-26.8	-26.4	11.6
Protein change (%)	19.0	-33.9	28.5	-12.9	-25.4	-24.9	-15.0
Carbohydrate change (%)	14.3	-46.7	-2.6	-43.3	-11.4	-28.3	19.2
Fat change (%)	26.7	-44.7	-29.4	-36.9	2.9	-22.3	37.3

Figure 11 PCD changes in individual energy and macronutrient intake

Five participants in the PCD group had a reduction in energy intake from baseline to week 12 and two had an increase of approximately 200 kcal/day estimated energy intake. In the PCD group two participants increased their carbohydrate intake by approximately 20g per day, whilst four reduced their intake and in one participant carbohydrate intake remained stable. Analysis of the dietary intake of participant one showed that their intake increased between weeks 0 and 12. As is shown in Figure 11 their weight did not change over the 12-week intervention period. Participant seven reported an intake at week 12 which was increased in energy and all nutrients except protein, however experienced a 2.8% weight loss during the intervention.

4.4 Glycaemic control

The secondary objective of this study was to establish hypoglycaemic safety of using intermittent fasting in people with T2DM. The differences in hypoglycaemia rates, HbA1c changes and diabetes medications are presented in this section.

4.4.1 Hypoglycaemic events

Four participants in each group failed to complete blood glucose diaries for all or some of the dietary intervention period. Those who failed to complete blood glucose diaries were asked at each group session / assessment session about the number of hypoglycaemic events they had experienced. None of these participants reported that they had experienced hypoglycaemic events. No participants in either group experienced a severe hypoglycaemic event, i.e. requiring the help of another to access treatment, unconsciousness or hospital admission due to hypoglycaemia. In clinical practice it is considered within acceptable blood glucose control if people with T2DM on insulin or OHA report up to two mild hypoglycaemic events per week (McNamara, 2013). Therefore, the total "acceptable" number of hypoglycaemic events for the IFD group was up to two hypoglycaemic events per participant per week; 2 hypoglycaemic events x 8 participants x 12 weeks = 192 events. The total "acceptable" number of hypoglycaemic events for the PCD group was 2 hypoglycaemic events x 7 participants x 12 weeks = 168 events. The IFD group had a combined number of eight reported mild hypoglycaemic events (4.2%), whilst the PCD group reported 21 mild hypoglycaemic events (12.5%). There was no significant difference in the number of hypoglycaemic events between intervention groups.

One participant in the PCD group and two participants in the IFD group reported experiencing more than two mild hypoglycaemic events a week. One participant in the PCD group experienced three hypoglycaemic events in one week during a hospital admission. This resolved after discharge from hospital. One participant (IFD group) experienced three hypoglycaemic events in one week when reducing

her insulin after a period on steroid treatment. One participant (IFD group) experienced five hypoglycaemic events in week two of the study due to the change to intermittent fasting, and contacted the research team for further modification of her insulin doses.

4.4.2 Hypoglycaemic awareness score

The hypoglycaemic awareness questionnaire (Clarke *et al.*, 1995) gives a score out of seven. A score ≤3/7 indicated a reduced level of hypoglycaemic awareness. A score ≥5/7 indicated an awareness of hypoglycaemia. One participant in the PCD group had a score of four out of seven at the initial assessment. Medical approval was sought for whether it was safe to continue in the study. After review it was deemed appropriate for the participant to continue. All other participants reported being aware of hypoglycaemic events, and all had a score of ≥5/7. Hypoglycaemic awareness scores remained consistent throughout the study.

4.4.3 HbA1c

Serum HbA1c is a long term (three month) measure of blood glucose control. HbA1c was measured at baseline and again at week 12. Table 16 shows the changes in HbA1c during the intervention period for both groups. One participant in the intermittent fasting group did not have their final blood tests performed, and so has been excluded from the analysis of biochemistry.

Table 16 Change in HbA1c

	PCD (n=7)	IFD (n=7)	Between group P value
HbA1c (mmol/mmol)			
Baseline	61 (52-63) [a]	73 (71-87) [a]	0.002 [b]*
Week 12	61 (49-63) [a]	66 (62-70) [a]	0.144 [e]
Change	-3 (-6-1) [a]	-11 (-18-7) [a]	0.003 [e]*
P value	0.108 [c]	0.018 [d]*	

Where non-parametric data exists, all results for that group are presented as median (25^{th}, 75^{th} centile) to assist in reading the table, however appropriate parametric or non-parametric tests were performed.

* P ≤0.05

[a] Median (25^{th}, 75^{th} centile)

[b] Mann Whitney U Test

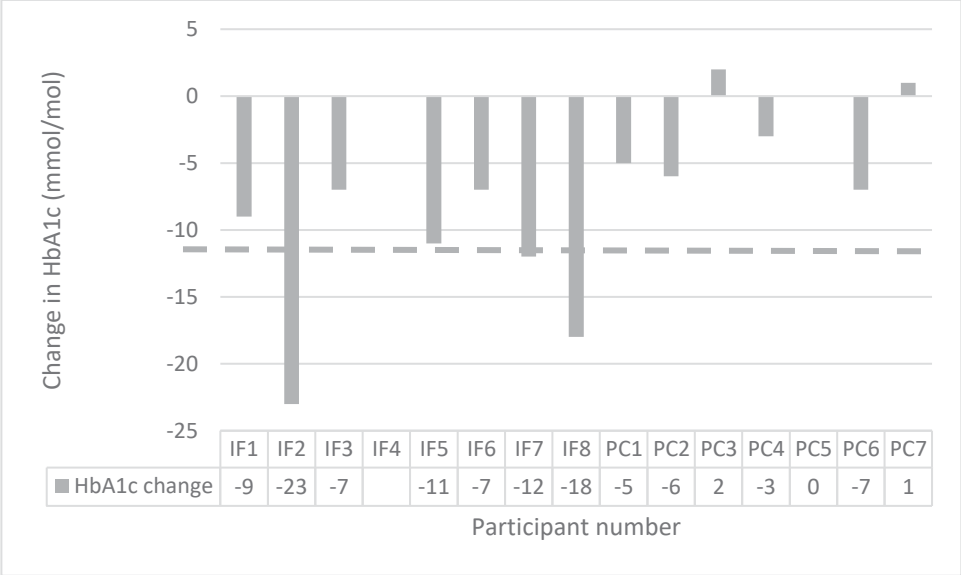
[c] Dependent T Test

[d] Wilcoxon Sign Rank

[e] Independent T Test

Both treatment groups experienced a decrease in median HbA1c. For the PCD group the median HbA1c decreased by 3 mmol/mol (not significant). At 12-weeks the IFD group had a significantly lower HbA1c (P=0.018) compared with baseline. For the IFD group HbA1c decreased by 11 mmol/mol, almost four times that experienced by the PCD group. This difference in change of HbA1c was significant (P=0.003).

Individual participant changes in HbA1c for both groups during the intervention period are shown in Figure 13. The dotted line denotes a clinically significant decrease of 11 mmol/mol (Anderson *et al.*, 2003, Genuth *et al.*, 2003, Aucott *et al.*, 2004)



Empty cell indicates weights that are missing due to participants missing group sessions or equipment not being available.

Figure 12 Changes in individual participant HbA1c levels (mmol/mol) over the 12-week intervention period

Participant IF4 had missing results and was excluded from the analysis. Participant PC5's HbA1c remained stable. All intermittent fasting group participants, who had both sets of blood tests performed experienced reductions in HbA1c. Four participants in the IFD group achieved a clinically significant decrease in HbA1c.

Four participants in the PCD group experienced reductions in their HbA1c, but none reached a clinically significant level of reduction. The HbA1c of participants PC3 and PC7 increased slightly.

4.4.4 Insulin and OHA doses

Participants in the IFD group were advised on insulin and oral hypoglycaemic agent (OHA) reductions as part of the treatment regimen for intermittent fasting. Participants in the PCD group were also advised of insulin and OHA changes if their blood glucose control indicated changes were required. Weekly insulin and OHA doses were calculated based on normal, fasting and non-fasting day doses. All

participants in the IFD had reductions in their insulin doses and two participants had reductions in OHA doses. Two participants in the PCD had reductions in insulin doses and none had changes made to OHA doses.

Table 17 Change in insulin doses during the intervention

	PCD (n=6)	IFD (n=8)	P-value
Total weekly insulin (units)			
Baseline	633 (± 430)	450 (± 191)	0.388 [b]
Week 12	607 (± 426)	262 (± 144)	0.052 [b]
Change	-1 (± 47)	-187 (± 106)	0.002 [b]*
P-value	0.133 [a]	0.002 [a]*	

* P= ≤0.05
mean ± standard deviation
[a] Dependent T test
[b] Independent T test

As is reported in Table 17 there was a significant difference in changes in insulin doses between treatment groups (P=0.002), and also within group reduction in the IFD group (P=0.002). One participant in the PCD group was excluded from the analysis as they changed type of insulin during the intervention period.

4.5 Cardiovascular disease risk measures

Cardiovascular disease is a leading cause of morbidity and mortality in those with T2DM (Fox *et al.*, 2015). In this section the results are presented regarding changes to anthropometric, clinical and biochemical measures of cardiovascular disease. Table 17 reports the results of baseline measurements at week 0, week 12 measurements and changes to waist circumference, waist: height ratio and blood pressure. The target range for waist circumference is <94 cm for men and <80 cm for women (World Health Organization, 2011). The goal range for waist: height ratio is <0.50 (Ashwell *et al.*, 2012). For people with T2DM the blood pressure goal is less than 120/80mmHG (American Diabetes Association, 2016b).

Table 18 Changes to cardiovascular measurements

	PCD (n=7)	IFD (n=8)	Between group P value
Waist circumference (cm)			
Baseline	123.5 (±13.4) [a]	124.0 (± 13.8) [a]	0.939 [c]
Week 12	121.5 (± 14.6) [a]	120.5 (± 13.6) [a]	0.893 [c]
Change	-2.0 (±4.6) [a]	-3.5 (± 2.1) [a]	0.402 [c]
P value	0.294 [b]	0.002 [b]*	
Waist: height ratio			
Baseline	0.74 (± 0.7) [a]	0.72 (± 0.5) [a]	0.603 [c]
Week 12	0.72 (± 0.7) [a]	0.70 (± 0.4) [a]	0.430 [c]
Change	-0.14 (± 0.26) [a]	-0.22 (± 0.15) [a]	0.455 [c]
P value	0.192 [b]	0.004 [b]*	
Systolic blood pressure (mmHg)			
Baseline	137 (± 16) [a]	138 (± 9) [a]	0.901 [c]
Week 12	131 (± 10) [a]	122 (± 27) [a]	0.426 [c]
Change	-7 (± 23) [a]	-17 (± 25) [a]	0.443 [c]
P value	0.456 [b]	0.099 [b]	
Diastolic blood pressure (mmHg)			
Baseline	81 (± 11) [a]	88 (± 19) [a]	0.394 [c]
Week 12	82 (± 9) [a]	79 (± 20) [a]	0.731 [c]
Change	1 (± 14) [a]	-9 (± 14) [a]	0.189 [c]
P value	0.894 [b]	0.109 [b]	

*P= ≤0.05

[a] Mean ± standard deviation

[b] Dependent T Test

[c] Independent T test

Table 18 shows no significant differences in between group changes in waist circumference, waist: height ratio, systolic and diastolic blood pressure. For the IFD group there was a statistically significant within group reduction in waist circumference (p=0.002) and waist: height ratio (p=0.004).

Four participants in the intermittent fasting group and five participants in the portion control group reported taking at least one medication to reduce blood pressure. No changes to these medications were reported by participants during the study period.

The “lipid profile” is the New Zealand standard blood panel to check serum measures of cardiovascular disease. A lipid profile includes total cholesterol, low density lipoprotein (LDL) cholesterol, high density lipoprotein (HDL) cholesterol,

triglycerides and total cholesterol: HDL cholesterol ratio. Table 19 shows the changes in cardiovascular biochemistry between and within treatment groups during the intervention period. One participant in the IFD group did not have their final blood test and so their results have been excluded from this analysis.

Table 19 Changes in cardiovascular biochemistry

	PCD (n=7)	IFD (n=7)	Between group P value
Total cholesterol (mmol/L) Reference range <5.0mmol/L			
Baseline	4.8 ± 1.3 [a]	3.8 ± 0.5 [a]	0.161 [c]
Week 12	4.9 ± 1.2 [a]	4.1 ± 0.4 [a]	0.169 [c]
Change	0.1 ± 0.7 [a]	0.3 ± 0.4 [a]	0.509 [c]
P value	0.688 [b]	0.086 [b]	
LDL cholesterol (mmol/L) Reference range <3.4mmol/L			
Baseline	2.6 ± 0.99 [a]	1.9 ± 0.65 [a]	0.278 [c]
Week 12	2.4 ± 1.10 [a]	2.0 ± 0.52 [a]	0.667 [c]
Change	-0.2 ± 0.76 [a]	0.2 ± 0.30 [a]	0.219 [c]
Pvalue	0.544 [b]	0.098 [b]	
HDL cholesterol (mmol/L) Reference range >1.0mmol/L			
Baseline	1.0 ± 0.29 [a]	1.0 ± 0.24 [a]	0.892 [c]
Week 12	1.0 ± 0.24 [a]	1.1 ± 0.30 [a]	0.595 [c]
Change	-0.08 ± 0.22 [a]	0.1 ± 0.15 [a]	0.080 [c]
P value	0.364 [b]	0.097 [b]	
Triglycerides (mmol/L) Reference range <2.0mmol/L			
Baseline	3.4 (2.0-3.6) [d]	2.3 (1.3-3.5) [d]	0.324 [f]
Week 12	3.5 (2.1-3.9) [d]	2.4 (1.3-3.4) [d]	0.250 [f]
Change	0.0 (-0.7-0.5) [d]	0.0 (-0.7-0.5) [d]	0.949 [f]
P value	0.873 [b]	0.883 [e]	
Total cholesterol: HDL cholesterol ratio Reference range <4.5			
Baseline	4.7 ±0.9 [a]	3.8 ± 0.6 [a]	0.324 [c]
Week 12	4.7 ±1.2 [a]	3.9 ± 1.1 [a]	0.250 [c]
Change	0.04 ±0.43 [a]	0.19 ± 0.55 [a]	0.598 [c]
P value	0.802 [b]	0.405 [b]	

Where non-parametric data exists, all results for that group are presented as median (25^{th}, 75^{th} centile) to assist in reading the table, however appropriate parametric or non-parametric tests were performed.

P ≤0.05

[a] Mean ± standard deviation

[b] Dependent T Test

[c] Independent T test

[d] Median (25^{th}, 75^{th} centile)

[e] Wilcoxon Sign Rank Test

[f] Mann Whitney U Test

No statically significant differences were found between groups or within groups. Seven participants in the intermittent fasting group and four participants in the portion control group reported taking a medication to reduce blood cholesterol levels. No changes to these medications were reported by participants during the study period.

4.6 Patient experiences of dietary interventions

As this feasibility study examined a novel dietary treatment against usual practice, at the completion of the intervention participants in both groups were asked to complete a questionnaire examining the acceptability of the dietary intervention they followed. Questions 1, 2 and 3 were scored on a 5-point Likert scale and questions 4 through 7 being free hand text. The results of questions 1-3 are shown in Table 20.

Table 20 Comparison of dietary acceptability questionnaire scores

	PCD (n=7) Mean (± SD)	IFD (n=8) Mean (± SD)	Between group p value Mann Whitney U test
Question 1: Did you find this diet easy or hard? (1 very hard: 5 very easy)			
Score	3.3 (± 0.5)	3.8 (± 1.4)	0.412
Question 2: Compared to other types of diets that you have done, was it 1 much harder: 5 much easier			
Score	3.6 (± 0.5)	3.7 (±1)	0.618
Question 3: Do you think you could stay on this diet for more than 12 weeks? (1 not at all: 5 definitely)			
Score	4.1 (± 1)	4.0 (± 1.4)	0.902

Participants rated the diets very similarly. Both groups found their diet to be neither easy nor hard, and compared similarly for effort to other weight loss strategies that they had attempted. Participants indicated that they could stay on their respective diet for longer than the 12-week study period.

Participants were also asked to comment on their experiences with the diets that they were following. Comments were grouped in to themes. These are reported in Table 21.

