Effect of Carbohydrate-Energy Replacement on Glycaemic Control Following High-Intensity Interval Training. Does Lactose Improve Glycaemic Control in Comparison to Sucrose?

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List of Abbreviations

Abbreviation	Term
AUC	Area under the curve
bw	Body weight
CGM	Continuous glucose monitoring
CHO	Carbohydrate
FFM	Fat free mass
GI	Glycaemic index
h	Hour
HIIE	High intensity interval exercise
HIIT	High intensity interval training
kg	Kilogram
LS Mean	Least square mean
MICT	Moderate intensity continuous training
min	Minute
OGTT	Oral glucose tolerance test
s	Seconds
SD	Standard deviation
SE	Standardised error
SMD	Standardised mean difference
TEE	Total energy expenditure
TTE	Time to exhaustion
VO_2max	Maximum volume of oxygen consumption
W	Watt
Wmax	Maximal workload
df	Degree of freedom

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Abstract

Background

High-intensity interval training (HIIT) is an increasingly popular training method due to its efficient, rigorous nature and proven benefit on glycaemic control and insulin sensitivity. There has been some research into how remaining in a carbohydrate-energy deficit post-exercise influences next-day glycaemic control, however there has been minimal research into how different types of carbohydrates affects glycaemic control. Lactose has a low glycaemic index of 46 which has been associated with both lower and more stable post-prandial blood-glucose concentrations. However, the effect of both lactose and HIIT on glycaemic control remains to be investigated.

Aims

The primary aim of the study were to identify the extent to which replenishing the exercise-induced energy deficit with different carbohydrates alters next-day glycaemic control following standard meal ingestion. Specifically, we were interested in evaluating if there was a difference in the glycaemic control in response to ingesting the milk sugar lactose compared to when ingesting ordinary sugar sucrose; two sugars with known different effects on the post-prandial blood-glucose response and liver metabolism.

Methods

Eight sedentary, untrained, lactose tolerant participants (n=4 males; n=4 females) with a VO_2max 29 $\pm$ 8 $ml \cdot kg^{-1} \cdot min^{-1}$ aged 20-70 years completed a crossover comprising three, two-day trials involving exercise and continuous glucose monitoring (CGM; Medtronic Guardian Connect, Northridge, CA, USA). Day 1 consisted of a HIIT session at 1700 h, comprising of 10 x 1-min cycle intervals at 80% maximal power, with 1 min recovery at 30% maximal power for 20 min total. A post-exercise carbohydrate beverage was ingested containing either lactose, sucrose, or a non-caloric control. Day 2 consisted of an oral glucose tolerance test (OGTT) at 0700 h, whereby a 75-g glucose drink was ingested after an overnight fast with blood samples collected overtaken ever 0, 30, 60, 90 and 120 min. To control for other glycaemic effects, a standardised controlled diet was consumed across the entire two-day period.

Results

There was a large mean increase in post-exercise glycaemic response represented by the 3-h area under the curve (AUC) with lactose (normalised AUC 2828 mmol·L^{-1}·$1h^{-1}$, ±90% confidence interval 1741; d=1.62, ±90% confidence interval 1.02) and sucrose (5172 mmol·L^{-1}·$1h^{-1}$, ±1877; d=2.03, ±2.19) ingestion compared to control (remaining in a carbohydrate deficit after HIIT), with the lactose-sucrose contrast eliciting a lower moderate response (-1344 mmol·L^{-1}·$1h^{-1}$, ±1719; d=-0.65, ±1.00). Overnight glycaemia (22:00 to 07:00 h) post-exercise was moderately greater after the consumption of sucrose (5730 mmol·L^{-1}·$1h^{-1}$, ±4685; d=0.61, ±0.57) and lactose (6202 mmol·L^{-1}·$1h^{-1}$, ±5329; d=0.66, ±0.64), relative to control, while the lactose-sucrose contrast was inconclusive (472 mmol·L^{-1}·$1h^{-1}$, ±4845; d=0.00, ±0.58). The next-day post-prandial glycaemic response to the standard meals revealed largely non-clear differences between carbohydrate types and the carbohydrates and control. Meanwhile, there was a trivial-moderate reduction in overall (7:00 – 24:00 h) mean glycaemia with post-exercise lactose was (-1539, ±2349; d=-0.27, ±0.40), while the sucrose-control contrast was unclear (505, ± 3503; 0.06, ±0.59).

Conclusion

In sedentary adults, overnight glycaemic responses provided evidence to suggest improved glycaemic response when consuming lactose compared to when remaining in a carbohydrate deficit after HIIT; an effect that trended lower compared to sucrose. However, the next day OGTT and post-prandial glycaemic responses were inconclusive. While the data is provisional, the results suggest that remaining in a carbohydrate-energy deficit after HIIT provides benefit to overnight glycaemia, and more research is required into the role of lactose.

Key Words

Exercise, glycaemic control, post-prandial, lactose, sucrose, continuous glucose monitoring, carbohydrate-energy deficit.

Chapter 1: Introduction

Glycaemic control is the control of blood glucose concentrations within the body and is an essential element to normal bodily function as it ensures that blood glucose levels are maintained in a healthy range, 4-8 mmol/L (Jensen et al., 2011). Blood glucose dysregulation is related to the development of chronic health conditions such as type 2 diabetes. Homeostatic control of blood glucose is achieved by an extensive and highly advanced network of hormones and neuropeptides released predominately in the brain, pancreas, liver, intestine, adipose and muscle tissue (Röder et al., 2016).

Insulin is a hormone which acts to maintain, as well as promote efficient utilisation of glucose. Insulin is able to carry out this action by stimulating an increase in glucose disposal in skeletal muscle and adipose tissue. The magnitude and duration of the rise of blood glucose and insulin concentration post prandially is dependent on the sensitivity of the peripheral tissue to insulin (insulin sensitivity), as well as pancreatic beta cell insulin secretion. Insulin resistance is when there is a reduced sensitivity / responsiveness to metabolic actions of insulin (e.g., insulin-mediated glucose disposal and inhibition of hepatic glucose production). Insulin resistance is associated with type 2 diabetes mellitus as well as a multitude of health problems such as, obesity, hypertension, dyslipidaemia, metabolic syndrome and coronary artery disease (Muniyappa et al., 2008).

Carbohydrate is one of the three macronutrients found in food and drink. Carbohydrates are broken down to glucose which is the bodies main source of energy, and the preferred substrate for energy metabolism (Mul et al., 2015). Carbohydrates influence the metabolism of glucose and insulin and are involved in cholesterol and triglyceride metabolism (Holesh et al., 2022). Sucrose is a simple carbohydrate, a disaccharide composed of glucose and fructose monomers (Queneau et al., 2007). It is commonly referred to as 'table sugar' and therefore is widely accessible and is derived from sugar cane and sugar beets (Queneau et al., 2007). Like sucrose, lactose is also a disaccharide, composed of galactose and glucose monomers and is the sugar found in milk and whey products (Arola & Tamm., 1994). Reaven et al. (1979) identified that the type of carbohydrate consumed had an impact on post-meal plasma glucose and insulin responses. When a sucrose beverage was consumed it elicited a higher plasma glucose response in comparison to glucose and starch, although the difference between glucose and sucrose was minimal (Reaven et al., 1979).

The effect of lactose in comparison to sucrose on blood glucose control in diabetic individuals has been shown to elicit a smaller glycaemic response (Gannon et al., 2001), however, it is worth noting that excess glucose that is not utilised by skeletal muscle can be stored as glycogen (Burke et al., 2004). Glycogen is the stored form of carbohydrate in the body with the majority of glycogen stored within the skeletal muscles (~80%, ~500g), due to skeletal muscle comprising of ~40-50% of total body weight in healthy young men, and ~20% of glycogen stored in the liver (Kanungo et al., 2018; Ivy et al., 1988; Hawley et al., 1997; Jensen et al., 2011). The concentration of glycogen stored in the skeletal muscle is 1-2%, in comparison to the liver where the concentration of glycogen stored is 5-6% (Guyton and Hall., 1986). The concentration of the glycogen in the liver is greater, however the liver is smaller (~1.5kg) than skeletal muscle and therefore total glycogen stored is less, ~100g (Taylor et al., 1996). In addition, a small amount of glycogen is stored in the brain and the heart in order to carry out important physiological functions (Murray and Rosenbloom., 2018).

High-intensity interval training (HIIT) is a recently popular training protocol which consists of alternating between intense periods of exercise where the aim is to reach >90% VO_2max or >75% of maximal power (Wmax), and short rest periods for recovery (Little et al., 2011). In a healthy population, HIIT has been shown to be effective in improving glycaemic control despite being of low exercise volume (Hearris et al., 2019). Research has also demonstrated the effectiveness of HIIT for individuals with type 2 diabetes. In a type 2 diabetic population, a single session of low volume HIIT, 10 x 1 minute cycling intervals with 1 minute rest intervals was shown to reduce post-prandial hyperglycaemia (Little et al., 2011). Additionally, this study also found that after HIIT the sum of the 3-h post meal glucose AUC, post meal peak glucose concentration and average glucose 60-120 minutes post-prandial were lower than when no exercise was completed (Little et al., 2011). Similarly, Adams. (2013) demonstrated that brief high-intensity exercise improved blood glucose 1 to 3 days post exercise, in both individuals with and without diabetes (Adams., 2013). In addition, research has shown that HIIT is one of the most effective means of improving cardiorespiratory and metabolic function, as well as physical performance (Buchheit et al., 2013). Cumulatively, this previous research suggests that individuals with, or who are at risk of diabetes, have improved cardiometabolic health following HIIT training (Tjønna et al., 2013)(Poon et al., 2020).

In a diabetic population the glycaemic response is altered with physical exercise, due to the complex metabolic stress it causes on the human body (Guthrie & Guthrie, 2004). As a result, to prevent hypoglycaemia during prolonged, aerobic (predominately) exercise, additional carbohydrate intake is

required (Colberg et al., 2016). Simultaneously, a major causal factor for the development of type 2 diabetes appears to be the reduction of physical activity. A review of 10 prospective studies established that individuals who achieved the population and age-appropriate recommendations of moderate-intensity physical activity were ~30% less likely to develop type 2 diabetes compared to those who were physically inactive (Jeon et al., 2007). In a study which compared the effects of HIIT to moderate-intensity exercise in individuals with metabolic syndrome over the course of 16 weeks, it was identified that insulin sensitivity reduced by 14.2% after the moderate-intensity exercise compared to baseline, whereas after HIIT exercise, insulin sensitivity increased by 15% ($p<0.05$) (Tjønna et al., 2008). This research suggests that HIIT exercise in comparison to moderate-intensity exercise may elicit improved glycaemic control within individuals with metabolic syndrome. However, more research is required to determine the effectiveness of HIIT training in individuals who have type 2 diabetes or are at risk of type 2 diabetes.

Previous research has shown that carbohydrate-energy replacement in comparison to when an exercise-induced carbohydrate deficit is maintained following exercise, impairs insulin sensitivity and glucose tolerance by ~20-25% the next morning following exercise (Taylor et al., 2018). These results suggest that an exercise-induced carbohydrate deficit is a key factor which stimulates muscle glucose uptake and insulin sensitivity (Taylor et al., 2018). In healthy adults, evidence suggests that replenishing the exercise-induced energy deficit with carbohydrate following moderate intensity continuous exercise blunts next-day improvements in insulin sensitivity (Newsom et al., 2010; Taylor et al., 2018) and post prandial glycaemic control (Schleh et al., 2020). A recent study investigated the effect of replacing energy lost with carbohydrates after a single-bout of HIIT, as well as the subsequent effects on 24 h glycaemic control in healthy women (Estafanos et al., 2022). The study involved three separate trials whereby the participants consumed either a low carbohydrate beverage, high carbohydrate beverage or a placebo non-carbohydrate beverage following a single-bout of HIIT. The study noted that when a carbohydrate beverage of equivalent energy value to the energy lost during exercise was consumed post exercise, a blunted 24 h mean and postprandial glycaemia 24 hours after the HIIT occurred. However, the effect size for the differences between the low carbohydrate group compared to the high carbohydrate group on next-day 24-h blood glucose concentrations was large, $d=0.87$. This research would suggest that a low-carbohydrate and or a low glycaemic index meal following exercise may aid in optimizing glycaemic control. However, there is limited research available which examines the effect of a carbohydrate-energy deficit or the effect of various forms of carbohydrate intake (low GI vs high GI, sucrose vs lactose) on glycaemic control after HIIT.

1.1 Summary and Justification of Research

Diabetes mellitus is a chronic disease affecting the metabolic system, which is characterized by elevated blood glucose levels, also known as hyperglycaemia (World Health Organisation., 2016). In 2022, 5% of the New Zealand population had diabetes, type 1 and 2 (Ministry of Health., 2022), while a more recent study found that the prevalence of New Zealanders with type 2 diabetes is expected to increase by 70-90% in the next 20 years (Diabetes New Zealand., 2021). There is a substantial amount of research which outlines the influence of physical activity and dietary factors on glycaemic control, insulin sensitivity and the risk of developing type 2 diabetes as detailed within Chapter 2 of this thesis. Different types of carbohydrates have different effects on the metabolism of glucose and insulin due to their chemical and structural differences (Holesh et al., 2022). There is limited research however on the effect of lactose on glycaemic control, the sugar naturally-derived from milk products. Research has shown that carbohydrates stored as glycogen in the muscle and liver are the primary fuel sources for high-intensity interval exercise as well as prolonged exercise (Burke et al., 2011). High-intensity interval training (HIIT) is a recently popular training protocol which consists of alternating between intense periods of exercise and short rest periods for recovery. During the exercise periods the aim is to reach >90% VO_2max or >75% of maximal power (Wmax) (Little et al., 2011). Previous exercise has delved into the effects of aerobic and/or continuous bouts of exercise on glycaemic control and insulin sensitivity. However, the effect of other exercise modalities on glycaemic control and insulin sensitivity is a growing area of research. Modifying the type of carbohydrate consumed after exercise, specifically lactose compared to sucrose and HIIT exercise, and the relative effects of the exercise and nutritional interventions on glycaemic control is an area which has not yet been considered. Investigating this will provide a more comprehensive insight into dietary and exercise strategies that could be used for the clinical prevention, management, and treatment of type 2 diabetes mellitus.

1.2 Purpose of the Study

The primary purpose of the study is to identify the extent to which replenishing the exercise-induced energy deficit with different forms of carbohydrate alters the next-day glycaemic control following standard meal ingestion. Specifically, the project will evaluate if there is a difference in the glycaemic control in response to ingesting the milk sugar lactose compared to when ingesting ordinary sugar sucrose; two sugars with known different effects on the blood glucose response and insulin sensitivity.

1.3 Aims

The primary aim of the study is to determine if a single session of low-volume high-intensity interval training improves the following day glycaemic control in sedentary males and females. The secondary aim is to investigate the effect of lactose or sucrose carbohydrate-energy replacements on post-exercise glycaemic response in sedentary males and females.

1.4 Objectives

To assess changes in blood glucose levels through continuous glucose monitoring in response to high intensity interval training.

To determine whether lactose in comparison to sucrose provided post-exercise, affects the glycaemic response following high-intensity interval training.

1.5 Hypothesis

We hypothesize that the provision of post-exercise carbohydrate-energy replacement would blunt next-day postprandial and 24 h glycaemic control and improve insulin sensitivity, when compared to maintaining an exercise-induced energy deficit following high-intensity interval training. Furthermore, we hypothesise that lactose will provide an improved glycaemic response following high-intensity interval training in comparison to sucrose post-exercise.

1.6 Thesis Structure

Chapter 1 sets the scene for the thesis providing and overview of the research area and concludes by outlining aims, objectives, and hypotheses for the research project. Chapter 2 is an extended literature review of relevant literature on the research project. Here the author discusses key concepts, such as;

carbohydrate types, blood glucose control, high-intensity interval training and carbohydrate-energy replacements that have previously been used or trialled in research in sedentary populations. Chapter 3 is the research manuscript which outlines the methods, results, discussion, and conclusion of the research project. Lastly, Chapter 4 provides a summary of the results and conclusions of the thesis, discusses study strengths and limitations and provides final recommendations from this study. Supplementary appendices include; the participant information sheet, study protocol and continuous glucose monitor data of individual participants.

1.7 Researchers Contribution

Researcher	**Contribution**
Rose Stirling – MSc Nutrition and Dietetics Student	Thesis primary author, HDEC ethics application, participant recruitment, data collection, data analysis and thesis write up.
Dr David Rowlands (Primary Supervisor)	Supervision of MSc student, MURF funding application, HDEC ethics application, assistance with data collection, assistance with statistical analysis, thesis review and support.
Dr Claire Badenhorst (Secondary Supervisor)	Supervision of MSc student, review of ethics, data collection protocol, thesis review and support.
Dr Wendy O'Brien (Secondary Supervisor)	Supervision of MSc student, review of ethics and data collection protocol.
PC Tong	Treatment blinding.

Chapter 2: Literature Review

2.1 Introduction

This literature reviews aims to provide a comprehensive overview on blood glucose control following high-intensity interval training and key factors that are directly related or influence this such as; carbohydrates, type of carbohydrate, trained state, insulin sensitivity and carbohydrate-energy replacement following HIIT.

An overview of the role of carbohydrates in the body is provided which follows on to a description of lactose in comparison to sucrose and how glucose is stored in the body. A discussion on diabetes mellitus is provided to help give the reader insight on blood glucose control and how postprandial glycaemia is measured. To conclude the review, a discussion on the association between exercise and insulin sensitivity is provided, with a focus on HIIT training and carbohydrate-energy replacement after exercise.

Over the period from April 2022 and March 2023, three electronic databases were used to review recent literature including; Google Scholar, PubMed and Scopus. In order to conduct a comprehensive search a variety of search terms were explored based on the study's purpose, aims and objectives. These included; 'carbohydrate', 'high intensity interval training', 'carbohydrates and HIIT', 'lactose', 'sucrose', 'blood glucose control and HIIT', 'carbohydrate-energy replacement after exercise'. For this narrative review, the most relevant (topic specific and human-based trials), full-text, English journal articles were selected.

2.2 Carbohydrates

Carbohydrate is one of the three macronutrients found in food and drink. Carbohydrates are broken down to glucose which is the human bodies main source of energy, and the preferred substrate for energy metabolism (Mul et al., 2015). Carbohydrates influence the metabolism of glucose and insulin and are involved in cholesterol and triglyceride metabolism (Holesh et al., 2022).

There are four different structural classes of carbohydrates; monosaccharides, disaccharides, polysaccharides and oligosaccharides, each class is determined by the number of structural units in which the carbohydrate contains (Oullette and Rawn., 2014). Monosaccharides are the fundamental units of a carbohydrate and are simple sugars, these include; glucose, galactose and fructose (Holesh et al., 2022). A disaccharide consists of two monosaccharides, which includes; sucrose (glucose and fructose), lactose (glucose and galactose) and maltose (glucose and glucose) (Ahnen et al., 2020). An oligosaccharide is a polymer which contains three to ten monosaccharides, with examples being, maltodextrins and raffinose

(Ahnen et al., 2020). Finally, a polysaccharide is a polymer which contains long chains of monosaccharides which are connected through glycosidic bonds, examples include, amylose and cellulose (Ahnen et al., 2020). Carbohydrates are classified into two different types; simple and complex carbohydrates. A simple carbohydrate is one or two sugars, a monosaccharide or a disaccharide, combined in a simple chemical structure (Holesh et al., 2022). These carbohydrates are easily broken down and therefore the energy released from carbohydrate metabolism is able to be easily utilised and subsequently blood glucose rises (Holesh et al., 2022). In comparison to a complex carbohydrate, e.g., oligosaccharide or polysaccharide, which are connected together in a complex structure and in turn take longer to digest. This is associated with blood glucose rising at a slower or constant rate (Holesh et al., 2022).

2.2.1 Lactose vs Sucrose

As previously stated, sucrose is a simple carbohydrate, a disaccharide composed of glucose and fructose monomers (Queneau et al., 2007). It is commonly referred to as 'table sugar' and therefore is widely accessible. It is derived from sugar cane and sugar beets (Queneau et al., 2007). Like sucrose, lactose is also a disaccharide, composed of galactose and glucose monomers and is the sugar found in milk and whey products (Arola & Tamm., 1994). When lactose is first ingested it cannot be immediately utilised and is required to be hydrolysed into galactose and glucose first. Glucose is transported to the liver, where liver glycogen synthesis and oxidation occurs, however a large proportion of the glucose enters the systemic circulation. As a result, insulin is released due to the rise in blood glucose concentration and glucose uptake by tissues which is initiated by this change in hormonal concentration. This process is elaborated more in section 2.4. The uptake of glucose from systemic circulation initiated by insulin occurs primarily in skeletal muscle which leads to the formation of glycogen through the action of glycogen synthase.

Galactose, like glucose is transported to the liver where galactose enters the leloir pathway which is the main pathway for galactose metabolism (Arola & Tamm., 1994). Through a multiple step pathway, galactose is converted into glucose-1-phosphate which allows for gluconeogenesis and glycolysis to occur (Koren and Palladino., 2016).

When galactose is co-ingested with glucose, in the form of lactose, at a rate of 33 $\mu mol \cdot kg^{-1}$ min^{-1}, plasma galactose decreased by 0.3 ± 0.1 mmol/L. Comparatively, when galactose is ingested alone, plasma

galactose increased by 2.3±0.3 mmol/L (Sunehag & Haymond., 2002). These results may suggest that blood glucose concentration will be less when ingesting lactose compared to galactose-alone when at rest. Additionally, the metabolic clearance of galactose is more than doubled when co-ingested with glucose through the first pass splanchnic pathway (Sunehag & Haymond., 2002). Conversely, sucrose is a disaccharide composed of glucose and fructose monomers. In a 6-week study, where 30% of the daily calories were derived from sucrose compared to starch, a significant increase in mean fasting serum insulin and glucose was observed ($P<0.005$; $P<0.025$). These findings suggest that ingestion of sucrose decreases insulin sensitivity in a healthy population when at rest (Bantle., 2009)

Galactose is oxidised at a rate ~50-60% less than glucose during exercise, which is likely due to the need for hepatic metabolism before substrate oxidation. A method to assess the degree of impact in which carbohydrates have on blood glucose is the glycaemic index (GI). The glycaemic index (GI) is a classification system which ranks foods based on their glycaemic response (Wolever., 1990). Glucose has a glycaemic index (GI) of 100 in comparison to lactose and sucrose which have glycaemic indexes of 46 and 61 respectfully. The GI of lactose is lower due to the presence of galactose which has a lower GI than fructose (GI of 19) which is present within sucrose (Foster-Powell et al., 2002). The consumption of lactose (11.0 ± 1.6) containing products has been shown to produce lower glycaemic fluctuations (represented as 3 h AUC mmol.min/L) in comparison to sucrose (10.8 ± 1.5) and control (11.2 ± 1.0) trials in individuals with non-insulin dependent diabetes mellitus (Wolever et al., 1985). These findings are suggested to be due to the slower rate of absorption of lactose, as well as the small hyperglycaemic effect of galactose (Gannon et al., 2001). However, in a study where individuals with diabetes ingested galactose at a 1g/kg/bw, little to no change in blood glucose concentration occurred (Roe & Schwartzman., 1932). Specifically, in the diabetic group, a significant decrease in blood glucose concentration occurred when insulin was administered, however there was little to no effect on galactose levels (Roe & Schwartzman., 1932). In addition, the tolerance of galactose was no greater in the diabetic individuals than in the non-diabetic individuals and galactose does not seem to cause a significant glycaemic excursion in the diabetic population, unlikely most other forms of sugar, carbohydrates. These results may indicate that galactose could be included as a form of dietary management for diabetes mellitus due to the findings establishing that diabetic individuals metabolise galactose at a similar, satisfactory rate as non-diabetic individuals (Roe & Schwartzman., 1932).

2.2.2 Glycogen Stores

Glycogen is the main energy substrate when exercise intensities are above 70% maximal oxygen uptake (Jensen et al., 2011). When glycogen stores are depleted, fatigue onset will occur (Ørtenblad et al., 2013). Post-exercise, the rate of glycogen synthesis is accelerated, particularly in the first 30 minutes post-exercise in order to restore glycogen stores (Ivy et al., 1991). In healthy individuals, the secretion of insulin post-exercise supports the uptake and storage of carbohydrates post prandially (Cartee., 2015). However, in instances where an individual presents with insulin resistance, uptake of carbohydrates post prandially is reduced, and maintenance of hyperglycaemia will increase the risk of type 2 diabetes (Scheen., 2003).

2.3 Insulin Resistance

Insulin resistance is defined as a clinical state in which a normal or elevated insulin level produces an attenuated biological glucose uptake response (Cefalu et al., 2001). This occurs when muscle and liver cells and adipose tissue neglect or resist against the bodies signal to secrete insulin. Insulin resistance is common in people who are overweight or obese and have adopted or are forced into a sedentary lifestyle; it is also the underlying mechanism behind elevated blood glucose levels - known as hyperglycaemia, type 2 diabetes mellitus, and is one of 4 to 5 features of metabolic syndrome (World Health Organisation., 2016). The elevated blood glucose levels occur due to the inability for glucose to be metabolized in the cells due to the inability of insulin produced by the pancreas to effectively signal the cells to increase glucose uptake (Jiang et al., 2020).

2.3.1 Causal Factors of Insulin Resistance

Within an individual with chronic or frequent periods of hyperglycaemia, long-term damage and dysfunction to the microvasculature of the kidney, eyes, nerves, heart, blood vessels and other tissues can occur, and is most extreme once hyperglycaemia is high and chronic (e.g., HbA1c >48 mmol/mol, fasting glucose >7.0 mmol/L), as in type 2 diabetes (American Diabetes Association., 2006). A major causal factor for the development of insulin resistance appears to be the reduction of physical activity. Furthermore, an increased weight to hip ratio, waist circumference and waist to height ratio has been shown to be causal (Xu et al., 2013).

Extensive research of type 2 diabetes has established two causal dietary factors: total energy intake and nutrient composition (Tinker et al., 2011; Villegas et al., 2009; Mendoza et al., 2007; Harding et al., 2008; Vessby et al., 2001). Energy intake that exceeds dietary requirements has been associated with an increase in fat mass and changes in body composition, alongside negative impacts on glucose metabolism (Hill et al., 2012; Nakrani et al., 2020).

A review article established that a high intake of dietary sugars is correlated with the development of chronic hyperglycaemia (Sami et al., 2017). Similarly, there is a correlation between type 2 diabetes, obesity, and metabolic syndrome with a high consumption of soft drinks (Nseir et al., 2010). In an eight year prospective study (Nurses' Health Study) which investigated the association between sugar sweetened beverage consumption and the risk of developing type 2 diabetes in a cohort of 51,603 women, reported that after adjustment for potential confounders, women who consumed one or more sugar-sweetened beverages daily had a 1.83 relative risk of developing type 2 diabetes ($P<0.001$), when compared to women who consumed less than 1 sugar sweetened beverages per month (Schulze et al., 2004). Middle-aged individuals who consume more than 1 soft drink per day had a 48% higher adjusted prevalence of developing metabolic syndrome than those who consumed less than 1 soft drink per day over the course of 4 years (Dhingra et al., 2007). Complementary to these results, a review article identified an association between dietary knowledge and type 2 diabetes. It was reported that in the group who were identified to be at high risk of developing type 2 diabetes, also had poor dietary knowledge (Sami et al., 2017). Cumulatively, these results may suggest that improved dietary knowledge may be associated with a reduced risk of developing type 2 diabetes (Primanda et al., 2011).

Furthermore, there is growing research on the link between the nutrient composition of a meal and post prandial blood glucose levels. Researchers have highlighted that high consumption of high GI carbohydrates, typically results in poorer glycaemic control (Willett et al., 2002). In addition, research has demonstrated that women in the highest quintile of glycaemic load had a 40% greater risk of type 2 diabetes than women who were in the lowest quintile ($P=0.03$). This elevated risk of type 2 diabetes development for women was noted after adjustment for age, body mass, alcohol intake, physical activity, and cereal fibre, all in which are confounding factors of type 2 diabetes (Salmeron et al., 1977)

In comparison, high dietary-fibre consumption is related to improved glycaemic control in individuals with type 1 and 2 diabetes (Chandalia et al., 2000; McIntosh et al., 2001; Giacco et al., 2000). Giacco et al.

