NORWEGIAN SCHOOL OF SPORT SCIENCES

Silje Løyning Sævareid

# The effect of different exercise intensities on glucose tolerance in young, healthy, and moderately active women

Master thesis in Sport and Exercise Science
Department of Physical Performance
Norwegian School of Sport Sciences, 2022

# Abstract

**Purpose:** Around 350 000 people have impaired glucose tolerance in Norway to this day. Among these, 1 out of 3 develops type 2 diabetes mellitus (T2DM) within 10 years' time. Physical activity and exercise have proven to increase glucose uptake in the skeletal muscle, and it is interesting to investigate if exercise of high intensity, low duration has a superior effect on glucose tolerance compared to continuous moderate exercise. Oral glucose tolerance test (OGTT) is normally used when investigating an effect on glucose tolerance. For this present study, it was used a continuous glucose measurement (CGM) device.

**Method:** Four adult, moderately active and healthy women (age=28± 3.5, BMI=22.8± 1.9, $VO_{2max}$=47.1± 3.9 ml/kg/L) completed a three-week training intervention wearing CGM device. The participants performed two high intensity interval exercise (HIIE) sessions at 85-95% $HR_{max}$ or two continuous moderate exercise (CME) sessions at 70% $HR_{max}$ on a bicycle, in a counterbalanced order with seven days of rest in between. They were given a standardized dinner after completed exercise and a standardized breakfast for the day after.

**Results:** Post-prandial glucose (PPG) after breakfast was reduced in the week with CME compared to HIIE (CME= 5.8±0.9 mmol/L to HIIE= 6.5±1.0 mmol/L, *p=0.*019), but not compared to control week. The PPG after dinner was reduced in the week with HIIE compared to CME (HIIE=5.3±0.3 mmol/L to CME=5.6±0.6 mmol/L, *p=0.028*) and in the control week compared to CME (CON= 5.3±0.2 mmol/L to CME= 5.6±0.6 mmol/L, *p=0.001*). No significant reductions in fasting glucose values.

**Conclusion:** This present study observed that a single bout of exercise improved glucose tolerance after a standardized breakfast and dinner.

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# Preface

This thesis marks the end of my master´s degree in Sport and Exercise Science at the Institute of Physical Performance, at the Norwegian School of Sports Sciences (NIH). The thesis work started in August 2021 and was completed in June 2022.

The experience has taught me a lot, and made me more independent both as a person and as a future professional. I have been responsible for recruiting participants and for completing the trials all by myself. Completing a master´s degree at NIH has given me an insight into the world of research, for which I am truly grateful.

I want to thank my main supervisor Jørgen Jensen for always being available and keeping your door open. I would also like to thank my co-supervisor Matthieu Clauss for useful discussions and for being available during my lab experiments. You were always available for all questions through this process, which has been of great help.

I must give a special praise to bioengineer Siri Taxerås Dalen. You have been supportive through the ups and downs of the process, and this has been of great importance to me. A big thank you to my fellow students Marte, Thea and Mai-Sissel for pushing and supporting one another, and to my roommate for her positivity and encouragement which have been of great motivation. Lastly, this would not have worked without the help and support from my family back home in Stavanger, so thank you.

It is important to note that the covid-19 pandemic was still apparent during this project, which largely affected the recruitment as well as the data collection. Therefore, I must give thanks to the four women who participated in this study.

*Silje Løyning Sævareid*

Oslo, June 2022

# 1. Introduction

## *1.1 Background*

Around 350 000 people have impaired glucose tolerance (IGT) in Norway to this day. Among these, 1 out of 3 develops type 2 diabetes mellitus (T2DM) within 10 years' time (Diabetesforbundet, 2021). Glucose tolerance is the body´s ability to restore normal glucose concentration after a meal. A normal blood glucose level will contain the highest concentration typically 30 minutes after ingestion. Blood glucose concentration will also go back to a normal blood glucose value, typically between 5-7 mmol/L for a person with normal glucose tolerance. The concentration of blood glucose in a person with reduced glucose tolerance will often have a higher fasted glucose concentration than one with normal glucose tolerance, but lower than one with diabetes mellitus. Impaired glucose tolerance can therefore be a pre-stadium for type 2 diabetes. Insulin resistance and IGT are possible risk factors for developing T2DM, as well as poor diet and a higher average weight in the population (Diabetesforbundet, 2021). Overweight and obesity can be leading causes in the development of T2DM, whereas physical activity (PA) can reduce the chances of both obesity and other risk factors of T2DM. Epidemiological studies suggest that PA can reduce the risk of T2DM by 30% to 50% in the general population (Bassuk, & Manson, 2005).

Physical activity (PA) is defined as "any bodily movement produces by skeletal muscles that results in energy expenditure" (Caspersen et al., 1985). Whereas exercise is defined as physical activity that is planned and repeated and is often chosen to do to improve or maintain one or more components of physical fitness (Caspersen et al., 1985). The amount of energy expenditure depends on the amount of total muscle mass that are being used, and on the intensity, duration, and frequency. Both exercise of high intensity, low duration, and low intensity, high duration has proven to have a positive effect on glucose tolerance (Grøntved et al., 2014; Jelstad et al., 2019) and insulin sensitivity (Adams, 2013). While most mode of exercise has proven to have a positive effect on glucose tolerance and insulin sensitivity, the majority of studies want to investigate if exercise of low duration, high intensity is superior to high duration, low intensity. The popular mode of endurance exercise (EE) of high intensity is called high intensity interval training (HIIT). This mode EE has proven to have superior effect on different physiological parameters (Helgerud et al., 2007) and is therefore of interest

within this field as well. In addition to the additional beneficial effect of high intensity, the World Health Organization (WHO) recommends 150-300 minutes per week of moderate physical activity or 75-150 minutes of vigorous PA to prevent different metabolic diseases including diabetes (WHO, 2022). However, a large portion of the population fail to meet these recommendations (Helsedirektoratet, 2016). It is therefore interesting to investigate if exercise of high intensity, short duration is sufficient to prevent IGT and diabetes in healthy adults, as the majority of research is done on exercise and glucose outcomes on obese, sedentary and/or individuals with diabetes.

The most commonly used method for determining the degree of glucose tolerance is an oral glucose tolerance test (OGTT) where one would drink 75g carbohydrate and draw blood samples 30, 60 and 120 minutes after intake. Continuous glucose measuring (CGM) devices can not only enclose information on glucose metabolism within a few hours of ingestion, but responses 24 hours post exercise and/or ingestion. CGM measures interstitial glucose concentration through subcutaneous adipose tissue via a sensor. The sensor then sends information to a transmitter that stores and displays the information on a receiver (Klonoff, 2017).

## *1.2 Present study*

### 1.2.1 Aim of the study

Physical activity and exercise have proven to have a positive effect on glucose metabolism in terms of improving glucose tolerance and insulin sensitivity. The majority of the research conducted on this topic has observed the effect of exercise on groups with risk of diabetes or diabetes itself. They have also used OGTT to observe the effect. The aim of this study was therefore to investigate the effect of exercise intensities on glucose metabolism in healthy, moderate active women using a continuous glucose measuring device.