Table 21 Themes from comments in dietary acceptability questionnaire

	PCD (n=7)	IFD (n=8)
What would stop you from staying on this diet for more than 12 weeks?	• Motivation (n=3) • Circumstances (e.g. sickness / stress / travel) (n=2) • Failure to lose weight (n=1) • Blood glucose levels (n=1)	• Motivation (n=1) • Circumstances (e.g. sickness / stress / travel / work) (n=5) • Doing physical activity (n=1) • Nothing (n=1)
What did you like about the diet	• Focus on portion sizes (n=3) • Affordable / Didn't have to buy special foods (n=2) • Felt better (n=1) • Helped to make choices (n=1)	• Simple (n=3) • Planned (n=2) • Felt better (n=2) • Support (n=1) • Seeing results (n=1)
What did you not like about the diet	• Not enough variation (n=1) • Nothing (n=5)	• Fasting (n=1) • Overeating on non-fasting days (n=1) • Measuring food (n=1) • Eating out experiences (n=1) • Paperwork / Blood testing (n=2) • Nothing (n=3)
Any other comments	• Support (n=3) • Diabetes education (n=1)	• Repetitive intake (n=1) • Pattern to eating (n=1) • Support (n=1) • Ease of diet (n=2)

Participants from both groups identified that motivation and change in circumstances such as work, sickness, travel or stress would be key reasons why they would not follow this diet for more than 12 weeks (PCD n=5; IFD n = 6). Individual comments included "Nothing except my head", "Nothing really, just a change in attitude or "Lack of focus and or motivation".

Participants rated both diets generally positively. Similar reasons were given for not continuing with the diets after 12 weeks and none of these reasons were because of the diet. Resources used in the portion control group were noted to be useful, and the simplicity of the intermittent fasting diet thought to be beneficial. Only one participant commented that they did not like to fast but reported that they found it easy to follow a pattern of eating.

4.7 Conclusion of results

Unfortunately, small numbers in each of the treatment groups prevented a robust statistical analysis comparing usual treatment (portion control) to the novel treatment (intermittent fasting). Presenting individual participant results provides insight in to what might be expected in a practice situation when people with T2DM treated using insulin choose to follow an intermittent fasting diet. Similar amounts of weight loss, rates of hypoglycaemia and changes in cardiovascular measures were seen. The participants in the IFD group had a statistically significant reduction in serum HbA1c (long term blood glucose control measure) when compared to the PCD group.

CHAPTER 5 DISCUSSION

This chapter discusses the research results presented in chapter four. The aim of this feasibility study was to investigate the effectiveness and safety of an intermittent fasting diet as an alternative to standard dietary advice for weight reduction in obese adults with insulin dependent T2DM. The IFD investigated was a two day per week reduced energy intake (550-650 kcal / 2300-270 kJ) and five days' normal intake making low fat choices. The PCD was the standard dietary treatment used for comparison. The PCD focused on energy reduction through reduction in portion sizes in line with current New Zealand dietary recommendations for those with T2DM and choosing low fat products (Dietitians New Zealand Diabetes Special Interest Group, 2014, Diabetes New Zealand, 2014). Both dietary interventions were presented as part of a monthly education and support group at which self-managed blood glucose (SMBG), motivation and change management were discussed. This twelve week intervention was conducted at Waitemata District Health Board (DHB), Auckland with participants recruited from the Diabetes Services. Secondary objectives of this study were to investigate the impact of an IFD on hypoglycaemia, glycaemic control and cardiovascular disease risk measures compared to standard treatment. Dietary acceptability of both diets was also investigated.

5.1 Characteristics of participants

The group of participants taking part in this feasibility study were 65% New Zealand European, 17% Maori and 17% from other ethnic groups. Because this was a feasibility study there was no specific sampling of population groups. According to the 2015 Waitemata DHB Population Health Profile, the total population covered by this DHB area is 582,765 of which 63% are NZ European / other, 9.7% Maori, 7.3% Pacific and 20% Asian. It has been estimated that 6% of the Waitemata DHB population has Diabetes, of which 4% are of Maori ethnicity, 10% of Pacific, 11% of Indian and 5% of European / other ethnic groups. Therefore, it can be said that although the participants recruited into the current study were representative of

the Waitemata DHB population, they were not representative of the Waitemata DHB population diagnosed with diabetes. The mean age of participants in this study was 54.6 years (PCD group) and 56.5 years (IFD group). Participants reported having been diagnosed with diabetes for a mean of 12.3 years (PCD group) and 14.9 years (IFD group). The United States Center for Disease Control and Prevention put the mean age of diagnosis of T2DM at 53.8 years in 2011 with 63% of people with T2DM being diagnosed between the ages of 40 and 64 years. Information from the New Zealand Adult Nutrition Survey (2008/09) and New Zealand's Virtual Diabetes Registry (Coppell *et al.*, 2013) show a peak in the reported rates of diabetes at 55 to ≥75 years. This indicates that the participants in the study were diagnosed with diabetes in line with this peak diagnostic age range of 40-75 years for New Zealand and the USA.

Twenty-three of the original forty participants did not complete the full intervention. There was no difference in withdrawal rates between groups. Of those who started the study 44% of the IFD group, and 36% of those in the PCD group did not complete the study. Other studies on intermittent fasting (IF) diets have withdrawal rates of 11% (Williams *et al.*, 1998), 20% (Harvie *et al.*, 2011) and 12% / 28% (Harvie *et al.*, 2013) have been reported, with 22% (Williams *et al.*, 1998), 13% (Harvie *et al.*, 2011) and 32% (Harvie *et al.*, 2013) for the control or daily energy restriction group. In studies on alternate day fasting (ADF) diets for weight loss withdrawal rates of 10% (Johnson *et al.*, 2007), 20% (Varady *et al.*, 2009), 36% (Bhutani *et al.*, 2013b), 50% (Eshghinia and Mohammadzadeh, 2013) and 6% (Varady *et al.*, 2013) have been reported. Therefore, it can be concluded that the withdrawal rates in the current feasibility study were towards the higher end of those reported by other fasting studies, and higher than the IF studies.

To help explain the high rate of participants who did not complete the study it is useful to consider the complexities of diabetes as a chronic condition. Although not investigated as part of this study, depressive symptoms and diabetes-related distress are common in people with T2DM and can be related to poor glycaemic

control and self-management (Aikens, 2012). People with T2DM have the challenge of having to practice high levels of self-control every day without respite (Jenkins *et al.*, 2016). Attrition rates from diabetes self-management education (DSME) can be as high as 57% (Gucciardi *et al.*, 2007), with older people and those who work being at highest risk of attrition. Asking people with a chronic health condition to participate in additional tasks such as dietary changes and increased blood glucose testing could therefore predispose to higher attrition rates.

5.2 Weight loss

No significant differences were observed in weight loss between the IFD group and the PCD intervention groups. Both groups lost weight with the IFD group losing a mean of 2.7 ± 3.0 kg and the PCD group losing a mean of 1.7 ± 2.5 kg over the 12-week intervention. This is equivalent to a weekly weight loss of 0.22 kg and 0.14 kg respectively. As can be seen in Table 22 when weight loss is broken down in to weekly amounts this is substantially less weight loss than was seen in other intermittent fasting diet studies.

Table 22 Weekly weight change in IF studies

	Weight change per week (kg)			
	Fasting group		**Standard treatment group**	**Length of study**
Current study	-0.22		-0.14	12 weeks
Williams *et al.* (1998)	-0.64		-0.36	15 weeks
Harvie *et al.* (2011)	-0.43		-0.25	24 weeks
Arguin *et al.* (2012)	-0.36		-0.47	15 weeks
Harvie *et al.* (2013)	-0.42 (protein limit)	-0.4 (protein free)	-0.31	12 weeks

Clinically, a weight loss of 5% has significant positive health benefits (Anderson *et al.*, 2003, Aucott *et al.*, 2004). A 5-10% reduction in weight has been shown to

reduce HbA1c by approximately 7 mmol/mol, improve serum lipids and reduce blood pressure (Aucott *et al.*, 2004, Anderson *et al.*, 2003). Only one participant in each group achieved ≥5% weight loss. Of participants who lost weight, the mean weight loss in the IFD group was 4% compared to 2.4% from the PCD group. Therefore, those in the IFD group had a more clinically significant amount of weight loss.

It is possible that in the current study obesogenic effects of insulin and OHA treatment resulted in less weight loss in both groups than might have been expected. What was not investigated in the current study was when participants had commenced on insulin therapy in addition to OHA. This might have explained differences in individual weight loss on the IFD intervention. Therefore, it could be argued the results reported in this study that showed noticeably less weight loss than other fasting studies could be due to weight loss being inhibited in people with T2DM who are treated using insulin or sulphonylureas. The only intermittent fasting study to examine the effect of IF on people with diabetes was the study by Williams *et al.* (1998), however participants discontinued their oral hypoglycaemic agents (OHA) before starting the intervention and were not taking insulin. The UK Prospective Diabetes Study Group (1998) found that people with T2DM treated using intensive treatment including insulin and sulphonylureas (an OHA) had significantly higher weight gain than those treated less aggressively, and those treated using insulin had the highest amount of weight gain. Weight gain of between 2-6kg within the first year of starting insulin therapy has been reported (Jansen *et al.*, 2014), however weight gain is not consistent. This weight gain has been attributed to excess food consumption when treating hypoglycaemic episodes which are more common on these treatments, reversing glycosuria so that glucose is stored as fat rather than lost in the urine, and the role of insulin as a growth hormone (Gottesman, 2004, Van Gaal and Scheen, 2015). Reduction in physical activity and an increase in depression has also been associated with commencing insulin therapy (Jansen *et al.*, 2014) which can impact on weight gain.

The number of fasting days each week and difference in energy intake on fasting days contributed to total weekly energy intake which in turn would influence weight loss. The current study used a five day non-fasting and two day (5:2) fasting per week IF regimen as used in the studies by Harvie *et al.* (2011) and Harvie *et al.* (2013). Participants in the IFD group were required to limit their food intake to 550-650kcal on any fasting day and to consume their normal diet, but choosing low fat options where possible on non-fasting days. No energy goals were set for non-fasting days. Results indicated that the mean energy intake was 604.7 ± 116.7 kcal on fasting days and 1166.5 ± 330.9 kcal on non-fasting days. Participants therefore seemed to be compliant with recommended energy intakes on fasting days, however reported a very low energy intake on non-fasting days which may indicate under-reporting by participants. Comparisons between the current study and other intermittent fasting studies as to compliance with fasting day dietary intake recommendations from this study cannot be made as other studies have either provided the fasting day intake in a way to ensure compliance (Williams *et al.*, 1998), or have not published data that specifically shows dietary intake on fasting days (Harvie *et al.*, 2011, Harvie *et al.*, 2013, Arguin *et al.*, 2012).

In the current study both groups reported a decrease in energy intake over the 12-week intervention. The PCD group had a significant (P=0.032) decrease in energy intake between baseline and week 12 of -15.9 ± 23.9%. The IFD group had a non-significant decrease of -33.2 ± 26.2%. At week 12 there was a significant difference between groups for reported daily energy intake (= 0.001) with a mean energy intake of 952 ± 211.9 kcal in the IFD group and 1488 ±301kcal in the PCD group. This is consistent with studies by Harvie *et al.* (2011), Harvie *et al.* (2013), Arguin *et al.* (2012) who reported that intakes in both groups decreased over the study period. Williams *et al.* (1998) did not report actual dietary intakes. A comparison of mean macronutrient intake change for the IF studies is shown in Table 23.

Table 23 Mean macronutrient changes in IF studies

IFD group		Estimated mean macronutrient change (%) from baseline			
		Energy	**Carbohydrate**	**Protein**	**Fat**
Current study		-33.2	-41.9	-25.9	-47.1
Williams *et al.* (1998)		Not reported			
Harvie *et al.* (2011)		-29.7	-25.3	-11.9	-40.1
(Arguin *et al.*, 2012)		Not reported			
Harvie *et al.* (2013)	**Protein limited**	-36.4	-43.2	-14.7	-40.6
	Protein free	-29.2	-42.9	-1.5	-25.4

Change in macronutrient intake in the fasting groups was comparable with other IF studies with the exception of a reduction in protein intake. This study reported a higher reduction in protein intake than in other IF studies.

Anecdotal feedback was received during this study that participants in the IFD group were being more mindful of food choices on non-fasting days, had reduced non-fasting day food portion sizes and were actively making healthier food choices than just choosing low fat options. This may help to explain the significant difference between energy intakes at week 12, and the difference in weight loss between groups. Harvie *et al.* (2013) reported that participants in both fasting diet groups had an energy and carbohydrate intake on non-fasting days which was lower than the dietary intake prescribed. Mean energy intake was 5-600 kcal (2000-2600 kJ) lower than prescribed on non-fasting days. Lack of compensatory intake on non-fasting days was also reported by Varady *et al.* (2013) in an ADF who also noted that feeling of fullness increased during the study period. The results of this study are in line with other fasting diet findings and indicate that intermittent fasting may not result in compensatory eating on non-fasting days.

To achieve a reduction in energy intake and therefore weight loss, participants in the PCD group were advised to reduce their portion sizes and frequency of consumption gradually in line with portion sizes and frequencies as advised by Diabetes New Zealand (2014) healthy eating guidelines. Participants were compliant with recommendations to reduce energy intake through modifications to

portion sizes and frequency. The PCD group had a significant decrease in energy intake between baseline and week 12 of 15.9 ± 23.9%. Daily estimated energy intake based on a three-day food record reduced by 384 ± 480kcal. The four research papers (Williams *et al.*, 1998, Arguin *et al.*, 2012, Harvie *et al.*, 2013, Harvie *et al.*, 2011) in which the effect of intermittent fasting were investigated all had a weight loss group treated by daily energy restriction (usual treatment) as a comparison. Participants in the Williams and Arguin studies were prescribed a daily energy intake, however it was not reported whether they were compliant with this recommendation. Energy intake for the standard treatment group in the study by Harvie *et al.* (2011) reported estimated energy intakes reduced by 410kcal between baseline and three months (-21.6%). Harvie *et al.* (2013) reported a 681.6 kcal (32.5%) reduction in daily energy intake for the standard treatment group. Comparing the percentage reduction in energy intake shows that for this study the standard treatment group had similar energy reductions than reported in other studies.

Amount of weight loss reported by this study when compared to other intermittent fasting studies may have been lower because of differences in activity recommendations during dietary interventions. In this study no recommendations were made to increase activity levels. Participants were encouraged to maintain activity levels during the intervention period. Activity recommendations were included in dietary interventions in the study by Williams *et al.* (1998) and Harvie *et al.* (2013). Although weight loss in the study reported by Williams *et al.* (1998) was highest at 0.64 kg per week, weight loss reported by Harvie *et al.* (2013) was similar to the studies by Arguin *et al.* (2012) and Harvie *et al.* (2011). Across the four studies there does not seem to be sufficient difference in weight loss to suggest that activity recommendations influenced rates of weight loss.

In summary, although weight reduction occurred in both groups in the current study the amount of weight loss was less than might have been predicted from reviewing the results of other intermittent fasting diet studies. These results may

highlight difficulties in comparing rates of weight loss between people with T2DM who are taking insulin and OHA to studies on people who are not taking these medications.

5.3 Glycaemic control

HbA1c is a long term measure of blood glucose and reflects circulating glucose over a three month period (Hare *et al.*, 2012). In the current study both intervention groups experienced a reduction in HbA1c however there was a significant difference in change in HbA1c between groups (P=0.003). Mean reduction in HbA1c in the IFD group was 11 mmol/mol and 3 mmol/mol in the PCD group. A reduction of ≥11 mmol/mol has been associated with clinically significant benefits: reduction in microvascular complications, all-cause mortality and reduction in myocardial infarction (Genuth *et al.*, 2003, UK Prospective Diabetes Study Group, 1998). Four out of eight participants in the IFD group achieved at least 11mmol/mol reduction in HbA1c compared with none of the participants in the PCD group. In this study there were no significant differences in hypoglycaemic rates between treatment groups. Hypoglycaemia rates were low in both groups. One participant in the IFD group had an increase in hypoglycaemia related to the dietary changes compared with no participants in the PCD group. This participant (participant 2) also showed the largest reduction in HbA1c during the study period. Because of the low numbers of participants in this study it is possible that the effect of these five hypoglycaemic events on HbA1c for this one participant skewed the combined HbA1c results from the IF group.