(2001) determined that in a type-1 diabetic cohort, a high-fibre diet in comparison to a low-fibre diet was shown to decrease both mean daily blood-glucose concentration ($P<0.05$) and the number of hypoglycaemic events ($P<0.01$)(Giacco et al., 2000). In individuals with type 2 diabetes, a high fibre diet (25g/day) over the course of six weeks improved glycaemic control, decreased hyperinsulinemia, and lowered plasma insulin concentrations in comparison to a moderate fibre diet (24g/day)(Chandalia et al., 2000). In individuals with type 2 diabetes, mean daily pre-prandial plasma glucose concentrations decreased by 13 mg per decilitre ($P=0.04$), plasma glucose AUC decreased by 10% ($P=0.02$) and plasma insulin AUC decreased by 12% ($P=0.05$) when consuming the high-fibre diet in comparison to the moderate fibre diet (Chandalia et al., 2000).

In addition to dietary factors, it has been identified that time spent being sedentary is an independent risk factor for cardiovascular disease, type 2 diabetes, and all-cause mortality (Biswas et al., 2015; Wilmot et al., 2012; Hu FB et al., 2003). It has been recommended by the American Diabetes Association that patients with diabetes should reduce their sedentary time and not sit for more than 90 minutes at a given time (American Diabetes Association., 2015). A meta-analysis which examined 10 studies established that there was a 112% greater pooled relative risk of diabetes associated with large quantities of television time (>7 hours per day) comparative to small quantities of television time (<2 hours per day) (Wilmot et al., 2012).

Finally, low levels of physical activity have been shown to be correlated to the risk of the developing type 2 diabetes (Hamasaki., 2016; Hamilton et al., 2014). A review article, which evaluated daily physical activity and type 2 diabetes risk identified that regular physical activity improved glycaemic control and reduced the risk of developing type 2 diabetes by 46–67.4%, in individuals with impaired glucose tolerance (Hamasaki., 2016). It was identified that individuals with type 2 diabetes had a lower energy expenditure, number of steps and duration of physical activity than healthy, non-diabetic individuals (Fagour et al., 2013). Walking for at least 30 minutes per day was shown to reduce the risk of cardiovascular disease by 50% in patients with type 2 diabetes (Hamasaki., 2016).

In a study which compared the effects of HIIT to moderate-intensity exercise in individuals with metabolic syndrome over the course of 16 weeks, it was identified that insulin sensitivity reduced by 14.2% after moderate-intensity exercise compared to baseline, whereas after HIIT exercise, insulin sensitivity increased by 15% ($p<0.05$) (Tjønna et al., 2008). This research suggests that HIIT exercise in

comparison to moderate intensity exercise may elicit improved glycaemic control within individuals with metabolic syndrome. However, more research is required to determine if HIIT exercise is in fact the best exercise modality to improve glycaemic control in individuals with type 2 diabetes.

2.4 Blood Glucose Control

An essential element to normal bodily function is maintaining blood glucose levels in a tight, healthy homeostatic range of between 4-5.4 mmol/L when fasting and 4-7.8 mmol/L two hours post prandial (Health Navigator., 2023) to prevent the detrimental effects on health of hyperglycaemia. Homeostatic control of blood glucose is achieved by an extensive and highly advanced network of hormones and neuropeptides released predominately in the brain, pancreas, liver, intestine, adipose and muscle tissue (Röder et al., 2016). The pancreas maintains blood glucose levels via the actions of the hormones, glucagon and insulin (Hantzidiamantis et al., 2019). When blood glucose levels rise, due to the breakdown of food into the associated macronutrients, such as carbohydrates, this stimulates insulin to be secreted from the beta cells in the islets of Langerhan in the pancreas. Insulin attaches to the corresponding receptors on the muscle and adipose tissue, enabling the insulin-dependent uptake of glucose into these tissues. Subsequently, blood glucose decreases within homeostatic range. Individuals who frequently experience hyperglycaemia or high blood glucose levels may be at risk of developing insulin resistance.

Postprandially blood glucose typically starts to rise 10 minutes after the start of meal ingestion in relation to the absorption of macronutrients into the bloodstream, specifically dietary carbohydrates. The trend of postprandial blood glucose is based on the absorption of carbohydrates, secretion of insulin and glucagon and their subsequent relationship on glucose metabolism in the liver and peripheral tissues. The degree and the timing of the peak of blood glucose concentration is dependent on a variety of factors such as; macronutrient composition, quantity and timing of food intake, rate of digestion, and insulin sensitivity of the individual (Black et al., 2005). In non-diabetic individuals, plasma glucose concentrations usually peak around 60 minutes and return to postprandial levels within 2-3 hours after food is ingested (Sabag et al., 2022).

Figure 1. Insulin sensitivity differing between a liver with normal glucose tolerance, compared to prediabetes compared to type 2 diabetes.

Note. This model was produced by Gillen et al. (2021) and illustrates how peripheral insulin resistance increases as glucose tolerance becomes increasingly impaired. From "Exercise-nutrient interactions for improved postprandial glycaemic control and insulin sensitivity" by Gillen, J. B., Estafanos, S., & Govette, A, 2021, *Applied Physiology, Nutrition, and Metabolism*, *46*(8), 856-865.

2.4.1 Effect of Food on Blood Glucose Control

The macronutrient composition of food plays a large role on blood glucose control. When fat is co-ingested with carbohydrates this delays gastric emptying. Similarly, when protein is co-ingested with carbohydrates this stimulates insulin secretion and slows gastric emptying (Gentilcore et al., 2006). Research has identified that there is a positive correlation between slower gastric emptying and protein stimulation of gut hormones (e.g., cholecystokinin and incretins) (Karamanlis et al., 2007). Fibre ingestion

will slow down the digestion of carbohydrates and therefore delays the absorption of glucose into the bloodstream (Heath et al., 1983).

Research has demonstrated that when carbohydrates are consumed alongside protein and fat, as part of a mixed macronutrient meal the post-meal plasma glucose response is reduced in comparison to when consumed in a drink as an isolated macronutrient (Reaven et al., 1979). In addition, Reaven et al. (1979) identified that the type of carbohydrate consumed had an impact on post meal plasma glucose and insulin responses. When a sucrose beverage was consumed it elicited higher plasma glucose in comparison to sucrose and starch, despite a minimal difference between glucose and sucrose (Reaven et al., 1979).

The effect of a mixed macronutrient meal in comparison to a carbohydrate only meal on glycaemic response has also been evaluated. Kim et al. (2019) investigated the effect of meal macronutrient composition on glycaemic response within healthy individuals and identified that blood glucose incremental AUC was significantly lower when consuming a mixed macronutrient meal (2,237.5 $mmol \cdot L^{-1} \cdot 1h^{-1} \pm 264.9$ $mmol \cdot L^{-1} \cdot 1h^{-1}$), consisting of rice, egg white, bean sprouts and oil compared to consuming a rice-only meal (3,691.3 $mmol \cdot L^{-1} \cdot 1h^{-1} \pm 473.4$ $mmol \cdot L^{-1} \cdot 1h^{-1}$) (Kim et al., 2019).

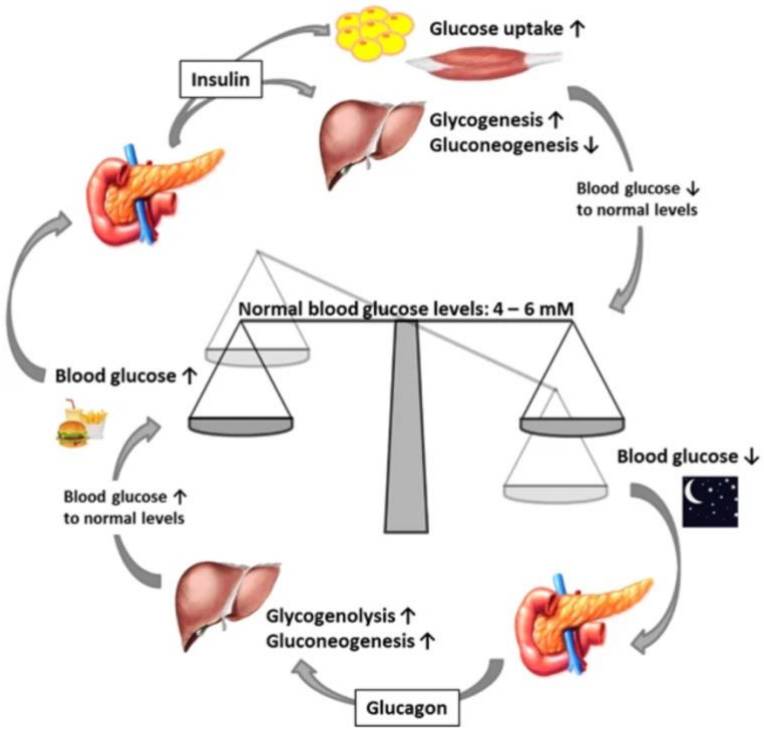


Figure 2. Blood Glucose Homeostasis.

Note. This model was produced by Röder et al. (2016) and illustrates how glucagon and insulin maintain blood glucose levels in a healthy range. From "Pancreatic regulation of glucose homeostasis" by Röder, P. V., Wu, B., Liu, Y., & Han, W, 2016, *Experimental & molecular medicine*, *48*(3), e219-e219.

A method to assess the degree of impact that carbohydrates will have on blood glucose is the glycaemic index (GI) (Wolever., 1990). A high GI food is ranked > 65% on the glucose scale and induces a rapid blood glucose response which results in blood glucose to spike (Cipryan et al., 2017). Foods that elicit this response and are classified as high GI foods include; watermelon, white and some wholemeal bread, rice cakes, honey, short-grain white rice and puffed wheat/cornflakes/rice flake cereal (NZ Nutrition Foundation., 2022). In comparison, a low GI food is ranked <40% on the glucose scale and induces a smaller blood glucose response and includes; wholegrain bread, oats, milk, yoghurt, legumes etc. Glycaemic control significantly improves ($P<0.05$) when a low GI diet was consumed in individuals with non-insulin dependent diabetes mellitus compared to a high GI diet (Jensen et al., 2011).

2.5 Measuring Postprandial Glycaemia

For real time measurements of blood glucose, CGM is used to depict trends in glucose levels and enables individuals to maintain tighter control of blood glucose levels, therefore avoiding hypoglycaemia or hyperglycaemia (American Diabetes Association., 2001). The use of CGM enables blood glucose concentrations to be measured under free-living conditions, therefore outside of the laboratory setting it provides in-depth detail on glucose levels throughout the day (Rovner et al., 2009). The validity of CGM in comparison with the gold standard for glucose testing, venous blood or capillary blood sampling has been supported through various research projects that have investigated the reproducibility of an individual's CGM derived postprandial glycaemic responses (Rohleing et al., 2019).

Another method to measure postprandial glucose tolerance is the OGTT (Bartoli et al., 2011). The OGTT has been widely used to diagnose diabetes and impaired glucose tolerance within individuals in a clinical setting. It provides a measure of insulin sensitivity which is a factor in the magnitude and duration of postprandial increases in blood glucose and insulin concentrations (Matsuda and DeFronzo., 1999). The test involves consuming a 75 g glucose beverage and then measuring blood glucose concentration in the

following 2 hours. Within the research setting, blood glucose concentration is measured through repeated blood sampling every 30 minutes within a 2-h period post beverage consumption. Measurements such as, glucose and insulin peaks, mean and AUC are calculated to assess changes in glucose and insulin levels.

In the OGTT the derived AUC is a measure of glucose excursion after glucose loading (75 g glucose drink) which is then used to assess glucose tolerance (Sakaguchi et al., 2016). Recent research has shown that a single OGTT is a valuable method of high clinical significance; testing for diabetes, insulin resistance, impaired beta-cell function, reactive hypoglycaemia, acromegaly, and other disorders of carbohydrate metabolism and could assist with the classification of prediabetes risk (Kuo et al., 2021; Eyth et al., 2021). Despite the OGTT providing specific and accurate data, it is a limited method for a thorough assessment of glycaemic response due to the localised time points in which glycaemia is measured. However, the use of CGM ensures the provision of an exhaustive data set and allows a greater time period of glycaemic response to be evaluated. This consequently allows for more comprehensive and insightful research to be completed.

2.6 Physical Activity and Blood Glucose Control

Physical activity is a recommended tool to improve insulin sensitivity and glycaemic control in both long term and acute research settings. In the acute research designs, consistent single-bouts of exercise enhanced insulin sensitivity and muscle glucose uptake in both insulin resistant (Devlin et al., 1987; Perseghin et al., 1996) and healthy individuals (Richter et al., 1989), although the effects of exercise on glucose tolerance are less clear in healthy individuals (Rose et al., 2001; Gonzalez et al., 2013).

In the insulin resistant population, participants consumed a carbohydrate-rich meal before a single-bout of 45 minutes of exercise on the elliptical trainer. Changes in muscle glycogen and fat content in the liver and the muscle were measured using ^{13}C and ^{1}H magnetic resonance spectroscopy which measures glucose concentration and the quantity of lactate produced from glycolysis (Rabol et al., 2011). The study showed that the single-bout of exercise reversed muscle insulin resistance and lead to increased postprandial muscle glycogen synthesis and decreased postprandial hepatic de novo lipogenesis and hepatic triglyceride synthesis increased (Rabol et al., 2011). This establishes that a single-bout of exercise can have notable effect towards the distribution and metabolic activity of ingested carbohydrates by deviating ingested carbohydrates away from the liver, and instead into the muscle cells (Rabol et al., 2011). Contrastingly, when a single-bout of prolonged moderate intensity exercise, 1 h of biking at 150W,

was completed in a healthy individual population there was an increase in insulin sensitivity and responsiveness of glucose utilisation, tending to last 48 hours after exercise (Mikines et al., 1988). Insulin sensitivity was measured using hyperinsulinemic clamps, which is the gold standard tool to measure insulin sensitivity. The findings of the study did not correlate with any change in plasma concentration of hormones or metabolites which influence glucose metabolism (Mikines et al., 1988). Rabol et al. (2011) included nutritional intervention prior to the exercise intervention and Mikines et al. (1998) did not include a nutritional intervention, however, Mikines et al. (1998) did include a set quantity of carbohydrates in which the participants were required to eat for the 3 days prior to completing the study.

Despite these findings, Rose et al. (2001) was unable to make a clear conclusion on the role of peripheral uptake and splanchnic output of glucose in altering glucose tolerance after exercise within healthy, trained males (Rose et al., 2001). The exercise intervention involved participants cycling for 1 h at 70% VO_2 max. At 30 minutes post exercise, an OGTT was completed to assess glycaemic response to the single-bout of exercise. Despite the study showing an exaggerated glycaemic response to oral glucose ingestion immediately after exercise (30 minutes), in comparison to when glucose was ingested 24 hours after exercise, the study did not control for any confounding factors, such as, dietary intake, hydration levels, or other lifestyle factors which could have influenced the study results. The study results were limited by a small sample size, influencing the ability to draw a definite conclusion (Rose et al., 2001). Gonzalez et al. (2013) identified that although acute exercise had no effect on glucose tolerance when no breakfast was consumed, reduced glucose tolerance was evident when breakfast was consumed prior to exercise. This may suggest that a carbohydrate deficit will result in a lower postprandial glycaemic response. However, these results may be interpreted with caution, as Gonzalez et al. (2013) study results were also limited due to a small sample size and consequently long-term effects cannot be determined from this short-term intervention (Gonzalez et al., 2013).

High-intensity interval training (HIIT) is a training protocol which consists of alternating between intense periods of exercise and short rest periods for recovery. During the exercise periods the aim is to reach >90% VO_2max or >75% of maximal power (Wmax) (Little et al., 2011). Previous exercise has delved into aerobic and/or continuous bouts of exercise however, the effect of other exercise modalities on glycaemic control and insulin sensitivity is a growing area of research. This is expanded on in section 2.7, insulin sensitivity and exercise.

2.7 Insulin Sensitivity and Exercise

Insulin is a hormone which acts to maintain full body glucose, as well as promote efficient utilisation of glucose. Peripheral insulin sensitivity is enhanced through insulin-dependent mechanisms for up to 48 hours following exercise in adults with and without insulin resistance (Devlin & Horton., 1985; Mikines et al., 1988; Perseghin et al., 1996; Koopman et al., 2005; Ortega et al., 2015). This is due to the increased contraction-mediated muscle glucose uptake which occurs during exercise, usually subsiding 3 hours after the exercise session. A sedentary lifestyle has been shown to be a factor that both directly and indirectly leads to insulin resistance (Henriksson., 1995). Findings have shown oxidative damage to be linked with physical inactivity due to an upregulation of enzymes (NADPH oxidase complex) which increases reactive oxygen species and induces oxidative damage (Hudish et al., 2019). Research has suggested that physical inactivity is correlated with increased inflammatory cytokines in plasma. Phillips et al. (2017) also identified that when replacing sedentary behaviours with physical activity in a healthy population, circulating cytokines are reduced and insulin sensitivity is improved (Phillips et al., 2017).

Richter et al. (2021) has shown that individuals who are trained have a higher insulin sensitivity in comparison to individuals who are untrained (Richter et al., 2021). However, improved glucose and insulin responses in sedentary young males has been achieved when completing HIIT for 2 weeks (Babraj et al., 2009). The HIIT involved six, 15-minute sessions over a 2-week period, with glucose and insulin activity measured via OGTT before and after HIIT sessions. The number of sprints increased from four during the first two sessions, to five in the third and fourth sessions, progressing to six in the last two sessions. The HIIT session comprising of four to six times 30 second cycle sprints interspersed with 4 minutes of recovery between sprints. The results demonstrated a 23% improvement in insulin sensitivity. Similarly, Little et al. (2011) established that low-volume HIIT, consisting of four to six, 30 second sprints and four to six recovery intervals, 3 times per week over the course of 12 weeks, reduced fasting glucose levels, improved glucose tolerance and increased mitochondrial capacity (Little et al., 2011). The effects of an acute bout of exercise on glucose transport are proportionally brief, usually returning to baseline in ~30-40 minutes. Nonetheless, once the acute effects of exercise have dissipated there is a period whereby glucose transport in stimulated due to increased effectiveness of insulin action. This increase in post-exercise insulin sensitivity is observed 48 hours after exercise in humans, however the mechanism for how this occurs is unknown (Mul et al., 2015).

Research on the effects of insulin action following short term exercise training, established that even after only 7 days of 30 minutes cycling and 30 minutes treadmill walking at ~70% of maximal aerobic capacity daily, without energy replacement, there was significant improvements in insulin action in patients with type 2 diabetes mellitus (Kirwan et al., 2009). The glucose disposal rate, which is a measure of the speed and efficiency that insulin is able to move glucose from the bloodstream into the cells, increased from 1.84 ± 0.32 to 2.67 ± 0.37 mg × kg^{-1} × min^{-1}; P < 0.0001 (40 mU) and 7.57 ± 0.61 to 8.84 ± 0.56 mg × kg^{-1} × min^{-1}; P = 0.008 (1,000 mU) (Kirwan et al., 2009). Suggesting that there does not need to be great quantity of HIIT, to make an impact on health outcomes.

The effects of HIIT on glycaemic control are less clear in the sedentary and overweight/obese population. A systematic review which reviewed the effectiveness of HIIT compared to MICT on glycaemic control in patients with type 2 diabetes, concluded that there was no significant changes in fasting glucose in the HIIT group compared to the MICT group (Liu et al., 2019). The systematic review identified that HIIT was more effective in reducing HbA1c (%) in comparison to MICT, however the quality of evidence was low which impacts the efficacy of this finding (Liu et al., 2019).

Research on glycaemic control in individuals who are sedentary and have type 2 diabetes is an ongoing area of research. Future research may consider investigating the effect of HIIT in comparison to moderate-intensity continuous exercise on glycaemic control, over a long-term period, with the use of CGM technology in this population group. This would provide insight into exercise as clinical management and treatment of type 2 diabetes.

2.8 Carbohydrates after Exercise and glycaemic response

Burke. (2011) identified that carbohydrates stored as glycogen in the muscle and liver are the primary fuel sources for high-intensity interval exercise as well as prolonged exercise (Burke et al., 2011). In order to maintain adequate glycogen content, high carbohydrate diets are recommended to ensure skeletal muscle has enough energy during training (Van Dijk et al., 2021). There is extensive research to state that carbohydrate rich foods with a moderate to high GI will provide a readily available source of substrate for glycogen synthesis (Murray et al., 2018; Kirwan et al., 2001).

Additionally, there is a wide range of sports nutrition research which recommends the importance of carbohydrates after exercise (Devlin & Williams., 1991; Thomas et al., 2016). Guidelines for carbohydrate needs for training and recovery state that "In the optimum diet for most sports, carbohydrate is likely to contribute about 60-70% of total energy intake." (Devlin & Williams., 1991). The recommendations for carbohydrates after exercise to optimise rates of muscle glycogen resynthesis is ~1.0-1.2 g/kg/h, beginning during the early recovery phase and continuing for 4-6 hours (Thomas et al., 2016).

2.8.1 Carbohydrate after exercise in healthy individuals

Roberts et al. (2013) established that the glycaemic response to carbohydrates is affected by protein consumed and exercise completed in healthy, active males and females (Roberts et al., 2013). A 45-minute cycle at 60% of their age-predicted maximum heart rate (220-age) was shown to significantly reduce the glycaemic response to carbohydrate-containing meals ($P<0.05$) (Roberts et al., 2013). Plasma insulin AUC was significantly higher when consuming glucose and protein after exercise compared to when just consuming glucose after exercise ($P<0.05$)(Roberts et al., 2013). Interestingly, there was a consistently higher post-exercise glucose response in studies which supplied a rapidly digestible liquid carbohydrate during the resistance training (Haff et al., 2000; Bird et al., 2013), when compared to studies which provided carbohydrate in the 10-60 minutes before resistance training where no increase in post-exercise blood glucose with carbohydrate ingestion was observed (Aoki et al., 2003; Wilburn et al., 2020). The results of this study suggest that consistent carbohydrate ingestion during exercise maximises blood glucose availability in healthy individuals.

2.8.2 Carbohydrate after exercise in people with insulin resistance

Contrastingly, in a diabetic population glycaemic response is altered with physical exercise as a result of the complex metabolic stress it causes on the human body (Guthrie & Guthrie., 2004). As a result, to prevent hypoglycaemia during prolonged, aerobic (predominately) exercise, additional carbohydrate intake is required (Colberg et al., 2016). When aerobic exercise is of a low to moderate intensity and lasts between 30 and 60 minutes, ~10-15 g carbohydrates may prevent the onset of hypoglycaemia. For exercise which is performed with relative hyperinsulinemia (after insulin bolus), 30-60g of carbohydrates per h of exercise may be required. This is similar to carbohydrate requirements to optimise performance in athletes with or without of diabetes.

There is a variety of factors which will influence the carbohydrate intake required such as, insulin regimens, timing of exercise, type of activity, as well as the blood glucose level at the beginning (Colberg et al., 2015). When insulin levels are lowered this may reduce or eliminate carbohydrate intake, which has been established by a 20% reduction in basal insulin for individuals on a multiple daily injection insulin therapy dosage, before and after exercise (Campbell et al., 2015). However, this strategy may not fully compensate for the decline in glucose which progressively occurs during exercise.

Arsa et al. (2015) investigated the effect of prior exercise on glycaemic responses following carbohydrate ingestion compared to no carbohydrate ingestion in individuals with type 2 diabetes mellitus, who were also sedentary. The participants completed a constant submaximal workload exercise session at 90% of lactate threshold. The study identified that a single exercise session consisting of 20 minutes at moderate intensity led to a decrease in glycaemia, however after carbohydrate consumption glycaemia was not affected (Arsa et al., 2015). This suggests that the decrease in glycaemia induced by training is counter-balanced with the consumption of carbohydrates after the exercise. Consequently, if individuals with diabetes do not consume carbohydrates after training, then they could be at risk of blood sugars dropping too low and a hypoglycaemic event occurring (Cockcroft et al., 2020; Cryer., 2008).

2.9 Carbohydrate Replacement after Exercise and Insulin Sensitivity

Previous research has shown that carbohydrate-energy replacement in comparison to when an exercise-induced carbohydrate deficit is maintained after exercise, impairs insulin sensitivity and glucose tolerance by ~20-25% in the morning following exercise (Taylor et al., 2018). These results suggest that an exercise induced carbohydrate deficit is a key factor, which stimulates muscle glucose uptake and insulin sensitivity (Taylor et al., 2018).

In healthy adults, evidence suggests that replenishing the exercise induced energy deficit with carbohydrates following moderate intensity continuous exercise, blunts next-day improvements in insulin sensitivity (Newsom et al., 2010; Taylor et al., 2018) and post prandial glycaemic control (Schleh et al., 2020). In contrast to this, when low carbohydrate iso-energetic meals containing protein and fat or a surplus of calories from fat post exercise, there has been improvements in next-day insulin sensitivity (Fox et al., 2004; Newsom et al., 2010). These two compelling pieces of research establishing that acute improvements in insulin sensitivity and glycaemic control are sensitive to carbohydrate intake. Despite

this finding, the effect may differ between exercise types, however, more research is needed in this area to determine the effect of various exercise types (e.g., HIIT) on insulin sensitivity.

Previous research investigating the effect of HIIT on insulin sensitivity was Fox et al. (2004). However, the design of the HIIT was following a 90-minute cycle at ~65% VO_2max and lasted a total of 30 minutes with no rest period in between efforts, instead lower intensity efforts interspaced between (Fox et al., 2004). Consequently, as a result of no rest periods included into the HIIT protocol, findings may not represent the changes to blood glucose control or insulin sensitivity which would be distinguished in a normal HIIT protocol. A recent study investigated the effect of replacing energy lost with carbohydrates after a single-bout of HIIT, as well as the subsequent effects on 24 h glycaemic control in healthy women (Estafanos et al., 2022). The study involved three separate trials whereby the participants consumed either a low carbohydrate beverage, high carbohydrate beverage or a placebo non-carbohydrate beverage following a single-bout of HIIT. The study noted that when a carbohydrate beverage of equivalent energy value to the energy lost during exercise was consumed post exercise, a blunted 24 h mean and postprandial glycaemia 24 hours after the HIIT occurred. However, the effect size for the differences between the low carbohydrate group compared to the high carbohydrate group on next-day 24-h blood glucose concentrations was large, d=0.87. This research suggests that a low-carbohydrate and or a low glycaemic index meal following exercise may aid in optimizing glycaemic control in females. In support of this, when consuming a low carbohydrate drink, next-day post prandial blood glucose was lower the 3 hours following breakfast (5.5 mmol/L ± 0.5, $P < 0.05$) in comparison to when consuming a high carbohydrate beverage (6.7 mmol/L ± 1.1) (Estafanos et al., 2022). It should be noted that there is limited research on the effect of carbohydrate-energy replacement following a single-bout of HIIT in women and accordingly is an on-going area of research.

Following a glycogen-depleting exercise session, ingestion of large amounts of carbohydrate can stimulate an increase in muscle glycogen content by 50-80% above normal resting values (Graham et al., 2010). Alternatively, restricting carbohydrates in the hours following endurance exercise has been shown to limit post-exercise muscle glycogen re-synthesis (Cartee et al., 1989; Newsom et al., 2010), which may contribute to heightened next-day insulin sensitivity upon subsequent carbohydrate ingestion. Taylor et al. (2018) demonstrated that after a 90 min endurance exercise session, maintaining a carbohydrate deficit enhanced insulin sensitivity the following morning to a greater extent, than in the non-exercise control condition (Taylor et al., 2018). However, in research where dietary fat was consumed post

exercise, next-day glucose tolerance and muscle glycogen resynthesis did not occur (Fox et al., 2004). Cumulatively, these results suggest that improved insulin sensitivity and glycaemic control following exercise is related to carbohydrate balance, rather than energy balance (Fox et al., 2004). Physiologically the insulin sensitizing effects of a carbohydrate deficit post-exercise have been correlated with reductions in muscle glycogen that occur during a single-bout of endurance exercise (Kawanaka et al., 1999). However, there is limited research available, which examines the effect of a carbohydrate-energy deficit or the effect of various forms of carbohydrate intake (low GI vs high GI, sucrose vs lactose) on glycaemic control after HIIT. Therefore, a field for future research prospects to investigate the effects of this on glycaemic control in both healthy and type 2 diabetic individuals.