### 1.2.2 Research questions

The research question is as follows:

1. Will there be a difference between the effect of exercise of high intensity, low duration (HIIE=high intensity interval exercise), exercise of low intensity, high duration (CME=continuous moderate exercise) and full rest control week (CON)

on post-prandial glucose response after a standardized breakfast?

2. Will there be a difference between the effect of exercise of high intensity, low duration (HIIE=high intensity interval exercise), exercise of low intensity, high duration (CME=continuous moderate exercise) and full rest control week (CON) on post-prandial glucose response after a standardized dinner?
3. Will there be a difference between the effect of exercise of high intensity, low duration (HIIE=high intensity interval exercise), exercise of low intensity, high duration (CME=continuous moderate exercise) and full rest control week (CON) on post-prandial glucose response during the night (fasting glucose concentration)?
4. Is exercise of high intensity, low duration (HIIE=high intensity interval exercise) superior to exercise of low intensity, high duration (CME=continuous moderate exercise)?

The hypotheses are as follows:

$H_0$= there are no differences in glucose tolerance between the two intensities (HIIE and CME) and control (CON).

$H_1$= there are differences in glucose tolerance between the two intensities (HIIE and CME) and control (CON).

# 2. Theory

## *2.1 General*

This chapter focuses on glucose metabolism. Glucose metabolism will first and foremost be described on a general basis. Secondly, the effect physical activity and exercise have on glucose metabolism will be explained, in particular the effect on glucose tolerance and insulin sensitivity. The current research conducted in this field will be presented and discussed. Finally, a description of CGM will be provided as well as research conducted on this measurement device.

## *2.2 Glucose*

### 2.2.1 Blood glucose and insulin

Glucose ($C_6H_{12}O_6$) is a carbohydrate that flows freely in the blood. This molecule must be replenished in order for the human body to survive. Glucose can enter the bloodstream via breakdown of carbohydrates ingested and absorbed by the intestine, and from breakdown of glycogen and lipids in endogenous storage (Martin & Klein, 1998), via glycogenolysis and gluconeogenesis (Wasserman, 2009). The body works in a way so that blood glucose concentration for a person weighing 70 kg is mostly maintained at 4 g, and this is especially important as the brain can only use glucose for energy yet not store it. Research has shown that even during exercise the blood glucose concentration will be constant, even after 2 hours post exercise (Wasserman, 2009). The body uses glucose for energy, both at rest and situations of stress. When glucose break down to pyruvate via glycolysis (figure 2.1) it produces energy in the energy-carrying molecule adenosine triphosphate (ATP) (Guo et al., 2012). Glucose metabolism and exercise will be further described in section 2.2.2 and section 2.3. Glucose is stored as glycogen mostly in liver and skeletal muscle (Adeva-Andany et al., 2016). A normal blood glucose level will be between 4-7mmol/L in healthy adults, and the insulin concentration is at 60 pmol/L. In post-absorptive state the liver glycogen storage will be 100 g and the muscle glycogen storage will be 400g (Wasserman, 2009). After ingestion of a meal, blood glucose concentration will rise, and the hormone insulin plays an important role. Insulin is secreted when the beta-cells from islets of Langerhans, located in the pancreas, are stimulated. Insulin decreases plasma glucose by starting processes which promotes glucose uptake into different cells, for example in hepatocytes and

skeletal myocytes (Markuns et al., 1999).

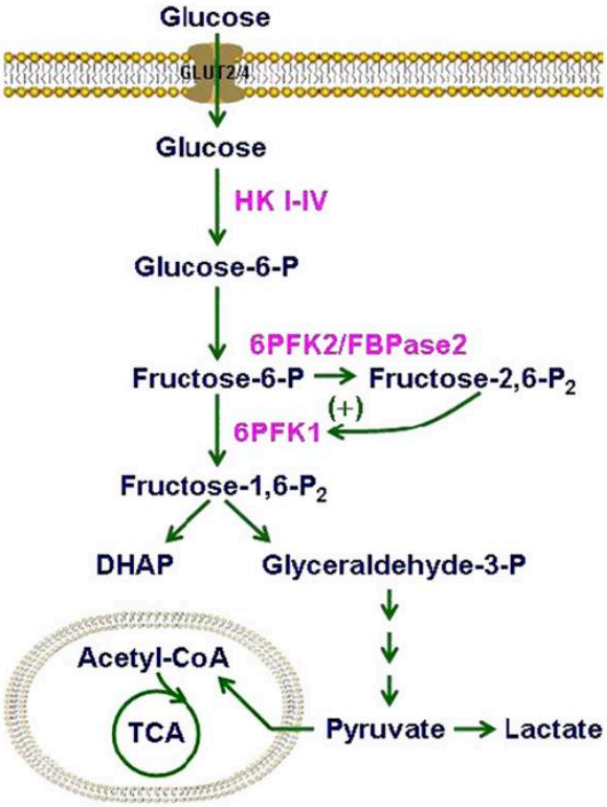


*Figure 2.1: The major steps of glycolysis. Glycolysis breaks down glucose into pyruvate. With oxygen available, pyruvate will enter the tricarboxylic acid cycle (TCA) and produces more adenine triphosphate (ATP) molecules. With absence of oxygen lactate will enter the liver to be recycled. Retrieved from Guo et al., 2012.*

Post-prandial glucose (PPG) reflects how the body reacts to food. A meal rich in carbohydrate will increase PPG more than a meal rich in fat or protein. After ingestion of a meal rich in carbohydrate one will also observe post-prandial glucose peaks. Post-prandial peaks can provide information about the glucose tolerance and post-prandial glucose response (Brand-Miller & Buyken, 2020). These peaks in the PPG may come from food with high glycaemic index (GI) which is a value that indicate the ability of the carbohydrate in the meal to increase the blood glucose (Wolever, 2017). A diet with a high amount of food with high GI, is often linked to T2DM and cardiovascular diseases (Brand-Miller & Buyken, 2020). Another value of significance when discussing glucose metabolism and the risk for T2DM and cardiovascular diseases, are elevated fasting blood glucose (FBG) (Adams, 2013).

### 2.2.2 Glucose metabolism in skeletal muscle

During the postabsorptive state, the blood glucose and insulin concentration is low. The main source of fuel for skeletal muscle is at this state non-esterified fatty acids (NEFA). Skeletal muscle tissue can use both glucose and NEFA as an energy source. When food is ingested, this stimulates insulin secretion from the pancreas, leading to suppression of lipolysis. The ability skeletal muscle has to switch from oxidation of fat during the fasting state (postabsorptive state) to oxidation of glucose during the postprandial state is called metabolic flexibility (Abduhl-Ghani & DeFronzo, 2010).