In the current study participants were already used to using self-monitored blood glucose (SMBG) at least twice a day. As part of the safety protocol participants were advised to test four times daily (before meals and before bed). Fasting may increase the risk of hypoglycaemic events in people with T2DM who are treated using insulin or some types of OHA because of changes to normal food intake (Loke *et al.*, 2010). Research on fasting during Ramadan has shown that people with

T2DM who are treated using insulin can safely fast, as long as appropriate education and insulin modifications are made (Ibrahim *et al.*, 2015). The results from the current study support these findings, and suggest that similar education packages can be used to minimise hypoglycaemia risk when following an IF diet.

The low number of individuals affected by hypoglycaemia as a result of medication changes also suggests that both the protocol used for calculating insulin and Sulphonylurea (as described in Chapter 3.5), and the design of the fasting day dietary intake (as described in Chapter 3.4.1) were appropriate.

What is also indicated from the results of the current study is that a 5:2 intermittent fasting regimen may result in a greater reduction in HbA1c than seen when following a portion controlled diet, and that reduction in HbA1c may not be attributed to an increase in hypoglycaemic events as reported events remained low in both intervention groups.

Comparison of findings between the current study and other studies is difficult because of lack of research in to the effects of fasting diets on people with T2DM who are taking insulin. The only other fasting study that included people with T2DM was conducted by Williams *et al.* (1998) in which participants were taken off their OHA before the study commenced. Williams *et al.* (1998) reported that in a group of participants with T2DM there was no significant difference between groups in HbA1c change. The group that undertook a 6:1 fasting regimen experienced a mean reduction in HbA1c of 8 mmol/mol while the standard group had no change in HbA1c. Participants in the study by Williams *et al.* (1998) were not routinely using SMBG but were taught to self-monitor blood glucose (SMBG) levels twice weekly. Hypoglycaemia was not reported although change in fasting plasma glucose at time points during the study was. One participant in the fasting group and three participants in the standard treatment group required to have their OHA re-started during the intervention period due to high blood glucose levels. The results from these participants were excluded from the final analysis in

recognition of the effect of OHA on HbA1c, glucose, lipid and insulin levels. It could be interpreted that any change in SMBG or HbA1c reported in the Williams *et al.* (1998) study may be affected by participants having higher than normal blood glucose levels because of the changes away from usual treatment.

5.4 Cardiovascular disease risk markers

People with T2DM are at higher risk of developing cardiovascular disease than people without T2DM (Daousi *et al.*, 2006, Fox *et al.*, 2015). Waist circumference and waist: height ratio are both indicators of cardiovascular risk (World Health Organization, 2011, Ashwell *et al.*, 2012). Although both groups experienced a decrease in waist circumference and waist: height ratio no significant changes were found between groups in changes to waist circumference or waist: height ratio. Results from studies investigating IF diets have varied with regards to success in reducing waist circumference. A non-significant decrease in waist circumference between groups was reported by Harvie *et al.* (2011), Arguin *et al.* (2012) and Harvie *et al.* (2013). Williams *et al.* (1998) did not report waist circumference. Harvie *et al.* (2011) also found a significant ($P<0.05$) reduction in waist circumference within the fasting group. In no other paper was waist: height ratio reported. The waist circumference results reported in this study are therefore comparable to those found in other IF studies.

Blood pressure remained stable in the PCD group (mean 137/81 mmHg at baseline, mean 131/82 mmHg at week 12) and there was a non-significant reduction in the IFD group (mean 138/88 mmHg at baseline, mean 122/79 mmHg at week 12). Four participants in the IFD and five in the PCD reported taking medication to treat hypertension and these medications did not change during the study. The results in the current study are in line with other IF studies which reported small non-significant reduction in systolic and diastolic BP in both groups (Harvie *et al.*, 2013, Harvie *et al.*, 2011). Williams *et al.* (1998) and Arguin *et al.* (2012) did not report blood pressure. The study by Harvie *et al.* (2011) and Harvie *et al.* (2013) included

participants who were taking antihypertensives, although any changes in blood pressure medications during the intervention period was not reported.

Therefore trends towards a reduction in blood pressure seen during the study period were unlikely to be due to medication (as antihypertensive medication did not change) .It has been reported that for every 1 kg weight loss systolic blood pressure may be reduced by 0.5% and diastolic blood pressure by 0.4% (Anderson and Konz, 2001). Anderson *et al.* (2003) reported in a meta-analysis that 10kg weight loss would result in a reduction of 4.9% and 3.8% in systolic and diastolic blood pressure respectively. Therefore, blood pressure reduction may be attributed to weight loss seen in fasting diets.

Klempel *et al.* (2013a) and Bhutani *et al.* (2013a) investigated alternate day fasting and vascular health and found that brachial artery flow-mediated dilation significantly increased after following an ADF diet comprising 25% energy intake from fat, which resulted in lower blood pressure. In the current study fat intake was less than 25% of daily energy requirements, however brachial artery dilation as a result of fasting is another possible mechanism that could influence blood pressure results.

In this study non-fasting serum lipids were analysed. A joint statement from the European Atherosclerosis Society and the European Federation of Clinical Chemistry and Laboratory Medicine Nordestgaard *et al.* (2016) recommended that the difference between fasting and non-fasting serum lipids are not clinically significant and that non-fasting blood samples be used for assessing serum lipids. By not specifying fasting blood tests in this study it was hoped that participant compliance with blood tests would be increased as it is acknowledged that fasting may lead to avoidance of blood tests (Nordestgaard *et al.*, 2016, Langsted *et al.*, 2008). Only one participant failed to have the final blood test performed.

Baseline and 12 week lipid levels were within recommended levels for total cholesterol, LDL cholesterol and HDL cholesterol in both intervention groups. In both groups triglyceride levels were above recommended levels (week 12 mean 2.4mmol/L IFD group and 3.5mmol/L PCD group). Total cholesterol: HDL ratio was within recommended levels at baseline and week 12 for the IFD group and above recommended levels for the PCD group.

Other IF studies tested lipid levels after a 12 hour fast (Harvie *et al.*, 2013, Harvie *et al.*, 2011, Arguin *et al.*, 2012, Williams *et al.*, 1998). The reporting of fasting lipid levels in other IF studies and non-fasting lipid levels in the current study could influence the comparison of study results. Although differences between non-fasting and fasting lipid levels may not be clinically significant (ref), there may be an effect when reporting research results. A comparison of lipid level changes between studies has been made to highlight variances and similarities in trends. A comparison of changes in lipid levels in fasting studies is shown in Table 24.

Table 24 Comparison of changes in lipid status during IF studies

Treatment Group	Change in mean lipid profile (mmol/L)				
	Total chol	**LDL chol**	**HDL chol**	**Triglyceride**	**Total Chol: HDL ratio**
Current study					
Fasting group	0.3	0.2	0.1	0	0.19
Usual treatment group	0.1	-0.2	-0.8	0	0.04
Williams *et al.* (1998) [a]					
Fasting group	-0.3	-0.15	0.03	-1.15	Not reported
Usual treatment group	-0.3	-0.19	-0.19	-0.66	
Harvie *et al.* (2011) [b]					
Fasting group	-0.3	-0.2	-0.1	0	Not reported
Usual treatment group	-0.8	-0.3	-0.1	-0.3	
Arguin *et al.* (2012) [c]					
Fasting group	-1.07*	-0.29	-0.02	-0.79	Not reported
Usual treatment group	-0.71	-0.44	-0.04	-0.5	
Harvie *et al.* (2013) [c]					
Limited protein fasting group	-0.25	-0.14	-0.02	-0.14	-0.13
Protein free fasting group	-0.23	-0.12	-0.05	-0.13	-0.01
Usual treatment group	-0.15	-0.1	0.02	-0.08	-0.45

[a] Results reported at 20 weeks
[b] Results reported at 12 weeks
[c] Results reported at 25 weeks
[d] Results reported at 12 weeks
* Significant P=<0.05

Taking medication (statins) to reduce serum lipid levels may have also influenced the trends seen in the current study when comparing to results from other studies. In comparison to changes seen from diet, statins have been reported to reduce LDL cholesterol by 18-50% or 0.7-1.4mmol/L, increase HDL cholesterol by 15-51% and reduce triclycerides by 7-30%. (Jacobson *et al.*, 2014, Stone *et al.*, 2015). Seven participants in the IFD group and four in the PCD group were taking lipid lowering medication to control cholesterol. Participants who were taking lipid lowering medications were excluded from the studies by Arguin *et al.* (2012), Harvie *et al.*

(2011). Williams *et al.* (1998) did not state whether participants were taking lipid lowering medications. Harvie *et al.* (2013) included participants who were taking lipid lowering and CVD medications.

5.5 Patient experience of dietary interventions

In the current study participants reported that they found the diet that they were assigned to be acceptable. Both groups found their diet to be neither easy nor hard, and compared similarly for effort to other weight loss strategies that they had attempted. Motivation and a change in circumstance (work / sickness / travel / stress) were given as key reasons for not continuing with either diet. Participants in both diets responded well to the support given. Arguin *et al.* (2012) and Williams *et al.* (1998) did not report on dietary acceptability. Harvie *et al.* (2011) reported quality of life in those on a 5:2 IF or daily energy restriction diet and that there were no major adverse effects of either diet. Changes in mood, hunger, fatigue, headache, constipation and feeling cold were reported as side effects of the IFD. Both groups reported feeling increased energy and health improvements. Limited choices of food was also highlighted by participants as a limitation. Similar results were seen by Harvie *et al.* (2013).

These results support the finding by Krebs and Parry-Strong (2013) that the optimal diet for people with T2DM is the diet that works for them. Both diets were equally well received by both intervention groups. After the study only two participants from the PCD group chose to start the IFD diet. None of the IFD group chose to start the PCD group. All but one participant from the IFD chose to continue with the IFD diet after the study conclusion. The participant who chose not to continue felt that it did not fit with their lifestyle and work shifts.

CHAPTER 6 CONCLUSION

This feasibility study was conducted to evaluate the effectiveness and safety of an intermittent fasting (5:2) style diet designed to result in weight loss in a population with Type 2 Diabetes who were treated with insulin. It was identified that there was a gap in the knowledge of whether fasting diets are an effective and safe weight reduction strategy for people with T2DM on insulin who may also be taking OHA. It was not known whether the obesogenic effect of insulin and certain types of OHA would result in similar rates of weight loss seen in studies on fasting diets in overweight or obese people without diabetes. It was not known whether fasting diets will result in increased rates of hypoglycaemia or hyperglycaemia in those on insulin. This 12-week intervention study compared standard dietary treatment (portion control diet) with an intermittent fasting diet to evaluate differences in weight change, glycaemic control and cardiovascular disease measures.

6.1 Summary of main findings

Similar weight loss was achieved in both groups (IFD: 2.7 ± 3.0kg, PCD 1.7 ± 2.5kg). No significant change in weight was observed between the intervention groups. Reduction in HbA1c was significant (P=0.003) in the IFD group only (IFD: 11 mmol/mol, PCD: 3 mmol/mol). Early indications are that a 5:2 IF diet may result in significant reductions in HbA1c compared to a daily energy restriction diet over a three-month period. With modification of insulin on pre-fasting and fasting day there was no increase in hypoglycaemia.

6.2 Study strengths

This is the first study in New Zealand to explore the feasibility of using a 5:2 intermittent fasting diet as a weight reduction strategy for people with T2DM who are treated using insulin. Other intermittent fasting studies have looked at healthy overweight and obese adults or people with T2DM who have had their medication discontinued. The study design was a randomised controlled trial and there was

regular support from specialist medical, dietetic and nursing staff. Another strength of the study is that the dietary intervention for the IFD used a self-selected meal plan that enabled participants to tailor the diet to their own personal and cultural preferences. Food selections for Maori, Pacific, Asian and Indian food choices were provided to help participants choose appropriate foods.

6.3 Study limitations

Unfortunately, the major limitation to this study was the poor recruitment and retention of participants. Having more subjects who completed the study may have increased the likelihood of attaining significant differences between groups in the results. As noted before, along with chronic diseases such as T2DM comes increased diagnosis of depression and diabetes-related distress (Aikens, 2012) and attrition rates for group education in people with T2DM can be as high as 57% (Gucciardi *et al.*, 2007). This study required a 12-week commitment to following a new diet, changing medications, increasing blood glucose testing and attending evening group sessions. Adding this to the daily burden of living with T2DM is likely to have over-ridden the perceived benefits of weight loss achieved by following a weight reduction diet. It is highly likely that the small sample size of eight participants in the IFD group and seven participants in the PCD group was not large enough to detect significant differences in weight change. Also, although the participants recruited to the study were representative of the Waitemata DHB population, they were not representative of the Waitemata DHB population diagnosed with diabetes. For this to have been the case, more Indian, Pacific and Māori participants would have been required. However, because this was a feasibility study there was no specific sampling of population groups.

The current study did not report when participants had commenced on insulin therapy in addition to OHA. In view of research reporting weight gain during the first year of commencing insulin therapy (Jansen *et al.*, 2011) knowing when

participants had started insulin therapy might help to highlight the different individual responses to IFD.

It is acknowledged that there are limitations to the accuracy of food records (Kirkpatrick *et al.*, 2014). Accuracy of food records can decrease if more than four consecutive days are reported (Thompson and Subar, 2008). Food records can also be compromised by participants willingness to complete a record of accurate and typical food intakes (Thompson and Subar, 2008). To reduce burden participants were requested to complete food records using household measures. To minimise errors the quantities, brands and missing foods were then checked at the initial and final assessment appointments by the primary investigator to reduce errors in recording (Thompson and Subar, 2008) and visual verification of portion sizes was used where appropriate using the Carbs and Cals app or book (Cheyette, 2013). Under reporting of dietary intake may still have occurred during this study as non-fasting day intakes were reported to be lower than expected.

Although lipid levels were reported as part of this study, the tests were non-fasting rather than fasting. This prevented a reliable comparison to be made with other IF studies.

6.4 Application to practice

Although the numbers in this study were small there are several recommendations that can be made with regards to the use of 5:2 IF diets in people with T2DM treated using insulin. It appears that the research from Ramadan fasting (Ibrahim *et al.*, 2015) can be transferred to intermittent fasting diets, and that education, medication changes and supervision are key to safe fasting without an increase in hypoglycaemia. This feasibility study has also indicated that 5:2 IF diets can be recommended as another tool for treatment of obesity in T2DM, and that these diets might reduce HbA1c levels more than other diets.

6.5 Future research

- With the safety and effectiveness of using IF for weight loss in people with T2DM treated using insulin have now been shown, larger studies utilising longer intervention periods to increase the likelihood of achieving significant results should be performed.
- Using both group-based, or one-to-one counselling may help provide comparison of results in real-life clinical settings.
- Larger studies would also show whether the significant results seen in the current study with changes in HbA1c were unique to this group or a benefit observed due to fasting.
- With the reduced amount of weight loss found in this feasibility study this area warrants further research. Studies comparing pre-diabetic, diabetics on OHA and diabetics on insulin to compare the obesogenic influence of insulin and sulphonylureas whilst following an IF diet should be performed.
- As ADF studies have shown an increased rate of weight loss it would be appropriate to investigate whether an ADF or 5:2 IF is more effective in achieving weight loss in people with T2DM.

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APPENDIX 1 Participant information and consent form

Participant Information Sheet
IFOOD Study

Waitemata District Health Board
Best Care for Everyone

Study title:	***IFOOD study* - Intermittent Fasting in Type 2 Diabetes**	
Locality:	Diabetes Service, Waitemata DHB	Ethics committee ref.: 14/NTA/11
Lead investigator:	**Katrina Pace**	Contact phone number: *(09) 486 8900 ext.2505*

You are invited to take part in the IFOOD study. This study is to find out if intermittent fasting diets help overweight people with type 2 diabetes who use insulin to lose weight. This study is being funded and run by the Diabetes Services, Waitemata DHB. It is also the thesis component of a Master of Science Degree in Human Nutrition from Massey University.

Whether or not you take part is your choice. If you don't want to take part, you don't have to give a reason and it won't affect the care you receive. If you do want to take part now, but change your mind later, you can pull out of the study at any time.