2.10 Conclusion

Carbohydrates and exercise are two factors in which have been widely established to influence glycaemic control in both healthy and diabetic individuals, both independently and dependently of each other. It has been identified that blood glucose concentration typically decreases after exercise, whereas blood glucose concentration increases when carbohydrates are consumed. The glycaemic excursions in which carbohydrates and exercise can cause are greater in individuals with type 2 diabetes, than within a healthy population and therefore adjusting these two variables may elicit improved blood glucose concentrations. Various exercise modalities and their relative effects on glycaemic control have thus been investigated, with the latest research identifying HIIT to induce improved insulin and glycaemic responses compared to other exercise modalities. The consumption of carbohydrates after exercise has been associated with smaller glycaemic excursions in both healthy and diabetic populations, specifically in the diabetic population, whereby carbohydrate consumption counter-balances the drop in blood glucose and avoids the risk of a hypoglycaemic event from occurring. There is emerging research on how different carbohydrate types influence glycaemic control after exercise, however this is limited. Furthermore, there is some research which outlines the effect of carbohydrate-energy replacement on glycaemic control after HIIT. However, more research on the effect of dietary intervention, such as, different carbohydrate types, is required to strengthen the current pool of research. This will provide greater insight into how dietary strategies can be used for regulating glycaemia, with possibility of impacting upon the prevention, management and treatment of insulin resistance and associated disease.

Chapter 3: Effect of lactose compared to sucrose on glycaemic control following HIIT

3.3 Methodology

3.3.1 Participants

A sample of 8 sedentary, lactose tolerant males (n=4) and females (n=4) aged 20-70 years completed the pilot study. Participant characteristics are in **Table 1.**

An initial study explanation and screening for inclusion/exclusion criteria was conducted over the telephone prior to the study beginning. To be included in the study, participants could either be male or female (post-menopausal), be between 18 and 70 years old and untrained. Participants had to complete less than 150 minutes of purposeful exercise per week of more than walking (VO_2max ≤43.9 ml·kg·min^{-1}). Participants must tolerant to lactose and have no known heart and respiratory conditions. Throughout the course of the study, activity level must remain the same as before the study, as this will affect study results; i.e., participants were to complete normal daily habits.

Participants and researchers involved in face-to-face procedures will be required to be non-symptomatic to COVID-19 prior to each laboratory visit. If you have recently tested positive for COVID-19 or you are unwell with a normal cold or the flu, or other infection, you will be excluded or participation postponed until you are well again, which is also normal practice outside of current pandemic conditions. You will be required to comply with the University COVID-19 requirements, as well as researchers.

The telephone consultation involved a health screening questionnaire to further assess participant suitability. The participant was able to ask any questions or clarify any concerns they had in regard to the study at this point. All protocols and procedures were approved by the Health and Disability Ethics

Committee (HDEC) prior to study commencing (2022 EXP 12240). All participants provided written consent prior to participation.

Table 1. Participant Characteristics.

Variable	Value
Participants (n)	8
Age (y)	52 ± 17
Height (cm)	168 ± 13
Body weight (kg)	84 ± 21
BMI ($kg \cdot m^2$)	29 ± 6
Fat free mass (kg)	56 ± 16
BMR ($kcal.day^{-1}$)	1585 ± 356
VO_2max ($ml \cdot kg^{-1} \cdot min^{-1}$)	29 ± 8
Wmax (W)	201 ± 58
TTE (minutes)	7 ± 3

Values are expressed as means +/- SD. BMI, body mass index; BMR, basal metabolic rate; FFM, fat free mass; VO_2max, Maximal oxygen uptake; Wmax, maximal workload; TTE; time to exhaustion.

3.3.2 Setting and Location

Participants were free-living and research protocols were conducted within the exercise, nutrition and sport science laboratory at Massey University, Albany, Auckland.

3.3.3 Study overview

The design of the study was a double-blind, block randomized (Williams design), crossover design comprising of three treatments: lactose, sucrose and a placebo control. The trial was conducted over a nine-week period per trial, per participant. Participants completed 3, 2-day trials with 10 visits to the laboratory. One week prior to starting the experimental trials, there was a baseline testing day and the day before each trial began the continuous glucose monitor was inserted **(Figure 3 & 4).** Details of the experimental conditions were:

1. **Lactose** added to a non-caloric beverage at a quantity (g) equivalent to energy (kJ) lost during the HIIT session.

2. **Sucrose** added to a non-caloric beverage at a quantity (g) equivalent to energy (kJ) lost during the HIIT session.
3. **Non-caloric placebo control**; a non-caloric beverage. The equivalent energy was provided as fat in the evening meal **(Table 3).**

Each experimental condition was randomised using a coded allocation sequence code. The sequence code was controlled by a third-party lab staff member who was not involved within the study to ensure double-blind conditions. At the end of data collection and statistical analysis, the treatment code was revealed to the researchers by the third party. The randomisation sequence is displayed in **Table 2.**

Table 2. Randomisation sequence for the trial, where A, B, C represent the three treatment conditions.

		Trial Number		
Participant	**Sequence**	**1**	**2**	**3**
01	1	A	B	C
02	2	B	C	A
03	3	C	A	B
04	4	C	B	A
05	5	A	C	B
06	6	B	A	C
07	1	A	B	C
08	2	B	C	A

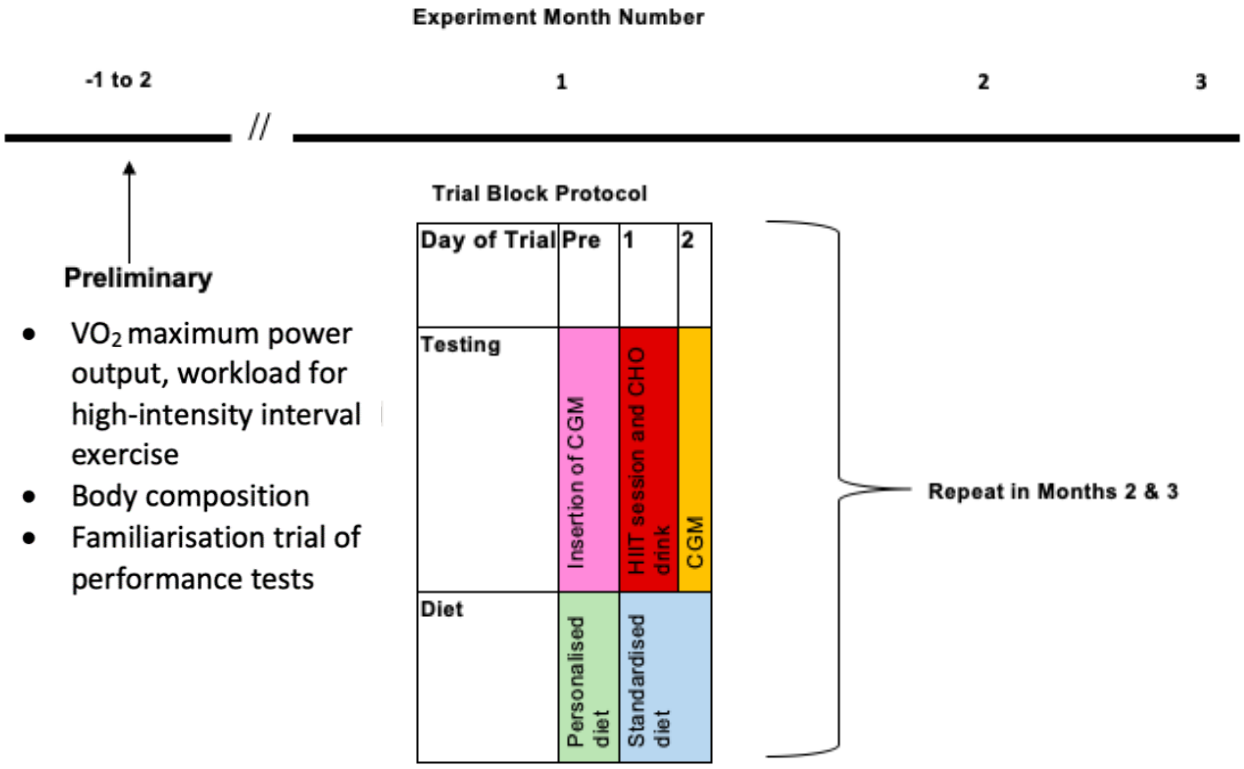


Figure 3. Research design and partition of exercise intervention and diet standardization.

3.3.4 Study Experimental Sessions

The study comprised of 10 visits to the laboratory; an initial visit, then three visits for each arm of the study. Participants conducted the trials approximately four weeks apart to ensure a satisfactory washout period between exercise trials (lactose and sucrose) and to reduce the training effect which could occur and effect glycaemic response. Female menstrual cycle phase was not accounted for as literature suggested that cycle phase had only negligible impact on post-exercise and fed glycaemic response (Oosthuyse & Bosch., 2010).

Visit 1, was a baseline testing day which consisted of body composition measurements using bioelectrical impedance analysis (BIA) (InBody 230, Seoul, South Korea). The fat free mass calculated during the scan was used to calculate energy requirements for each individual participant. This was then followed by a VO_2max/Wmax test on a cycle ergometer (Velotron, Racermate, Seattle, USA), which consisted of an incremental TTE, whereby intensity gradually increased from moderate to high intensity.

During all exercise sessions, participants breathed through an on-line gas analysis system (Moxus, AEI Technologies, Naperville, IL, USA) that covered the mouth and nose, and attached to a 0.2 micro filter system, which filters microorganisms. The study was completed during the COVID-19 pandemic within New Zealand, therefore all participants wore masks while on University premises, as required by the university's COVID-19 policies.

Visit 2, was conducted at the laboratory around 24-h before experimental trial at 15:00 to 17:00 h. At this time, a CGM (Medtronic Guardian Connect, Northridge, CA, USA) was inserted into the subcutaneous tissue on back of the upper arm. Participants remained in the lab for ~2-h while a calibration routine involving finger-prick blood samples (lancet device) was conducted; at the 2.00 h and 2.5 h time points. Participants in the meantime were instructed on the calibration and data recording procedure, and were informed on the feeding protocol for the standardized diet that was provided to participants to consume over the following two days of the metabolic trial.

Visit 3, was day 1 of the metabolic trial. The participant conducted a finger-prick calibration in the morning upon wakening / before eating breakfast. The participants consumed standardized mixed-macronutrient meals (~55% carbohydrate, 30% fat and 15% protein) at standardised times; 9:00 h (breakfast), 12:00 h (lunch) and 15:00 h (snack). If the participant did not consume the meal at the given time, they reported to the lead researcher who noted this in data analysis for temporal adjustment. Participants then reported to the laboratory at 16:30 h wearing exercise-suitable clothing. Before commencing the exercise test, the CGM was recalibrated using a HemoCue RT201+ (HemoCue AB, Ängelholm, Sweden). The participant was then fitted to the bike in preparation to perform a supervised session of high-intensity interval exercise.

Post-exercise (5 min), the test drink or placebo beverage was ingested. The lactose and sucrose was consumed within an artificially-flavoured, zero calorie beverage (Sprite Zero, Coke, NZ) at a quantity equivalent to the exercise-induced energy expenditure (aerobic metabolism). This was determined from a regression equation of oxygen consumption to bike power output established during the VO_2max test during baseline testing, in Visit 1. Using the VO_2max / Wmax regression equation, the maximal oxygen uptake (VO_2max) was plotted against the maximal work capacity (Wmax) and a linear regression equation was calculated. This regression equation was then used to calculate the energy (calories) expended in both the 30% and 80% efforts. Carbohydrate quantity was then calculated based on the energy expenditure to match the energy burnt in the HIIT session. The quantity of the beverage (ml) was 10 fold

of the carbohydrate quantity. The calculated energy, carbohydrate and quantity values were used to determine the composition of the carbohydrate beverages consumed after the exercise session.

The control (no sugar placebo) condition consumed a non-caloric placebo beverage (Sprite Zero, Coke, NZ), with the exercise calories added as fat in the form of butter and macadamia nuts to the evening meal (**Table 3**). After exercise and drink ingestion, participants showered if desired and remained in the laboratory until 19:00 h where they then consumed a low-carbohydrate high-fat (LCHF) dinner meal. Participants were then able to leave the laboratory under instructions to abstain from consuming any food or drink, other than water for the rest of the evening. Participants were required to complete a finger prick calibration before bed.

Visit 4. On Day 2 of the metabolic trial, the participants reported to the lab at 06:30 h. The CGM was recalibrated using the HemoCue RT201+ (HemoCue AB, Ängelholm, Sweden). A venous catheter was placed into an antecubital vein by a trained individual for fasting and postprandial blood collection. A high glucose drink (75 g dextrose, 300 ml water) was ingested at 07:00 h for assessment of the OGTT response over the course of 2 h. The meals for the remainder of the day were mixed macronutrient meals following the same macronutrient split as day 1 (**Table 4**).

Blood glucose was continuously monitored via GCM until the end of Day 2, with special note to post-prandial responses to all meals throughout Day 2.

The CGM transmitter devices and hand held glucometer was collected by the researcher from the participant or was returned by the participant. This process was completed two more times, ~4 weeks apart each time.

3.3.5 Protocols.

Exercise tests were conducted using the electronically braked cycle ergometers (Velotron, Racer Mate, Seattle, WA) and gas analysis using a calibrated Moxus MaxII Metabolic System (AEI Technologies, Naperville, IL, USA).

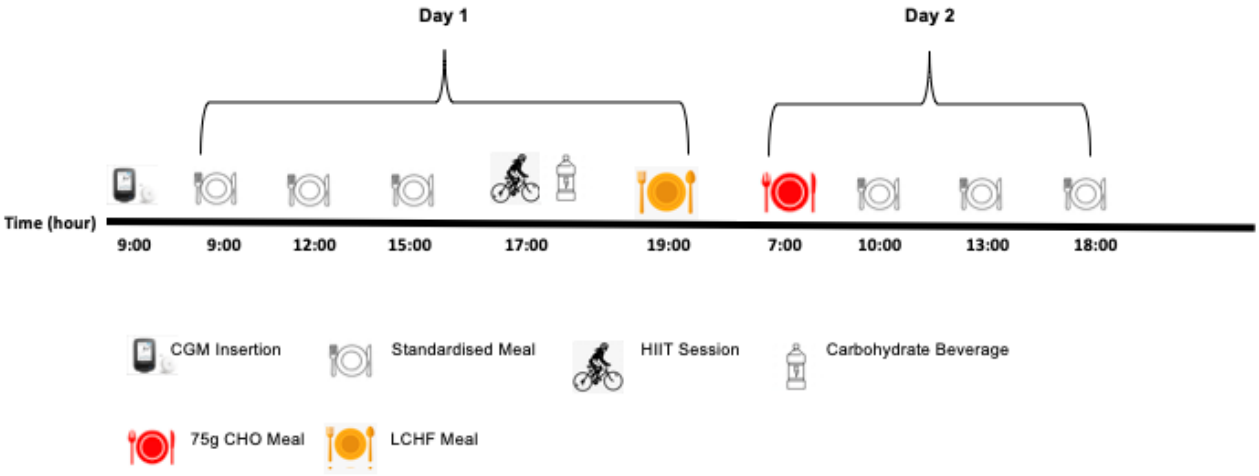


Figure 4. Metabolic Test Protocol.

3.3.6 Exercise Protocol

A 5 minute warm-up at 50 W was completed before the participants complete 10 x 1-min sprint intervals at ~80% Wmax interspaced between 1-min recovery intervals which will involve slow riding at ~30% Wmax. The exercise finished with a 5 minute cool down at 50 W (Gillen et al., 2013). The workload for the high-intensity intervals was determined for each participant by prescribing ~80% Wmax achieved during the VO_2max test in visit 1, baseline testing of the study. The ~30% Wmax recovery interval were also determined from this test.

3.3.7 Exercise-Induced Energy Expenditure

In visit 1, baseline testing, VO_2max was measured continuously using a metabolic cart with an online gas collection system (Moxus MaxII Metabolic System, AEI Technologies, Naperville, IL, USA). Participants breathed into a mouth piece which was connected to the system and wore a nose peg, both in which allowed us to determine the quantity of O_2 consumed during the test. To determine the total energy expenditure (kcal/min), total VO_2 (ml/min) was used. The energy of the carbohydrate beverages was

matched to the exercise-induced energy expenditure measured from the within-subject VO_2 power regression established during the VO_2 max test during baseline testing.

3.3.8 Standardised Diet

Each participant received the same food, the quantity was relative to resting energy expenditure (REE). To individualise diets to each participant, daily energy intake was calculated by the Cunningham equation, with energy from basal physical activity accounted for using 1.4*RRE (Harris & Benedict, 1918) (Dietitian New Zealand Handbook, 1988). On day 1, 90% of daily energy was provided at main meals; 30% at each breakfast (7:00 h), lunch (12:00 h), and dinner (19:00 h) and 10% of daily energy was a mid-afternoon snack (15:00 h). The macronutrient composition of the breakfast, lunch and snack meals were; ~55% carbohydrate, ~30% fat and ~15% protein. On day 1, the breakfast comprised of berry yoghurt (250g) and honey flavoured oats (90g). Lunch was butter chicken. Afternoon tea was raisins and peanuts. Dinner was a low carbohydrate, high fat meal which consisted of tinned salmon, steamed vegetables, butter and macadamia nuts (~5/80/15% carbohydrate/fat/protein). All subsequent meals were consumed under free-living conditions and were pre-packaged mixed-macronutrient meals following the same macronutrient slit as day 1. Breakfast was ingested at 7:00 h, which was a high glucose meal consisting of 75g of glucose in water. Morning tea was berry yoghurt (125g), peanuts (20g) and raisins (10g) (10:00 h). Lunch was a butter chicken meal and peanuts (13:00 h). Lastly, dinner was beef lasagne with edam cheese (18:00 h). The nutrient composition of each meal is displayed below in **Tables 3 and 4.**

Table 3. Nutritional Composition of next-day meal (day 1).

Meal	**Energy (kJ)**	**CHO (g)**	**Protein (g)**	**Fat (g)**
Breakfast (~30% EI)	2372 ± 171	94 ± 6	21 ± 2	9 ± 1
Lunch (~30% EI)	2435 ± 134	83 ± 4	19 ± 1	19 ± 1
Afternoon Tea (~10% EI)	930 ± 169	12 ± 5	3 ± 2	18 ± 1
Low-CHO Dinner (~30% EI)	3145 ± 532	6 ± 0	26 ± 7	70 ± 12
Total Daily Intake	7858 ± 424	194 ± 13	61 ± 3.7	92 ± 3.5

Values are expressed as meals ± SD. EI, energy intake

Table 4. Nutritional Composition of next-day meal (day 2).

Meal	Energy (kJ)	CHO (g)	Protein (g)	Fat (g)
Breakfast (~15% EI)	1200	75	0	0
Morning Tea (~15% EI)	1141 ± 100	27 ± 3	12 ± 1	13 ± 1
Lunch (~35% EI)	2834 ± 235	88 ± 8	23 ± 2	25 ± 2
Dinner (~35% EI)	2907 ± 235	74 ± 8	31 ± 2	29 ± 2
Total Daily Intake	8082 ± 571	264 ± 18	65 ± 5	68 ± 5

Values are expressed as meals ± SD. EI, energy intake

Participants were required to eat at the scheduled times, if they failed to eat at the given time they were to contact a researcher, who took note of this and controlled for this when calculating glucose response. Water and other non-caloric beverages were allowed within a prescribed maximum quantity of caffeinated beverages of 3 per test day

3.3.9 Continuous Glucose Monitoring

To measure blood glucose levels, CGM was used throughout each of the 2-day trials. GCM is a tool to identify glycaemic response to food and exercise outside of the laboratory setting (Nardacci et al., 2010). The CGM sensors recorded interstitial blood glucose concentration and were inserted into the upper arm ~12 hours prior to the first meal of the trial to be consumed on day 1. Blood glucose data measured on the sensor were read through a transmitter and recorded through the specific software downloaded on participant's device. To calibrate the CGM, a finger prick calibration was carried out using a glucometer. We analysed various glycaemic parameters over the course of the trial (placebo-control, lactose and sucrose groups). The main results which were assessed the day following the exercise/carbohydrate beverage interventions were; post-exercise glycaemia, overnight glycaemia, postprandial glycaemia and overall glycaemia (7:00 – 24:00 h).

Postprandial glycaemic responses were assessed for all of the following day meals; breakfast, morning tea, lunch and dinner. This was assessed by calculating the 3-h post meal average glucose concentration, the postprandial peak glucose concentration (highest glucose concentration attained over the 3-h postprandial period) and the 3-h AUC using the trapezoidal rule (Little et al., 2011; Gillen et al., 2012). The next-day mean average blood glucose concentration and 24-h blood glucose concentration and 24-h

glucose AUC were assessed from midnight to midnight following the exercise/carbohydrate beverage interventions. Meal overall glycaemia was assessed from 7:00 h to 24:00 h the day following exercise and carbohydrate beverage intervention.

The mean glucose concentration and the AUC were analysed 1-h after consuming the carbohydrate beverage and 3 hours following the LCHF dinner. Overnight glycaemia was defined as the 12-h period prior to the next-day OGTT consumption and was analysed by calculating the 12-h average glucose concentration and 12-h glucose AUC.

Unfortunately, in a number of trials the CGM stopped recording data on day 2 of the metabolic trial after lunch or dinner. The reason for this are unknown and because of this, full data was not able to be calculated over that period and is coded as missing data within the linear mixed model analysis (**Table 6**).

3.3.10 Oral Glucose Tolerance Test

An OGTT was conducted on day 2 of the metabolic trial, the morning after the HIIT exercise session. The purpose of the OGTT was to determine following day glucose tolerance and insulin sensitivity. An intravenous cannula was inserted into the forearm vein of the participant by a trained phlebotomist for repeated blood samples to be performed at the given time points; 0, 30, 60, 90, 120 minute. The catheter was maintained patent through a saline flush and removed after the final sample. At the 7:00 h following a 12 h overnight fast, the participant consumed a 75g glucose solution (100% Dextrose Brewing Sugar) within 2 minutes. Immediately after drawing the blood the plasma ethylenediaminetetraacetic acid (EDTA), was separated in the centrifuge (10 min) and 30 minutes post blood draw the serum plasma was separated in the centrifuge (10 min). Plasma glucose at each of the given time points was analysed immediately through the use of a lancet device.

All samples were stored at -80 degrees celsius and remained to be stored at -80 degree celsius for the next 10 years. Blood samples were not analysed due to non-significant findings, secondary to unable to reach the statistically significant, calculated sample size (n=12). If samples were to be analysed in the future, this would include analysis of plasma insulin, glucose and free fatty acids.

3.3.11 Statistical analysis

The sample size was estimated from the difference of the glucose response to a standard 75g load following high-intensity exercise with or without post-exercise carbohydrate replenishment (Taylor et al.,

2018). To detect a significant difference ($p \leq 0.05$) between conditions with 80% power, it was calculated that n=12 was required.

Treatment effects on outcomes were estimated with linear mixed models in SAS (9.4, Cary, NC, USA). All data was log-transformed prior to analysis to manage heteroscedasticity and to express outcomes as percentages. Fixed effects was treatment; period and sequence was dropped because of insufficient repeats of these design parameters due to reduced sample size **(Table 1).** AUC were baseline adjusted with the CGM average 15-min glucose concentration prior to each AUC as a numeric covariate. Cohen's *d* was calculated to assess effect size between treatments for select outcomes of interest, where the denominator was the SD of in the control condition. The cohen's *d* is classified by the size of effect, a trivial effect size is a cohen's *d* of 0 – 0.2, a small effect size is a cohen's *d* of 0.2 – 0.6, a moderate effect size is a cohen's *d* of 0.6 – 1.2, a large effect size is a cohen's *d* of 1.2 – 1.6, a very large effect size is a cohen's *d* of 1.6 – 2 and an extremely large effect size is cohen's *d* of greater than 2. To adjust for the low sample size we completed a correction factor equation to cohen's d using the equation, 1-3/ (4*df - 1).

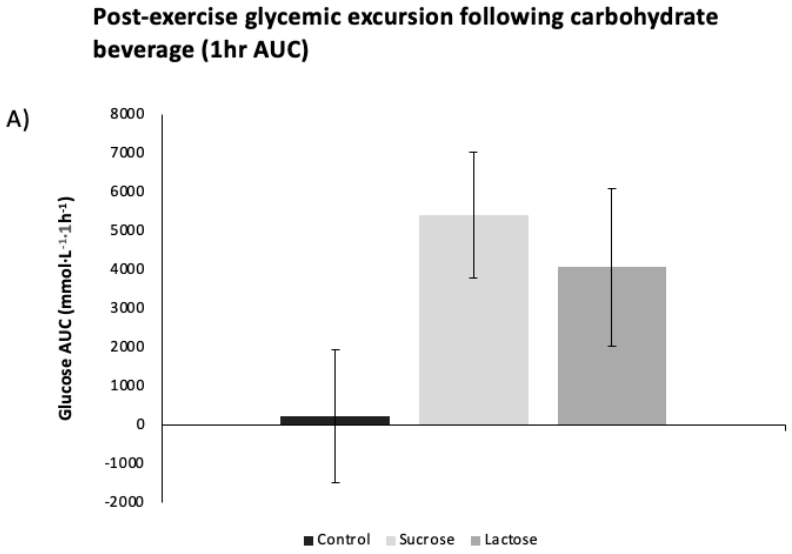
Confidence limits have been calculated to assess the range of data and measures the limit between which measurement error is with a probability. Comparatively, to confidence intervals provide an indication of how reliable the results are by using the sample to estimate the interval of probable values of the population.

The coefficient of variation of the GCM outcome, otherwise known as the test-retest within-subject SD or the typical error of measurement, was calculated from the average SD expressed as a percent of the baseline mean glucose concentration of the difference in 30 min fasting morning glucose on day 1 for each of the 3 conditions, with each difference divided by root two, then the 3 within-SDs converted to variance and pooled to CV%. This CV contains both technical and within-subject biological error and was able to be compared to the instrument value that we were given.

3.4 Results

3.4.1 Post Exercise Glycaemic Parameters

After consumption of sucrose compared to lactose the 1 h and 2 h post-exercise glycaemic excursion was greater, as displayed in **Figure 5.** The effect size of the post-exercise interstitial glycaemic excursion (1 h and 2 h AUC) was greater for sucrose (1 h d=2.03, ±Cohen *d* 90% confidence limit 1.1, ±90% confidence limit 1876; 2 h d=1.88, ± Cohen *d* 90% confidence limit 0.63, ±90% confidence limit 1071) than after lactose consumption (1 h d=1.62, ±1.0, ±1740; 2 h d=1.58, ±0.58, ±982).



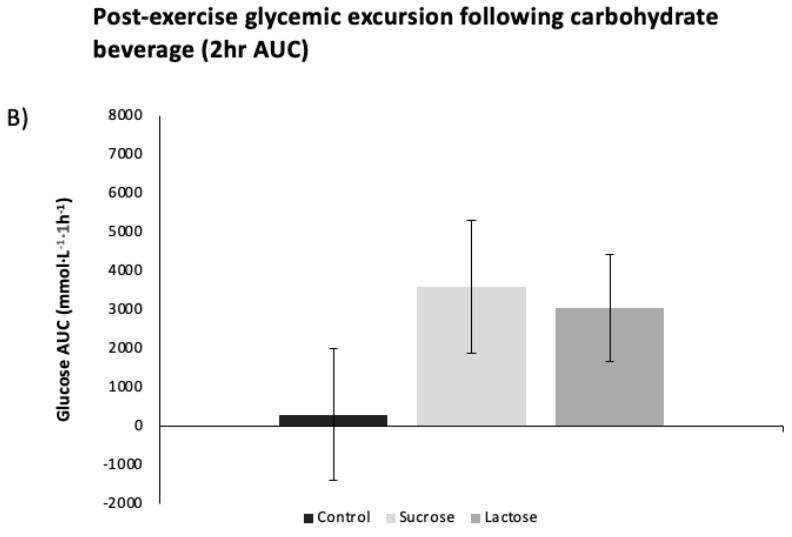


Figure 5. Post-exercise glycaemic excursion represented as AUC measured with CGM, following the post-exercise test drinks for the first 1 h and total combined 1 and 2 h AUCs. Values are expressed as means ± SD.

3.4.2 Overnight Glycaemic Control

Overnight blood glucose concentration is (22:00 to 07:00 h) displayed in **Figure 6.** The interstitial blood glucose concentration was lower in the control group compared to lactose and sucrose. The effect size for overnight mean interstitial blood glucose concentration was moderate for both sucrose-control (5730 mmol·L^{-1}·1h^{-1}, ±90% Confidence Limits, CL, ±4685, d=0.61, ±0.57) and lactose-control (6202 mmol·L^{-1}·1h^{-1}, ±5329, d=0.66, ±0.64).