As mentioned in section 2.2.1, plasma glucose and insulin secreted from the pancreas will rise at the post-prandial state. Glucose transport through the cell membrane (figure 2.2) will happen with the help of glucose transporter proteins (GLUTn). As glucose is a hydrophilic molecule and the membrane is impermeable, glucose transport happens through facilitated diffusion via glucose transporters in the skeletal muscle called GLUT4. Insulin will bind to an insulin receptor (IRS) at the skeletal muscle cell membrane and the intracellular vesicles of GLUT4 will incorporate with the cell membrane (Jensen et al., 2011). This leads to more GLUT4 availability for glucose to be transferred into the cell. When plasma insulin is decreased, GLUT4 return to their intracellular vesicles (Adeva-Andany et al., 2016).

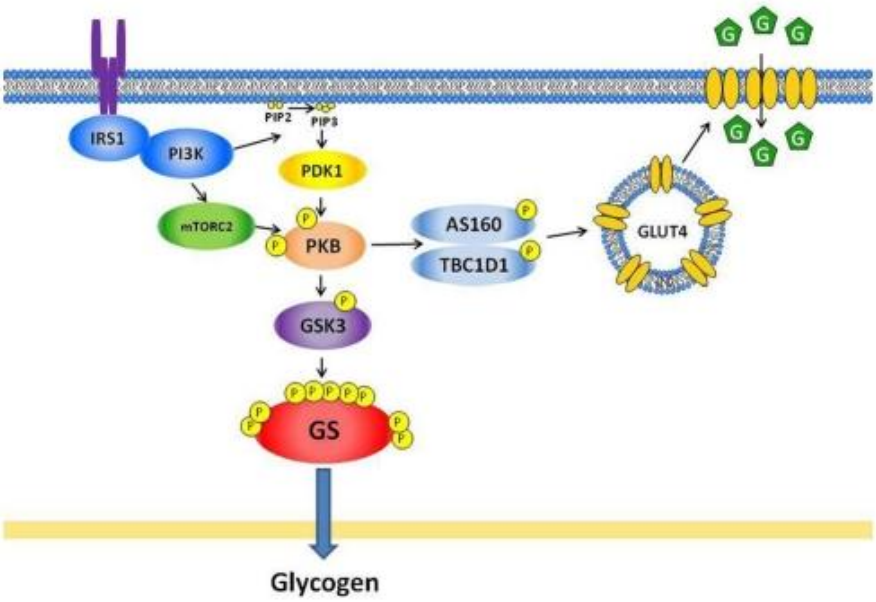


*Figure 2.2: The insulin signalling pathway to glucose uptake and glycogen storage in the skeletal muscle. When insulin binds to IRS it activates protein kinase B (PKB) via through phosphatidylinositol 3-kinase (PI3K) and namely phosphoinositide-dependent protein kinase-1 (PDK1; phosphorylates PKB at threonine 308) and the mammalian target of rapamycin complexed with Rictor (mTORC2). PKB activates both glycogen synthase and the regulation of GLUT4 translocation. Retrieved from Jensen et al. (2011)*

Glucose tolerance (GT) is the body´s ability to restore a normal level of blood glucose concentration after a meal. This is normally determined using an oral glucose tolerance test (OGTT) where after an overnight fast one would drink 75 g glucose dissolved in water. People with a normal glucose tolerance (NGT) will often see the highest level of glucose in the blood after 30 min post ingestion and decrease towards more normal levels (5 mmol/L) within two hours (Takahashi et al., 2018). If an individual´s glucose level stays high (7.8 – 11.1 mmol-1) after these two hours, this could be an indication of IGT. Impaired glucose tolerance is often referred to as insulin resistance due to insulin´s impaired effect on insulin stimulating tissues such as skeletal muscle. With insulin resistance, normal insulin level will not be sufficient for glucose disposal. IGT can be a pre-stadium to type 2 diabetes (Nathan et al. 2007). The pathogenesis of IGT suggest that the site of insulin resistance in an IGT individual is mainly in the skeletal muscle whereas impaired FBG is linked more to hepatic insulin resistance (Nathan et al., 2007). Both Nathan et al. (2007) and Wasserman (2009) report that too much glucose in the bloodstream over time (glucose toxicity) can contribute to the dysfunction of the β-cell in the pancreas, and that this is the pathology behind diabetes. In addition, it is

suggested that in these individuals there can be reduced GLUT4 translocation (Abduhl-Ghani & DeFronzo, 2010).

### 2.2.3 Risk factors for development of impaired glucose tolerance

As mentioned, too much blood glucose over time can contribute to poor insulin signalling and secretion. Abduhl-Ghani and DeFronzo (2010) suggest that elevated plasma NEFA plays a causative role in the pathogenesis of insulin resistance in skeletal muscle. In insulin resistant individuals, both non-diabetic obese and diabetic people, there will be an increased rate of lipolysis, therefore an elevated plasma NEFA. This is due to the impaired effect of insulin as a lipolysis inhibitor. The effect of plasma NEFA on insulin resistance is called lipotoxicity (Unger, 1995). It has also been suggested that there is a significant correlation between insulin resistance and intramyocellar fat compared to extromyocellar fat (Boden et al., 2001; Perseghin et al., 1999). This could therefore be an explanation as to why overweight, and obesity increase the risk of diabetes due to IGT and insulin sensitivity. Namely because overweight and obesity are characterized by increased plasma NEFA. It is well established that an increase in body mass index (BMI) increases the risk of impaired glucose tolerance (Jani et al. 2008; Kahn et al. 2008; Krssak & Roden 2004). Both obese NGT individuals with and without family history for T2DM, and individuals with hypertension, have a decrease in insulin-mediated glucose disposal. Therefore, there will be an increased risk for IGT (Abduhl-Ghani & DeFronzo, 2010). This theory has also been demonstrated by Hansen et al. (2010), who showed that weight, intake of high-energy diet and absence of strenuous physical activity can lead to impaired glucose tolerance and diabetes. It has been suggested that weight loss in obese NGT individuals can reverse the insulin resistance in skeletal muscle.

## *2.3 Exercise*

### 2.3.1 Exercise intensity

It is well established that exercise improves glucose metabolism and T2DM (Grøntved et al., 2014). It is recommended to perform 150-300 minutes per week of moderate physical activity or 75-150 of vigorous PA to prevent different metabolic diseases including diabetes (WHO, 2022). Exercise is often divided into two types: anaerobic and aerobic. Anaerobic exercise is characterized as activity of short duration and high intensity while aerobic is more the continuous, longer types of activities with lower

intensity. The aerobic system has the capacity of the cardiovascular system and contracting muscle to utilize oxygen, whereas the anaerobic system relies on energy sources within the contracting muscle and independently of oxygen (Patel et al., 2017). Exercise intensity refers to "the rate of metabolic energy demand during exercise" (Maclntosh et al., 2021). The intensity of the exercise can be expressed in several different terms such as oxygen uptake in litres per minute, power output in watts, heart rate in beats per minute and speed in meters per second or per hour. It can also be expressed in more relative terms such as maximal oxygen uptake and maximal heart rate (Maclntosh et al., 2021). These terms are of objective methods. Rating of perceived exertion (RPE) is a subjective method to describe the intensity of the exercise. There are different protocols for this method where one of them is the Borg Scale. Borg´s RPE scale ranges from 6 to 20, from no exertion at all to extremely hard (Borg, 1982).