This Participant Information Sheet will help you decide if you'd like to take part. It tells you why we are doing the study, what your participation would involve, what the benefits and risks to you might be and what would happen after the study ends. You do not have to decide today whether or not you will participate in this study. Before you decide you may want to talk about the study with other people, such as family, whānau, friends, or healthcare providers. Feel free to do this. There are contact details at the end of this sheet. Please contact us if you have any questions you would like to discuss with us before signing the Consent Form. We will go through this information again with you and answer any questions you may have at the first visit.

If you agree to take part in this study, you will be asked to sign the Consent Form on the last page of this document. You will be given a copy of both the Participant Information Sheet and the Consent Form to keep.

This document is 8 pages long, including the Consent Form. Please make sure you have read and understood all the pages.

What is the purpose of the study?
If you are overweight and want to lose weight there are many diets to choose from. The most successful way to lose weight is the one that individuals finds works for them. This means that health professionals need to investigate new diets and make sure that they are safe for people with diabetes.

Recently a type of eating plan has been used to help people to lose weight. Intermittent fasting - you might have heard it called the "5:2 diet" or "the fast diet". We want to see how this diet measures up against the usual advice that dietitians give to help people lose

weight. Other research suggests that this might be a successful way to lose weight. But no research has been done with people with Type 2 Diabetes who are treated using insulin. We want to make sure that this type of dietary advice can help people with Type 2 Diabetes lose weight, and doesn't lead to an increase in low blood sugars.

The IFOOD study will compare two groups. One group will be asked to follow a healthy eating plus intermittent fasting diet, the other group will be asked to follow a healthy eating plus portion control diet. Healthy eating plus portion control is the usual dietary advice given to help people with Type 2 Diabetes lose weight. You will be randomly put in to either group. By randomly putting you in a group it means we can't influence the results by putting people who might do well in one group or the other. By having a group following our usual advice, which we know generally works well, we can make a comparison of how this new type of diet measures up.

Whether you decide to take part in the study or not, the Diabetes Service at Waitemata DHB offer diabetes Specialists, nurse and dietitians to help you to manage your diabetes.

Ethics for this study have been granted from Northern A Health & Disability Ethics Committee, Reference number 14/NTA/11.

What will my participation in the study involve?

<u>Who are we looking for?</u>

We are looking for 40 men and women to take part in the study. To take part in this study you should:

Have type 2 diabetes
Be taking insulin
Be between 35 and 65 years old
Be overweight with a Body Mass Index (BMI) between 30 and 39
Have an HbA1c between 55 and 90 mmol/mol within the last 3 months
Regularly test your blood sugar at home
Be able to feel when your blood sugar levels go too low
Have no other medical conditions that may prevent you from following a weight loss diet, like kidney disease, severe heart disease or a condition your doctor has told you is "unstable" or not well controlled
Not be pregnant, breastfeeding or planning to be so in the near future
Be able to understand written and spoken English without a translator
Think you can follow a weight loss diet for 12 weeks

<u>What are the two diets?</u>

Healthy eating plus intermittent fasting

Two days a week you will be restricted to eating three very small meals.
Five days a week you will be encouraged to make low fat food choices, with high fibre carbohydrate at each meal. How much you eat of these foods will be the same as you have been eating before starting on the study.

Healthy eating plus Portion Control

Every day of the week you will be asked to choose low fat foods, high fibre carbohydrates at each meal and change your portion sizes to meet the recommendations given by Diabetes New Zealand. The recommendations given by Diabetes New Zealand is the usual dietary advice that all people with Diabetes are encouraged to follow. They are also the recommendations that Dietitians base their advice on.

What does the study involve? What do I have to do?

If you want to take part in the study we will send you a questionnaire to make sure that you can tell if your blood sugar levels go too low. If you can tell if your blood sugars go too low then you meet the criteria for the study. You will be invited to come to North Shore Hospital Diabetes Service for a **first visit**.

At this first visit we will go through the patient information sheet and the consent form with you again and give you a copy.

At the first visit we you will need to bring with you a three day diary of the food that you have eaten (we will give you a diary to fill in).

The Dietitian will take your weight, height, measure your waist and hips, and take your blood pressure.

If you have not had a blood test in the month prior to the study starting you will be given a blood test form to get your Lipid profile (cholesterols and triglyceride) and HbA1c checked.

Expect to put aside about one hour for the interview and the blood test.

You are welcome to bring a support person with you to this meeting.

The study will start within two weeks of you having your first visit.

Come to **three group sessions**, held either during the day or evening once every 4 weeks. Each session will approximately last one hour.

Group sessions will be held to teach you about the diets and give you support and motivation.

You are welcome to bring a support person with you to this meeting.

Come to a **final interview** which will take about one hour.

You will see the Dietitian who will take your weight, height, measure your waist and hips, and take your blood pressure.

They will also complete a questionnaire with you about your awareness of low blood sugar levels, and how you found the dietary and medical advice you were given.

You will be given a blood test form to get your Lipid profile (cholesterol and triglyceride) and HbA1c checked.

You can get this blood test done whilst you are at the hospital.

The study will run for **12 weeks** (three months). You will be randomly put in to one of the diet groups.

For the study you will have **two sets of blood tests** taken – at the start and the finish of the study. These are the usual blood test checks that you would have as part of your diabetes care (HbA1c and cholesterol, triglycerides). When you come to the group sessions you will be weighed and have your waist and hips measured again. Your blood pressure will be checked at the first visit and at the end of the study.

During the study we will be asking you to

Fill in a **diary** every day with your blood sugar readings

Fill in a three day food diary four times over 12 weeks

If you are in the group who is following the intermittent fasting weight loss programme we will ask you to write down how many days that week you managed to fast

At the end of the study you will return to your usual diabetes team appointments.

If you choose not to be in the study at any time, your usual care with the diabetes team and dietitian will continue. Whether you decide to take part in the study or not, the Diabetes Service at Waitemata DHB offer diabetes Specialists, nurse and dietitians to help you to manage your diabetes. This includes helping you to manage your insulin and other medications, checking your blood sugar levels, treating low and high blood sugar levels and dietary advice.

What are the possible benefits and risks of this study?
The main benefit of this study is that, regardless of which group you are in hopefully you will lose weight. By losing weight your blood sugar levels may also improve, and you may feel better.

A possible risk of this study is an increase in how often you have low blood sugar levels. With any diet that cuts down the amount of carbohydrate there is more of a risk of low blood sugar (hypoglycaemia). Usually low blood sugar can be identified and treated quite quickly and easily. This leads to no harm. If low blood sugar is not picked up and treated then it can cause unconsciousness and in extreme cases, death. There is also the potential for high blood sugar levels during the study if your medication is reduced too far. This is less of a risk to health in the short term.

In the group sessions you will be taught about the symptoms of high and low blood sugar and how to treat them. If you are chosen for the intermittent fasting group we will change your medication doses on fasting days. The research doctor will tell you of your new doses on fasting days. You will also be taught how to identify patterns in your blood sugar readings. You will have access to the research team if you feel that you are not managing your blood sugar levels, or need more help. This is the same for both treatment groups, and is the level of care you could expect to receive if you were not involved in the study.

Who pays for the study?
The study is being paid for by Waitemata DHB Diabetes Services. You will not be charged to attend the groups or for any tests associated with the study.

What if something goes wrong?
If you were injured in this study, which is unlikely, you would be eligible for compensation from ACC just as you would be if you were injured in an accident at work or at home. You will have to lodge a claim with ACC, which may take some time to assess. If your claim is accepted, you will receive funding to assist in your recovery.

If you have private health or life insurance, you may wish to check with your insurer that taking part in this study won't affect your cover.

What are my rights?
You do not have to participate in this study. Participation is voluntary. You can withdraw from this study even if you have given consent, at any time. Do you not have to give a reason why you are withdrawing from the study. If you decide not to participate, or withdraw from the study then your usual care from the Diabetes Service will resume.

You will be given access to all information collected about you during the study – weight, waist and hip measurements, blood pressure readings, blood tests, nutrition analysis and questionnaire results.

If any new information about either treatment (intermittent fasting or healthy eating diets) becomes available during the study that may have an impact on your health then we will let you know.

All your information will be kept confidential. Your will be given a study number which all information will be held against. We will use this instead of your name to help privacy.

What happens after the study or if I change my mind?
There may be the opportunity to try the healthy eating plus intermittent fasting diet if you were not in that treatment group, but still keen to try it. At the final interview the dietitian will discuss with you what your needs are for continuing to lose weight or maintaining your weight loss.

Your usual care with the Diabetes Service will start again after the study has finished. You will return to see your usual Diabetes nurse, doctor and dietitian.

Information collected during the study will be kept for 10 years in secure storage facilities.

Blood collected for blood tests during the study will be destroyed as part of usual practice.

You can choose to be informed of the study results within six months of the study finishing.

Who do I contact for more information or if I have concerns?
If you have any questions, concerns or complaints about the study at any stage, you can contact:

Katrina Pace, Dietitian
(09) 486 8900 ext. 2505
Katrina.pace@waitematadhb.govt.nz

Dr Catherine McNamara
(09) 486 8900 ext. 2505
Catherine.McNamara@waitematadhb.govt.nz

If you want to talk to someone who isn't involved with the study, you can contact an independent health and disability advocate on:

Phone: 0800 555 050
Fax: 0800 2 SUPPORT (0800 2787 7678)
Email: advocacy@hdc.org.nz

For Maori health support please contact :

If you require Māori cultural support talk to your whānau in the first instance. Alternatively you may contact the administrator for He Kamaka Waiora (Māori Health Team) by telephoning 09 486 8324 ext 2324

If you have any questions or complaints about the study you may contact the Auckland and Waitematā District Health Boards Maori Research Committee or Maori Research Advisor by telephoning 09 486 8920 ext 3204

You can also contact the health and disability ethics committee (HDEC) that approved this study on:

Phone: 0800 4 ETHICS
Email: hdecs@moh.govt.nz

Consent Form

IFOOD Study

Please tick to indicate you consent to the following

I have read and I understand the Participant Information Sheet.	Yes ☐	No ☐
I have been given sufficient time to discuss with family / whanau or a friend whether or not to participate in this study.	Yes ☐	No ☐
I have had the opportunity to use a legal representative, whanau/ family support or a friend to help me ask questions and understand the study.	Yes ☐	No ☐
I understand that taking part in this study is voluntary (my choice) and that I may withdraw from the study at any time without this affecting my medical care.	Yes ☐	No ☐
I consent to the research staff collecting and processing my information, including information about my health.	Yes ☐	No ☐
If I decide to withdraw from the study, I agree that the information collected about me up to the point when I withdraw may continue to be processed.	Yes ☐	No ☐
I consent to my GP or current provider being informed about my participation in the study and of any significant abnormal results obtained during the study.	Yes ☐	No ☐
I agree to an approved auditor appointed by the New Zealand Health and Disability Ethic Committees, or any relevant regulatory authority or their approved representative reviewing my relevant medical records for the sole purpose of checking the accuracy of the information recorded for the study.	Yes ☐	No ☐
I understand that my participation in this study is confidential and that no material, which could identify me personally, will be used in any reports on this study.	Yes ☐	No ☐
I understand the compensation provisions in case of injury during the study.	Yes ☐	No ☐

I know who to contact if I have any questions about the study in general.	Yes ☐	No ☐
I wish to receive a summary of the results from the study.	Yes ☐	No ☐

I am satisfied with the answers I have been given regarding the study and I have a copy of this consent form and information sheet.	Yes ☐	No ☐
I understand my responsibilities as a study participant.	Yes ☐	No ☐

I hereby consent to take part in this study.

Participant's name:

Signature: Date:

Declaration by member of research team:

I have given a verbal explanation of the research project to the participant, and have answered the participant's questions about it.

I believe that the participant understands the study and has given informed consent to participate.

Researcher's name:

Signature: Date:

APPENDIX 2 Example food record form

IFOOD Study - Intermittent Fasting in Type 2 Diabetes
Three Day Food Diary

Candidate number: **Screening / 1 /2 /**
Final
Date:

If you have any questions or concerns about the form please feel free to contact Katrina Pace, Dietitian on (09) 486 8900 ext 2505

This food diary will show us what you are eating and drinking. It will help us to adjust your insulin and medication amounts.

Please make sure you keep to foods that you usually eat. Write down everything you eat and drink and how much you had of them.

When you have filled out this 3 day food diary please bring it with you to your next IFOOD session.

Here is an example of how to fill out the diary.

Date / Time	Food / Drink	Amount	Comments
25.7.14 *8am* *10am*	*Weetbix* *Milk for weetbix* *Coffee* *Muffin - blueberry (from muffin break)* *Flat white*	*4* *250ml* *100ml milk, 1 tsp sweetener* *1* *Regular size from muffin break*	*Running late for work*

DAY 1

Date / Time	**Food / Drink**	**Amount**	**Comments**

APPENDIX 3 Hypoglycaemic awareness score

IFOOD Study - Intermittent Fasting in Type 2 Diabetes
Hypoglycaemia awareness Questionnaire

Candidate number: **Screening / Final**
Date:

We would appreciate it if you could answer the questions below. If you have any questions or concerns about the form please feel free to contact Katrina Pace, Dietitian on (09) 486 8900 ext

When you have filled out this form please send it back in the postage-paid envelope to Katrina Pace, Dietitian, Diabetes Service, North Shore Hospital, Private Bag 93503, Takapuna, Auckland 0740

1. Check the category that best describes you: (check one only)

I always have symptoms when my blood sugar is low	
I sometimes have symptoms when my blood sugar is low	
I no longer have symptoms when my blood sugar is low	

2. Have you lost some of the symptoms that used to occur when you blood sugar was low?

Yes	
No	

3. In the past six months how often have you had moderate hypoglycaemic episodes? (episodes where you might feel confused, disorientated, or lethargic and were unable to treat yourself)

Never	
Once or twice	
Every other month	
Once a month	
More than once a month	

4. In the past year how often have you had severe hypoglycaemic episodes? (episodes where you were unconscious or had a seizure and needed glucagon or intravenous glucose)

Never		1 time	
2 times		3 times	
4 times		5 times	
6 times		7 times	
8 times		9 times	
10 times		11 times	
12 or more times			

5. How often in the last month have you had readings less than 4mmol/l with symptoms?

Never		1 time / week	
1 to 3 times		2-3 times / week	
4-5 times / week		Almost daily	

6. How often in the last month have you had readings less than 4mmol/l without any symptoms?

Never		1 time / week	
1 to 3 times		2-3 times / week	
4-5 times / week		Almost daily	

7. How low does your blood sugar need to go before you feel symptoms?

3.3 – 3.8 mmol/l	
2.7 – 3.2 mmol/l	
2.2 – 2.6 mmol/ l	
< 2.2 mmol/l	

8. To what extent can you tell by your symptoms that your blood sugar is low?

Never	
Rarely	
Sometimes	
Often	
Always	

Thank you.

Clarke et al 1995

APPENDIX 4 Portion control diet resources

Waitemata District Health Board
Best Care for Everyone

IFOOD

HEALTHY EATING

+

CLEVER PORTIONS

all you need to know

Name:

Contact

Katrina Pace, IFOOD Dietitian

Dr Catherine McNamara

Diabetes Service, North Shore Hospital

(09)486 8920 ext 2505

Katrina.pace@waitematadhb.govt.nz

IFOOD group sessions:

Tēnā koutou katoa.

Welcome to the IFOOD group session. There are three group session. All the groups are held here at North Shore Hospital. You are welcome to bring a support person to all your group sessions and interviews.

Session	Time	Date
Session 1 [week 0]		
Session 2 [week 4]		
Session 3 [week 8]		

In Session 1 we will talk about

- What is diabetes
- Taking control of your health
- The IFOOD plan
- Managing your diabetes on the IFOOD plan

In Session 2 we will talk about

- Support and motivation
- Sharing experiences
- Keeping up your changes and goal setting
- How you are managing your diabetes on the IFOOD plan

In Session 3 we will talk about

- Support and motivation
- Sharing experiences
- Keeping up with the IFOOD plan
- Keeping up your changes and goal setting

Please make sure that you bring this book to every session.
At each session you will be weighed.

Four weeks after group session 3 you will come to a final interview at North Shore Hospital. At this appointment we will talk about what support you need to keep up the changes you have made.