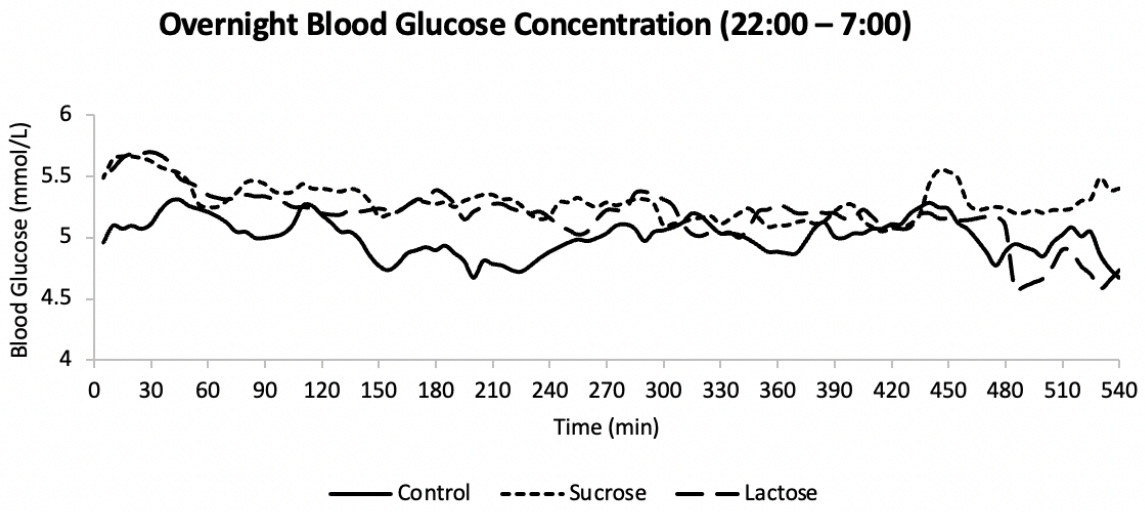


Figure 6. Overnight interstitial blood glucose concentration measured with CGM.

Data represent the 3-h post dinner to next-day OGTT (22:00 – 7:00). Values are expressed as means.

3.4.3 Oral Glucose Tolerance Test (OGTT) in Plasma Samples and Continuous Glucose Monitoring

There was a trivial to small effect size for sucrose-control (1233 mmol·L^{-1}·1h^{-1}, ±2340, d=0.20, ±0.51; **Table 5**) compared to lactose-control which elicited a extremely trivial effect size (257 mmol·L^{-1}·1h^{-1}, ±2566, d=0.01, ±0.56; **Table 5**). Lactose-sucrose had a negative small effect size (-976 mmol·L^{-1}·1h^{-1}, ±2012, d=-0.26, ±0.44; **Table 5**).

Plasma glucose concentration in response to next-day 75g glucose ingestion attenuated a lower mean glycaemic response after sucrose (6.9 mmol/L) in comparison to lactose (7.0 mmol/L) and control (7.6 mmol/L). Although the difference was acute between treatment groups, a difference of 0.1 mmol/L between lactose and sucrose.

When comparing the average blood glucose concentration in response to next-day 75g glucose ingestion of the OGTT to CGM between treatments we found the following; a 26% difference in the control group (OGTT 7.6 mmol/L; CGM 6.1 mmol/L; **Figure 7&9**), a 12% difference in the sucrose group (OGTT 6.9 mmol/L; CGM 6.2 mmol/L; **Figure 7&9**), and 14% difference in the lactose group (OGTT 7.0 mmol/L; CGM 6.2 mmol/L; **Figure 7&9).**

3.4.4 Post-prandial Glycaemic Response to Standardised Meals

The 3-h post-prandial blood glucose response to next-day meals (75g glucose ingestion, snack, lunch and dinner) are outlined in **Table 5** and **Figures 7, 8, 9 & 10.** The mean blood glucose concentration was lower, with a larger effect size in sucrose-control group following all next-day meals (75g glucose ingestion 1233 $mmol \cdot L^{-1} \cdot 1h^{-1}$, ±2340, d=0.20, ±51; snack 4635 $mmol \cdot L^{-1} \cdot 1h^{-1}$, ±19449, d=-0.41, ±2.51; dinner -3950 $mmol \cdot L^{-1} \cdot 1h^{-1}$, ±12511, d=-0.37, ±1.3; **Table 5**) except after lunch where difference in effect size was trivial in all contrasts (sucrose-control 168 $mmol \cdot L^{-1} \cdot 1h^{-1}$, ±17958, d=-0.18, ±1.88; lactose-control 42 $mmol \cdot L^{-1} \cdot 1h^{-1}$, ±19073, d=-0.41, ±2.0; lactose-sucrose -126 $mmol \cdot L^{-1} \cdot 1h^{-1}$, ±18703, d=-0.15, ±2.0; **Table 5**). There were no significant differences in the 3-h mean blood glucose concentrations and/or AUC between sucrose-control, lactose-control and/or lactose-sucrose **(Table 5, Figures 7, 8, 9 & 10).** Post-prandial glucose concentrations after 75g glucose ingestion (2 h), snack and lunch were the lowest after consumption of lactose in comparison to sucrose and control **(Figure 8, Figure 10A&B).**

3.4.5 Overall glycaemic response

Next day overall glycaemia (AUC) from 7:00 h – 24:00 h inclusive was similar in control (8325 $mmol \cdot L^{-1} \cdot 1h^{-1}$, SD 6058) and sucrose (8830 $mmol \cdot L^{-1} \cdot 1h^{-1}$, SD 9885) trial, but lower with lactose (6785 $mmol \cdot L^{-1} \cdot 1h^{-1}$, SD 5686). Whereas, the lactose-control AUC difference was -1539 $mmol \cdot L^{-1} \cdot 1h^{-1}$ (±2350; d=-0.27, ±0.40); sucrose-control 506 $mmol \cdot L^{-1} \cdot 1h^{-1}$ (±3503; d=0.06, ±0.59); and the lactose-sucrose contrast -2045 $mmol \cdot L^{-1} \cdot 1h^{-1}$ (±3523; d=-0.35, ±0.59), where the lactose-control contrast expressed in terms of Cohen *d* standardised difference, was small with uncertainly (confidence interval) ranging from trivial to moderate.

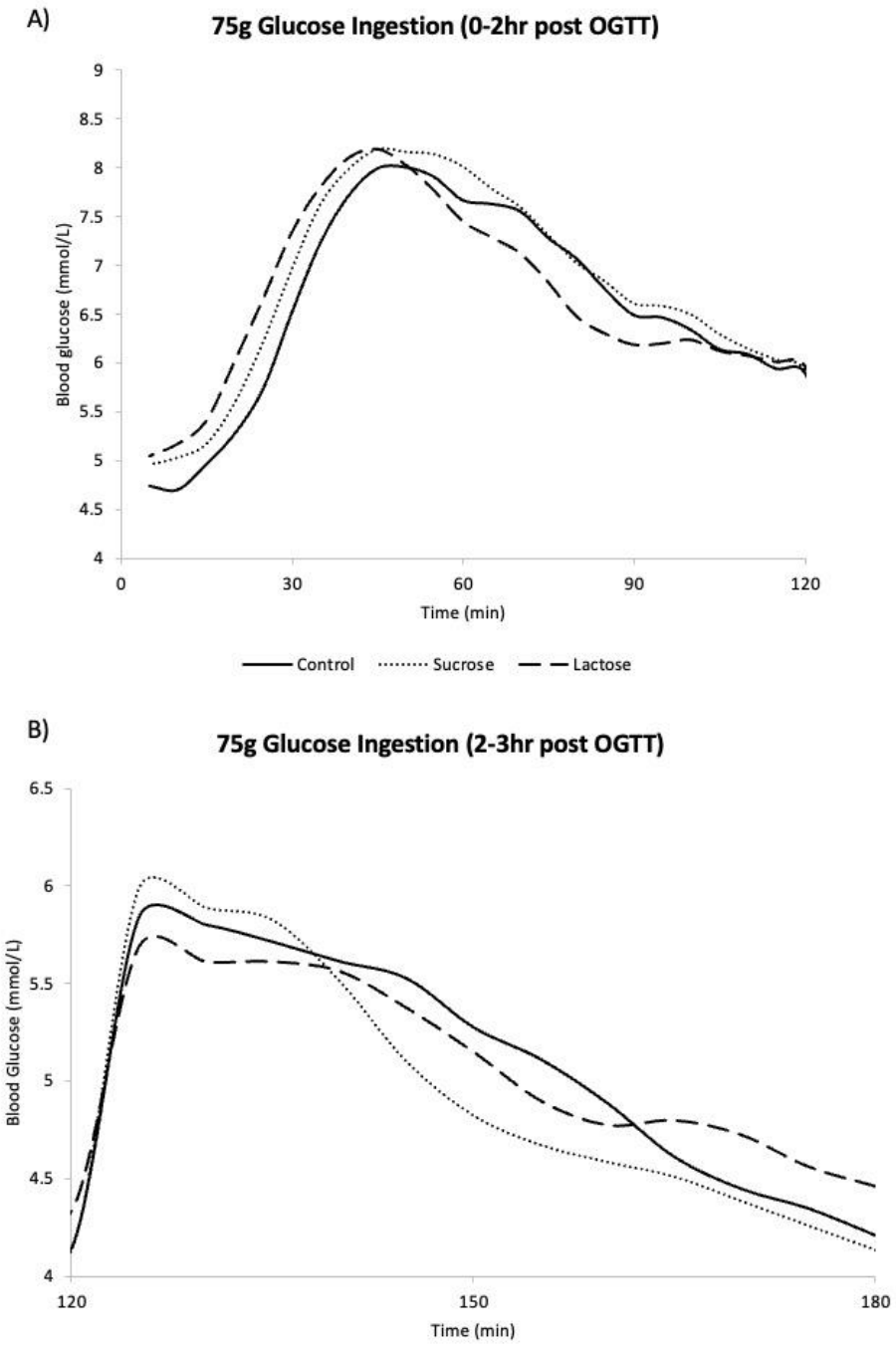
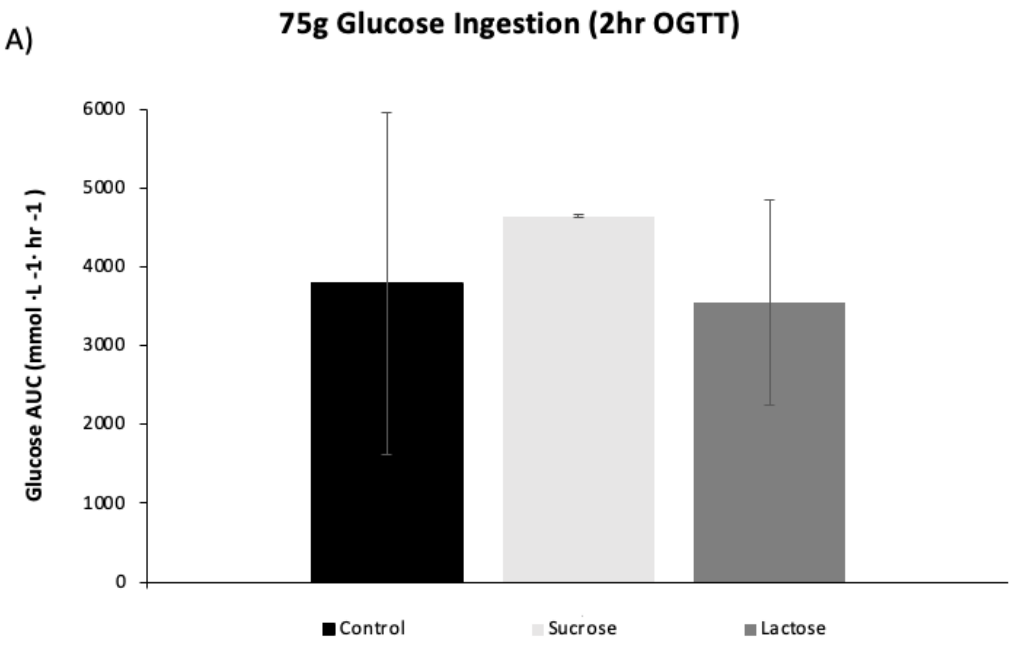


Figure 7. Interstitial glucose concentration measured with CGM during the OGTT. Values are expressed as means.

Data was analysed (A) 0-2 h post ingestion and (B) 2-3 h post ingestion.



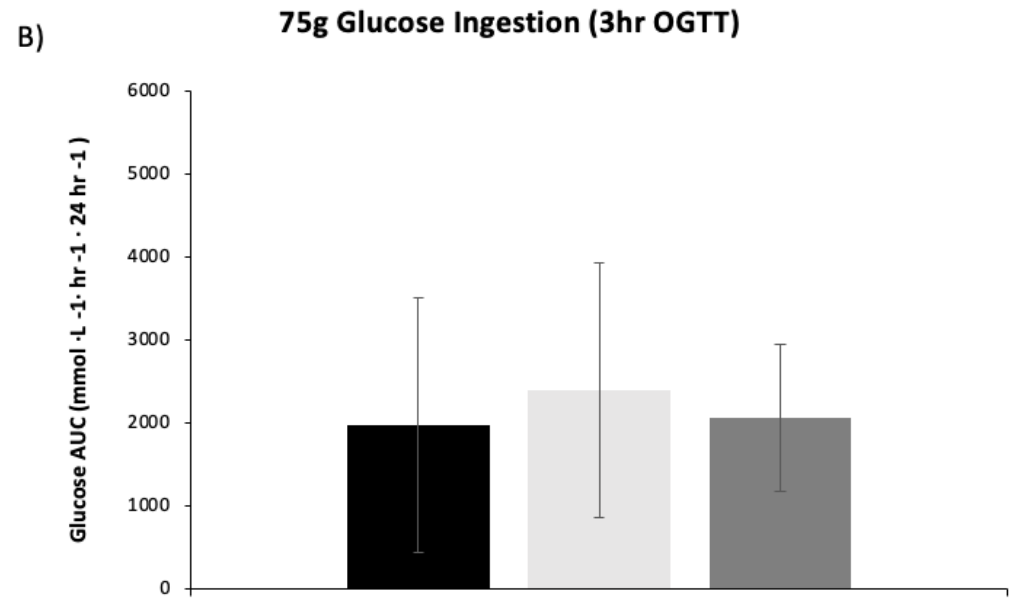


Figure 8. Interstitial glucose concentration AUC. Measured with CGM during the OGTT. Values are expressed as means ± SD.

Data was analysed (A) 0-2 h post ingestion and (B) 2-3 h post ingestion.

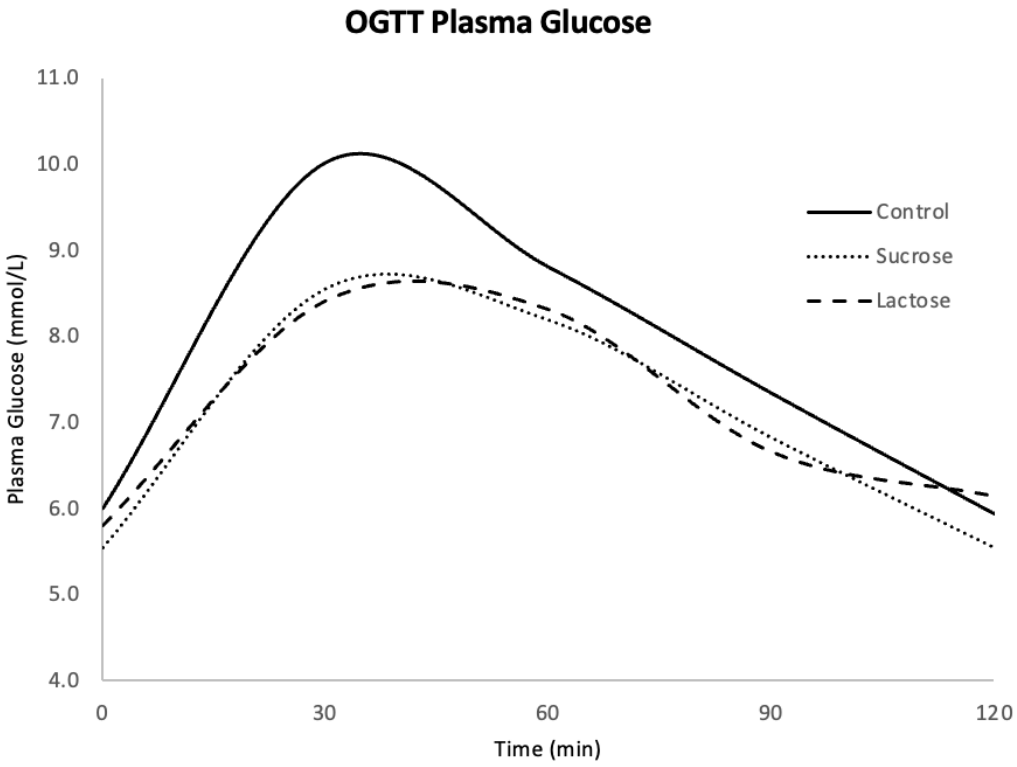


Figure 9. Plasma glucose concentration during the OGTT. Values are expressed means.

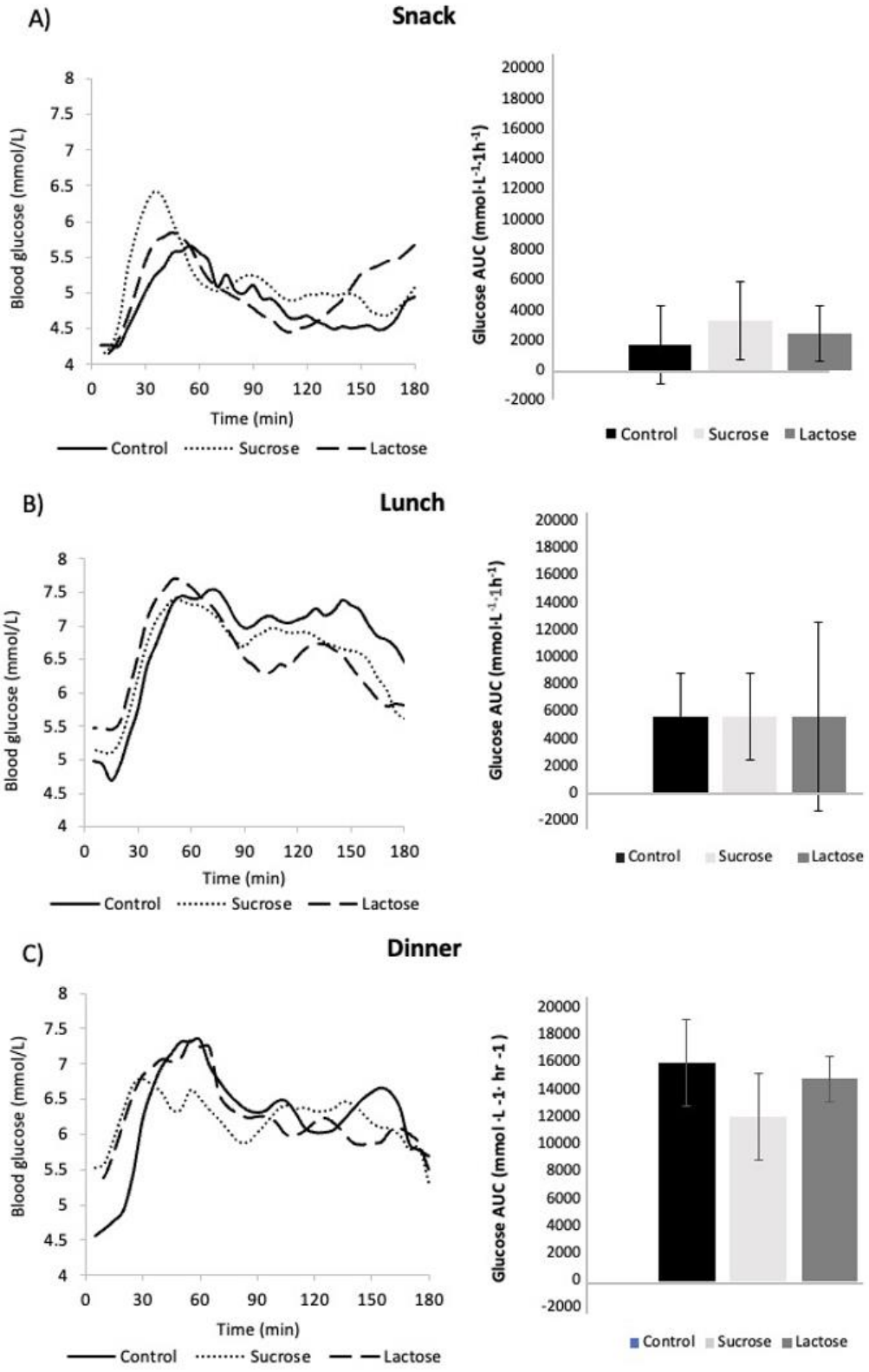


Figure 10. Interstitial glycaemic responses 3 hours following snack, lunch, and dinner meals consumed the day after exercise from continuous-glucose monitoring. Values are expressed as means ± SD.

Table 5. Analysis of 3 h postprandial glycaemic responses from continuous-glucose monitoring to next-day meals.

	Group Contrast LSmean Differences and 90% Confidence Limits (CL) for glucose AUC ($mmol \cdot L^{-1} \cdot h^{-1}$)				
Contrast	**Est**	**90% CL**	**p-value**	**Cohen *d***	**Cohen *d* 90% CL**
			OGTT		
Sucrose – Control	1233	±2340	0.37	0.20	±0.51
Lactose – Control	257	±2566	0.86	0.01	±0.56
Lactose – Sucrose	-976	±2012	0.41	-0.26	±0.44
			Snack		
Sucrose – Control	4635	±19449	0.39	-0.41	±2.51
Lactose – Control	2170	±12673	0.63	-0.29	±1.64
Lactose – Sucrose	-2466	±5630	0.45	-0.34	±0.73
			Lunch		
Sucrose – Control	168	±17958	0.99	-0.18	±1.88
Lactose – Control	42	±19073	1.00	-0.41	±2.0
Lactose – Sucrose	-126	±18703	0.99	-0.15	±2.0
			Dinner		
Sucrose – Control	-3950	±12511	0.57	-0.37	±1.3
Lactose – Control	-1230	±14129	0.88	-0.18	±1.5
Lactose – Sucrose	2720	±10577	0.65	0.09	±1.1

Data are least-squares mean (LSmean) estimates and 90% confidence limits adjusted for pre-intervention baseline within a linear mixed model.

Oral glucose tolerance test, OGTT.

Area under the curve, AUC.

Least squares mean, LSmean.

Estimate, Est.

3.4.6 CGM Reliability

The inter-day reliability of the Medtronic Guardian Connect CGM is shown in **Table 6**. The average within-SD expressed as a coefficient of variation relative to the mean was 5.0%.

Table 6. Reliability of the Medtronic Guardian Connect CGM.

Day 1 fasting contrast	Average Variance ($mmol \cdot L^{-1}$)	Within-subject SD or typical error in glucose units ($mmol \cdot L^{-1}$)	Within-subject SD (% of the average mean difference)
Sucrose – Control	0.33	0.41	5.1
Lactose – Control	0.31	0.39	5.2
Lactose – Sucrose	0.14	0.26	3.4

3.5 Discussion

3.5.1 Overview of Findings

The primary aim of the study was to identify the extent to which replenishing the HIIT-exercise induced energy deficit with carbohydrate attenuates the normal increase in glucose tolerance. This was observed with a single-bout of HIIT, as a mechanism to examine the next-day glycaemic control with continuous-glucose monitoring (CGM) following the ingestion of glucose and standard meals. Specifically, we were interested in evaluating if there was a difference in the overall (7:00 – 24:00 h) and post-prandial glycaemic control in response to ingesting the milk-sugar, lactose, compared to the ingestion of ordinary table sugar, sucrose. Both of these sugars having known different effects on the blood glucose response and on liver metabolism (Wolever et al., 1985; Bantle., 2009; Roe & Schwartzman., 1932). However, contrary to our hypothesis the next-day post-prandial glycaemic response to the standard meals revealed largely non-clear differences between carbohydrate types and the carbohydrates and control. Additionally, we hypothesised that lactose ingestion would provide an improved glycaemic response following completion of HIIT exercise in comparison to after sucrose ingestion. Our findings provide some evidence in support, as seen by a pattern for a small overall glycaemic AUC of lactose (lactose-control, d=-0.27; 90% CL=0.14, -0.65; lactose-sucrose d=-0.35; 90% CL=10.25, -0.93; **Table 5**). Although this finding was not statistically significant with the uncertainty (confidence interval) being substantial, there was many contributing factors to this. One of the contributing factors to the uncertainty was that the sample size (n=8; **Table 1**) was less than the pre-study power calculation (n=12). This is a likely result of recruitment challenges associated with the COVID-19 pandemic and post-COVID-19 reluctance of people wishing to volunteer. It is proposed that a larger sample size would have likely reduced the confidence interval of our results. To place the results in context, the above lactose-sucrose effect equates to a reduction in glucose concentration of 0.5 mmol/L. A study conducted by Asia Pacific Cohort Studies Collaboration identified a strong continuous relationship between usual fasting glucose and the risk of cardiovascular disease death (Asia Pacific Cohort Studies Collaboration., 2004). It was established that a 1 mmol/L lower usual fasting glucose level was associated with a 15-22% lower risk of cardiovascular death (Asia Pacific Cohort Studies Collaboration., 2004). Effects of approximately 10% or more are considered relevant for clinical health outcomes in the community (Hopkins et al., 2009). Therefore, if the estimated effect size was maintained over a chronic timeframe, post exercise lactose ingestion may result in a near clinically relevant effect size. This suggests that either non-biologically important or substantial effects cannot be discounted. Therefore, these findings support previous insight on the attenuating effect of post-

exercise carbohydrate consumption on the HIIT-induced improvements on next-day glycaemic control after exercise and provide some preliminary data on the effect of a low-glycaemic index carbohydrate type, lactose, on post-prandial glycaemia.

3.5.2 Oral Glucose Tolerance Test

In our study we used OGTT to evaluate the glycaemic response to the 75-g glucose ingested the morning after the HIIT exercise session and post-exercise carbohydrate beverage. Despite sucrose displaying a larger effect size of glycaemic control and plasma glucose, compared to lactose and the non-carbohydrate control, the results were trivial. Due to this result and having a sample size less than the pre-study power calculation (n=12), our study did not complete the analysis of plasma free-fatty acids, plasma insulin and serum glucose as initially intended. Inconclusive results were most likely to have been observed. Furthermore, to support our resource decision, within another study which investigated the effectiveness of high-intensity interval training in comparison to endurance training on glycaemic control in individuals with type 2 diabetes, no changes to any OGTT variable were observed between the three groups (HIIT, endurance and control), however fasting glucose, HbA1c levels and glycaemic variability were all reduced in the HIIT group (Winding et al., 2018).

3.5.3 Continuous Glucose Monitoring

Within the study, CGM was the primary tool to assess acute glycaemic changes in response to the consumption of carbohydrates following high-intensity interval training. Continuous glucose monitoring provides instant, 24/7 reading of glucose levels, glucose trends and alerts forthcoming hyper-or hypoglycaemia. CGM technology therefore provides rapid information that may be used by the individual to make decisions on exercise or nutrition. The mean average relative difference of the CGM unit used in the current study (Medtronic Guardian Connect, Northridge, CA, USA) compared to self-monitoring of blood glucose concentration values by finger prick sampling was 11.5% (Freckmann et al., 2019). In comparison to other CGM models on the NZ market, for example, Dexcom had a mean average relative difference of 16% (Huang et al., 2020). While we did not compare blood glucose concentration, the plasma glucose concentration measured within the OGTT was 80-89% higher than CGM data.

The day-to-day within-subject coefficient of variation is an important measure of the combined typical error of measurement and the within-subject variability contributing to current variability (standard error) in outcomes and in the current study was 5% **(Table 6).** In comparison, the published Dexcom coefficient

of variation was 17 ± 3% (Shah et al., 2019). Therefore, in comparison to other CGM devices on the market, the CGM used in the study, Medtronics Guardian Connect CGM, within-subject variability contributing to current variability was 3.5 times smaller than Dexcom, thus justifying our resource decision.