A popular term or form of exercise of high intensity is HIIT. These intervals are defined by periods of exercising at high intensity with rest periods at low to moderate intensity in between (Kessler et al., 2012). Two typical protocols for HIIT can be the "30 seconds all-out sprint" or exercise composed of longer intervals. Exercise such as HIIT is characterized by anaerobic capacity. These longer intervals mentioned above, are called high intensity exercise (HIIE) due to the concept HIIT may often be associated with very short duration intervals with all-out effort. During longer intervals of high intensity the skeletal muscles use both anaerobic and aerobic systems to release energy when ATP is converted to adenosine diphosphate (ADP) (Guo et al., 2012). A popular protocol for these longer intervals is the 4x4 minutes intervals. These exercises are often set at 4 minutes at 80-95% of $VO_{2max}$ with recovery of 3-4 minutes at low to moderate intensity (Kessler et al., 2012). The "30 seconds all out sprint" can inflict potential safety risks as well as motivational challenges, and are therefore used more in protocols for young, healthy, and trained individuals. High intensity exercise (HIIE) is often compared to continues moderate exercise (CME) to investigate which one has the superior effect. CME can be defined by 50-75% of $VO_{2max}$ (Kessler et al., 2012).

The different intensities have different adaptations and influences different physiological aspects on physical health. Kessler et al. (2012) reports that both protocols for high intensity exercise have a superior effect on glucose metabolism outcomes when compared to CME. This research is often investigated on individuals

with risk for metabolic syndrome (such as hypertension, obesity etc.) and diabetes, and therefore these studies should be interpreted accordingly. Their findings might not be applied for a wider population. These studies will be illustrated in table 2.1. There has been research showing the opposite (Manders et al., 2010) where CME has a significant better effect compared to control and HIIT.

*Table 2.1: Overview of the different studies conducted on the effect of different exercise intensities on glucose tolerance and insulin sensitivity.*

| **Author** | **Design** | **Subjects** | **Intervention** | **Effect** |
|---|---|---|---|---|
| Young et al. (1989) | Randomized Crossover | 14 healthy young men | OGTT morning after overnight fast 1) 40 h after the last training session (control), 2) 14 h after 40 minutes of exercise (40% $VO_{2max}$), and 3) 14 h after 40 minutes of exercise (80% $VO_{2max}$). | No effect on glucose tolerance. 30% decrease in insulin area at 40% $VO_{2max}$, and 45% decrease at 80% $VO_{2max}$ |
| King et al. (1996) | Randomized Crossover | 12 sedentary, obese men (n=6 NGT, n=6 NIDDM). | Participants completed two 7-days blocks: cycling 50% $VO_{2peak}$ for 70 minutes and 70% $VO_{2peak}$ for 70 minutes. OGTT were performed before and after each block. | No effect on glucose tolerance. Insulin had decreased 20.37% after 7 days of exercise at 70% $VO_{2peak}$ |
| Babraj et al. (2009) | RCT | 16 sedentary healthy men | 2 weeks of HIIT (all-out protocol) with pre- and post-OGTT, or control with OGTT | Glucose tolerance reduced 12% after HIIT compared to pre-training OGTT. Unchanged FBG. |

| | | | | |
|---|---|---|---|---|
| Manders et al. (2010) | Randomized crossover | 9 sedentary men with type 2 diabetes | Three blocks with single bout of exercise. Randomized whether they started with low-intensity (LI) exercise, high-intensity (HI) exercise or 60 min seated control day | Average 24-h glucose concentrations were reduced after the LI exercise bout (10.34%) compared to control days. There were no significant lower glucose concentrations when compared with HI exercise. |
| Little et al. (2014) | Randomized crossover | 10 overweight or obese sedentary (8 females and 2 males) | Randomized whether they started with HIIT (10x1 minute intervals) and CME with 7 days apart (control week). CGM to measure glucose. | HIIT improved postprandial glycemia after dinner, and both HIIT and CME improved post-prandial glucose peak. |
| Ross et al. (2015) | RCT | 300 obese women and men | Randomized into one of the four groups: 1) control, 2) LALI (300 kcal/session at 50% $VO_{2peak}$), 3) HALI (360-600 kcal/session at 50% $VO_{2peak}$), 4) HAHI (360-600 kcal/session at 75% $VO_{2peak}$). OGTT for all participants. | HAHI had a greater reduction in glucose tolerance compared to the control group. HAHI and HALI had reduced insulin AUC. |

| | | | | |
|---|---|---|---|---|
| Cockcroft et al. (2015) | Randomized crossover | 9 adolescent boys | Randomized whether they started with 1) HIIT, 2) CME, 3) control (rest). OGTT 10 minutes after. | 28.9% reduction in glucose tolerance from HIIE and 23.9% reduction from CME. No effect on FBG |
| Lithgow et al. (2018) | Randomized crossover | 16 healthy males and females | Two blocks: 1) HIIT 10x1 minute interval set at 100% $VO_{2peak}$ and 2) CME (29 minutes of continuous cycling at ~65% of $VO_{2peak}$. OGTT before and after each trial. | No difference for glucose tolerance.<br><br>24.6% more insulin was produced during OGTT following HIIT. |

*Abbreviations for table 2.1: OGTT=oral glucose tolerance test, NGT= normal glucose tolerance, NIDDM= non-insulin dependent diabetes mellitus, RCT= randomized control trial, HIIT= high intensity interval training, FBG= fasting blood glucose, LI= low intensity exercise, HI= high intensity exercise, CME=continuous moderate exercise, LALI= low-amount, low-intensity, HALI= high-amount, low-intensity, HAHI= high amount, high intensity.*

### 2.3.2 Energy substrates during exercise

Carbohydrate and fat are the major energy substrates used by skeletal muscle during exercise. The energy is utilized from breakdown of glycogen into glucose and triacylglycerols into NEFA, where most of the glycogen utilized during exercise comes from intramuscular stores. Lipid is predominantly the energy source at rest for skeletal muscle. As the demand for energy increases with increasing intensity, the muscles depend more on glycogen storage. The reason for this is that breakdown of lipid will take longer compared to carbohydrates as well as it requires oxygen (Borghouts & Keizer, 2000). It was previously mentioned in the section 2.2.1, that the body wants to maintain a normal blood glucose concentration at all times. During extreme situations,

such as exercise, blood glucose concentrations will be “protected” by breakdown of glycogen by increasing glucose 6-phosphate which inhibits the hexokinase (HK) reaction (whereas HK is a vital step (first step) in glycolysis, see figure 2.1). This provides a source for energy without removal of blood glucose. Only after extensive and prolonged exercise (>4 hours) will blood glucose concentration decrease (Wasserman, 2009).