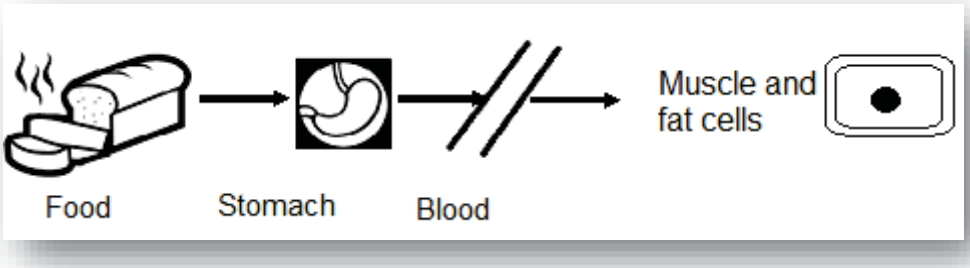
The study will last 12 weeks (3 months).

If you can't come to a group session please contact us on (09) 486 8920 ext 2505

What is diabetes?

Diabetes happens when you have too much sugar (glucose) in your blood.

Your body makes **insulin** that helps keep your **blood sugar** levels under control.

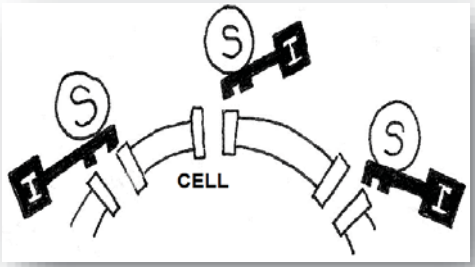


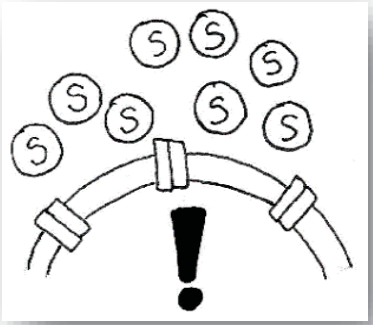
Sugar from starchy carbohydrates travels from the stomach through the blood stream to your body's muscle and fat cells.

Insulin acts like a key unlocking the doors to the muscle and fat cells, and allowing sugar to get in to the cells. Cells then use the sugar as fuel to give energy to the body.

When this works properly sugar entering the blood stream from the stomach is able to exit the blood stream through the muscle and fat cells.

In this way the body can keep control of the amount of sugar in the blood. It keeps the blood sugar in the normal range (4.5 – 9 mmol/L).

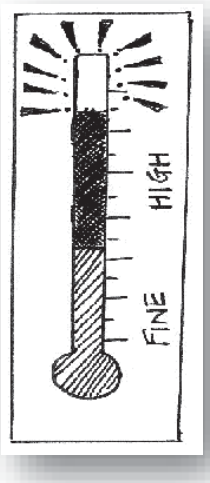




In Type 2 Diabetes the insulin does not work properly, or your body doesn't react to the insulin the way it should.

The cell doors remain closed causing sugar to get backed up in the blood stream. Your blood sugar will go above 9 mmol/L.

Sugar backing up in the blood stream makes blood sugar levels rise, which can create several problems.



- Because sugars are not able to get into muscle and fat cells, your body is not getting the fuel it needs. You might feel tired or fatigued.

- Your body may try to dilute the excess sugar in the blood stream by pulling fluid out of your cells making you dehydrated and thirsty.

- More importantly, over time high blood sugar levels may cause damage to your eyes, kidneys, nerves and heart.

- If blood sugar levels are not controlled properly diabetes can lead to serious complications such as blindness, amputation, kidney failure, heart attack and stroke.

Keeping your blood sugars in the normal range (4.5 – 9 mmol/L) can help stop these problems from happening.

There are four ways to help keep your blood sugar levels in the normal range:

1. Taking the medication that your doctor prescribes you
2. Choosing healthy foods
3. Keeping your weight in the recommended range for you
4. Exercise and physical activity

1. There are medications, tablets and injections which can help you keep your blood sugar levels in the best range. We will be talking more about medications and blood sugar levels later.

2. Choosing healthy foods can help you control your blood sugar levels and your weight.

3. Losing weight is something you can do to help make managing your diabetes easier. Losing weight can make you more sensitive to any insulin you are still making. It can also help you lower your risk of getting serious health problems that can happen with diabetes. Not only that but losing weight can help you to feel better and move better.

4. Exercise and activity can help your own insulin work. It also helps you to lose weight and can help your mood too.

Taking control of your health

There are lots of things that you can do to help keep healthy when you have diabetes. Because you have diabetes you will have access to a doctor or diabetes specialist, practice or diabetes nurse and dietitian. **But the most important person that can help you live a full, active and healthy life is you.**

Your whānau, friends and health professionals can all tell you what you need to do, but you are the one who needs to make the changes. Taking control of your diabetes is one of the most important things you can do to keep healthy. But change and keeping healthy just doesn't happen. Being aware that **you need to take actions** to keep your diabetes in-check is an important step towards taking control of your diabetes.

Change has to start somewhere.

What is your motivation?

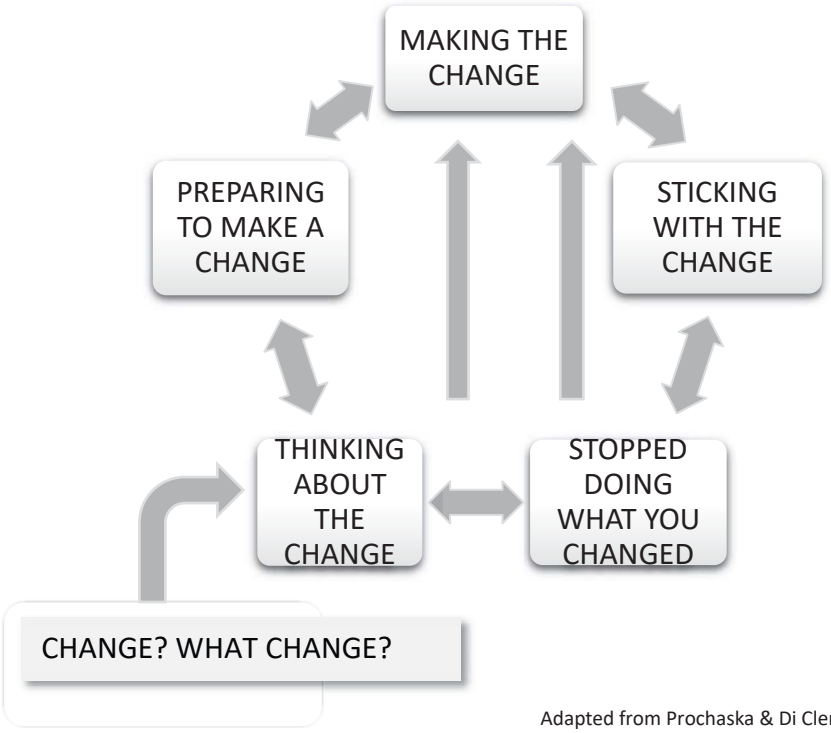
Think about where you want your health and wellbeing to be in the future. Does you diabetes or weight affect your relationships with yourself or others, or activities that you want to do.

If you are going to make changes WHY are you doing it?

Why I want to make changes.

Making changes

Having the reason to make a change and knowing what to do is one thing, but making those changes can be different. It can be useful to know if you are ready to change. Have a look at the picture below.



Adapted from Prochaska & Di Clemente's model of change

Change? What change?	You think everything is okay with what you are doing (but it might not be).
Thinking about the change	You are thinking about changing what you are doing, or making lifestyle changes, but not making any changes yet. There may have to be other things that happen before you can start to think about making changes.
Preparing to make the change	You are thinking of practical ways to help you change what you are doing. You are starting to make plans and setting yourself up to succeed.
Doing the change	Well done, you are making those changes.
Sticking with the change	Well done, you have made those changes and are sticking with them!
Stopped doing what you changed	Your old behaviour has come back again as a regular thing.

Things to think about:

- Where are you in the circle?

- Do you want to get to the next step?

Being mindful

Taking care of yourself is important for everyone, but having diabetes means you should take a bit more care (be mindful) when taking care of yourself.

> Being **mindful** means being present in the moment and making conscious decisions about things.

Learning to be more mindful in your day to day activities can help you focus on keeping your diabetes in-check.

Remember, being mindful means being present in the moment and making conscious decisions about things. Being mindful can help you to decide what changes need to happen in your life to help you achieve your goals.

- Be more aware …
- Be aware of what is going on inside and outside of you – your emotions, your feelings, your environment, the people around you
- Be aware without judgement, criticism or being negative (especially towards yourself)
- Accept things for what they are, not what you want them to be or expect them to be

Diabetes is a long-term condition - it doesn't go away. Everyone can have a bad day and it is important not to be too self-critical about things. It is one day out of one week out of one month out of one year … Try to make decisions and choices in the future which will help you manage your diabetes more effectively.

Things you can do to practice being more mindful

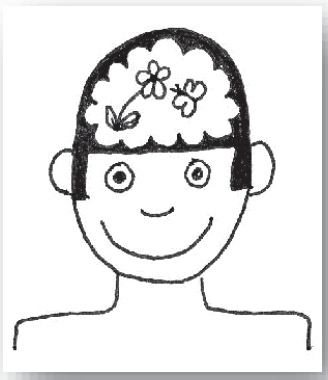
- Don't watch TV or read a magazine while you are eating. Don't judge what you are eating, whether you should be eating it or what will happen to your blood sugars. Focus on your food – the taste, texture, flavours, temperature.

- Walk down the road. Pay attention to the sounds, smells, birds, trees, temperature.

- Live in the moment. For ten minutes each day try not thinking about all the things you have to do / need to do / shopping lists / projects / what-if's. Think clearly about what is going on with your for those 10 minutes. Where are you? How are you feeling? Enjoy being there, breathe and be grateful for the break you have given yourself.

- **[write another idea here that you could do]**

MIND FULL
OR
MINDFUL?



Setting yourself up for success

The last step in successful change is to plan for the future. Life happens. Thinking about what you might do if things get in your way can help you keep to the changes and choices that you make. This will set you up to succeed and make long-lasting changes.

You have already written down your motivation to make changes. You have decided if you are in the right place to change, and what you might need to help you get to a place where you can make changes. You have thought of one way to help you be more mindful. Now let's look at how to set goals.

Think about one goal that you have. Write it down here.

How important is this to me?

Not important → Very important

1 2 3 4 5 6 7 8 9 10

What is my first step to make this happen?

What could stop me making this happen?

If this happens, what can I do to make sure I can keep making this step?

Do I need any support to help me?

Now, how confidence do I feel about making this step?

Not confident → Very confident

1 2 3 4 5 6 7 8 9 10

The IFOOD-CP Plan

Healthy eating + clever portions

Healthy eating + clever portions is how to make sure you are eating the right amounts of the right foods. Being aware (mindful) of what you are eating, and why you are eating it. Sometimes we just need to take some time to make sure we are eating what we think we actually are.

- Having high fibre carbohydrate foods at each meal
- Trying to have similar amounts of carbohydrate at each meal
    - If you stop losing weight but are following the rest of the advice then cutting down your carbohydrate by a serving at each meal
- Eating at least 3-4 servings of fruit and at least3-4 servings of vegetables each day
- Having 2-3 serving of milk or yoghurt each day
- Eating 1-2 servings of meat, chicken, fish, eggs or beans each day
- Choosing low fat products instead of high fat foods
- Choosing low sugar foods
- Choosing low salt options where possible or limiting the amount of salt used
- Drinking at least 6-8 cups of fluid a day

This is how everyone should eat, not just people with diabetes. Helping your family and friends to eat this way can help make sure they keep healthy too. And your family and friends can support you by eating this way.

How can I change my portion sizes?

The "Diabetes and Healthy Food Choices" leaflet tells us about portion sizes as well as how many servings you should have eat day.

Here are some good ideas of how to change your portion sizes

- Spend a few days paying attention (being mindful) of what your portion size is and how many servings you are eating each day.

- If you are having more, or less, than the recommended portions then work at **cutting them (or increasing them) by one serving every few days**.

- If you cut down your meat portions then increase your vegetables to keep you full.

What do I eat now?

Food group	What is my portion size now?	What should it be?
Carbohydrates		1 slice of bread, 1 cup pasta or rice, 1 cup cassava, 1 medium potato, kumara or taro, 1 cup cereal, ½ cup muesli
Fruit		1 fruit, ½ cup canned fruit
Non-starchy vegetables		½ cup cooked, 1 cup salad, 1 tomato / carrot
Meat, fish, chicken, eggs, beans		Fits in to the palm of your hand
Milk and yoghurt		1 cup milk, 1 pottle yoghurt
Drinks		200ml

Food group	How many portions do I have a day?	How many should I have?
Carbohydrates		6-8
Fruit		At least 3-4
Non starchy vegetables		At least 3-4
Meat, fish, chicken, eggs, beans		1-2
Milk and yoghurt		2-3
Drinks		At least 6-8

How can I make a change?

What change can I make to my portion sizes / numbers?

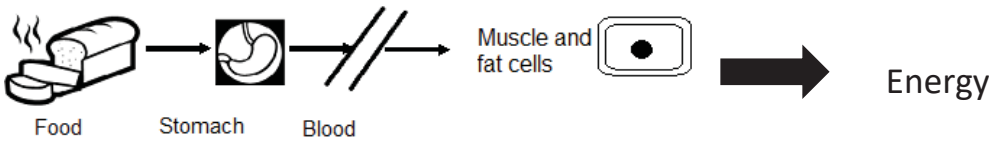
What is something that could stand in my way?

If this happens, how can I keep on track?

How to choose low fat

If you	Try this
Have dark blue or light blue top milk (Whole milk or low fat milk)	Green top milk (Trim milk)
Use butter or margarine	Low fat margarine
Keep the skin on your chicken	Taking the skin off
Keep the fat on your meat	Taking the fat off your meat
Fry food	Grill, bake or stir fry
Use oil	Use oil spray or baking paper
Can see a "low fat" yoghurt, sauces or chips choice on the supermarket shelves	Choose the low fast option instead
Eat pies and pastries	Don't have them so often
Use coconut milk	Choose low fat

Why have carbohydrates at each meal?



Carbohydrates break down in to sugar in your body. Remember you need this carbohydrate to give your body energy. Having carbohydrates at each meal will help to keep your blood sugar level. If you miss carbohydrates but still have taken your insulin then your blood sugar level may go too low.

It is important to have similar amounts of carbohydrate at each meal.

What are the best kinds of carbohydrate to have?

The best kinds of carbohydrate to have are high fibre. These are:

- Wholemeal, wholegrain or brown breads, cereals, chapatti, roti
- Pasta or rice
- Starchy vegetables, like potato, kumara or taro
- Fruit

Managing your diabetes on the IFOOD plan

You are using insulin and diabetic tablets (oral hypoglycaemic agents) to control your diabetes. As you start to change your portion sizes and serving numbers your blood sugars might change.

It is very important that you record your food intake and monitor your blood sugar readings in your diary. This will help us make sure that your insulin and medication doses are right.

It is possible that during the IFOOD plan your insulin or diabetic tablet doses will change.

Understanding your blood sugar readings

Testing your blood sugar may seem just one more thing to fit in to life. Having an understanding about what the readings mean and what you can do to improve things is really important in you taking control of your health.

The best range for blood sugar readings is 4.5 - 9mmol/l

Keeping your blood sugar readings in this range will help you stay well and cut down the risk of developing long-term complications.

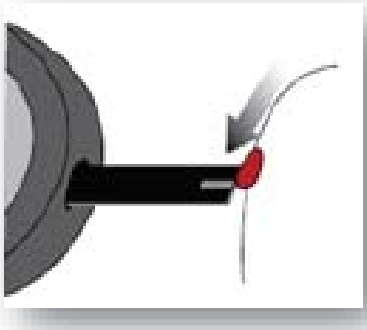
Knowing what your blood sugar readings are will help you and your doctor or nurse work out if you are on the right treatment. This means testing your blood sugars and understanding what to do about the readings if they are outside the best range.

- You might need to do more blood sugar tests if your lifestyle, diet or exercise changes, such as starting the IFOOD-CP diet!
- Eating more, having more stress and exercising less can all make your blood sugar levels higher.
- Eating less and exercising more can make your blood sugar levels lower.