Within the research setting, rapid and continuous sampling serves as an advantage as it provides researchers with immediate data availability (post-processing) and also the flexibility to assess the trend of the blood glucose concentration over an extended period of time, rather than a snapshot. The most traditional and common method to measure blood glucose is by a finger prick capillary sample with a lancet device, however, this does not provide the continuity and dynamics of information in which CGM does. An earlier study concluded that conventional glucose testing such as, finger prick capillary sample, misses day-to-day excursions in plasma glucose levels, the missed high and low values are pertinent in the diagnosis of type 1 diabetes (Boland et al., 2001). Finger prick capillary blood sampling is more taxing and invasive and increases participant burden compared with GCM (Heinemann et al., 2008). We were able to assess the trend across the 24-h period in response to the HIIT and carbohydrate ingestion, despite the current study showing minimal effect within 24-h glycaemic control between the selected carbohydrates and relatively minor effects relative to the carbohydrate-deficit group. The trend showed lower next-day postprandial and overnight glycaemic excursions after lactose consumption in comparison to sucrose and non-carbohydrate control after a single-bout of HIIT. While these results were not statistically significant, the trend corresponds with results from Estafanos et al. (2021) who observed a reduction in select next-day post-prandial glycaemic excursions; however, they only saw minimal changes within overall glycaemic control following HIIT when assessed by CGM technology. Similarly, Schleh et al. (2019) used CGM to assess glycaemic control in response to acute endurance exercise and found no effect on next-day 24 h mean or peak glucose concentration, however revealed lower post-prandial hyperglycaemia the following day (Schleh et al., 2019). These conclusions may be attributable to findings from a meta-analysis investigating the effect of exercise on glycaemic control as assessed by CGM within patients with type 2 diabetes (MacLeod et al., 2013). MacLeod et al. (2013) findings established that short-term exercise might preferentially target postprandial hyperglycaemia and glucose fluctuations, which are conveniently sense by CGM. With respect to our study, these findings suggest that CGM technology is proficient in sensing the postprandial dynamic changes, which was a primary outcome in the data analysis of results. Thus, again justifies the use of CGM technology within the study.

The constant assessment feature of the CGM allows for exhaustive information of the change in blood glucose over the given time period. The pivotal time points that were assessed within our study were next-day post-prandial glycaemic excursions. Within the study, there was a notable difference in the glycaemic response between all three groups after the 75g glucose ingestion, snack and dinner meals. However, glycaemic response to the lunch meal was relatively similar between all three groups. There is increasing research which illustrates that hyperglycaemic excursions throughout the day are independent risk factors for developing cardiometabolic complications (Monnier and Colette., 2008; Rawlings et al., 2011). Consequently, CGM technology captures glycaemic excursions and the use of this technology within the study magnifies the clinical relevance of the benefit of 24-h glycaemic assessment within patients with type 1 and 2 diabetes and/or metabolic syndrome.

Despite CGM technology providing many strengths such as, the ability to capture the dynamic changes of glycaemic control, this method was not executed optimally within the study due to the CGM sensors frequently losing connection and consequently losing data. Unfortunately, the CGM sensor predominately lost connection overnight between days 1 and 2 (8.33%) and day 2 between lunch and dinner (50%). The frequency in which this occurred is referred to in **Table 6**. This loss in connection reduces the accuracy of the data reported, especially the blood glucose concentration data. This was a primary finding within the study, overnight glycaemia 22:00–6:00 and therefore to assess this measure with the missing blood glucose values, glucose AUC was calculated, which provided an average. In cases whereby three or more consecutive data points were missing, the average of the three previous data points were used to calculate the glucose AUC value. This provided an estimate figure in order to assess the predicted data trend, nonetheless extensive time (~25 hours) was dedicated to post-collection data stream analysis in excel to match data dropout with time series, in order to ensure reliable AUC data was calculated. Unfortunately, due to the missing data of the CGM technology the weight of the effect size and statistical significance was also reduced in overnight glycaemia results (possible type-1 error). Overnight glycaemia within the study was the only glycaemic parameter which displayed statistical significance for the sucrose-control group (p=0.05; **Figure 6**) and the lactose-control group (p=0.005; **Figure 6**). Therefore, the unreliable nature of the CGM technology served as a key limitation of the study.

3.5.4 HIIT and glucose control

The findings of the study showed improved next-day (7:00-24:00 h) glycaemic control after HIIT when remaining in a carbohydrate-energy deficit compared to when consuming sucrose and lactose. However, the finding is not significant ($P \geq 0.05$) and it poses the question, if it was the HIIT training which produced the greatest effect towards glycaemic control in comparison to the carbohydrate deficit? The design of the study included a low-carbohydrate, high-fat dinner after the exercise and carbohydrate-beverage treatment. However, the mechanism of why restricting carbohydrates post exercise results in next-day glycaemic improvements is unable to be determined from the study design. Nevertheless, inferences from prior literature leads us to hypothesise that the relative hypoglycaemic pattern, if shown in future research to be robust, may be attributable to enhanced skeletal-muscle glycogen content and post-exercise insulin action. A negative correlation has been previously shown between skeletal-muscle glycogen and post-exercise insulin action, showing that insulin-stimulated glucose uptake is increased when glycogen is depleted due to exercise utilisation being greater (Bogardus et al., 1983; Holtz et al., 2008).

Borgardus et al. (1983) identified that muscle glycogen depletion after exercise is associated with reduced basal and insulin stimulated carbohydrate oxidation rates (low dose insulin infusion, $P<0.04$; high dose insulin infusion, $P<0.03$)(Bogardus et al., 1983). It was also concluded that even when 100 g of carbohydrates were re-fed after a single bout of glycogen-depleting exercise, there is still an increase in the rate of insulin-stimulated carbohydrate oxidation (18% increase)(Bogardus et al., 1983). Holtz et al. (2008) identified that carbohydrate-restriction after exercise resulted in an increase in insulin-stimulated glucose storage and elevated fasting fat oxidation in sedentary, overweight individuals ($r= 0.82$, $p=0.003$) (Holtz et al., 2008). Greater full-body glucose and lipid metabolism in sedentary, overweight individuals are two characteristics often associated with the healthy, active population and therefore this finding is notable.

The exercise protocol within the study comprised of 1 minute at 80% Wmax followed by 1 minute at 30% Wmax repeated 10 times. Due to the short and intense nature of the session, we can assume that the primary substrate that was used was muscle glycogen (van Loon et al., 2001). In a study that measured muscle glycogen utilization using the same protocol, of 1 minute at 80% Wmax followed by 1 minute at 30% Wmax repeated 10 times, a ~20-24% reduction in muscle glycogen concentrations was observed after the HIIT and this did not influence potential reductions in liver glycogen stores (Skelly et al., 2017). It is

these potential reductions in liver glycogen stores which have an insulin sensitising effect (Richter et al., 2001).

3.5.5 Lactose as an alternative carbohydrate post-exercise

The importance of carbohydrates after exercise to replenish muscle glycogen has been widely recognised within the literature to assist with muscle recovery (Ivy et al., 2004; Williams., 2004). The extensive research is primarily targeted to the athletic population with respect to the importance of muscle glycogen on performance (Bergström et al., 1967), with minimal research targeting individuals in a state of disease such as, type 2 diabetes or metabolic syndrome.

Odell et al. (2021) stated that in order to promote optimal combined liver and muscle glycogen replenishment post exercise, glucose must be combined with a carbohydrate that heavily influences hepatic metabolism, such as, galactose or fructose. It is likely that lactose, a disaccharide of glucose and galactose, may be adequate to promote combined muscle and liver glycogen resynthesis, due to the structural combination of glucose and galactose. There are limited other studies which investigate muscle or liver glycogen replenishment and/or recovery of exercise performance with consumption of lactose.

Within the study, glycaemic variability was not directly assessed, however we were able to make predictions on the variability by evaluating the cohen's *d* standard deviation (SD), as well as prediction of the uncertainty of the least square mean, identified through confidence limits (CL). The spread of the confidence limits were larger within the lactose group across all next-days meals, except the snack (**Table 5**). Thus, despite lactose showing potential for improved glycaemic control after exercise, the uncertainty of the mean estimate (CL) suggests that more research is required to confirm this glycaemic pattern. As a result, we are unable to make a firm statement regarding the use of lactose to improve glycaemic control following exercise.

3.5.6 Post-exercise carbohydrate-energy deficit and glycaemic control

Our study established that there were probable improvements in glycaemic control when remaining in a carbohydrate-energy deficit after HIIT, within a sedentary population. This was demonstrated by a lower overnight blood glucose concentration within the control group compared to sucrose and lactose groups. In a study that also investigated the effects on glycaemic control when remaining in an energy deficit after HIIT (Estafanos et al., 2022), showed improved next-day glycaemic control when remaining in a

carbohydrate-energy deficit opposed to when replenished following a single-bout of HIIT after breakfast ($p<0.05$, $d=1.3$) and snack meals ($p<0.05$, $d=1.2$). This data suggests that next-day glycaemic control after HIIT can be manipulated by consumption of carbohydrates post-HIIT within a sedentary population. However, Estafanos et al. (2022) investigated glycaemic control after HIIT within a female only sample. Our study investigated females as well as males, on the effect of glycaemic control after HIIT and carbohydrate intervention, and while the sample size was too small to differentiate a sex difference, the similar outcomes to Estafanos et al. (2022) suggests effects may be robust across sexes, but a larger sample size study would be required to confirm this.

Comparable findings to the present study have been established in two studies, which investigated the effects of maintaining an exercise-induced energy (Schleh et al., 2019) and carbohydrate-energy (Taylor et al., 2018) deficit after acute endurance exercise of 45-90 minutes at 65-70% VO_2 peak in healthy populations. Both studies showed improved next-day glycaemic control and insulin sensitivity. Regardless, of these similar findings the methodology was different. Taylor et al. (2018) only measured next-day insulin sensitivity through the use of a 2-h OGTT the morning following exercise, therefore, only measured a narrow time period of glycaemic control. In a more comparative study design to the current study, Schleh et al. (2019) refed participants mixed-macronutrient meals post-exercise, whereas our study refed with a low carbohydrate high-fat meal. Schleh et al. (2019) investigated exercise-induced energy deficit on next-day glycaemic control, whereas we investigated exercise-induced carbohydrate deficit on next-day glycaemic control. Both of these previous studies involved moderate-intensity continuous exercise (~65% VO_2max), whereas our study involved low-volume, high-intensity exercise. In relation to our study, these findings suggest that it is the exercise intervention which provides the greatest impact on improved next-day glycaemic control and insulin sensitivity, rather than the carbohydrate intervention.

It was established that when comparing the intervention sugars to the non-carbohydrate control, lactose had the greatest effect size ($d=-0.27$, ±0.40; **Table 5**) compared to sucrose ($d=0.06$, ±0.59; **Table 5**) for overall glycaemic response (7:00am – 24:00). Despite the difference shown between lactose compared to sucrose, this is a small effect size nonetheless and thus a trivial result. Notably, we were able to observe next-day post prandial glycaemic excursions and evaluate how glycaemic control varied across the day. We concluded that although the results unfortunately showed a trivial size of effect and were not statistically significant, it revealed that ingestion of lactose in comparison to sucrose after HIIT resulted in a smaller mean post prandial glycaemic excursion following 75g glucose ingestion (2064 $mmol \cdot L^{-1} \cdot 1h^{-1}$,

2390 mmol·L^{-1}·$1h^{-1}$; **Figure 8**), snack (7411 mmol·L^{-1}·$1h^{-1}$, 9876 mmol·L^{-1}·$1h^{-1}$; **Figure 10**) and lunch (16843 mmol·L^{-1}·$1h^{-1}$, 16969 mmol·L^{-1}·$1h^{-1}$; **Figure 10**). This aligns with research reporting that lactose has a consistently lower impact on blood glucose concentration post ingestion than sucrose (Wolever et al., 1985).

Postprandial glycaemic response the day following exercise and carbohydrate beverage ingestion was a key outcome evaluated in our study. Estafanos et al. (2021) observed a transient improvement in postprandial glycaemic control the day following exercise (breakfast $p<0.05$, $d=1.3$; snack $p<0.05$, $d=1.2$). These finding can be linked to a negative correlation between glycaemic control and muscle glycogen content, as previous research suggests, ingesting carbohydrates subsequently increases muscle and liver glycogen concentrations and reverses the exercise-induced improvements to glycaemic control, which occur as glycogen stores increase (Cartee et al., 1989; Kawanaka et al., 1999). Post-prandial glycaemia is an independent risk factor associated with cardiovascular disease that causes a larger effect than fasting hyperglycaemia (Hanefeld et al., 1996; Kuusisto et al., 1994). Postprandial hyperglycaemia is characterised by hyperglycaemic spikes that stimulate oxidative stress when combined with soluble, advanced glycation end products and lipid peroxidation products (Giugliano et al., 1996; Schmidt et al., 1999). The lipid peroxidation products act as an activator of upstream kinases that triggers endothelial dysfunction and expression of inflammatory genes and thus postprandial hyperglycaemia is a paramount disturbance in the pathogenesis of vascular failure (Node and Inoue., 2009). Thus, it can be inferred that this study's finding provides clinical relevance for type 2 diabetes and metabolic syndrome, providing management strategies for these patients, as well as prevention strategies for the onset of type 2 diabetes for patients categorised as prediabetic.

3.5.7 Effect of HIIT in a sedentary population

Babraj et al. (2019) assessed and demonstrated glycaemic control and insulin sensitivity in response to HIIT in sedentary young males. Babraj et al. (2009) conducted 2-6 HIIT sessions over the course of two-weeks, in contrast our study conducted a single session of HIIT. Babraj et al. (2009) identified a significant reduction in plasma glucose and insulin AUC after the 2 weeks of HIIT, whereas our study did not exhibit a significant reduction in plasma glucose and was unable to determine plasma insulin due to not completing blood sample analysis. However, due to the opposing characteristics of study participants within Babraj et al. (2009) to our study, a direct comparison cannot be made. This then poses the question, does the quantity of HIIT sessions completed influence the effect on glucose and insulin metabolism? Like our study, Babraj et al. (2009) conducted a VO_2max test in order to determine baseline physiological

markers of fitness. Babraj et al. (2009) study consisted of 16 participants which had a VO_2max of 47 ± 11 ml·kg^{-1}·min^{-1}, in comparison to our study which contained 8 participants and had a VO_2max of 29 ± 8 ml·kg^{-1}·min^{-1}. Despite both studies classifying participants as 'sedentary', there is a significant difference in VO_2max between participants and in fact a VO_2max of 47 ± 11 ml·kg^{-1}·min^{1} would classify the participants of Babraj et al. (2009) as recreationally-active. Therefore, training status of the individual or individuals' within a study may have a potential influence on the glycaemic control and insulin sensitivity after HIIT. However, this remains to be fully investigated.

Chapter 4: Conclusion

4.1 Overview and Achievements of Study Aims and Objectives

The study completed was a pilot study, aiming to identify the extent to which replenishing the energy deficit induced by a single session of low volume HIIT with carbohydrate, alters next-day glycaemic control following standard meal ingestion in sedentary, healthy males and females. Specifically, we were interested in evaluating if there is a difference in the glycaemic control in response to ingesting the milk sugar, lactose, compared to when ingesting ordinary table sugar, sucrose and comparing both sugars to a placebo-designed, non-carbohydrate control. The main finding of the study is that when remaining in a carbohydrate-energy deficit, there seemed to be improved overnight glycaemic control after high-intensity interval training, with some indication that lactose can also elicit an improved glycaemic response. While the data contained some sampling uncertainty, the results support previous work, suggesting that replenishing carbohydrates blunts the subsequent postprandial hypoglycaemic effect of exercise compared to when remaining in a carbohydrate-energy deficit. However, more research is required to validate the efficacy of these results.

4.2 Contribution of Research

To date there is limited data on the interaction of exercise and post-exercise carbohydrate type on the subsequent glycaemic response. Therefore, our research will provide new information into if carbohydrate type affects glycaemic response following exercise. If the study or follow up larger-sample trials were to get published this may influence further research on the choice of carbohydrate type following exercise to elicit improved glycaemic response and overall health of the population.

Additionally, investigating the effect of post-exercise carbohydrate type on glycaemic response will also provide relevant information for people with insulin resistance. Informing these individuals about which carbohydrate type provides them with improved glycaemic control, especially following exercise will be beneficial as for some individuals with diabetes this can be difficult and stressful to manage (Riddell et al., 2009).

4.3 Strengths and Limitations

A perceived strength of the study was the inclusion of the OGTT on day 2 of the study. The OGTT provides a measure of insulin sensitivity which is a factor in the magnitude and duration of postprandial increase in blood glucose and insulin concentrations. The OGTT also serves as a comparison to CGM data.

In the OGTT the derived AUC is a measure of glucose excursion after glucose loading (75g glucose drink) which is used to assess glucose tolerance (Sakaguchi et al., 2016). Measurements such as, glucose and insulin peaks, mean and AUC are calculated to assess the glucose and insulin action over the course of 2 hours, assessed every 30 minutes (0, 30, 60, 90, 120 minute). This provides more in-depth analysis of next-day glycaemic response in response to either lactose, sucrose, or the control group post-exercise in comparison to the CGM data. Especially considering that the CGM devices frequently lost data overnight, prior to the OGTT assessment. Therefore, determining insulin sensitivity using equations which are validated against the gold standard measurement (Matsuda and DeFronzo, 1999) increased the validity of the study design, providing acute data in respect to glucose tolerance. However, the OGTT also served as a limitation of the study. The OGTT was the longest visit into the laboratory and required participants to be there early in the morning (6:30am). Individuals who expressed interest in the study, yet did not proceed to participant commonly reported the addition of the OGTT, involving needles and blood samples taken, was the key factor to why they decided to not partake. This identified barrier to participation was unexpected but was a subsequent factor in the reduced sample size (n=8) compared to the statistically significant, calculated sample size (n=12). Majority of participants who completed the study reported the OGTT to be the greatest burden and vexatious aspect of the study design.

A key factor to the extremely challenging participant recruitment was the COVID-19 pandemic. Despite, the study providing a reimbursement for the participants time and travel cost, it was smaller compared to the amount that was asked from the participants. In addition, recruiting sedentary-overweight individuals aged 50-70 years was more challenging than anticipated. This resulted in the amendment to HDEC to modify the participant criteria in order to target to aim to include the student population who are already on campus to remove the travel barrier. Furthermore, another key limitation in the study was the minimal time to conduct the research due to unfortunately having to change research projects because of COVID-19 protocol enforcements by the University administration, and doing so whilst completing clinical placement responsibilities.

A strength of the study was the inclusion of the standardised diet on day 1 of the study. Despite, data from the CGM devices on day 1 prior to the ingestion of the carbohydrate beverage (lactose, sucrose or control) and exercise intervention not being assessed, standardised diet was provided for the full day 1, to provide a baseline measure. This created consistency among the participants in terms of the true effect of the exercise intervention and carbohydrate beverage on blood glucose control.

A limitation of the study design was the unawareness of participants HbA1c level prior to participation in the study. Despite the exclusion criteria including, type 1 and 2 diabetes mellitus, no pre-participant HbA1c blood samples were completed to assess current HbA1c status and therefore insulin sensitivity pre-trial. According to fasting blood glucose concentrations, taken at 0 minutes on day 2 of the metabolic trial prior to the OGTT, two of the eight participants had apparent hyperglycaemia (blood glucose≥7mmol/L). Therefore, some sample heterogeneity in glucose tolerance may account for the lack of any clear effect of lactose compared to sucrose on postprandial glycaemia.

4.4 Directions for Future Research

Our study was a pilot study, as a result of being unable to achieve the target sample size and the exploratory nature of the intervention. The findings of our study suggest probable and insightful information on carbohydrate-energy replacement after a single session of high-intensity exercise. Specifically, the effect of lactose in comparison to sucrose on glycaemic control and insulin sensitivity. A larger sample size would be able to provide more clarity towards the extent of the effect size and therefore essential for future research within this field. Although, an approximate post-hoc sample size estimation suggests that n>30 would be required to identify any carbohydrate differences, which may be at a biologically trivial effect size.

4.5 Final Conclusion and Recommendations

From the findings of this research the following recommendations can be made. However, to assess the accuracy and efficacy of these recommendations further testing in a larger sample size is encouraged.

- Overnight glycaemic responses provided evidence to suggest improved glycaemic response when consuming lactose compared to when remaining in a carbohydrate deficit after HIIT; an effect that trended lower compared to sucrose.

For future research within the field, our study recommends the following:

- To conduct research among a larger sample size to be able to quantify a significant effect and/or large effect size.
- To conduct the study using CGM units with a greater user reliability, and if available, units that don't require calibration (we were unable to access Dexcom units due to Licencing blocks for any research on non-diabetic cohorts).
- To conduct research within a type 2 diabetic population group to assess glycaemic response in a cohort with disordered glycaemic control.
- Participants to consume the post exercise meal 3 hours after consuming the post-exercise drink, rather than 2 hours. This allows a 3-h glycaemic response and AUC for the carbohydrate beverage to be assessed.
- Include analysis of plasma insulin after a next-day OGTT, by collecting blood samples and sending to a laboratory to be analysed. This allows researchers to be able to quantify the insulin response to different carbohydrates and/or carbohydrate deficit after exercise.
- Include analysis of plasma free-fatty acids after a next-day OGTT, by collecting a blood sample and sending it to a laboratory to be analysed. This allows researchers to be able to assess the correlation between plasma free-fatty acids and blood glucose concentration. This will enable researchers to assess the link between blood glucose and cardiovascular health.
- Include measurements of muscle glycogen content, AMPK and distal insulin signalling targets in skeletal muscle biopsy samples. This would add an in depth understanding into the skeletal muscle response of the carbohydrate type and/or carbohydrate-energy deficit.

It is key to note that the recommendations based on the findings of the study are of relevance to individuals who have type 2 diabetes and/or metabolic syndrome to assist with disease prevention, management and treatment. These recommendations do not consider the impact in which a carbohydrate-energy deficit may have towards muscle recovery and athletic performance. Therefore, more research is required to assess the effect of a carbohydrate-energy deficit after exercise as well as, lactose consumption post-exercise within an athletic population.

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Appendices

Appendices A: Participant Information Sheet

Participant Information Sheet

High-Intensity Exercise Benefits to Blood Glucose Control – Is the Milk-Sugar Lactose better than Sucrose?

Formal Study title: Effect of Carbohydrate-energy Replacement on Glycaemic Control Following High-Intensity Interval Training. Does Lactose Improve Glycaemic Control in Comparison to Sucrose?

Primary Contact and Researcher: Miss Rose Stirling.

Contact phone number: [redacted]

Email: r.stirling@massey.ac.nz

Lead and Student Supervisor: Prof. David Rowlands

Study Site: School of Sport, Exercise and Nutrition, Massey University, Albany Campus

Contact phone number: [redacted]

Email: d.s.rowlands@massey.ac.nz

Ethics committee referee: Dr Kaio Vitzel

Purpose of the Study

The primary aims of the study is to identify the extent to which replenishing the exercise-induced energy deficit with carbohydrate alters next-day glycaemic control following standard meal ingestion. Specifically, we are interested in evaluating if there is a difference in the glycaemic control in response to ingesting the milk sugar lactose compared to when ingesting ordinary sugar sucrose; two sugars with known different effects on the blood glucose response and on liver metabolism.

This study will provide data for a Masters of Nutrition and Dietetics thesis and insight into how lactose might be a useful alternative sugar to sucrose in the diet of people with elevated risk of later developing diabetes.

Voluntary Participation and Withdrawal from the Study

You are invited to take part in a study on the effect of carbohydrate-energy replacement on glycaemic control following high intensity interval training. 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 any care you receive or future relationships with the University. 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 sets out 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. We will go through this information with you and answer any questions you may have. 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.

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.

If you wish to withdrawal from the study then please inform Miss Rose Stirling, Masters Student. If you do withdrawal from the study after the second tests are completed then your data will be used in the study. However, if you withdrawal before this point then your data will not be used in the study and your information will be deleted.

Please make sure you have read and understood all the pages before proceeding to the consent form.

Study Design and Involvement

The study involves the continuous monitoring of blood glucose levels through a device called a continuous glucose monitor (CGM). The CGMs comprises a sensor unit placed on your skin that samples from a very small wire inserted just below your skin surface. The CGM remains on your skin for the duration of each study of three blocks, and sends the glucose data collected to an App that we will load onto your phone or iPad or Android device. The CGM allows us to measure the body's glucose concentration (glycaemic) response every 5 min following an exercise test and meals. The CGMs are now becoming very popular in people with diabetes to better control blood glucose levels. In order to calibrate the CGM a blood sample is required to be taken and is outlined in the consent form.

The design of the study isa double-blind, randomized, cross over, where you will ingest following a bout of high-intensity interval training (HIIT) exercise one of the three test drinks containing either lactose, sucrose, or placebo. conducted over 3 months per participant, comprising 3 trials and 10 visits to the laboratory. The visits are summarised in Figure 1 and Table 1 below, with more specific detail of activities provided in Figure 2. You and the researchers will not know which carbohydrate beverage being tested (blinding) at each trial to control for any pre-existing information which may influence outcomes. There are 12 participants total completing this study.

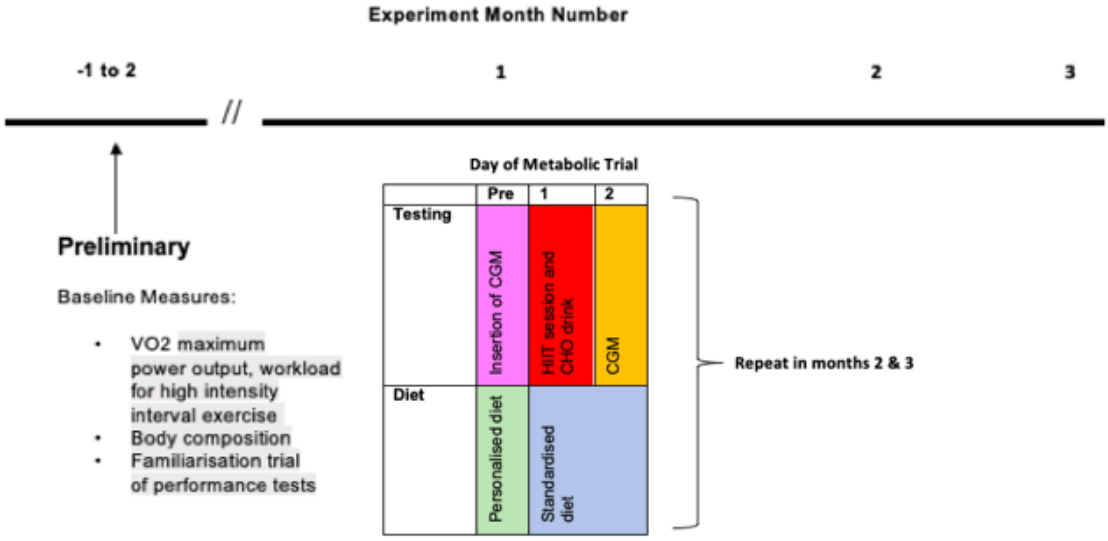


Figure 1. Research design and partition of weekly exercise and diet.

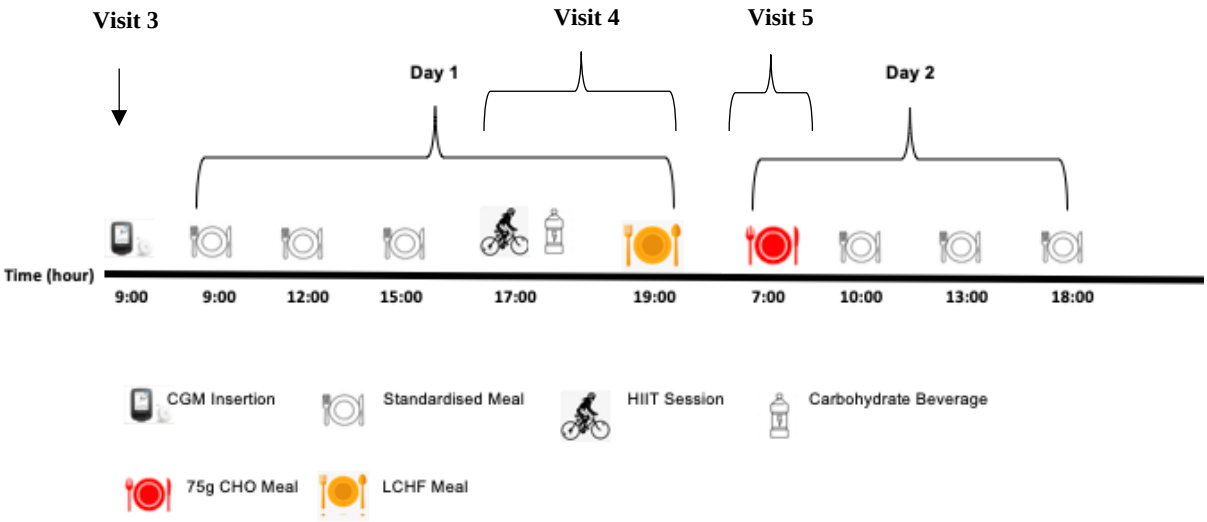


Figure 2. Metabolic test protocol

An initial meeting will be conducted between yourself and MSc Dietetics Masters Student, Rose Stirling, which will provide an explanation of the study and screening for inclusion/exclusion criteria will be provided by a telephone or online consultation. You will be able to ask any questions and have the questions answered. If you are the research team are both happy then you will be invited to sign the consent form. Following which, you will be asked to complete the health screening questionnaire. If no health issues are revealed, then a date and time for the Visit 1 will be arranged.