The primary energy source depends on the intensity of the exercise. Lipolysis of triglycerides is the predominant energy substrate at exercise set <65 % $VO_{2max}$. The primary source of energy will then shift to more breakdown of carbohydrates (Romijn, 1993) and up to 85 % $VO_{2max}$ the skeletal muscle will use both energy substrates (Martin & Klein, 1998). After exercising approximately 60 min, glycogen storages will be depleted, and lipid will then again be the main source of energy. After secession of exercise, most of the ingested glucose post exercise will be stored as glycogen in the skeletal muscles, as opposed to the post absorptive state where ingested glucose will mainly be stored in the liver (Borghouts & Keizer, 2000).

### 2.3.3 Effect of exercise on glucose metabolism

It is known that physical activity can improve glucose homeostasis and reduces the risk of metabolic diseases such as diabetes type 2 (Grøntved et al., 2014; Jelstad et al., 2019; Munan et al., 2020). Impaired glucose tolerance and insulin resistance are possible risk factors for diabetes type 2, and physical activity has been recommended to improve glucose tolerance (Jelstad et al., 2019) and insulin sensitivity (Adams, 2013). Impaired glucose tolerance and insulin resistance stem from insulin not adequately dispose blood glucose. The limited step in glucose disposal may be due to its transport into the cell via GLUT4 translocation. Increased GLUT4 concentration with endurance training has been suggested to be an important factor regulating insulin sensitivity (Babraj et al., 2009).

GLUT4 distributes striated muscle and adipose tissue with glucose and is an important regulator of whole-body homeostasis. The GLUT4 transport proteins are stored in vesicles inside the cell and with both insulin signalling and contraction the GLUT4 translocation will increase (Huang & Czech, 2007). Insulin and exercise alone or combined, increase translocation of GLUT4 to the plasma membrane (Whitehead et al.,

2000). The mechanism behind the insulin-dependent way may be better understood than the mechanism behind exercise-induced glucose uptake through GLUT4 translocation. Muscle contractions increase glucose permeability in skeletal muscle cells. This is due to an increase in blood flow and mechanical work, which contributes to a large amount of the exercise-induced glucose uptake in skeletal muscle through GLUT4 translocation. The mechanism behind exercise-induced GLUT4 translocation is suggested to be activation by sarcoplasmic reticulum calcium ion ($Ca^{2+}$) release (Richter & Hargreaves, 2013) and increased level of adenosine monophosphate (AMP) to ATP due to high energy expenditure (AMP will bind itself to AMP-activated protein kinase). This will lead to increased glucose uptake in the skeletal muscle cells (Borghouts and Keizer, 2000, Huang and Czech, 2007).

This effect has been observed in both prolonged submaximal exercise as well as more intense exercise (Richter and Hargreaves, 2013), where Terada et al. (2001) suggest that exercise of high intensity have a superior effect on GLUT4 expression. Exercise has proven to increase GLUT4 expression both at the end of exercise and 3 hours post exercise (Borghouts & Keizer, 2000; Kraniou et al., 2006; Richter & Hargreaves, 2013). Exercise and insulin can also have the same effect in glycogen synthase while this process may be decreased during exercise of high intensity and will then rapidly increase at the end of exercise (Jensen & Richter, 2011). What this may suggest is that glycogenesis is put on hold during intense exercise as energy is more needed elsewhere (Nielsen & Wojtaszewski, 2004).

This post-exercise effect in the skeletal muscle displays an increased sensitivity to insulin. This will lead to an increased glucose uptake after a meal in the exercised muscles who are in need of replenish their glycogen stores (Jensen & Richter, 2011). Acute exercise has proven to enhance insulin stimulated glucose uptake in trained individuals compared to untrained (Borghouts & Keizer, 2000), and Huang and Czech (2007) reports that where there is a response to exercise there is an upregulation in GLUT4 expression in skeletal muscle. Jensen et al. (2011) also rapports that glycogen storage capacity is greater in trained individuals than in untrained individuals.

## 2.4 Continuous glucose measurement (CGM)

### 2.4.1 CGM technology

A continuous glucose measurement (CGM) device is a wearable body sensor that measures blood glucose frequently in regular intervals (5–15-minute intervals). Glucose concentration is measured by the CGM through the interstitial fluid via a sensor implanted in the subcutaneous adipose tissue, often attached to the abdomen. It consists of a wearable sensor that connects with a transmitter. The transmitter sends the information to a receiver that works as storage and continuous display of glucose in mmol/L. The technology of CGM is illustrated in figure 2.3. There are different types of CGM were the wearable sensors have different lifetime. The lifetime varies from 3-10 days (Rodard, 2016), whereas the one used for this project, Dexcom G6 (Dexcom G6; Dexcom, San Diego, CA, USA), needs to be changed after 10 days. The newer versions of CGM (Dexcom G6 for example) includes a sensor applicator that intends to make the insertion of the sensor easier and result in a more consistent sensor deployment (Wadwa et al., 2018).

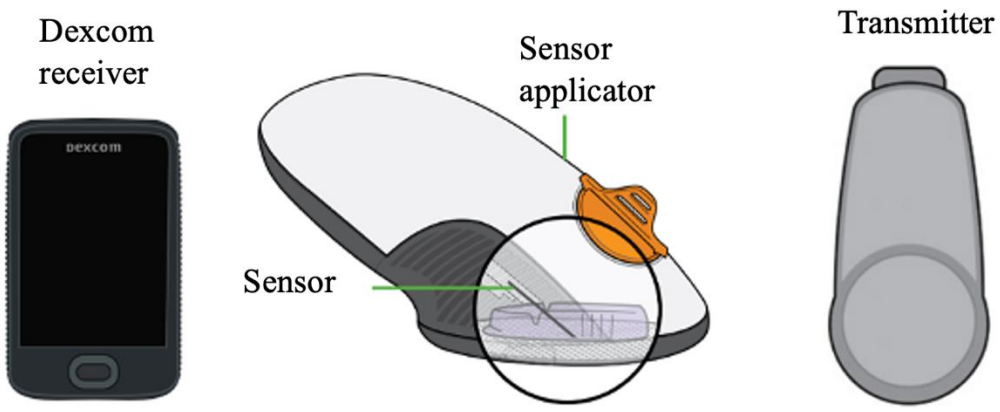


*Figure 2.3: The technology of the continuous glucose measurement device. CGM consisting of 3 parts; from left to right A) Dexcom receiver, B) sensor with an applicator, and C) a transmitter. Retrieved from Dexcom, 2022.*

### 2.4.2 CGM reciprocates

Devices for continuous glucose measurement was initially made for patients with diabetes (Klonoff, 2017). The purpose is to make it easier for them to regulate and pay attention to their glucose level. This device has also been used in research. Several studies have applied CGM in their methods (Manders et al. 2009, Praet et al. 2006, Little et al. 2014). It has been applied in research to see if the method itself provides a

sufficient monitor for diabetes patients (Laffel et al. 2020, Wadwa et al., 2018). Furthermore, there are studies using CGM to see the effect of exercise (Manders et al. 2010, Praet et al. 2006, Little et al. 2014) or diet (Rasmussen et al. 2020) on glucose metabolism. When it comes to research on glucose tolerance and insulin sensitivity, a more commonly used method is an OGTT. This is apparent in most of the research shown in table 2.1.