In the IFOOD study we will be making changes to the foods that you eat. This is why it is important to test your blood sugar and keep the diaries we give you.

How to test your blood sugar

1. Wash your hands with warm water. Dry your hands.
2. Get these items ready:
    - testing meter
    - test strips
    - lancet device & lancet (finger-pricker)
    - diary & a pen
3. Put the test strip in the meter to turn it on.
4. Prick your finger and squeeze out a drop of blood. Put the blood on the end of the strip.
5. Wait for the blood sugar number to show up on meter.
6. Write the blood sugar test result in your diary.



How often to test your blood sugar?

As you are taking insulin it is good to test your blood sugar between 1 and 4 times a day. This might be before meals, before bed or when you think your blood sugar levels might be too low or too high.

During the IFOOD study we would like you to test your blood sugar levels

- **Before breakfast**
- **Before lunch**
- **Before evening meal**
- **Before bed**

And

- **If you feel your blood sugars are too low or too high**

Why test so often? By reducing your food intake two days a week we need to make sure that your insulin doses are correct – in other words, your blood sugar levels are not too high or too low. The only way to find out is for you to test your blood sugars.

What does your blood sugar reading mean?

If your blood sugar is	**This means it is**
Below 4	Too low! Call us if you have more than 2 lows in a week.
4.5-9	The right target for before meals.
9-11	A little high before meals.
11-16	Too high! Call us if it stays this high for a week.
Over 16	Too high! Call us if it stays this high for 2-3 days.

Low blood sugar

Low blood sugar is also called “hypoglycaemia” or just “hypo”.

If your blood sugar is	This means it is
Below 4	Too low! Call us if you have more than 2 lows in a week.

When your blood sugar is below 4 mmol/L you might feel:

What to do if your blood sugar is below 4

Have **one** of these choices

- 7-8 large jelly beans
- Have 4-5 dextrose tablets
- 150ml (half a glass) of coke, lemonade (the full sugar drinks) or fruit juice

Sit down and wait for 10 – 15 minutes. Test your blood sugar again.

If your blood sugar in still less than 4 mmol/L then have another 7-8 large jelly beans, 4-5 dextrose tablets or another 150ml of coke or lemonade.

If your blood sugar is over 4 mmol/L then have a meal or a snack such as

- 1 glass (250ml milk)
- A slice of wholegrain bread
- A piece of fruit
- A pottle of low fat yoghurt

As you are taking insulin, always make sure you carry jelly beans or dextrose tablets with you.

Contact us if you have MORE THAN TWO blood tests BELOW 4 in a week.
Make sure you write your blood sugar reading in your diary.

High blood sugar

Too high blood sugar is also called “hyperglycaemia” or “hyper”.

If your blood sugar is	This means it is
Over 16	Too high! Call us if it stays this high for 2-3 days in a row.
11-16	Too high! Call us if it stays this high for a week.

Most people can’t tell how high their blood sugar is without testing. However very high blood sugar levels can make you

- Tired or fatigue
- Depressed or low mood
- Not able to concentrate
- Thirsty
- Passing lots of urine

If your blood sugars are high for a long time then this can lead to serious health problems. Sometimes it is not easy to tell if you have symptoms of high blood sugar. This is why it is important to test your blood sugar levels.

If you are sick or unwell contact your GP. It might be the reason why your blood sugar readings are high.

Contact us if your blood sugar is over 16 mmol/L for 2-3 days in a row, or 11-16 mmol/L for a week.

Make sure you write your blood sugar reading in your diary.

Managing your blood sugar patterns

It may look like your blood sugar diary is just a list of numbers. But understanding patterns in your blood sugar readings can help you and your doctor or nurse to figure out if changes in your medication and/or lifestyle are needed to improve your diabetes control. If your blood sugar control is better then you may feel better and have better health.

Try to work out what the main problem with your blood sugar reading is. Is it going too high or too low? Are you always low before breakfast but high before your evening meal? Keeping a regular record of your blood sugar readings can help you get an idea about when the readings may be out of target.

Recording other information like when you take medication and amount of carbohydrate you eat, stress, exercise etc. can help you understand your blood sugar readings.

Is the problem happening at a particular time, and how often does it happen?

Once you have kept a diary for a few days, you should be able to tell if your blood sugar readings are outside the target at a particular time of day or night.

Don't forget we recommend blood sugar readings are checked:
1. First thing in the morning before breakfast.
2. Before lunch or evening meal
3. Before bed

And
4. If you feel like your blood sugar is too low or too high

A pattern is something that happens frequently – maybe two days out of three, at the same time of day. It can show a problem that needs to be

What's causing the problem?

With practice you can learn to see what is causing your blood sugar readings to be too high or too low at a particular time of day or night. **This skill is called Pattern Management.** Here are some useful tips for good pattern management:

- Blood sugar readings: try to test your sugar readings at the same time each day.
- Medication: try to take them just as they have been prescribed
- Carbohydrate: try to stick to similar amounts at most meals
- Exercise: keep active and try to keep this consistent when you are trying to look for patterns.

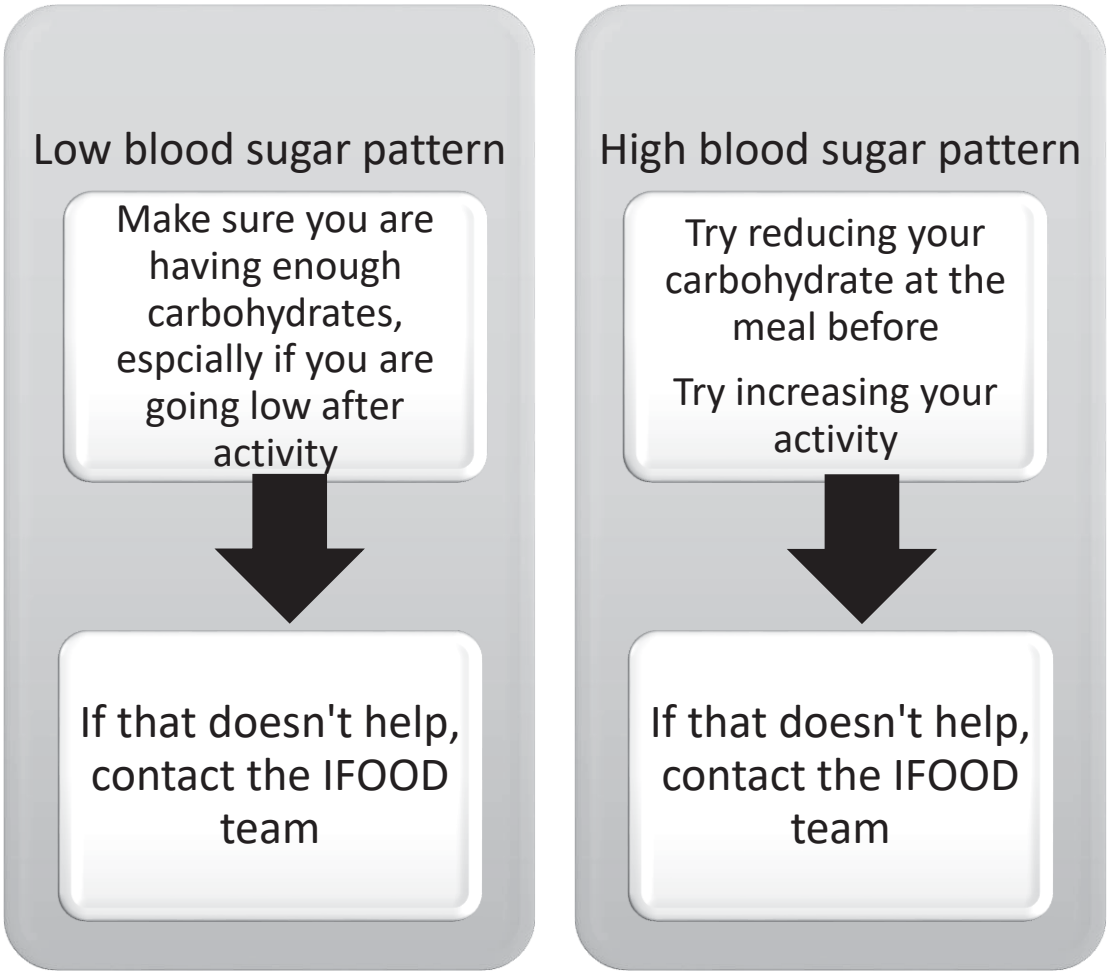
What can you do to fix the problem?

If you have seen a pattern in your blood sugar readings, a change in your medication and/or lifestyle may be needed. For example

- If you are having lots of hypos (low blood sugars), your medication will probably need to be reduced.

- If your before breakfast readings are above target, you may need to have your evening medication increased, possibly reduce dinner time carbohydrate intake or do some activity in the evenings.

- If your readings are mainly high after meals, you could look at reducing your carbohydrate portions or talk to your nurse or doctor about increasing your medication.



The IFOOD team will decide if you need to change your medications, and by how much.

Let's look at an example

Walter has his long acting insulin two times a day – at breakfast and before bed. Here are some of his blood sugar readings. What do you think he needs to do with his medicines?

Day	Before breakfast	Before lunch	Before evening meal	Before bed	In the night
Monday	3.9	8.3		7.5	
Tuesday	4.1		9.4	7.1	3.9
Wednesday	6.6	10.1		8.4	
Thursday	4.0			7.9	

Walter's blood sugar readings before bed are in target. This is good. But he is waking up with very low blood sugar readings. It looks like his blood sugar levels are dropping too low over night.

Walter should …

What to remember about managing your blood sugar patterns …

- Testing and writing down your blood sugar readings will help you to see patterns.
- Patterns might be your blood sugar always being low or high at certain times of the day, or after some meals or activities.
- If you know the patterns, you can fix the problem.

- **Contact the IFOOD team to see if your medication needs to be changed.**

Things to remember

Make healthy choices (green traffic light) from your Diabetes New Zealand leaflets.

Food group	Portion size	Serving number
Carbohydrates	1 slice of bread, 1 cup pasta or rice, 1 cup cassava, 1 medium potato, kumara or taro	6-8, or gradually cut down from where you are now
Fruit	1 fruit, ½ cup canned fruit	3-4
Non-starchy vegetables	½ cup cooked, 1 cup salad, 1 tomato / carrot	3-4
Meat, fish, chicken, eggs, beans	Fits in to the palm of your hand	2-3
Milk and yoghurt	1 cup milk, 1 pottle yoghurt	1-2
Drinks	200ml	6-8

Test your blood sugars four times every day and write down the readings.

This will help you to spot your blood sugar patterns
If changes to carbohydrate or activity don't help improve your patterns then contact the IFOOD team

Contact the IFOOD team if you feel that you are having

- more than 2 low blood sugar (blood sugar less than 4 mmol/l) readings a week
- Over 16 mmol/L for more than 2-3 days in a row
- 11-16 mmol/L for a week.

IFOOD study: Session 2 Information

Managing your blood sugar patterns

It may look like your blood sugar diary is just a list of numbers. But understanding patterns in your blood sugar readings can help you and your doctor or nurse to figure out if changes in your medication and/or lifestyle are needed to improve your diabetes control. If your blood sugar control is better then you may feel better and have better health.

Let's just remember … what can change your blood sugar readings?

Exercise	Will lower your blood sugar
Carbohydrate foods / sugary foods	Will increase your blood sugar
Stress or anxiety	May increase your blood sugar Especially if you comfort eat But might lower your blood sugar if you stop eating
Illness	May increase your blood sugar
Medications	Insulin and your diabetic tablets will lower your blood sugar Other medications may increase your blood sugar

A pattern is something that happens frequently – maybe two days out of three, at the same time of day. It can show a problem that needs to be fixed.

A pattern might be your blood sugars

- Being too high before meals
- Being too low before meals
- Going low (below 4 mmol/l) at the same time each day
- Having to have a snack or else your blood sugars go too low

The best range for blood sugar readings is 4.5 - 9mmol/l

Try to work out what the main problem with your blood sugar reading is. Is it going too high or too low? Are you always low before breakfast but high before your evening meal? Keeping a regular record of your blood sugar readings can help you get an idea about when the readings may be out of target.

Recording other information like when you take medication and amount of carbohydrate you eat, stress, exercise etc. can help you understand your blood sugar readings.

Is the problem happening at a particular time, and how often does it happen?

Once you have kept a diary for a few days, you should be able to tell if your blood sugar readings are outside the target at a particular time of day or night.

Don't forget we recommend blood sugar readings are checked:

- First thing in the morning before breakfast.
- Before lunch or evening meal
- Before bed

And

- If you feel like your blood sugar is too low or too high

What's causing the problem?

With practice you can learn to see what is causing your blood sugar readings to be too high or too low at a particular time of day or night. **This skill is called Pattern Management.** Here are some useful tips for good pattern management:

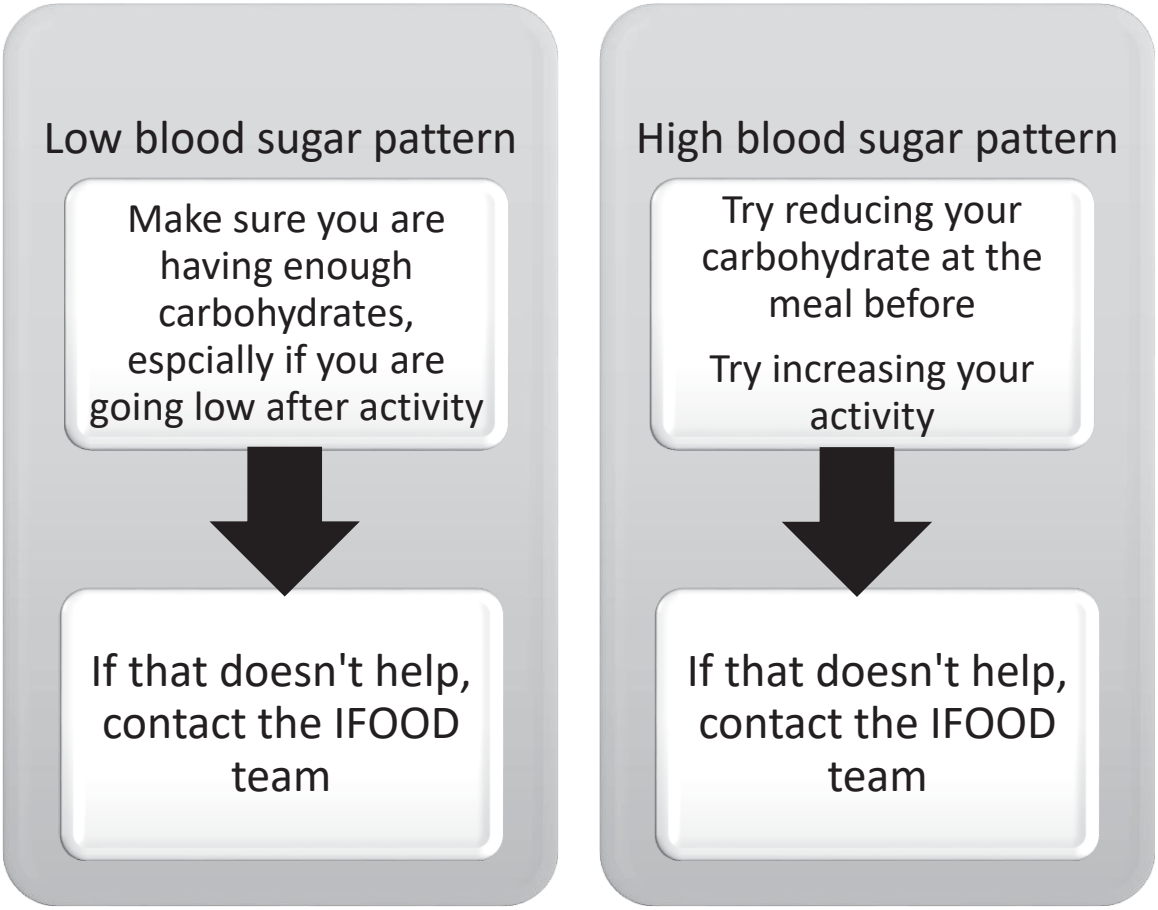
Blood sugar readings: try to test your sugar readings at the same time each day.
Medication: try to take them just as they have been prescribed
Carbohydrate: try to stick to similar amounts at most meals
Exercise: keep active and try to keep this consistent when you are trying to look for patterns.