Table 1. Summary of study visits.

Visit	
1	• Recap of study involvement. Opportunity to answer any further questions and gain consent (if not done in the initial meeting). • Laboratory and cycle ergometer familiarization comprising a short 3-5 min low intensity ride after bike fit. Please bring appropriate clothing to ride a bicycle. • Detailed study information sheets will be provided at this time.
2	• At an agreed time, you will report to the University laboratory. Please bring clothing and footwear suitable for riding a lab/gym bicycle. • We will determine your body composition to determine body mass and body fat percentage using a bioelectrical impedance scale. • You will then perform an exercise test on the lab bicycle to determine your fitness level (maximal oxygen uptake and maximum watts), called a VO_2max/W test. This test involves starting with easy pedalling, then gradually increasing exercise workload until you reach your exercise limits or exhaustion from breathing or muscle effort (or both). • After this exercise test, you will rest for about 10 min then we conduct a familiarization trial of the HIIT exercise comprising 1 interval at 80% of your Wmax. • During the VO_2max test and HIIT exercise you will breathe through an on-line

	gas analysis facemask that covers the mouth and nose. From this we collect a sample of your expired breath to determine your metabolic rate. The breath is also filtered through 0.2 micro filter system, which filters microorganisms. At other times, you will need to comply with the University site visit requirements for COVID, at the time.
3	• In the evening the day prior (Pre) to the first experimental day (Day 1) you will come to the lab around 16:00 to 17:00h. • At this time, a continuous glucose monitor (CGM) (Medtronic Guardian Connect) will be placed on back of the upper arm or if more suitable, on the outer upper thigh. • You will remain in the lab for ~2-h while a calibration routine involving finger-prick blood samples is conducted (2 samples – 2 hours and 2 ½ hours after placement). • In the meantime, you will be instructed on the calibration and data recording procedures using the iPad or Android App. • You will also be instructed on the feeding protocol for the standardized diet that we will provided to you to consume over the following 2-day metabolic trial. • From the insertion to the removal of the CGM device no paracetamol is to be taken as this can affect the accuracy of the CGM sensors. • Following each experimental block, we can show you the glucose response and how the technology works if you are interested.
4	• In the morning prior to breakfast, you will conduct a calibration procedure of the CGM under video instruction from the researchers (Zoom, Teams, Skype). • There after you will be in your usual home or work environment and consume a standardized mixed-macronutrient meal at standardised times; 9:00 h (breakfast), 12:00 h (lunch) and 15:00 h (snack) and other drinks. • Depending on your personal schedule, the meal and exercise times on both

	Day 1 and Day 2 may be moved back or forward 1 h, but must be ingested at the specified times, as this is part of the fine control the blood glucose response to the exercise and meals. • Later in the day you will next report to the laboratory at 17:00 h with exercise-suitable clothing. After changing your CGM will be recalibrated. • Next, you will perform a the HIIT exercise (10x1-min cycle intervals at 80% maximal power, with 1 min recovery at 30% maximal power, total 20 min). • Post-exercise (5 min), you will ingest the test drink or placebo. • The lactose and sucrose will be consumed from an artificially-flavoured 500-ml beverage (lemonade flavour) at a quantity equivalent to the exercise-induced energy expenditure (aerobic metabolism). The control (no sugar) condition will comprise a taste-matched zero calorie placebo beverage, with the exercise calories added as fat to the following evening meal. • After exercise and drink ingestion, you have the option to shower if desired and rest seated in the laboratory prior to consuming a low-carbohydrate high-fat (LCHF) dinner meal at 19:00h (or + 2 h post exercise). • You will then leave the laboratory, under instructions to abstain from consuming any food or drink other than water for the rest of the evening.
5	• On Day 2 of the metabolic trial, you will report to the lab at 06:30h. • The CGM will be recalibrated. • A venous catheter will be placed into a vein on the inside of the mid arm by a trained person (David Rowlands, Claire Badenhorst, or other certified person) for fasting and postprandial blood collection. • You then then ingest a high glucose drink containing 75g at 07:00h for assessment of Oral Glucose Tolerance response. Blood samples will be collected from you at time=0, 30, 60, 120 min. • You will then leave the lab for work or elsewhere. The remaining meals will be provided and following the same macronutrient split as day 1 and need to

	be ingested at the precise standardised meals at the given times; 10:00h, 13:00h and 18:00h. • Some of the study meals will contain animal products (meat, dairy) are not suitable if you follow a vegetarian or vegan diet. • Blood glucose will be monitored via GCM to the end of Day 2.
6	• On an agreed day following Visit 5, the researchers will collect, or you will return, the CGM transmitter devices to the lab for cleaning and reuse for another participant.

Who can take part in the study?

18-70 year old untrained male and females (post-menopausal) who complete less than 150 minutes of purposeful exercise per week of more than walking (VO_2max ≤43.9 ml·kg·min^{-1}.) You must be tolerant to lactose and have no known heart and respiratory conditions. Throughout the course of the study, activity level must remain the same as before the study, as this will affect study results; i.e., just keep up your normal daily habits.

Participants and researchers involved in face-to-face procedures will be required to be non-symptomatic to COVID-19 prior to each laboratory visit. If you have recently tested positive for COVID-19 or you are unwell with a normal cold or the flu, or other infection, you will be excluded or participation postponed until you are well again, which is also normal practice outside of current pandemic conditions. You will be required to comply with the University COVID-19 requirements, as well as researchers.

Potential Risks of the Study

As a result of heavy physical exercise there is a very small increase in the risk of a heart attack, and a small increase in risk of a muscle, tendon, or ligament injury, such as a strain. You may also experience fatigue and may experience muscle cramps, and there is a chance of gut discomfort.

There is a small risk of localised infection associated with pin-pricks and venous catheterisation for blood sampling. This will be mitigated by use of alcohol swabs of the skin prior and band aid covering after. For a small percentage of the population with genetic blood clotting disorder, there is a risk of a thrombosis with venous catheterisation.

Potential Benefits of the Study

The direct benefit of this study is identifying your blood glucose level across the day; resting and after consumption of food and drink. As well as, how this differs between different meals of the day and different foods consumed. Furthermore, you will gain insight of your glycaemic control following exercise. This study may therefore help you to maintain good health or provide you with critical information to seek help from a healthcare professional.

The indirect benefits of this study are contributing to scientific research that is intended for publication in an international journal, and assisting in a study contributing towards the completion of a Master of Nutrition and Dietetics thesis. Additionally, contributing to this study provides the foundation data for future research into glucose control and the role of lactate in metabolism, health and endurance performance.

Reimbursement

Participation in the study may incur some travel costs. The study will reimburse a total of $100 to contribute to travel at the completion of the entire study.

Recruitment

Participants are being recruited through Massey University previous study databases, social media, word of mouth and community group notices.

What if something goes wrong?

If you were to get injured in this study, you will be eligible to apply for compensation from ACC just as you would be if you were injured in an accident at work or at home. This does not mean that your claim will automatically be accepted. 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.

Can I get my unused blood samples back?

Upon request, we can provide your unused blood samples back for culturally-preferable disposal. We are unable to provide Karakia.

What will happen to my information?

During this study Drs David Rowlands, Wendy O'Brien and Claire Badenhorst and masters student, Miss Rose Stirling, as well as other on-site staff will record information about you and your study participation. This includes the results of any study and the pre-screening health assessments. You cannot take part in this study if you do not consent to the collection of this information.

Identifiable Information

- Identifiable information is any data that could identify you (e.g., your name, date of birth, or address). However, only Drs David Rowlands, Wendy O'Brien and Claire Badenhorst and masters student, Miss Rose Stirling will have access to your identifiable information. As well as, Auditors of Health and Disability Ethics Committee (HDEC) and regulatory bodies for audit purposes.

1. Only research staff and masters student will complete study assessments.
2. Research staff, to process and report your screening and safety tests.
3. The ethics committees, or government agencies from New Zealand or overseas, if the study or site is audited. Audits are done to make sure that participants are protected, the study is run properly, and the data collected is correct.
4. Your usual doctor, if a study test gives an unexpected result that could be important for your health. This allows appropriate follow-up to be arranged.
5. The Medical Officer of Health, if you return a positive test for COVID-19.
6. Rarely, it may be necessary for Dr David Rowlands to share your information with other people – for example, if there is a serious threat to public health or safety, or to the life or health of you or another person OR if the information is required in certain legal situations.

De-identified (Coded) Information

To make sure your personal information is kept confidential, information that identifies you will not be included in any report generated by Drs David Rowlands, Wendy O'Brien and Claire Badenhorst and masters student, Miss Rose Stirling (researchers). Instead, you will be identified by a code. Researchers will keep a list linking your code with your name, so that you can be identified by your

coded data if needed. All information will be stored in password protected files and computers with access only by the researchers on the project.

The results of the study may be published or presented, but not in a form that would reasonably be expected to identify you. All information will be presented as summarised statistics rather than individual data. This therefore limits your data from being identified when presented.

Future Research Using Your Information.

If you agree your coded information may be used for future research related to lactose or other metabolic or nutrition studies. This is outlined in a second consent form also.

This future research may be conducted overseas. You will not be told when future research is undertaken using your information. Your information may be shared widely with other researchers or companies. Your information may also be added to information from other studies, to form much larger sets of data.

You will get a short report about any research that is done using your information. This will be provided by the email provided.

Your information may be used indefinitely for future research unless you withdraw your consent. However, it may be extremely difficult or impossible to access your information, or withdraw consent for its use, once your information has been shared for future research.

Security and Storage of Your Information.

Your identifiable information is held at exercise science laboratory at Massey University, Albany Campus during the study. After the study, it is transferred to a secure archiving site and stored for at least 10 years, then destroyed. Your coded information will be entered into electronic spreadsheets and stored in a secure sever and kept by the researchers indefinitely. All storage will comply with local and/or international data security guidelines.

Risks.

Although efforts will be made to protect your privacy, absolute confidentiality of your information cannot be guaranteed. Even with coded and anonymised information, there is no guarantee that you cannot be identified. The risk of people accessing and misusing your information (e.g., making it harder for you to get or keep a job or health insurance) is currently very small, but may increase in the future as people find new ways of tracing information.

This research includes basic information such as your geographic region and. It is possible that this research could one day help people in the same groups as you. However, it is also possible that research findings could be used inappropriately to support negative stereotypes, stigmatize, or discriminate against members of the same groups as you.

Rights to Access Your Information.

You have the right to request access to your information held by the research team. You also have the right to request that any information you disagree with is corrected.

Please ask if you would like to access the results of your screening and safety tests during the study. You may access other study-specific information before the study is over, but this could result in you being withdrawn from the study to protect the study's scientific integrity.

If you have any questions about the collection and use of information about you, you should ask Dr David Rowlands or Miss Rose Stirling.

Rights to Withdraw Your Information.

You may withdraw your consent for the collection and use of your information at any time, by informing your Study Doctor.

If you withdraw your consent, your study participation will end, and the study team will stop collecting information from you.

Information collected up until your withdrawal from the study will continue to be used and included in the study. This is to protect the quality of the study.

Accessing Study Results

At the end of the intervention, participants will be emailed a document with the full breakdown of the results with relevant explanations.

Study Funding

The study has received funding from the Massey University Research Funding (MURF).

Study Approval

This study has been approved by Health and Disability Ethics Committee (HDEC), who check that studies meet established ethical standards.

Who do I contact for more information or if I have any concerns?

If you have any questions, concerns or complaints about the study at any stage, you can contact:

Prof *David Rowlands*

Professor of Nutrition, Metabolism and Exercise. School of Sport, Exercise and Nutrition. Massey University, Albany

Telephone number: [redacted]

Email: d.s.rowlands@massey.ac.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@advocacy.org.nz

Website: https://www.advocacy.org.nz/

For Maori health support please contact:

Dr Bevan Erueti, Senior Lecturer, School of Health Sciences

Kaiarataki Māori / Associate Dean Māori

Telephone number: + 64 6 356 9099 ext. 83087

Email: B.Erueti@massey.ac.nz

For Pacific health support please contact:

Mr Jack Scanlan, Lecturer, School of Social Work

Telephone number: +6492136353

Email: J.Scanlan@massey.ac.nz

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

Phone: 0800 4 ETHIC

Email: hdecs@health.govt.nz

Appendices B: Consent Form

Consent Form

Glucose Control after Exercise.

Comparing Lactose vs High-Fructose Carbohydrate.

*An interpreter is available on request

Please tick to indicate you consent to the following:

I have read, or have had read to me in my first language, and I understand the Participant Information Sheet.
I have been given sufficient time to consider whether or not to participate in this study.
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.
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.
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.
I consent to the research staff collecting and processing my information, including information about my health.
I understand that the study requires a venous catheter to be inserted in a vein in the mid arm and blood samples will be collected.
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.

I agree to an approved auditor appointed by the New Zealand Health and Disability Ethics 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.		
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.		
I understand the compensation provisions in case of injury during the study.		
I know who to contact if I have any questions about the study in general.		
I understand my responsibilities as a study participant.		
I agree for my coded information to potentially be used for future studies related to lactose or other metabolic nutrition studies.	Yes ☐	No ☐
I agree for my coded information to be sent overseas for a potential future study.	Yes ☐	No ☐
I agree to indefinite storage of coded study data.	Yes ☐	No ☐
I wish to have the remainder of my blood sample returned.	Yes ☐	No ☐
I wish to receive a summary of the results from the study.	Yes ☐	No ☐

Declaration by participant:

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: Dr David Rowlands

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: Dr Claire Badenhorst

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: Dr Wendy O'Brien

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: Rose Stirling

Signature: Date:

DATA AND TISSUE MANAGEMENT PLAN

Version: 1.25

Date: 26/12/21

Protocol: Effect of Carbohydrate-energy Replacement on Glycaemic Control Following High-Intensity Interval Training. Does Lactose Improve Glycaemic Control in Comparison to Sucrose?

Sponsor: Massey University Research Funding

Site: School of Sport, Exercice and Nutrition, Massey University, Albany

Co-ordinating Investigator: Dr David Rowlands and Miss Rose Stirling

1. INTRODUCTION

This Data and Tissue Management Guide outlines how data will be handled during the study- High-Intensity Exercise Benefits to Blood Glucose Control – Is the Milk-Sugar Lactose better than Sucrose and after its completion.

2. STUDY STRUCTURE

TABLE 1. STUDY STRUCTURE

Sponsor	School of Sport, Exercise and Nutrition (Funding) Massey University Research Funding (MURF)
Contract Research Organisation	School of Sport, Exercise and Nutrition, Massey University Massey University East Precinct Albany Expressway, SH17 Auckland 0632
Contact Person	Andy Foskett – Head of School a.foskett@massey.ac.nz

CONSENT FOR DATA AND TISSUE COLLECTION AND USE

Consenting: All participants will be informed of, and provide consent for, the collection and use of their data and tissue for the purposes of this study, and for any mandatory secondary uses.

DATA AND TISSUE COLLECTION

Data will be collected from the following sources:

Direct communication with the participant
Study assessments, including laboratory test results and a questionnaire
Tissue will be collected as follows:
Venous blood sample will be collected from the participant during the study.
Data and tissue will be collected primarily by the Investigator or designated study staff. All study personnel involved in data and tissue collection will be trained in GCP, study protocol, and collection requirements.
Collection of data and tissue will be limited to that necessary for the specified purposes of the study, or for additional purposes that the participant has explicitly consented to.

PRIVACY AND CONFIDENTIALITY

Participants' privacy and confidentiality will be respected through the protection of their data and tissue as outlined in this plan. The Investigator will comply with legal and regulatory requirements regarding the privacy and confidentiality of participants' data and tissue.
Participants have the right to access and correct personal data held by the site. Other results may be available on request, and will not result in the participant being withdrawn from the study.

BREACH OF PRIVACY / CONFIDENTIALITY

A breach of privacy means unauthorised or accidental access to, or disclosure, alteration, loss, or destruction of a participant's information.
In the event participant privacy and confidentiality is breached during the study, the following steps will be taken:
Action will be taken to reduce the risk of harm following the breach. Where possible, the recipient will be contacted and asked to destroy or return any electronic disclosed material.
The participant will be informed of the breach as soon as practicable (unless the participant is under the age of 16 and notification would be contrary to his/her interests; or notification would be likely to prejudice the health of the participant (after consultation with the participant's health practitioner, where practicable), and provided with support as required.
The approving HDEC will be informed.
For notifiable privacy breaches of privacy under the Privacy Act 2020, the New Zealand Privacy Commissioner will be notified in accordance with that Act.

FORMS OF DATA AND TISSUE

IDENTIFIABLE DATA AND TISSUE

Study data and tissue will be collected in identifiable form which only Miss Rose Stirling, Dr David Rowlands, Dr Claire Badenhorst and Dr Wendy O'Brien have access to.
Source documents refer to identifiable data and tissue collected for the purposes of this study.
All information will be stored in password protected files and computers with access only by the researchers on the project.

De-identified Data and tissue

De-identified data and tissue in this study includes but is not limited to:
Screening results: Age, gender, BMI, VO_2 max, activity level, COVID-19 results / symptoms. -
Testing results: Glycaemic response following ingestion of lactose, sucrose and placebo beverages. -

To make sure your personal information is kept confidential, information that identifies the participant will not be included in any report generated by Drs David Rowlands, Wendy O'Brien and Claire Badenhorst and masters student, Miss Rose Stirling (researchers). Participants will be identified by a code only, with a master code file linked to participant stored in password protected files and computers with access only by the researchers on the project.

Access to and Use of Data and tissue

Collected data and tissue will be used to answer the research questions and fulfil the study requirements described in the study protocol, and for the secondary purposes outlined in Sections 7.4 and 7.5.

Identifiable Data and tissue

Identifiable data comprises of the participant's name, date of birth, contact details, address, GP, emergency contacts and any other relevant information which may distinguish the participant.
Identifiable data may be accessed by the following groups:
The Investigator and designated study staff, to fulfil protocol requirements; Miss Rose Stirling, Dr David Rowlands, Dr Claire Badenhorst, Dr Wendy O'Brien.
Auditors of Health and Disability Ethics Commitee (HDEC) and regulatory bodies for audit purposes.

De-identified Data and Tissue

De-identified data may be accessed and used by the following groups:
The Investigator and suitably trained and experienced study staff, to conduct the study; Miss Rose Stirling, Dr David Rowlands, Dr Claire Badenhorst, Dr Wendy O'Brien.
De-identified data may be included in published study results including, but not limited to, peer-reviewed publications, clinical trial registry websites, scientific meetings, and regulatory / marketing submissions.
De-identified tissue will be used for analyses as described in the protocol.
De-identified data may be included in clinical trial registries and data banks (refer to Section 8.7).

Future Use of Data and Tissue

Pending participant consent, coded information may be used for future research related to lactose or other metabolic or nutrition studies.

Storage and Destruction of Data

Identifiable Data and Source Documents

During the study, study-specific source documents will be maintained. Health Screening Questionnaire will be stored in locked filing cabinet in the laboratory during the duration of the study. Following data collection it will be moved into secure storage.
The only identifiable data will be in Health Screening Questionnaire and an Excel spreadsheet title Participant Details, which will contain the participant code.

Identifiable information is held at exercise science laboratory at Massey University, Albany Campus during the study. After the study, it is transferred to a secure archiving site and stored for at least 10 years, then destroyed. Your coded information will be entered into electronic spreadsheets and stored in a secure sever and kept by the researchers indefinitely. All storage will comply with local and/or international data security guidelines.

De-identified Data

Study deidentified data will be recorded on datasheets and transferred to Excel worksheets and SAS datasets for storage and processing.
Data entry will be limited to designated study staff trained and experienced in transcribing data for this purpose.
The spreadsheets and stored in a secure sever and kept by the researchers indefinitely. All storage will comply with local and/or international data security guidelines.

Storage and Destruction of Tissue

New Zealand Laboratory

School of Sport, Exercise and Nutrition, Massey University, Albany is responsible for the storage, testing/analysis, and destruction of the tissue samples described in sections 6.1 and 6.2.
Tissue samples will be labelled as detailed in Section 6.
The laboratory is Good Laboratory Practice (GLP) compliant. The facilities are secure with tissue access restricted to those staff directly involved in their analysis.
Tissue samples will be retained for up to 3 years then destroyed by biohazard disposal or returned to the participant on request.

Consultation

Consultation regarding data and tissue management is outlined in the participant information sheet in which the participant consents to understanding and agreeing with when signing the consent form.

Māori Data and Tissue Sovereignty

During the study, data and tissue may be collected from participants identifying as Maori. Taking of tissue is a major cultural issue for Māori as it is linked to whakapapa and continuation of Māori as a nation. For some Māori, tissue is considered tapu & imbued with wairua.
Options for karakia will be discussed with participants during the informed consent process. Personal and health information is a tāonga (treasure) and will be treated accordingly.

Formal Māori consultation for this study will be completed as part of the Locality Approval Process for New Zealand study site. Any recommendations for additional measures to improve Māori rights and interests in relation to data and tissue will be acted upon.

RETURN OF RESULTS

Screening and safety results will be provided to participants on request.
Participants have the right to request a lay summary of study results.

INCIDENTAL FINDINGS

In the event that a study assessment returns a result of potential clinical significance, the participant will be informed. The participant's usual doctor and / or an appropriate specialist will be notified, and follow-up will be arranged.

RESULTS ARISING FROM FUTURE RESEARCH

Data

Participants will not be told when future research is undertaken using the study (de-identified) information. De-identified data may be shared with other researchers or companies. Information may also be added to information from other studies, to form much larger sets of data.
Information may be used indefinitely for future research unless participant consent is withdrawn. It may be extremely difficult or impossible to access individual participant information, or withdraw consent for its use, once information has been shared for future research.

Tissue
No future unspecified research is planned for tissue collected in this study.

WITHDRAWAL OF DATA AND TISSUE

Participants may withdraw consent for the collection of data at any time, without providing a reason.
Should a participant withdraw consent, no further data and tissue will be collected by study staff.
Data collected prior to the participant's withdrawal will continue to be used and analysed, depending on the stage of withdrawal. If enough data has been collected then data will still be used if not enough this data will be discarded.
Tissue collected prior to the participant's withdrawal will continue to be used and analysed for the purposes of the study.

Appendices D: Advertisement

Glucose Control after Exercise Study

The School of Sport, Exercise and Nutrition at Massey University are conducting a study investigating the effect lactose has on glucose control after exercise as compared to sucrose

What the study involves?

- Continuous Glucose Monitoring
- 4 exercise trials at the laboratory, comprising of a modern exercise approach called high-intensity exercise training (HIIT)
- 2 day standardised diet
- Ingesting carbohydrate beverage after exercise
- Blood sample collected

Who we are looking for?

- 50-70 year old males and females (post-menopausal)
- Sedentary (none or up to 150 minutes purposeful exercise per week) & overweight
- Eat a mixed diet (non-vegetarian, non-vegan)
- Tolerate Lactose
- Based in Auckland

$100 travel cost reimbursement!

Interested?

If you are interested in the study or would like further details please don't hesitate to contact MSc Dietetics student Rose Stirling for more details

rstirling@massey.ac.nz
[redacted]

MASSEY UNIVERSITY
TE KUNENGA KI PŪREHUROA
UNIVERSITY OF NEW ZEALAND

Appendices E: Study Guidelines

Study Diet Instructions and Background (non-study) Exercise

Thank you for consenting to take part in the study investigating the effect of carbohydrate-energy replacement on glycaemic control following high-intensity interval training.

General Instructions:

- **Only eat the meals provided.** Do not eat anything else apart from the provided meals and snacks.
- **Only at the prescribed times.** This require is so we can accurately track the glycaemic response against time for everyone participating in the study and to control for diurnal (time of the day on metabolism) effects. Please arrange your day schedule so that this is possible.
- **Finish your meals or snack within 10 minutes** after the on-time start of eating your meal.
- Salt and pepper can be added to meals if desired.
- Drink only water and if desired black coffee or tea. Do not add any milk or sugar or other additions to coffee or tea.
- Nuts and raisins will be portioned and labelled with day, meal and time to consume to avoid confusion.

Study Diet Details

Pre day 1:

Once you have collected the food from the laboratory, please place yoghurt and cheese in the refrigerator. Remaining ingredients are fine at room temperature.

Day 1:

At home or workplace.

9:00: Breakfast – 2x yoghurt pottles, 2x oat sachets and ensure drink

- Empty oat sachets into a bowl and add 1 cup water. Cook in the microwave for 90 seconds or until cooked to desired consistency. Top with yoghurt or eat yoghurt separately.
- DO NOT add anything else e.g; milk, brown sugar, cream etc.
- Mix ensure powder with water, until desired consistency/taste.

12:00: Lunch – Butter chicken and rice meal and ensure drink.

- Cook in the microwave for 90 seconds or until desired temperature.
- Mix ensure powder with water, until desired consistency/taste.

15:00: Snack – Macadamias, raisins and ensure drink.

- Mix ensure powder with water, until desired consistency/taste.

16:30: Report to the laboratory in exercise clothing for the HIIT exercise starting at 17:00.

19:00: Dinner – Salmon, steamed vegetables, butter and macadamias.

- Not included in your pack as this is provided and consumed in the laboratory.

Day 2:

Report to the laboratory at 6:30 for the oral glucose tolerance test (OGTT). A catheter will be placed in a vein in your forearm.

7:00: Breakfast – 75g glucose drink

- Not included in your pack as this is provided and consumed in the laboratory.

At home or work.

10:00: Snack – 1x yoghurt pottle, peanuts, raisins and ensure drink.

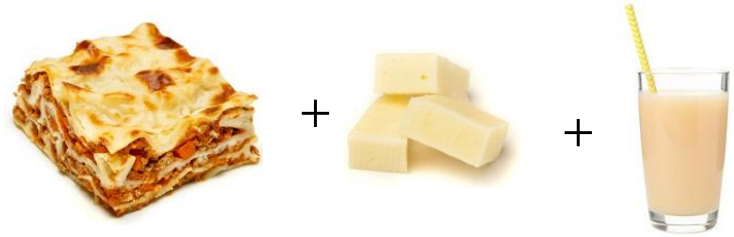
- Mix ensure powder with water, until desired consistency/taste.

13:00: Lunch – Butter chicken and rice meal, peanuts and ensure drink.

- Cook butter chicken and rice in the microwave for 90 seconds or until desired temperature. Add peanuts in top of meal or eat separately.
- Mix ensure powder with water, until desired consistency/taste.

18:00: Dinner – Lasagne, cheese and ensure drink.

- Cook lasagne in the microwave for 150 seconds or until desired temperature. Either grate cheese on top of lasagne or eat separately.
- Mix ensure powder with water, until desired consistency/taste.



Thank you in advance for participating! Your compliance to this protocol has a great impact on the study results, so it is very important that these are meet.

If you have any questions, feel free to contact Rose Stirling, MSc Nutrition and Dietetics student at any time.

Email: rstirling@massey.ac.nz

Phone: [redacted]

Appendices F: Letter of Ethical Approval and Amendment from Health and Disability Ethics Committee

Health and Disability Ethics Committees
Ministry of Health
133 Molesworth Street
PO Box 5013
Wellington
6011
hdecs@health.govt.nz

Ethics reference: 2022 EXP 12240

10 May 2022

Professor David Rowlands

Massey University East Precinct Albany Expressway, SH17
Albany
Auckland
0632
New Zealand

Tēnā koe Professor Rowlands

APPROVAL OF APPLICATION

Study title: Effect of Carbohydrate Energy Replacement on Glycaemic Control Following High-Intensity Interval Training. Does Lactose Improve Glycaemic Control in Comparison to Sucrose?

I am pleased to advise that your application was **approved** by the Central Health and Disability Ethics Committee (the Committee). This decision was made through the EXP pathway.

Conditions of HDEC approval

HDEC approval for this study is subject to the following conditions being met prior to the commencement of the study in New Zealand. It is your responsibility, and that of the study's sponsor, to ensure that these conditions are met. No further review by the Central Health and Disability Ethics Committee is required.