### 2.4.3 Benefits

CGM might be more efficient compared to self-monitoring of blood glucose. This measurement device gives more measurements (288 measurements compared to 4-7 measurements generated by self-monitoring), and it is also less painful and less blood waste (Klonoff, 2017). Most CGMs will give notifications when glucose level is low (<3.1 mmol/L). This is an additional benefit when comparing CGM with self-monitoring and a huge benefit for individuals with diabetes.

### 2.4.4 Errors

The measurement errors for CGM has improved compared to when it was initially available. The cofactors of glucose oxidase, that are used by CGM, compete with tissue oxygen, and can therefore overestimate the glucose concentration in case of hypoxia. A new oxygen-independent technology is being developed. The new sensors can therefore be implanted without being toxic as some oxygen CGM technology has been proven to be (Klonoff, 2017). Due to measuring from the extracellular fluid and not direct from the blood stream, the display will have a 5–15-minute delay depending on which type of CGM being used. Calibration with capillary blood glucose measuring is therefore normally performed twice a day. Due to this delay, it is recommended to not perform calibration right after ingestion and after exercise, because there may be rapid increases and decreases in glucose concentration (Klonoff, 2017). According to Dexcom and research (Wadwa et al., 2018) performed on Dexcom G6, it does not require calibration to be accurate due to factory calibration i.e. calibration conducted during the manufacturing process. Wadwa et al. (2018) still reports that calibration can be useful if one is not familiar with CGM and if the value displayed on the receiver appears wrong.

# 3. Methods

## *3.1 Participants*

### 3.1.1 Recruitment

Recruitment of participants was done by means of advertisements in social media and posters (appendix 1) at Myrens gym, a fitness gym in Torshov, Oslo. It was also announced in different group fitness classes at Myrens gym. A total of 10 women were interested to participate. 5 healthy, moderately active women were included for this project, the characteristics of whom are presented in table 3.1.

Inclusion criteria were as follows:

- Women
- 18-45 years old
- Healthy → evaluated through a health examination questionnaire (appendix 2)
- No known diseases
- Moderate endurances-based physical activity (PA) level (some experience with endurance training, such as running and cycling, around 2 sessions a week for the last 3 months).

Participants were excluded if they had any known metabolic disease, cardiovascular disease and/or eating disorder, as well as medication that could affect the outcome. The objective was to test these women for 3 subsequent weeks.

*Table 3.1: Characteristics of participants, registered at pre-tests.*

| | **Group 1 (n=2)** | **Group 2 (n=2)** | **Total (n=4)** |
|---|---|---|---|
| **Age (years)** | 30 (± 4.2) | 26 (±1.4) | 28 (± 3.5) |
| **Body mass (kg)** | 62.1 (± 1.1) | 63.9 (± 9.1) | 63 (± 5.4) |
| **Height (cm)** | 162 (± 2.8) | 170.8 (±2.5) | 166.4 (± 5.5) |
| **BMI (kg/m²)** | 23.7 (± 1.3) | 21.9 (± 2.5) | 22.8 (± 1.9) |
| **$VO2_{max}$ (ml/kg/L)** | 47 (± 4.3) | 47.3 (± 5.2) | 47.1 (± 3.9) |

*Data is represented as mean and standard deviation*

After pre-testing one participant dropped out due to knee problems. Her characteristics from pre-testing are therefore not represented in table 3.1. The process of recruitment and enrolment are illustrated in figure 3.1.

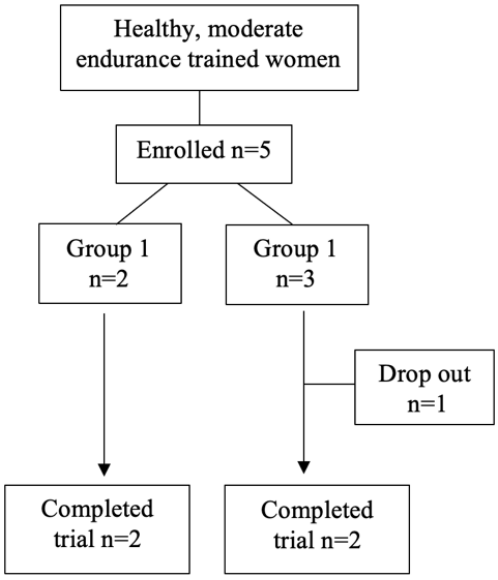


*Figure 3.1: Flow chart over recruitment and included participants in the intervention.*

### 3.1.2 Ethics

This project required approval by the ethical committee of the Norwegian school of Sport´s Science (NIH). Application number 198_02092 (appendix 3) was approved in October 2021. The project was also approved by the Norwegian Centre for Research Date (NSD). Ethical rules and guidelines for data collection in human trials were in accordance with the Helsinki declaration (Førde, 2014).

Prior to any testing, the participants were given information and asked to confirm this in writing by signing an information and consent form (appendix 4).

## *3.2 Design*

### 3.2.1 Design overview

The design used for this project was a crossover study. The project involved participation in a three-week intervention (not included the pre-test week conducted in advance). The participants wore a continuous glucose measuring (CGM) device (figure 2.2) during the entire intervention (figure 3.2). Two weeks, containing two sessions of exercise at different intensities, were separated with 7 days rest (i.e., control week) in between them. The intervention also had 3 standardized meals (figure 3.2) provided by the master student at NIH. Prior to the intervention, the participants did pre-tests (section 3.3.2).

| | | | | |
|---|---|---|---|---|
| **Pre-tests** | ⬇ | | | |
| **CGM** | | ⬇ | ⬇ | ⬇ |
| **Standardized meal at NIH** | | ⬇ | ⬇ | ⬇ |
| **Standardized training session at NIH** | | ⬇ | | ⬇ |
| **Week** | 0 | 1 | 2 | 3 |

*Figure 3.2: Overview of the entire participation period. Pre-test were performed 1-2 weeks prior to the intervention. Continuous glucose measurement (CGM) device was worn every day throughout the intervention. Standardized meal at NIH every Thursday, and exercise sessions in week 1 and 3.*

The participants were divided into two groups with different start-up dates (first group with start-up in January, and the second one in February) due to limited amount of CGMs. The exercise intensity was randomized. The first group started the intervention performing exercise with high intensity intervals whereas the second group started the intervention performing exercise with CME. The exercise days are represented in figure 3.3.