What can you do to fix the problem?

If you have seen a pattern in your blood sugar readings, a change in your medication and/or lifestyle may be needed. For example:

If you are having lots of hypos (blood sugars below 4 mmol/l),	your medication will probably need to be reduced	You can reduce your insulin by 1-2 units and keep a close eye on your blood sugar levels to make sure you are not running too high, or need to cut your insulin more
If your before breakfast readings are above target (but okay at night)	you may need to have your evening medication increased possibly reduce dinner time carbohydrate intake or do some activity in the evenings.	You can increase your evening insulin by 1 unit and keep a close eye on your blood sugar levels to make sure you are not going low
If your readings are mainly high before meals	you could look at reducing your carbohydrate portions	You can increase your morning insulin by 1 unit and keep a close eye on your blood sugar levels to make sure you are not going low

If you are going to bed high and waking in target or low	Your medication overnight might need to be reduced	Even although you are high at bed, you are dropping overnight. Try reduce your insulin by 1-2 units and keep a close eye on your blood sugar levels to make sure you are not running too high, or need to cut your insulin more



Let's look at an example

Walter has his long acting insulin two times a day – at breakfast and before bed. Here are some of his blood sugar readings. What do you think he needs to do with his medicines?

Day	Before breakfast	Before lunch	Before evening meal	Before bed	In the night
Monday	3.9	8.3		7.5	
Tuesday	4.1		9.4	7.1	3.9
Wednesday	3.3	10.1		8.4	
Thursday	4.0			7.9	

Walter's blood sugar readings before bed are in target. This is good. But he is waking up with very low blood sugar readings. It looks like his blood sugar levels are dropping too low over night.

Walter should …

IFOOD study: Session 3 Information

"Worst case scenario" goal setting: What to do when life gets in the way

Think about the changes that you have made to achieve your health goals. In the box below write down the "worst case scenario" of what could happen if you stop these changes.

How important is it to me that this DOESN'T happen?

Not important → Very important

1 2 3 4 5 6 7 8 9 10

Why did I choose this number and not a lower number?

What might make this "worst case scenario" happen?

Imagine that this happens. What can I do to help myself keep on with these changes?

What support do I need to help me?

Now, how confidence do I feel about doing things to go back to what I was doing before?

Not confident → Very confident

1 2 3 4 5 6 7 8 9 10

Why did I choose this number and not a lower number?

IFOOD study: Session 3 Information

Reading Food Labels

All the information you need to choose healthy foods can be found on food packets or food labels. Being able to read food labels will help you compare different products of the same food type to make better choices.

Try to choose foods that are low in fat, low in salt, sugar and high in fibre

The **ingredients list** starts with the ingredient in the largest amounts first. Foods that may contain ingredients that people may be allergic to such as: gluten, wheat, soy, milk, nuts, shellfish) may be highlighted.

The **Nutrition Information Panel** lists all the main nutrients in the food. Usually listed are energy (KJ and kcal), protein, fat, carbohydrate, sugars, fibre and sodium (salt). The amount of each nutrient is listed per 100g/ 100ml and for each serve.

Use these steps to help you make a healthy food choice

Look at the per 100g or per 100ml column on the Nutrition Information Panel

Nutrition Information Panel (cereal)
Serving Size: 40g
Servings per pack: 10

	Per serve	Per 100g
Energy - KJ	588	1470
- Cal	141	352
Protein (g)	2.9	7.3
Fat – Total (g)	**0.7**	**1.7**
- Saturated	**0.2**	**0.4**
Carbohydrate-Total (g)	28.8	72
- Sugars (g)	**10**	**25**
Dietary Fibre (g)	**2.9**	**7.3**
Sodium (mg)	**123**	**308**
Potassium (mg)	77	193
Iron (mg)	2.7	6.7
Calcium (mg)	178	444

Fat
Look at total fat and saturated fat. Choose products with **less than 10g per 100g total fat and less than 2g per 100g saturated** fat

Sugars
Choose products **with less than 10g per 100g, and less than 5g per 100g for drinks.** If a cereal or muesli bar has dried fruit, then aim for **less than 25g per 100g**

When comparing similar products look for the **lowest in total fat, saturated fat and sugars,** and the **highest in fibre**

Sodium (Salt)
A low salt product **is less than 120mg per 100g** and a high salt product has more than 450mg per 100g. Try to choose products **less than 450mg/100g**

Fibre
Choose products with **more** than **6g per 100g dietary fibre**

Making sense of nutritional claims

The packet of the food you are looking at may also give you information to make healthy choices.

Nutrition claim	What it means
98% Fat Free	These products have only 2% fat but may still be high in sugar and/or salt (sodium), e.g. some crackers, sweets.
'Lite' or 'Light'	These may have less energy, fat, sugar and/or salt but the term 'lite' may be referring to the colour or flavour, e.g. 'Lite' Olive oil – lighter colour. 'Lite' yoghurt – may be lower in sugar or fat.
Low Fat	These products are low in fat but could be high in sugar, e.g. some low fat muesli.
Reduced Fat	The fat content is lower than the standard product but may still be a high fat snack product, e.g. reduced fat potato chips still contain a lot of fat.
No Added Sugar	The product will have no sugar 'added' but may be high in 'natural' sugars, e.g. fruit juice, canned fruit.
Pick the Tick Two Ticks	These foods have met the NZ Heart Foundation criteria for being lower in saturated fat, salt and calories and higher in fibre and calcium. They may not be low in total fat or sugar. Many foods without the label may still be healthy food choices. Check the food labels. The "Two Tick" label shows core healthy food products that are low in fat and often low in sugar too.
'No Added Salt' or 'Salt Reduced'	This means that no salt is added or the salt content is reduced compared to the 'original' product, e.g. no 'added' salt Peanut Butter, salt reduced Baked Beans with less salt than the original.
Cholesterol Free	Often written on foods that may never have cholesterol in, e.g. Rice and sunflower oils. Cholesterol in foods has little effect on your blood cholesterol.
'Diet'	These products are often sweetened with artificial sweeteners and therefore have little or no calories, e.g. 'Diet' soft drinks.
Low Glycaemic Index (GI)	Glycaemic index is an indication of how quickly sugar is used in the body. A food that has a low GI does not always mean that a food is an everyday healthy food choice. It may still be high in sugar, carbohydrates, fat and or calories, e.g. chocolate. Use the food label reading guidelines along with the certified GI logo to make a healthy food choice.
Gluten free	Gluten is a protein found in food. Gluten has not been detected in these products. They may also have the crossed grain logo meaning that it has been approved by Coeliac NZ as being safe for people who need gluten free food.

This information sheet has been developed for use by Waitemata DHB Dietitians. It may be used by other healthcare professionals if appropriate training has been given. Please consult Waitemata DHB Dietitians if you have questions about using this information

Waitemata District Health Board
Best Care for Everyone

YOUR
IFOOD
HEALTHY EATING
+
CLEVER PORTIONS
PORTION CHECKLIST

Name:

Contact
Katrina Pace ,IFOOD Dietitian
Dr Catherine McNamara
Diabetes Service, North Shore Hospital
(09)486 8920 ext 2505
Katrina.pace@waitematadhb.govt.nz

August 2014

IFOOD STUDY Clever Portions:

How many portions are you having?

Food group	Serving size	Food group	Serving size
Breads, cereals & starchy veg	1 slice of bread, 1 cup cooked pasta or rice, 1 cup cassava, 1 medium potato, kumara or taro, 1 cup cereal, ½ cup muesli	Meat, fish, chicken, eggs, beans	Fits in to the palm of your hand
Fruit	1 fruit, ½ cup canned fruit, ½ banana	Low fat milk and yoghurt	1 cup milk (250ml) , 1 pottle yoghurt
Vegetables	½ cup cooked, 1 cup salad, 1 tomato / carrot	Drinks	200ml
Fats and oils	1 teaspoon margarine or oil 2 teaspoons "low fat" margarine 1 tablespoon low fat salad dressing / mayonnaise		

Tick off each box as you eat a portion of that food group. Use the portion size information above to estimate how much you are having. If you are ticking the grey boxes, try to cut down by one grey box (portion) every 2-3 days until you are keeping in the numbered boxes.

If you are not eating all your portions of fruit, vegetables, dairy, meat or drinks, try to slowly increase every 2-3 days.

Date:												
Fruit and vegetables	1	2	3	4	5	6	7	8				
Breads, cereals & starchy veg	1	2	3	4	5	6	7					
Meat, fish, chicken, eggs & beans	1	2	3									
Low fat milk, cheese and yoghurt	1	2										
Fats & oils	1	2	3									
Drinks	1	2	3	4	5	6	7	8				

This resource has been condensed for reproduction purposes. The original contains six of these check lists.

IFOOD STUDY Fridge poster: Clever Portions

Make healthy choices (green traffic light) from your Diabetes New Zealand leaflets.

Food group	Portion size	Serving number
Carbohydrates	1 slice of bread, 1 cup pasta or rice, 1 cup cassava, 1 medium potato, kumara or taro, 1 cup cereal, ½ cup muesli	6-8, or gradually cut down from where you are now
Fruit	1 fruit, ½ cup canned fruit	3-4
Non-starchy vegetables	½ cup cooked, 1 cup salad, 1 tomato / carrot	3-4
Meat, fish, chicken, eggs, beans	Fits in to the palm of your hand	2-3
Milk and yoghurt	1 cup milk, 1 pottle yoghurt	1-2
Drinks	200ml	6-8

If you	Try this
Have dark blue or light blue top milk (Whole milk or low fat milk)	Green top milk (Trim milk)
Use butter or margarine	Low fat margarine
Keep the skin on your chicken	Taking the skin off
Keep the fat on your meat	Taking the fat off your meat
Fry food	Grill, bake or stir fry
Use oil	Use oil spray or baking paper
Can see a “low fat” yoghurt, sauces or chips choice on the supermarket shelves	Choose the low fast option instead
Eat pies and pastries	Don’t have them so often
Use coconut milk	Choose low fat

Test your blood sugars four times every day and write down the readings.

- This will help you to spot your blood sugar patterns
- Try to have similar amounts of carbohydrates at each meal to help keep your blood sugars level

Contact the IFOOD team **(09 486 8920 ext 2505)** if you are having

- more than 2 low blood sugar (blood sugar less than 4 mmol/l) readings a week
- Over 16 mmol/L for more than 2-3 days in a row
- 11-16 mmol/L for a week.

Waitemata District Health Board

Best Care for Everyone

YOUR

IFOOD

HEALTHY EATING

+

CLEVER PORTIONS

DIARY

Name:

Contact

Katrina Pace ,IFOOD Dietitian

Dr Catherine McNamara

Diabetes Service, North Shore Hospital

(09)486 8920 ext 2505

Katrina.pace@waitematadhb.govt.nz

August 2014

Your tablets (your doctor will fill this in for you)

Name (tablet)	**Normal** dose + time	**New** dose + time (date:)

Changing your insulin

Your insulin (your doctor will fill this in for you)

Name (insulin)	**Normal** dose + time	**New** dose + time (date:)

What does your blood sugar reading mean?

If your blood sugar is	This means it is
Below 4	Too low! Call us if you have **more than 2 lows in a week.**
4.5-9	The right target for before meals.
9-11	A little high before meals.
11-16	Too high! Call us if it stays this high for a week.
Over 16	Too high! Call us if it stays this high for 2-3 days.

During the IFOOD study we would like you to test your blood sugar levels

- Before breakfast
- Before lunch
- Before evening meal
- Before bed

And

- If you feel your blood sugars are too low or too high

How to fill in your diary:

Date:	**8.30am**		**12.45**		**6.30**		
Sugar reading	*e.g. 9.3*		*e.g. 5.4*		*e.g. 10.2*		
Insulin	*4 units novomix 30*						
Medication	*Metformin 500mg*						
Comments	*e.g. after dinner went to the movies had popcorn*						

You will be asked to give this diary back to us at your next session. If you would like a copy for your records, please let us know.

Date:							
Sugar reading							
Insulin							
Medication							
Comments							
Date:							
Sugar reading							
Insulin							
Medication							
Comments							

This resource has been condensed for reproduction purposes. The original contains enough to record five weeks of blood glucose levels.

APPENDIX 5 Intermittent fasting diet resources

Waitemata District Health Board
Best Care for Everyone

IFOOD

HEALTHY EATING

+

INTERMITTENT FASTING

all you need to know

Name:

Contact

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The information provided in the work book is identical to that provided for the Portion Control Diet intervention, except for the following pages.

Other hand-outs used for group sessions 2 and 3 are the same as for the portion control group.

The IFOOD-IF Plan

"Intermittent" fasting means that for two days a week you eat a lot less than you normally eat. We call these days your "fast" days. Some fasting diets have either no food during the fasting day, or fast during the day and only eat a breakfast and dinner. In the IFOOD-IF plan you still eat three times a day, only what you eat has a lot less energy (or calories). This is because having a regular intake of foods is safer for people with diabetes. For the five other days of the week you eat a healthy diet – making low fat choices, having carbohydrate at each meal, and eating the same amount of these foods as you usually would.

The days where you eat only three mini-meals are the days that we call "fast" or "fasting" days.

You are being asked to fast for 2 days out of 7 days in the week, for 12 weeks.

It doesn't matter which days of the week you fast.

- You might not want to fast during the weekend if you are at home with your family.
- It might be easier to fast on days that you work.

You don't need to fast on the same days every week. But if you do it might make it easier for you to get in to the routine of fasting.

- You might not want to fast on a day that visitors are coming.
- You might want to fast on days that you are busy or have a lot of appointments so you don't have time to think too much about food.
- You might want to swap days if you have to go to a hui or tangihanga.

You don't need to fast on two days together.

- You could fast on Monday and Wednesdays.
- You might find it works better for you if you fast on Monday and Tuesdays.

You can change the days of the week that you fast.
If you forget or can't fast on one or even two days in a week then still keep going with the study. It is important that we still get your information.

What to remember

Healthy Eating + Intermittent fasting

- Two days a week –
  - choose your foods from the list in this book
- Five days a week –
  - choose low fat foods
  - have carbohydrates at each meal

What to eat on fasting days

What you eat on your fasting days is based on the choices below. Make sure that you have **three "meals" a day**. This will help to keep your blood sugars stable.

Carbohydrates. Each of these is 10g of carbohydrate. You need 20g carbohydrate at each meal (three meals a day). **Choose TWO of these choices AT EACH MEAL.**			
1 thin (sandwich cut) slice bread	½ thick (toast) slice bread	1 weetbix	½ cup porridge cooked in water
1/3 cup cereal	1 cup blueberries	1 mandarin	½ small banana
1 apple	1 small kiwifruit	¼ cup cous cous	3 crackers (e.g. Vitawheat)
1/3 cup mashed potato	1 small egg-sized potato	¼ cup cooked white rice	30g rice / egg noodles
3cm slice kumara	¼ cup cooked pasta	50g (½ medium) boiled green banana	½ small roti
2 small pieces sushi	30g (¼ cup) taro	250ml trim milk	1 pottle diet yoghurt

Add to this

Protein. Choose TW0 choices A DAY			
1 egg	1 small grilled chicken breast / chop	½ cup beef or lamb mince	1 grilled low fat sausage
1 small fish fillet	½ small can tuna in spring water	½ cup dahl, lentils, beans, chickpeas	¾ cup firm tofu

And

Non-starch vegetables. Choose TW0 choices A DAY			
1 cup green salad (lettuce, 1 tomato, cucumber, capsicum)		½ cup boiled mixed vegetables (carrot, broccoli, silverbeet, spinach, peas)	
Drinks. Have at least 6-8 drinks A DAY			
Tea (no sugar – sweetener is okay)	Coffee (no sugar – sweetener is okay)	Herbal tea	Water
Diet fizzy drinks (1-2 maximum)	You have an extra 250ml trim milk allowance a day for tea and coffee or one drink of milk.		