Standard conditions:

- Before the study commences at *any* locality in New Zealand, all relevant regulatory approvals must be obtained.
- Before the study commences at *any* locality in New Zealand, it must be registered in a clinical trials registry. This should be a registry approved by the World Health Organization (such as the Australia New Zealand Clinical Trials Registry, www.anzctr.org.au or https://clinicaltrials.gov/).
- Before the study commences at *each given* locality in New Zealand, it must be authorised by that locality in Ethics RM. Locality authorisation confirms that the locality is suitable for the safe and effective conduct of the study, and that local research governance issues have been addressed.

After HDEC review

Please refer to the *SOPs* for HDEC requirements relating to amendments and other post-approval processes.

Your next progress report is due by 10th May 2023.

Participant access to compensation

The Central Health and Disability Ethics Committee is satisfied that your study is not a clinical trial that is to be conducted principally for the benefit of the manufacturer or distributor of the medicine or item being trialed. Participants injured as a result of treatment received as part of your study may therefore be eligible for publicly-funded compensation through the Accident Compensation Corporation.

Further information and assistance

Please contact the HDECs Secretariat at hdecs@health.govt.nz or visit our website at www.ethics.health.govt.nz for more information, as well as our General FAQ and Ethics RM user manual.

Nāku noa, nā

Mrs Helen Walker

Health and Disability Ethics Committees
Ministry of Health
133 Molesworth Street
PO Box 5013
Wellington
6011
hdecs@health.govt.nz

Ethics reference: 2022 AM 12240

7 June 2022

Professor David Rowlands

Massey University East Precinct Albany Expressway, SH17
Albany
Auckland
0632
New Zealand

Tēnā koe Professor Rowlands

APPROVAL OF AMENDMENT

Study title: Effect of Carbohydrate Energy Replacement on Glycaemic Control Following High-Intensity Interval Training. Does Lactose Improve Glycaemic Control in Comparison to Sucrose?

I am pleased to advise that this amendment was **approved** by the Central Health and Disability Ethics Committee (the Committee). This decision was made through the post-approval pathway.

Further information and assistance

Please contact the HDECs Secretariat at hdecs@health.govt.nz or visit our website at www.ethics.health.govt.nz for more information, as well as our General FAQ and Ethics RM manual.

Nāku noa, nā

Mrs Helen Walker

Chair

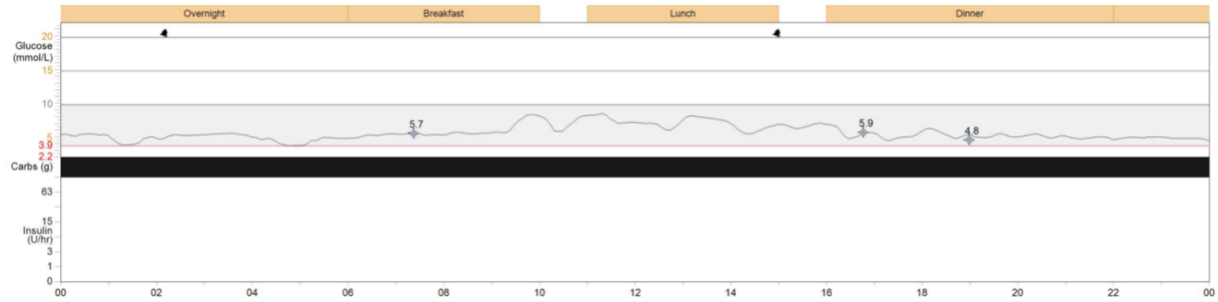
Central Health and Disability Ethics Committee

Encl: Appendix A: documents submitted

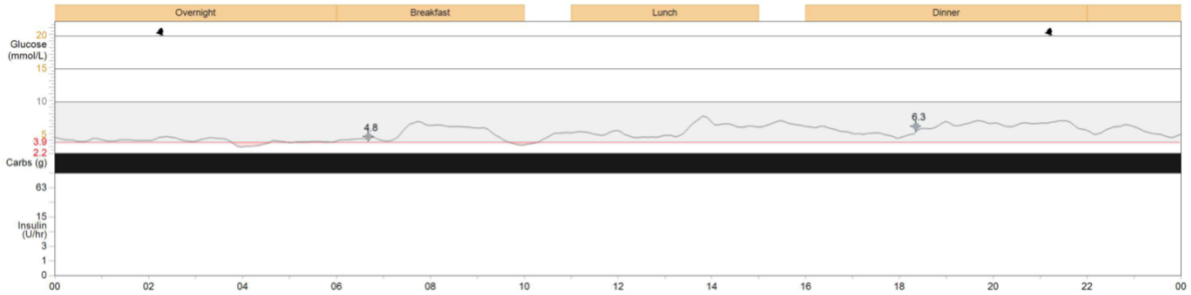
Appendices G: Continuous Glucose Monitor Data

Participant 01

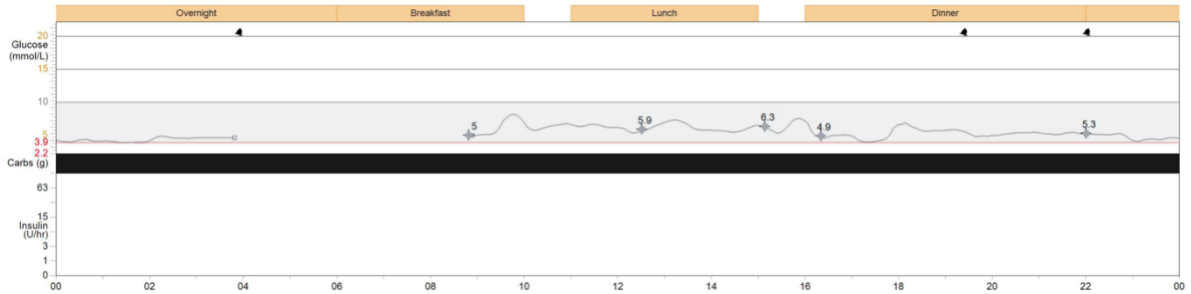
Trial 1: Day 1



Trial 1: Day 2



Trial 2: Day 1



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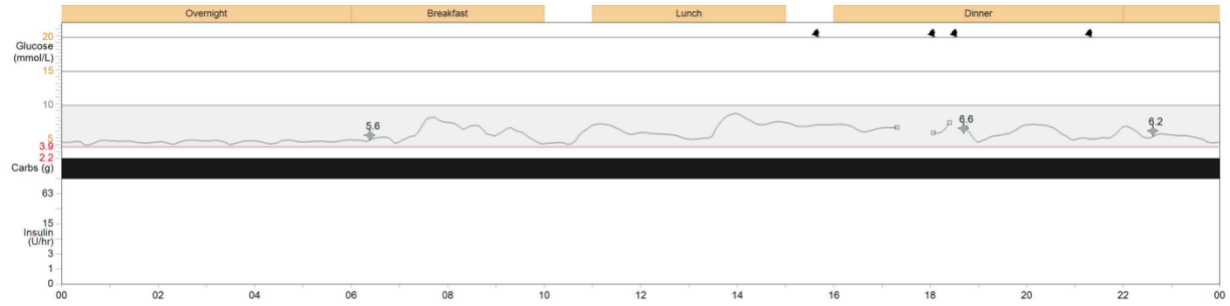
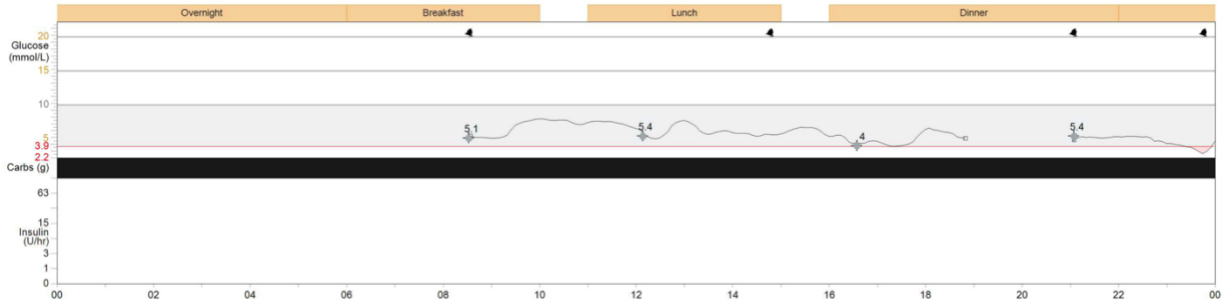


Trial 3: Day 1



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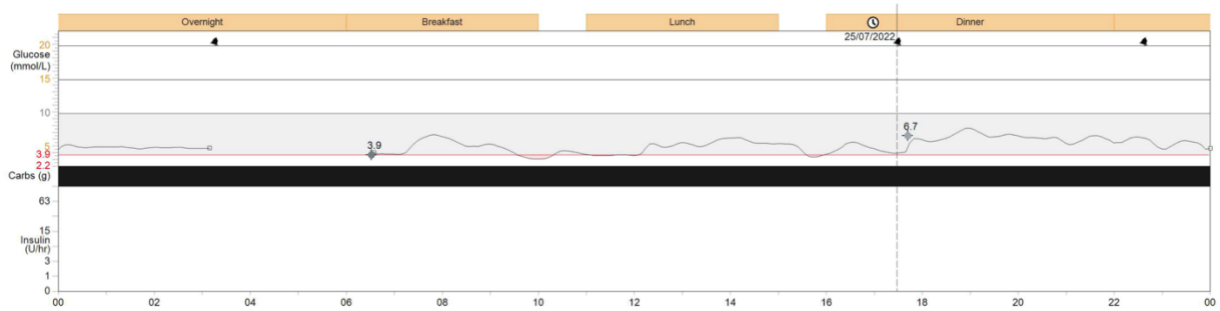

Participant 02

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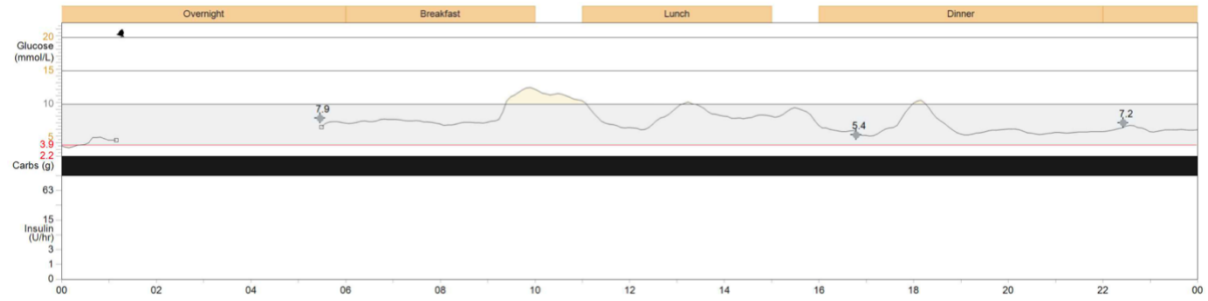

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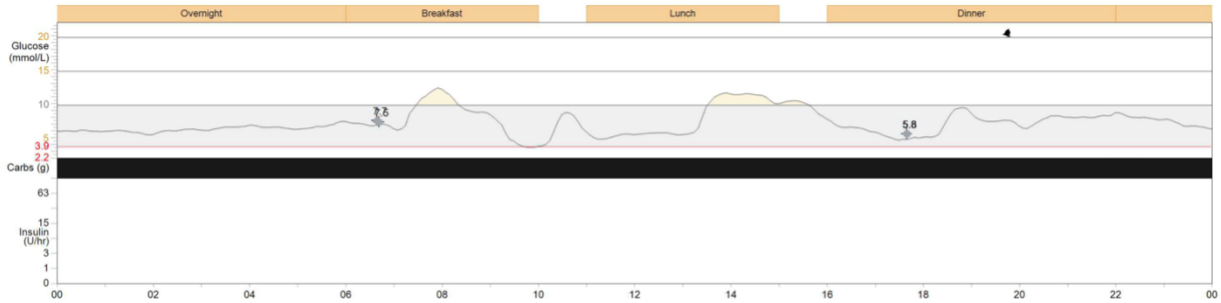

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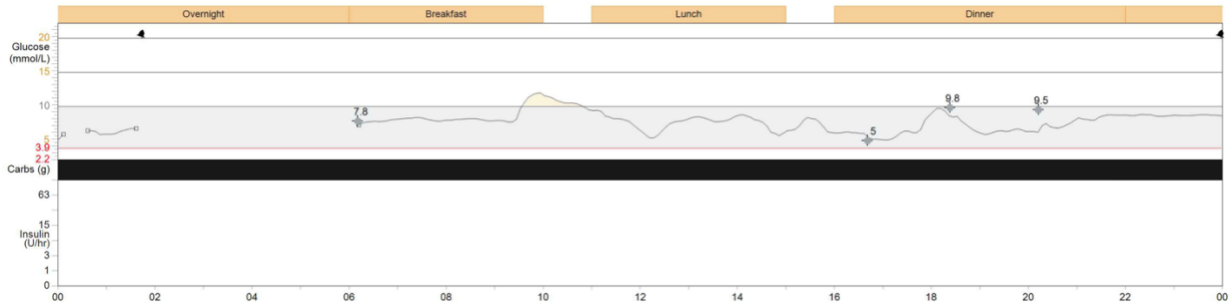

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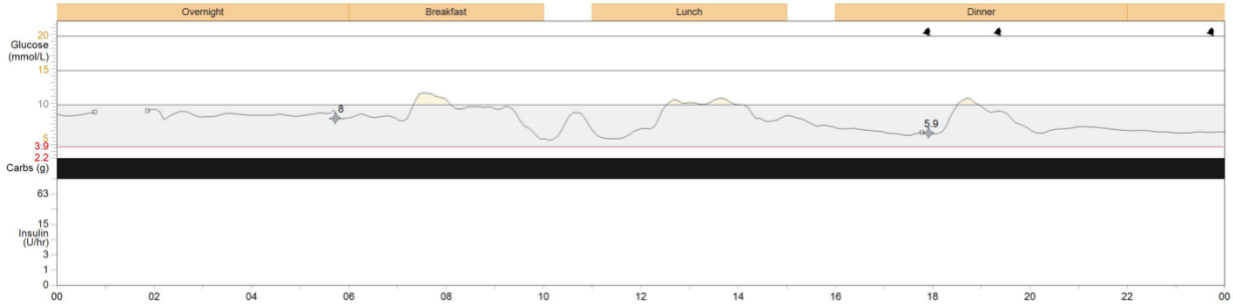

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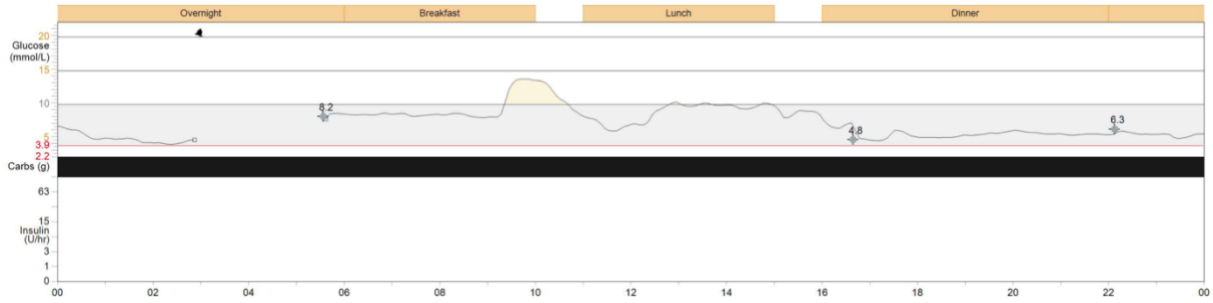

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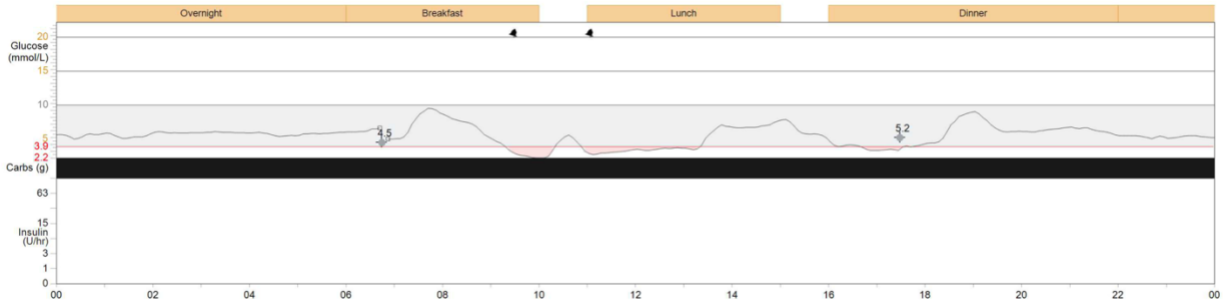

Participant 03

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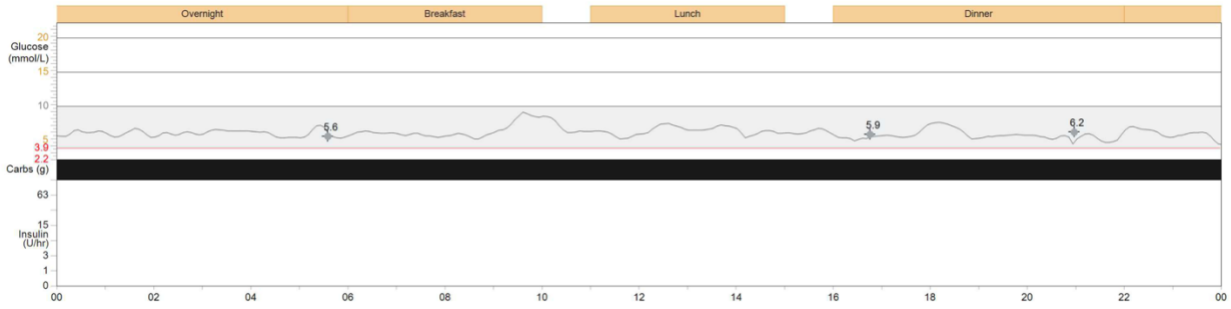

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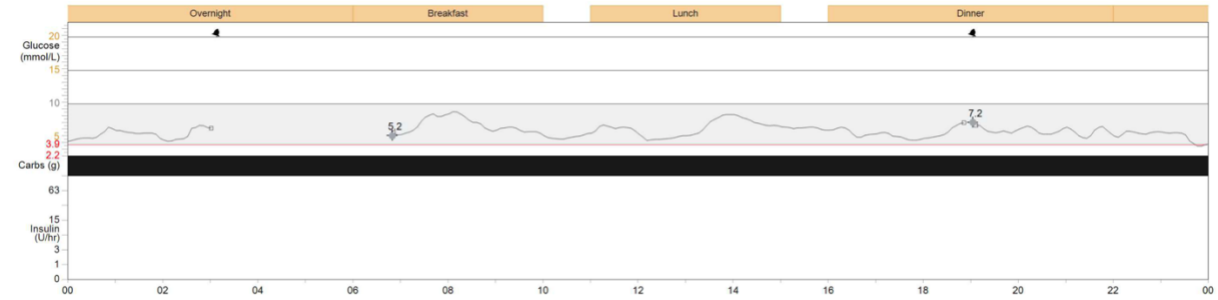

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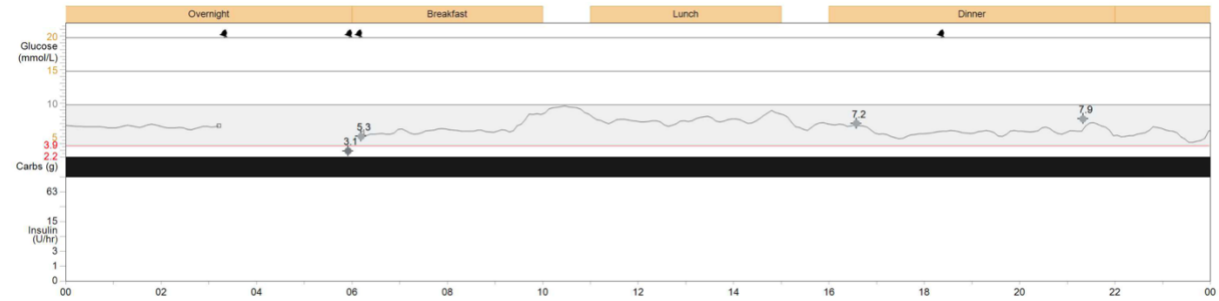

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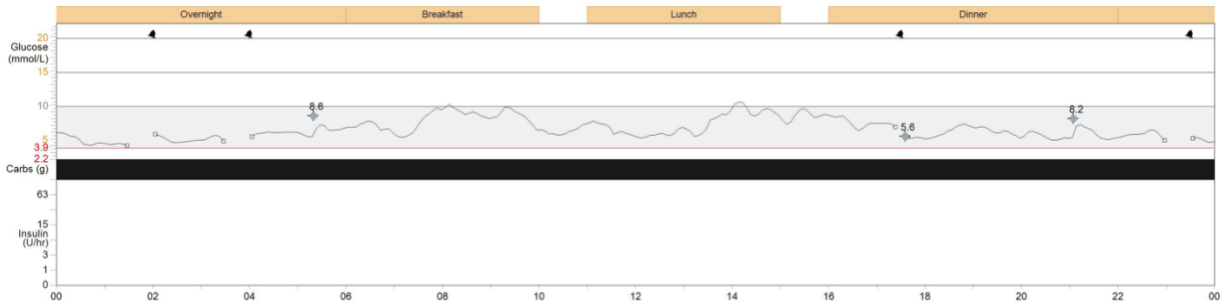

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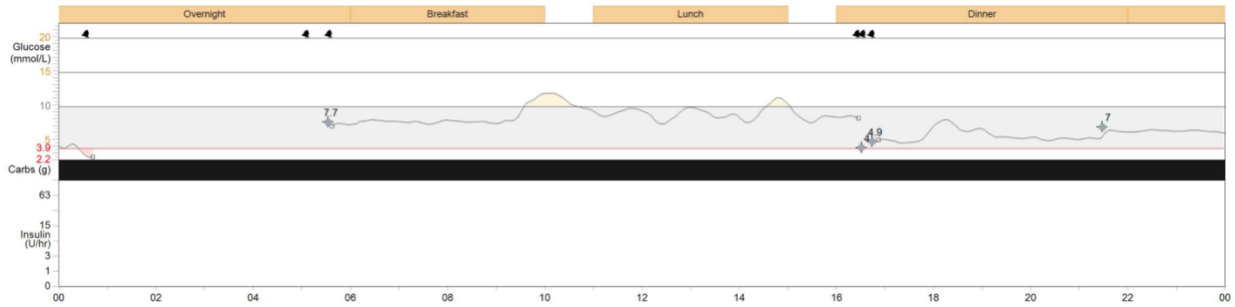

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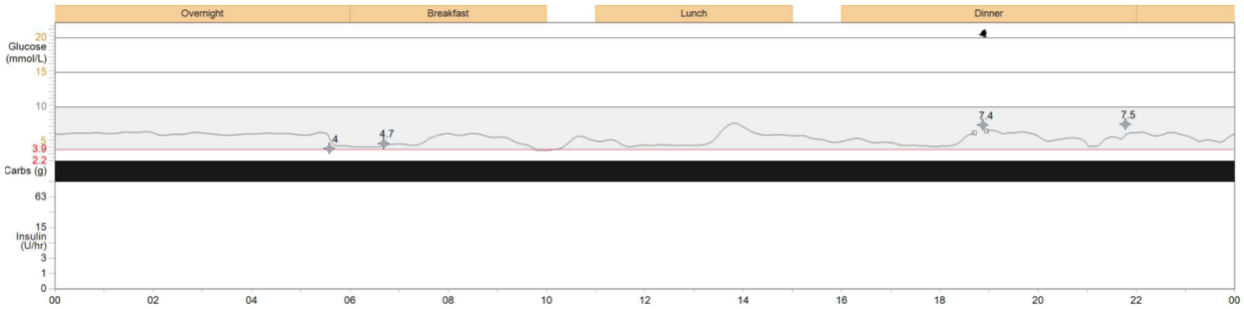

Participant 04

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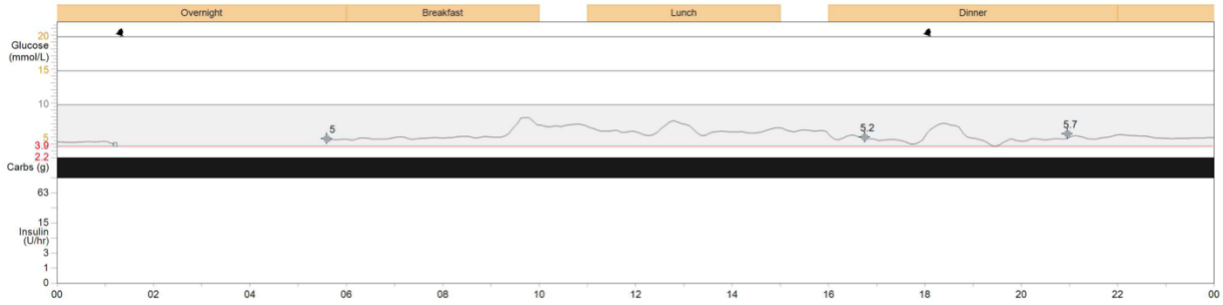

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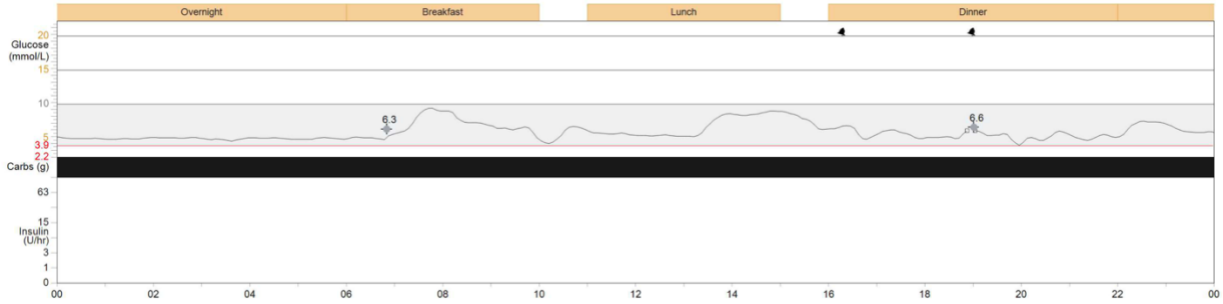

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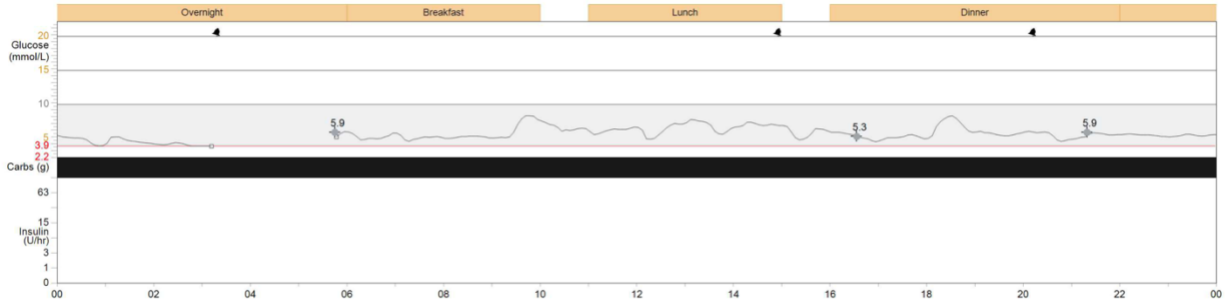

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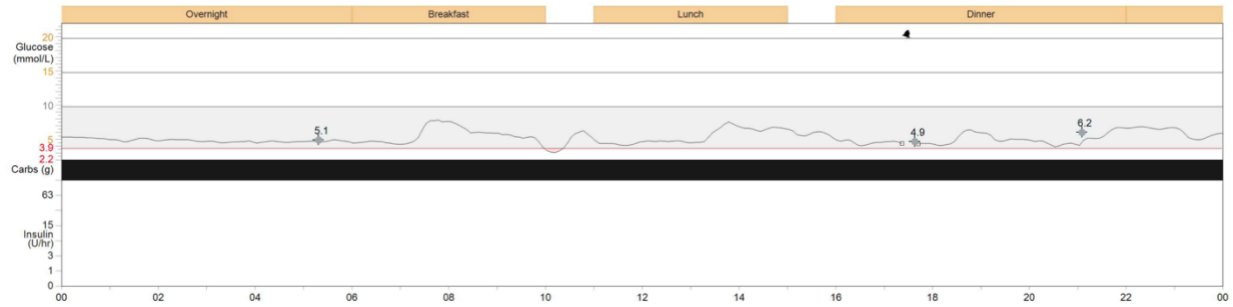