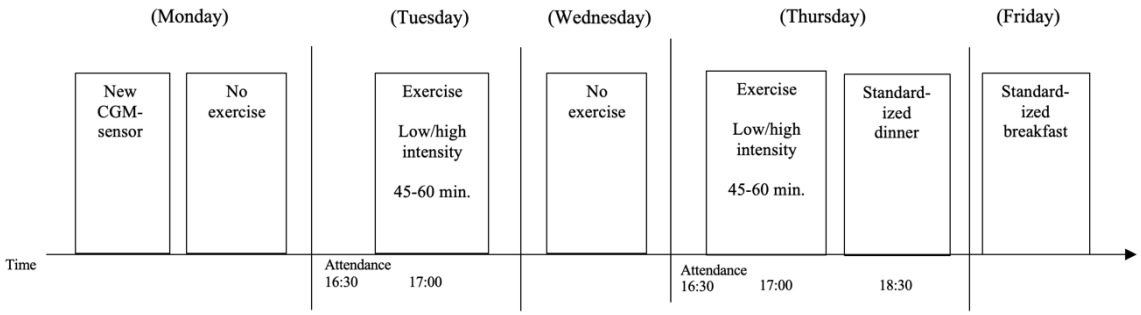


*Figure 3.3: Overview of a week with exercise. The participants changed sensors every Monday, workout Tuesday and Thursday during the exercise weeks (week 1 and week 3). Thursdays they were given a standardized dinner, in all of the intervention weeks.*

On the first day of the first week, the participants reported to the laboratory at NIH before 18:00 and attached the CGM to the abdomen and received a short training in the use of the CGM. The day after the CGM was attached, the participants reported to the cycling room at NIH for their first workout, at 16:30. Both types of exercise sessions started with a 10-minute warm up on a stationary bicycle, at 50-70% of their $HR_{max}$. This was followed by either exercise of high intensity or exercise of low intensity, both on a stationary bicycle. After the first exercise of the week, the participants went home and returned to NIH 48 hours later for their second session with the same intensity they did the first day. This session was followed by a standardized dinner (described in section 3.4). Next time the participants reported for a training session was 11 days later. The same procedure was followed for this week with the opposite intensity for the exercise (standardized workouts are described in section 3.3). The days of attendance are illustrated in figure 3.2. The participants reported to NIH at 18:25 Thursday in the control week as well, for a standardized dinner.

## *3.3 Standardized workouts*

The intensity for each participant was calculated from their maximum HR in the $VO2_{max}$ test. The intensity for the continuous moderate exercise (CME) was set at 70% $HR_{max}$ and the high intensity interval exercise (HIIE) was set at 85-95% $HR_{max}$. The CME was continuous work for 45 minutes, whereas the HIIE consisted of 4 minutes of high intensity times 4. Between each interval they had 2 minutes of active recovery set at 70% $HR_{max}$. The participants were recommended to maintain a pace of 70-80 revolutions per minute per minute (RPM) in each exercise session. They were also recommended to maintain the rating of perceived exertion (RPE) of 15-18 for the HIIE,

and an RPE of 10-12 for the CME, using the Borg´s scale (Borg, 1982).

## 3.4 Standardized meals

The standardized meals were prepared by the master student and were adapted to each participant´s body weight. The energy intake for the breakfast was 4 kcal * kg (figure 3.2 show the mean energy content for the standardized breakfast) and 8 kcal * kg for the dinner (figure 3.3 show the mean energy content for the standardized dinner). In addition, they were given a small chocolate pudding (YT chocolate pudding rich in protein with 190g – 74 kcal) after dinner and a banana (125 kcal) for breakfast. The banana was given to add flavour to the breakfast. The standardized breakfast was porridge made from large, flaked oatmeal.

*Table 3.2: Energy content in the standardized breakfast*

| **Standardized breakfast (kcal)** | **Banana (kcal)** |
|---|---|
| 253.1 (± 20.7) | 125 |

*Data is represented as mean and standard deviation*

The dinner consisted of pasta, minced meat and tomato sauce. The standardized dinner consisted of 49.8 % carbohydrates, 23.2 % protein and 27 % fat. This meets the recommendations of the Norwegian Ministry of Health and Care Services which is 45-60 % carbohydrates and 25-40 % fat with approximately 10-20 % protein. The participants were given the protein pudding as additional protein to the carbohydrate rich meal and as dessert.

*Table 3.3: Energy content in the standardized dinner*

| **Standardized dinner (kcal)** | **Tine protein pudding (kcal)** |
|---|---|
| 504.2 (± 42.5) | 140.6 |

*Data is represented as mean and standard deviation*

## 3.5 Continuous glucose measurement (CGM)

The Dexcom G6 CGM (Dexcom, San Diego, CA, USA) (figure 2.2) consists of three components: 1) a wearable sensor, 2) a transmitter and 3) a receiver that receives the transmitted data and displays the information to the user. The receiver had to be within a 6-meter radius from the participant. The sensor and the transmitter each had a serial number that was linked to the receiver. The sensor was attached to the stomach using a sensor applicator. Following this, the transmitter was attached to the sensor and the receiver had a two-hour warm up before it was activated. The sensor needed to be changed out after 14 days, but for this project the sensors were changed every Monday (total number of sensors per participant: 3). The participants could have their sensor changed at NIH with assistance, but they were also given a lesson in how to change the sensor themselves.

The participants were to calibrate the CGM equipment at least two times a day (in the morning and in the afternoon) and whenever they would get a low value (<3mmol/L). They were also told not to calibrate within two hours after ingestion. Calibration was done by finger stick blood test and the collected blood sample was retrieved into cuvettes (HemoCue Glucose 201 RT Microcuvettes, HemoCue AB, Ängelholm, Sweden). The cuvettes were analysed in a glucose analyser (Fotometer HemoCue Glucose 201 RT, HemoCue AB, Ängelholm, Sweden). The participants were given cuvettes to perform the calibration at home. The test leader (master student) also performed calibration at NIH before the exercise on Tuesdays and Thursdays. The CGM provided glucose concentration values every 5 minutes throughout the intervention (i.e., 288 values per 24-h period) and continuous data were collected for three weeks.

## 3.6 Pre-tests

### 3.6.1 Incremental- and $VO_{2max}$ test

Every participant performed an incremental test and a $VO_{2max}$ test before the intervention. The intensity of the standardized workouts was calculated from the results of these pre-tests.

The pre-tests were performed on a Lode bike (Lode Excalibur Sport, Lode B.V., Netherland). The participants started with a three-step incremental test as a warm-up,

where each step lasted for 5 minutes. The start load for each participant were set between 50-70 W. The load was increased with 15 W for each step. After 5 minutes they started the maximum oxygen uptake test ($VO_{2max}$), at 100 W. Each minute the participant was able to complete, 15 W was added until exhaustion or if they went below 65 RPM. The heart rate (HR) was measured using a sports watch connected to a belt monitoring the HR (Polar RS400, Polar AS, Kempele, Finland), and RPM and RER were logged from the computer screen (program: Lab manager). Every 30 seconds, HR and RPM were recorded in addition to respiratory exchange ratio (RER) and VO2/kg when load was increased.

### 3.3.3 O2, CO2 and RER measuring

Oxygen uptake was measured by an ergo spirometry using Oxygen Pro (Jaeger Instruments, Friedberg, Germany). The participants breathed through a two-way valve using a mouthpiece (Hans Rudolph Inc., Kansas City, Missouri, USA). Expiration air is mixed in a chamber before it is measured. Volume calibrates manually via a 3 litres pump. $O_2$ and $CO_2$ are calibrated against surrounding air (20,93 % $O_2$ / 0,03 % $CO_2$) and a known gas with approx. 16 % $O_2$ and approx. 6 % $CO_2$.