An example of what a fast day meal plan would look like is:

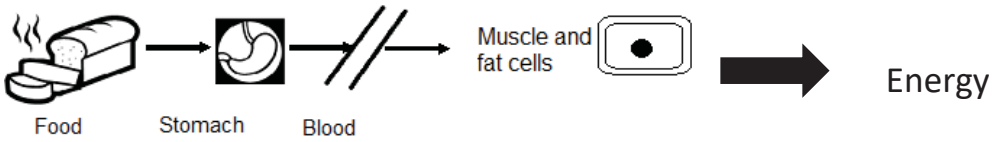
	Fasting day 1	**Fasting day 2**
Breakfast	1 Weetbix with 250ml trim milk	½ cup porridge oats cooked in water 1 cup blueberries
Lunch	1 poached egg, 1 thin (sandwich cut) slice of wholemeal toast, 1 cup of salad and a kiwifruit	3 crackers (e.g. Vitawheat), ½ can tuna in spring water, 1 cup salad and a pottle of diet yoghurt
Evening meal	1/3 cup of mashed potato, 1 small grilled chicken breast, ½ cup cooked veg and a mandarin	½ cup cooked pasta with ½ cup minced beef and 1 cup of salad
Drinks	Tea, herbal tea, coffee, water – 1.5 – 2 litres a day. 250ml trim milk each day in tea and coffee (with optional sweetener)	

Remember, fasting is only for TWO days a week. The rest of the week you eat your usual healthy eating meals.

How to choose low fat

If you	Try this
Have dark blue or light blue top milk (Whole milk or low fat milk)	Green top milk (Trim milk)
Use butter or margarine	Low fat margarine
Keep the skin on your chicken	Taking the skin off
Keep the fat on your meat	Taking the fat off your meat
Fry food	Grill, bake or stir fry
Use oil	Use oil spray or baking paper
Can see a "low fat" yoghurt, sauces or chips choice on the supermarket shelves	Choose the low fast option instead
Eat pies and pastries	Don't have them so often
Use coconut milk	Choose low fat

Why have carbohydrates at each meal?



Carbohydrates break down in to sugar in your body. Remember you need this carbohydrate to give your body energy. Having carbohydrates at each meal will help to keep your blood sugar level. If you miss carbohydrates but still have taken your insulin then your blood sugar level may go too low.

It is important to have similar amounts of carbohydrate at each meal.

What are the best kinds of carbohydrate to have?

The best kinds of carbohydrate to have are high fibre. These are:

- Wholemeal, wholegrain or brown breads, cereals, chapatti, roti
- Pasta or rice
- Starchy vegetables, like potato, kumara or taro
- Fruit

Things to remember

You are only fasting for two days out of every week.

- choose foods from the list on these two days

On the other five days a week –

- choose low fat foods
- have similar amounts of carbohydrates at each meal
- eat the same amounts as you usually do

Test your blood sugars four times every day and write down the readings.

This will help you to spot your blood sugar patterns
If changes to carbohydrate or activity don't help improve your patterns then contact the IFOOD team

Contact the IFOOD team if you feel that you are having

- more than 2 low blood sugar (blood sugar less than 4 mmol/l) readings a week
- Over 16 mmol/L for more than 2-3 days in a row
- 11-16 mmol/L for a week.

IFOOD STUDY Fridge poster: Intermittent fasting

IFOOD STUDY Name:

Make sure that you have three "meals" a day on your fasting days. Breakfast, lunch and dinner

Carbohydrates. Each of these is 10g of carbohydrate. You need 20g carbohydrate at each meal (three meals a day). Choose TWO of these choices AT EACH MEAL.			
1 thin (sandwich cut) slice bread	½ thick (toast) slice bread	1 weetbix	½ cup porridge cooked in water
1/3 cup cereal	1 cup blueberries	1 mandarin	½ small banana
1 apple	1 small kiwifruit	¼ cup cous cous3 crackers (e.g. Vitawheat)	
1/3 cup mashed potato	1 small egg-sized potato	¼ cup cooked white rice	30g rice / egg noodles
3cm slice kumara	¼ cup cooked pasta	50g (½ medium) boiled green banana	½ small roti
2 small pieces of sushi	30g (¼ cup) taro	250ml trim milk	1 pottle diet yoghurt

Add to this

Protein. Choose TW0 choices A DAY			
1 egg	1 small grilled chicken breast / chop	½ cup beef or lamb mince	1 grilled low fat sausage
1 small fish fillet	½ small can tuna in spring water	½ cup dahl, lentils, beans, chickpeas	¾ cup firm tofu

And

Non-starch vegetables. Choose TW0 choices A DAY	
1 cup green salad (lettuce, 1 tomato, cucumber, capsicum)	½ cup boiled mixed vegetables (carrot, broccoli, silverbeet, spinach, peas)

Drinks. Have at least 6-8 drinks A DAY			
Tea (no sugar – sweetener is okay)	Coffee (no sugar – sweetener is okay)	Herbal tea	Water
Diet fizzy drinks (1-2 maximum)	You have an extra 250ml trim milk allowance a day for tea and coffee or one drink of milk.		

You are only fasting for two days out of every week.
choose foods from the list on these two days
On the other five days a week –
- choose low fat foods
- have carbohydrates at each meal
- eat the same amounts as you usually do

Contact the IFOOD team **(09 486 8920 ext 2505)** if you feel that you are having
more than 2 low blood sugar (blood sugar less than 4 mmol/l) readings a week
Over 16 mmol/L for more than 2-3 days in a row
11-16 mmol/L for a week.

Medication changes

	Breakfast	Lunch	Dinner	Bed
Non fasting day insulin				
Non fasting day medication				
Pre Fasting day insulin				
Pre Fasting day medication				
Fasting day insulin dose				
Fasting day medication dose				

Waitemata District Health Board
Best Care for Everyone

YOUR

IFOOD

HEALTHY EATING

+

INTERMITTENT FASTING

DIARY

Name:

Contact

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August 2014

Your tablets (your doctor will fill this in for you)

Name (tablet)	**Normal dose + time**	**New dose + time (date:)**

Changing your insulin

Your insulin (your doctor will fill this in for you)

Name (insulin)	**Normal dose + time**	**New dose + time (date:)**

What does your blood sugar reading mean?

If your blood sugar is	**This means it is**
Below 4	Too low! Call us if you have **more than 2 lows in a week.**
4.5-9	The right target for before meals.
9-11	A little high before meals.
11-16	Too high! Call us if it stays this high for a week.
Over 16	Too high! Call us if it stays this high for 2-3 days.

During the IFOOD study we would like you to test your blood sugar levels

- Before breakfast
- Before lunch
- Before evening meal
- Before bed

And

- If you feel your blood sugars are too low or too high

How to fill in your diary:

Date: ~~**Fasting**~~	**8.30am**		**12.45**		**6.30**		
Sugar reading	*e.g. 9.3*		*e.g. 5.4*		*e.g. 10.2*		
Insulin	*4 units novomix 30*						
Medication	*Metformin 500mg*						
Comments	*e.g. after dinner went to the movies had popcorn*						

You will be asked to give this diary back to us at your next session. If you would like a copy for your records, please let us know.

Date: Fasting							
Sugar reading							
Insulin							
Medication							
Comments							
Date:							
Sugar reading							
Insulin							
Medication							
Comments							

This resource has been condensed for reproduction purposes. The original contains enough to record five weeks of blood glucose levels.

APPENDIX 6 Group education teaching plans

Title:	**IFOOD study: Session 1**
Time:	70 minutes
Aim:	To introduce the study and give an overview of motivation for self-management of diabetes and weight loss, dietary interventions and blood sugar management.
Objectives:	By the end of the session, participants will be able to: Identify strategies to help behaviour change Describe the principles of the allocated weight reducing diet Describe best practice for blood sugar testing Identify symptoms of hypoglycaemia and hyperglycaemia Describe how to manage hypoglycaemia and hyperglycaemia, including when to contact the research team

General resources	IF Group	CP group
	Healthy eating + intermittent fasting handbook Fasting day information leaflet HE + IF diary Food diary Fridge sheet	Healthy eating + clever portions handbook Clever portion checklist HE + CP diary Food diary Fridge sheet DM healthy food choices leaflet Blank plate model
	Pens Whiteboard pens	

What is diabetes
Taking control
The IFOOD plan
Managing your diabetes on the IFOOD plan

Time	Content	Activity	Resources
5 minutes	Introduction / mihi: Who we are Who group participants are Overview of IFOOD study Overview of sessions	Group discussion	Study packs
10	What is diabetes What food effect blood sugar levels	Open question: Key points: Sugar needs insulin to get in to cells. Otherwise backs up in blood Blood sugars kept under control by diet (regular cho), medication, exercise, keeping to normal weight Carbohydrates are the only food group that effect blood sugar levels	Handbook page 5-6
Review knowledge of type 2 diabetes, briefly. Insulin acts as a key to get sugar in to cells Type 2 diabetes, insulin is either not as sensitive as it used to be, or not produced in enough amount Too much sugar damages blood vessels in the heart, eyes, kidneys, feet. = Complications. Keeping blood sugars as near normal as possible keeps you healthy. Normal = 4-9mmol/L. Diet,			

meds, insulin all help. Losing weight helps by increasing insulin sensitivity, cutting down risk of heart attacks. Foods that effect blood sugar levels Carbohydrates effect blood sugar levels – starchy veg, bread, sugar, pasta, rice Other foods contain energy but don't change blood sugar levels.			
15 minutes	Taking control of your health Motivation Importance of change in weight reduction Process of change Goal setting	Many people can tell you what you need to do but you are the one who needs to make the change. Page 7 – it helps to write down your motivation – you can reflect on this when times get tough. Activity: Draw on whiteboard. Go through stages. Complete section page 9. Setting yourself up for success: Page 11. If time go through steps. If not, describe and encourage use. ? Come back to this at end of session.	White board / pens Handbook
What does health mean to you? [Links to Diabetes by carrying on theme of controlling weight & blood sugars to keep healthy] White board – open discussion – what does "health" mean to the group? Who feels that they have "health"? Process of change Look at cycle picture in book Discuss cycle of change. Ask people to mark on in book where they think they are in the cycle of change (secret – don't need to share). Link in to what is their motivation to show how to move forward in the cycle			
15 minutes	Diet information Fasting: What intermittent fasting means Making food choices on fasting days Choosing low fat foods Portion control What is healthy eating How to reduce portion sizes / serving frequencies	Both diets: Go through diet info. Clever portions: Activity: Plate model. Circle on paper, draw proportions of veg, meat & starch. Discuss. Show checklist leaflet – how to reduce portion size. FOCUS point – regular carbs, similar amounts. Fasting: Discussion: how to manage appetite on fasting days FOCUS point – only these diet choices, not any other IF info. Activity: choosing low fat foods	Handbook pages 12-14 Quick reference sheet Diabetes healthy food choices leaflet
15 minutes	Blood sugar testing How to / when to Hypo & hyper management	Insulin changes – page 15 Those on Lantus should use fasting day dose on evening BEFORE fasting day. FOCUS point: How to test, when to test – make sure have blood testing machine.	Handbook

		Offer prescriptions. Why testing important – need to make sure insulin adjustments correct. Ensure can tell when low and what to do. When to contact us.	
What is the ideal target range for blood sugars? What is hypo? Who has gone hypo? What does it feel like? What is hyper? Who has gone hyper? What does it feel like? Check knowledge, reinforce correct information. Treatment of hypo / hyper according to protocol			
5 minutes	Diaries Your IFOOD diary Food diaries	Discussion	Food diaries Your IFOOD diary
5 minutes	Review next four week plan Reminder dates of next session Reminder phone calls	Discussion	

Teacher Notes:

[All anthropometry will have been done at screening interview within the two weeks preceding group session 1.]

On Arrival
Participants + support person (if desired)
Groups will have been randomised prior to session 1. It is important that groups are able to get to know each other through mihi and sharing of experiences e.g. length of time diagnosed with diabetes.

Aims of course / session:
Spend a short time with the group reviewing the study outline and what the sessions will cover. Any outstanding questions?

Title:	**IFOOD study: Session 2**
Time:	1 hour
Aim:	To provide encouragement, support and reinforce dietary change and blood sugar monitoring. To give participants and opportunity to share experiences.
Objectives:	By the end of the session, participants will have been given the opportunity to: Share experiences, give feedback, have questions answered. Reviewed goal setting Discuss blood glucose pattern management By the end of the session IFOOD team will have Checked knowledge (diet and blood sugar monitoring), reinforced changes, ensured safe management.

General resources	IF Group	CP group
	HE + IF diary Food diary Goal setting sheet Blood sugar patterns handout	HE + CP diary Food diary Goal setting sheet Extra CP checklists as needed Blood sugar patterns handout
	Pens Whiteboard pens	

Review
Goal setting
Blood glucose pattern management

Time	Content	Activity	Resources
5 minutes	Weight review	Weight	Scales
15 minutes	Review & support	General discussion	White board pens
Check Blood glucose levels – have they been managing blood glucose levels Experiences with diet, insulin adjustment, blood glucose			
15 minutes	Motivation Goal setting	General discussion	White board / pens Goal setting sheet
Did they keep up with goal setting? Review goals from session one Did they focus on this / review this over previous month New goals to set			
15 minutes	Blood glucose patterns	Work through example in handbook Bring out example in own diaries Focus on: What increases blood glucose What decreased blood glucose What is a “pattern” How to decide whether to increase / decrease insulin	Handbook Blood sugar pattern handout

10 minutes	Review next four week plan Reminder dates of next session Reminder phone calls	Discussion	

Title:	**IFOOD study: Session 3**
Time:	1 hour
Aim:	To provide encouragement, support and reinforce dietary change and blood sugar monitoring. To give participants and opportunity to share experiences.
Objectives:	By the end of the session, participants will have been given the opportunity to: Share experiences, give feedback, have questions answered. Reviewed goal setting Discuss establishing healthy lifestyle choices and changes (when life gets in the way) By the end of the session IFOOD team will have Checked knowledge (diet and blood sugar monitoring), reinforced changes, ensured safe management.

General resources	IF Group	CP group
	HE + IF diary Food diary Goal setting sheet Worst case scenario sheet Reading food labels information sheet	HE + CP diary Food diary Goal setting sheet Worst case scenario sheet Reading food labels information sheet Extra CP checklists as needed
	Pens Whiteboard pens	

Review
Goal setting
Establishing healthy lifestyle choices and changes

Time	Content	Activity	Resources
5 minutes	Weight review	Weight	Scales
15 minutes	Review & support	General discussion	White board pens
Check Blood glucose levels – have they been managing blood glucose levels Experiences with diet, insulin adjustment, blood glucose			
15 minutes	Motivation Goal setting	General discussion	White board / pens Goal setting sheet
Did they keep up with goal setting? Review goals from session one and two Did they focus on this / review this over previous month New goals to set			
15 minutes	Establishing healthy lifestyle choices & changes – when life gets in the way	General discussion Reading food labels Eating out “Worst case scenario” goal setting activity	Reading food label info sheet Worst case scenario goal setting sheet

10 minutes	Review next four week plan Reminder dates of next session Reminder phone calls	Discussion	

APPENDIX 7 Standardised assessment form

Baseline date		**Baseline time**	
Final date		**Final time**	
Collected by			

Participant number				
Sex	Male		Female	
Age at baseline (years)				
Duration diabetes at baseline (years)		**Year of diagnosis**		

Ethnic group	Description	Code

Height (cm) A	
Height (cm) B	
Height (cm) C	
Median / Average	
Height (m^2)	

	Baseline **Date:**	**Week 4** **Date:**
Weight (kg)		
	Week 8 **Date:**	**Final** **Date:**
Weight (kg)		

	Baseline	**Final**
BMI (kg/m^2)		
Waist circ A (cm)		
Waist circ B (cm)		
Waist circ C (cm)		
Median / Average		
Hip circ A (cm)		
Hip circ B (cm)		
Hip circ C (cm)		
Median / Average		
Waist hip ratio		
Blood pressure		

Medication / Nutritional supplements

	Baseline		**Final**	
Name	Dose	Frequency / time	Dose	Frequency / time

APPENDIX 8 Dietary acceptability questionnaire

Candidate number:
Date:

1. How hard did you find this diet?				
1 (very hard)	2	3	4	5 (very easy)

2. Compared to other types of diets that you have done, was it				
1 (much harder)	2	3	4	5 (much easier)

3. Do you think you could stay on this diet for more than 12 weeks?				
1 (not at all)	2	3	4	5 (definitely)

4. What did you find good about the diet?

5. What did you not like about the diet?

6. Are there any other comments you would like to make about the diet?