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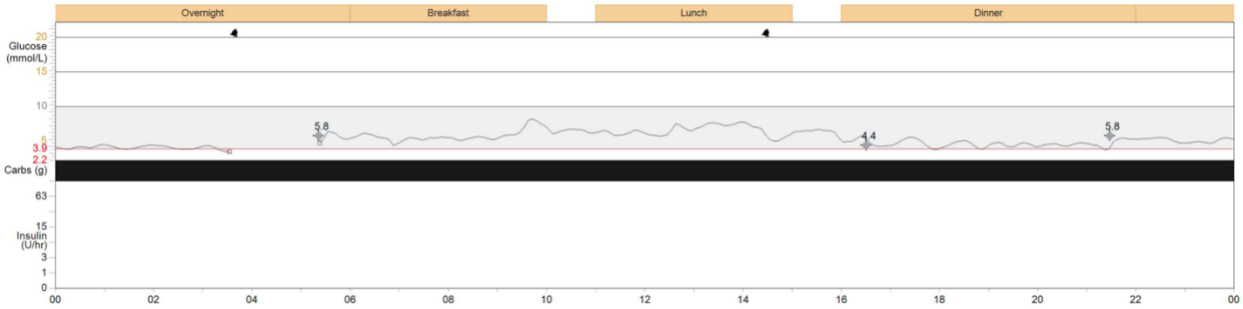

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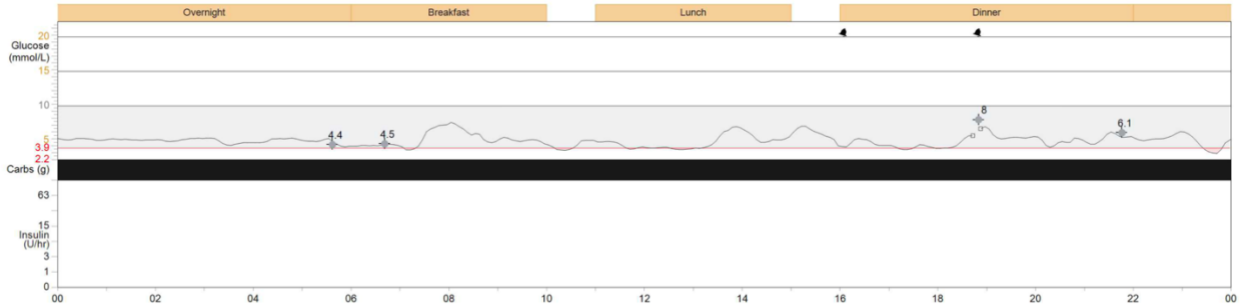

Participant 05

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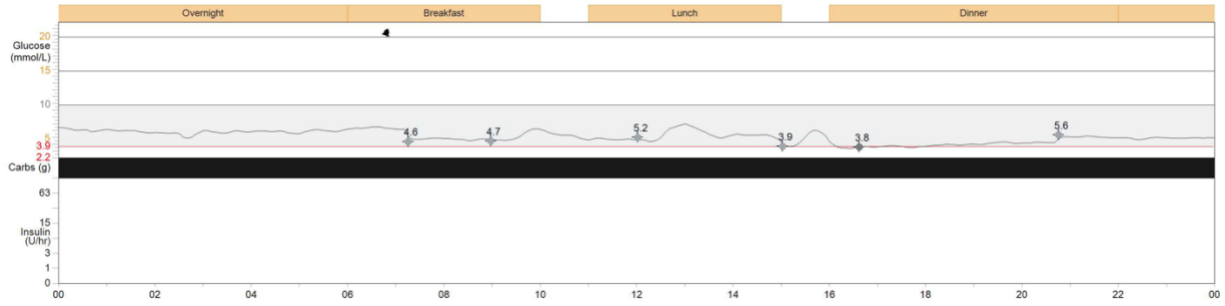

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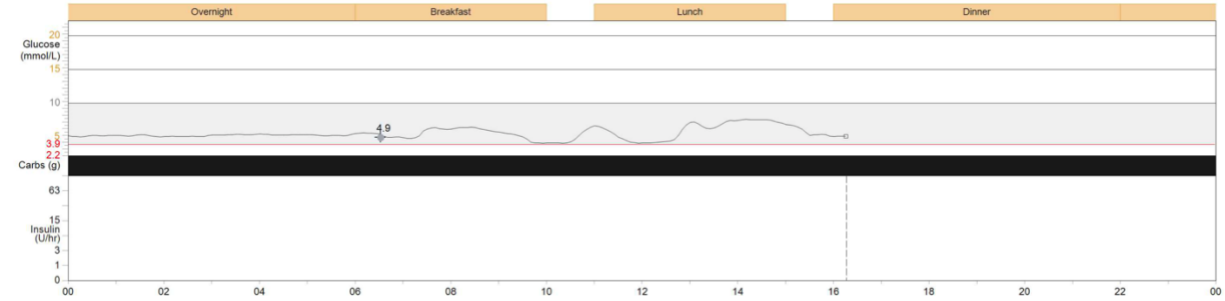
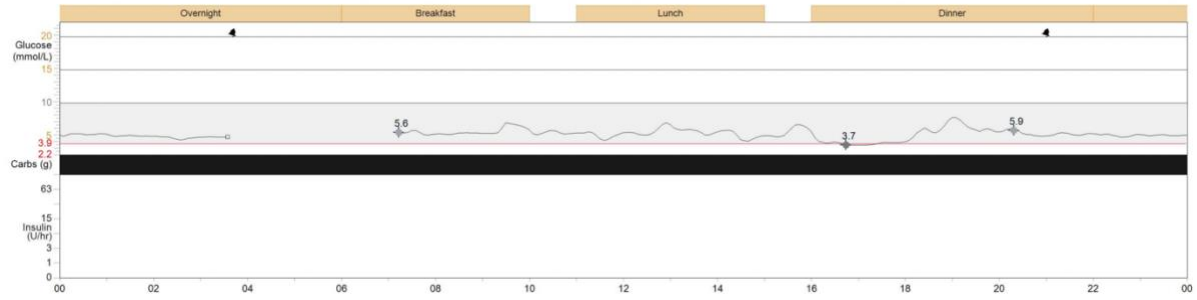
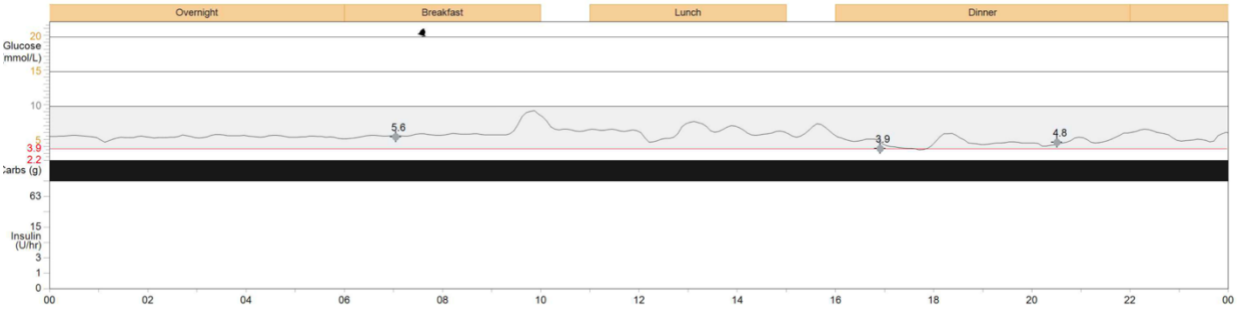


Trial 2: Day 1

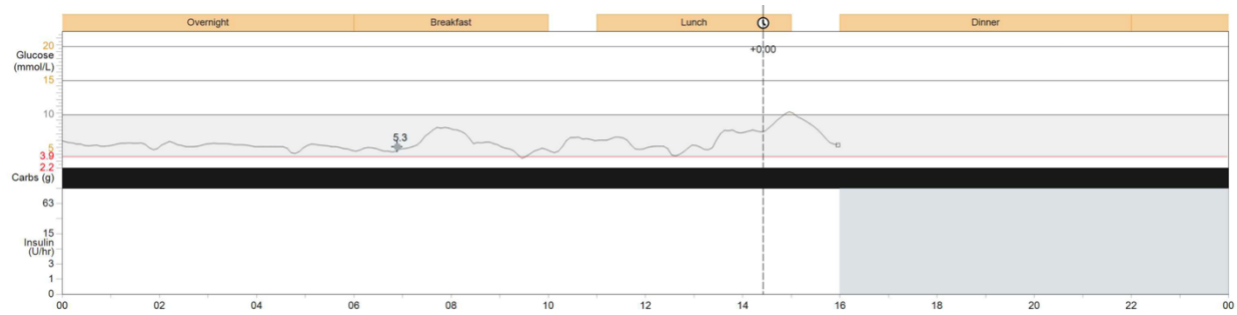


Trial 2: Day 2

Trial 3: Day 1

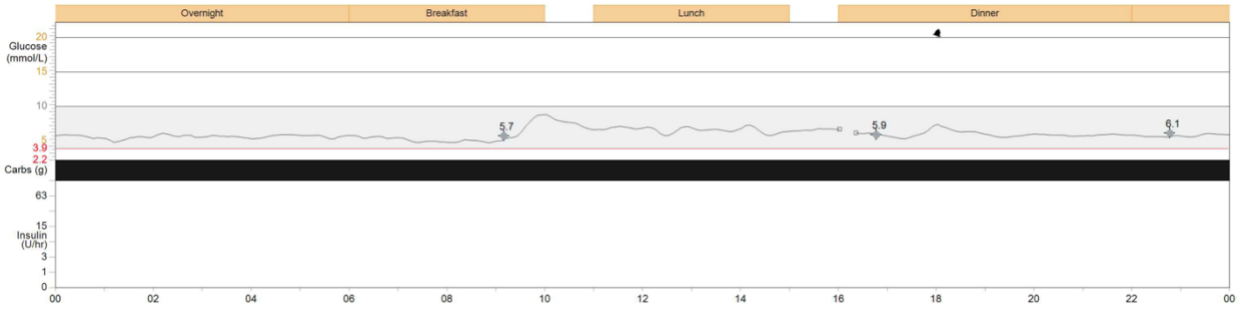


Trial 3: Day 2

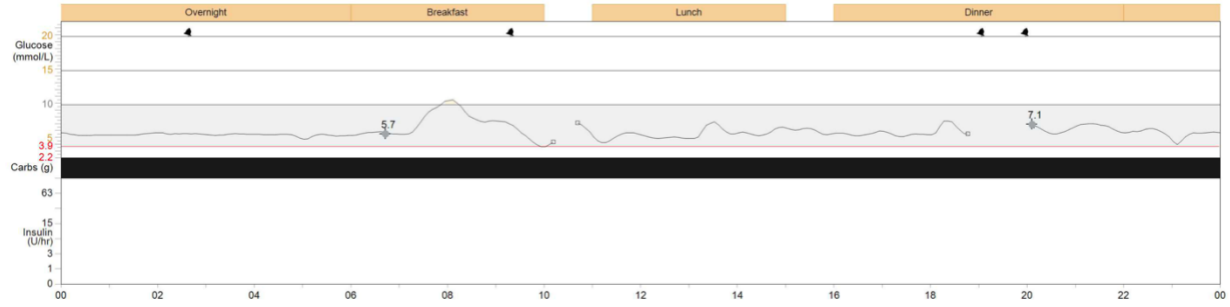


Participant 06

Trial 1: Day 1

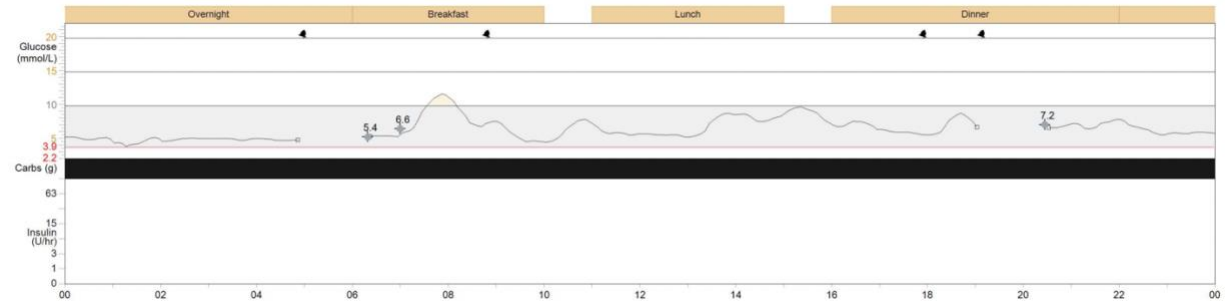


Trial 1: Day 2

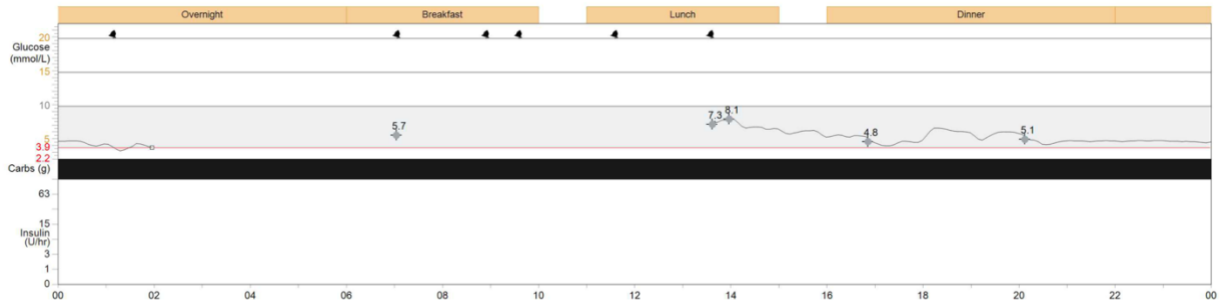


Trial 2: Day 1

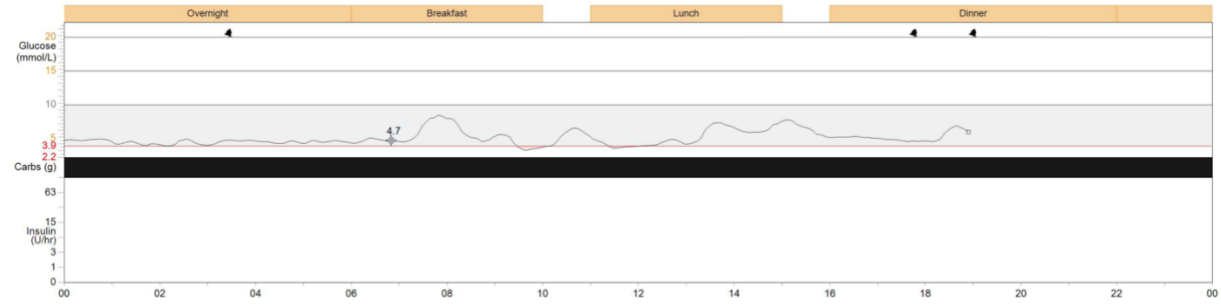
Trial 2: Day 2



Trial 3: Day 1

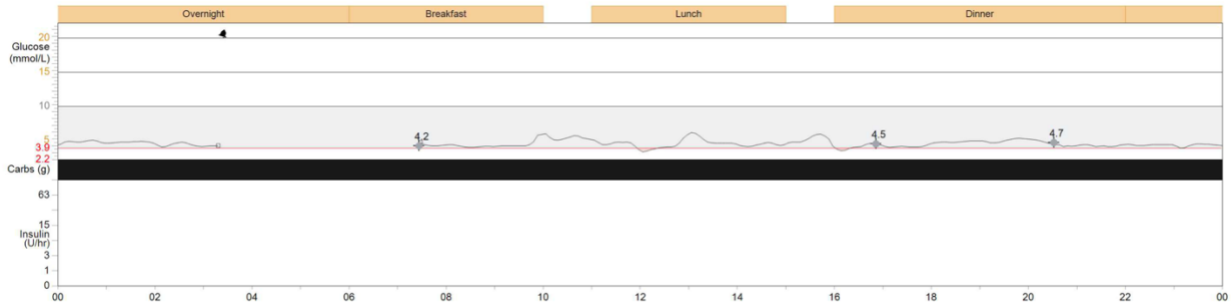


Trial 3: Day 2

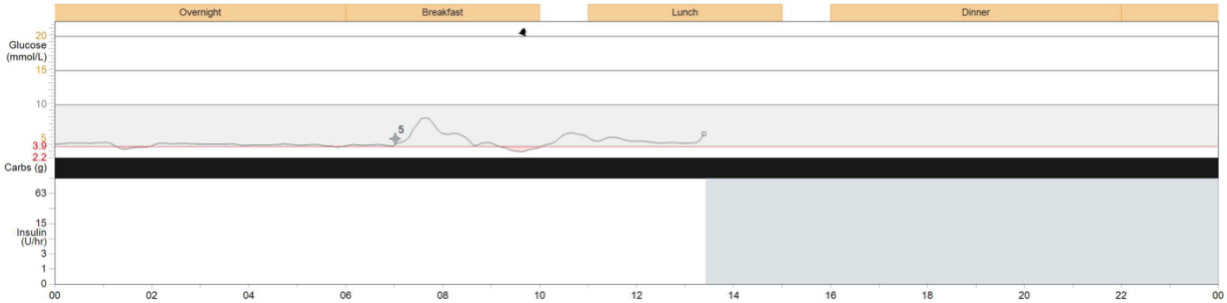


Participant 07

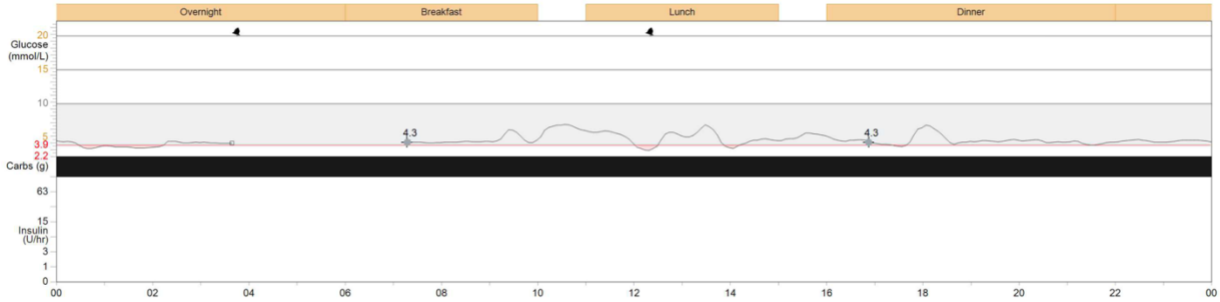
Trial 1: Day 1



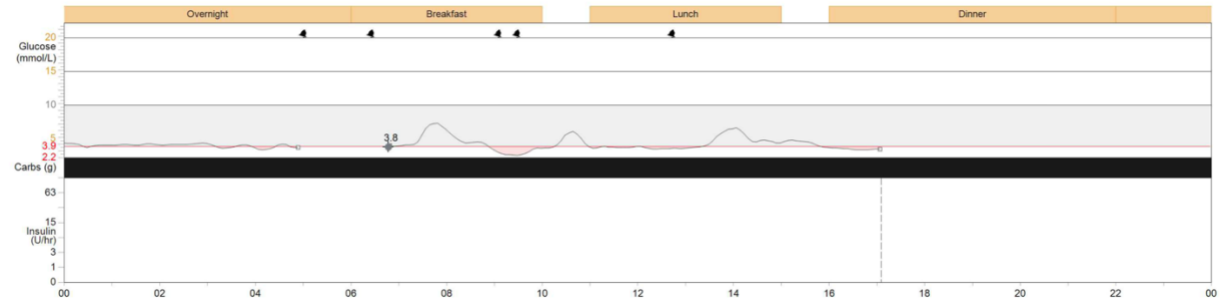
Trial 1: Day 2



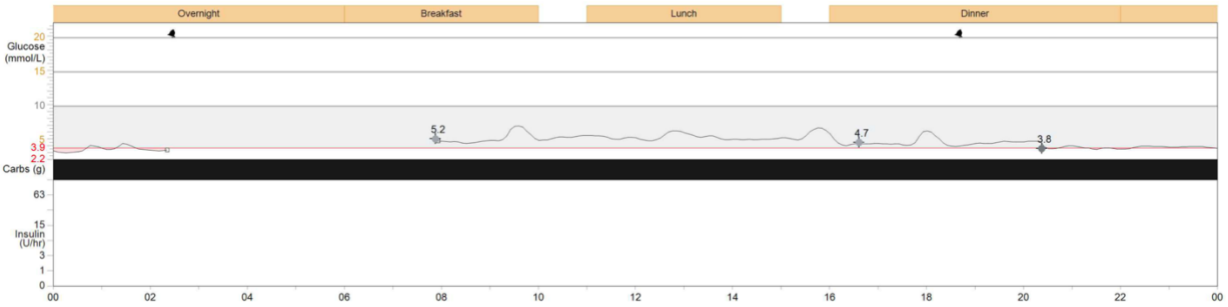
Trial 2: Day 1



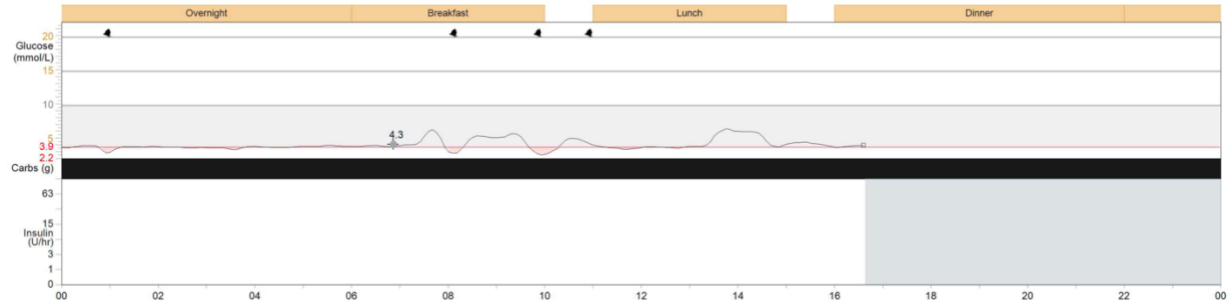
Trial 2: Day 2



Trial 3: Day 1

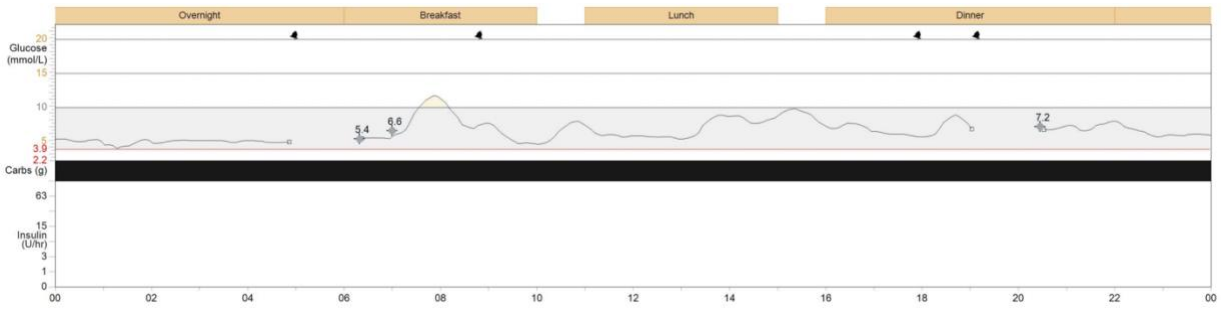


Trial 3: Day 2

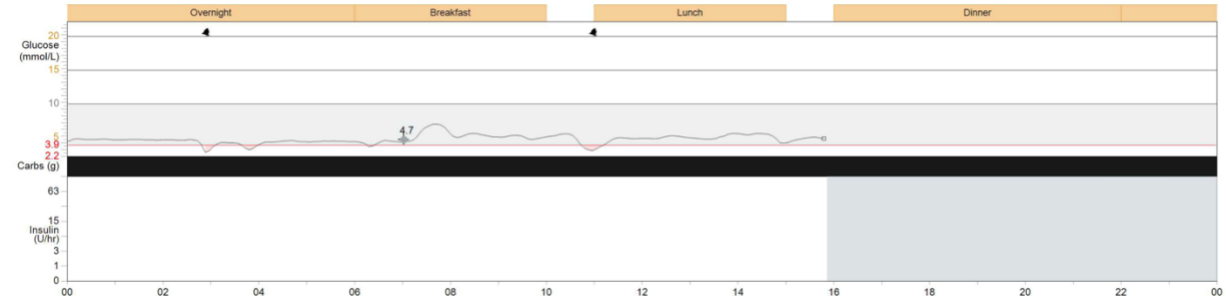


Participant 08

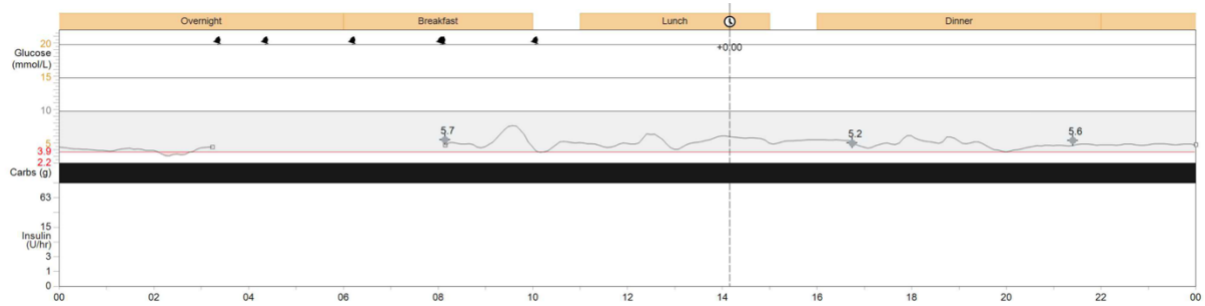
Trial 1: Day 2



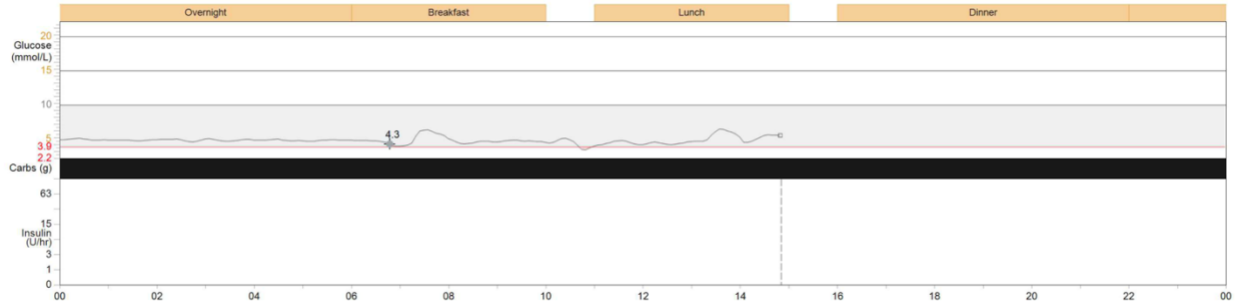
Trial 2: Day 2



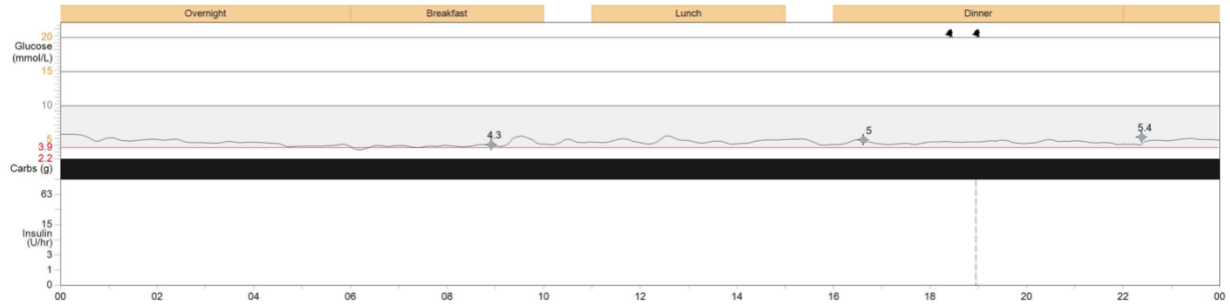
Trial 2: Day 1



Trial 2: Day 2



Trial 3: Day 1



Trial 3: Day 2