## *3.7 Registration of physical activity and meals*

The participants were asked to standardize their food intake and beverage 24 hours before attending the second test day of the week (17:00 Wednesday – 17:00 Thursday). This information was reported in a form they were given by the master student (appendix 5). They were encouraged to refrain from exercising other than the one prescribed, during the intervention. In addition, they were encouraged to refrain from caffeine before and until three hours after the standardized breakfast.

## *3.8 Statistical analysis*

Continuous glucose measurement data was downloaded to a MacBook Pro with Dexcom software according to the manufacturer's instructions. Data were exported to Microsoft Excel for Mac IOS 11.6.5, version 16.61, for initial inspections and analysis. The initial inspection of the CGM data involved identification of meal and physical activity entries and selection of data of interest. This also required identification of entries from the registration form (appendix 5) because some of the participants forgot to log it into the Dexcom receiver. Mean glucose concentration, and mean HR and RPE

were calculated using the AVERAGE-function in Microsoft Excel, 2022. The same method was used calculating the standard deviation, with the STDEVA-function in Excel. The tables and figures illustrated in this study have been prepared in Microsoft Excel for Mac and GraphPad Prism 9 (GraphPad Software, La Jolla, California, USA). All data were analysed using IBM SPSS Statistics for Windows, Version 20.0 (IBM Corp. 2011, Armonk, NY, USA). The results are represented as mean and standard deviation. Significance is set at 5 % ($p<0.05$). The statistical tests performed were done to compare means within three groups (1) HIIE, 2) CME, and 3) CON). Due to not all the data being normally distributed and the sample size being small, both parametric test (one-way ANOVA) and non-parametric test (Kruskal Wallis test) were performed to see if the outcomes were similar.

# 4. Results

## *4.1 Continuous glucose measurement (CGM) parameters*

The CGM provided glucose concentration values every 5 minute for three weeks in the present study. This provided a mean of 5965.8±142.4 observations, depending on how often participants calibrated and how many entries logged from meals and activities. The time periods included in the analysis were: two hours post-meal for dinner on the day of exercise/control day and two hours post-meal breakfast on the day after exercise/control day. In addition, mean FBG concentration value per hour was included from midnight to 6:00 (00:00-06:00). The statistical tests compared means of time of ingestion to two hours post-ingestion, and mean glucose concentration during the six hours during the night.

## *4.2 Characteristics of the exercise sessions*

All participants were able to complete all four exercise sessions. Mean HR in the HIIE session is represented in figure 4.1. Table 4.1 represent mean RPE in the HIIE sessions. Mean HR and RPE in the CME session are represented in table 4.1. As expected, both mean HR and mean RPE were higher in the HIIE compared to the CME sessions ($p<0.001$).

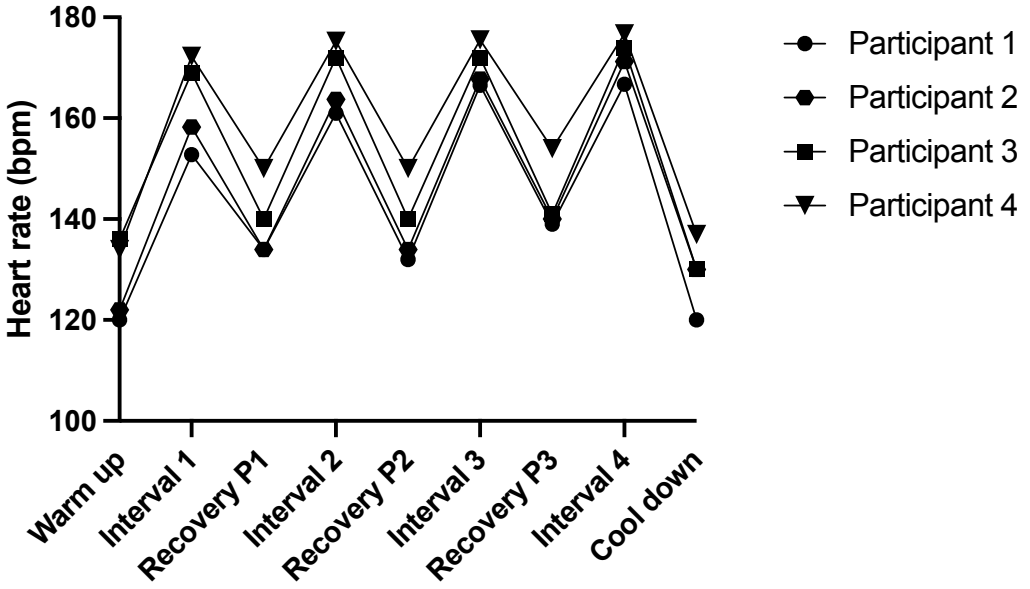


*Figure 4.1: mean heart rate (HR) of all participants during the high intensity interval exercise (HIIE). Recovery Px, recovery period 1-4.*

Figure 4.1 shows BPM peaks for each participant, for each interval contained in the high intensity exercise session. The peaks increased for each interval. Figure 4.2 shows an example of the 4 minutes contained in one interval. Following the same pattern as that of mean heart rate in figure 4.1, the highest BPM peak is at the last part of the represented interval.

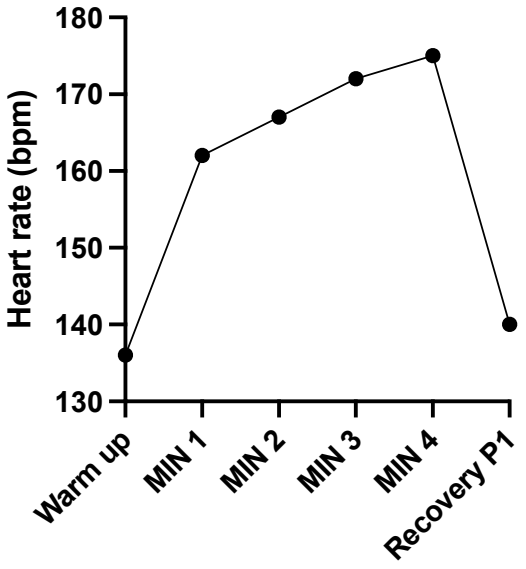


*Figure 4.2: mean heart rate (HR) for one participant, 4 minutes contained in one interval (Recovery P1, recovery period 1).*

RPE in the HIIE sessions was similar for each participant, with a smaller variation for participant 2. They were all within the recommended RPE range for HIIE (15-18) except for participant 1 who reported that the RPE for the first interval in the second HIIE session was at 14.

*Table 4.1: mean ratings of perceived exertion (RPE) in high intensity interval exercise (HIIE) sessions.*

| Participant ID | Mean RPE |
|---|---|
| **1** | 15.8 (± 1.3) |
| **2** | 16.1 (± 0.6) |
| **3** | 15.9 (± 1) |
| **4** | 15.8 (± 1) |

*Data is represented as mean and standard deviation*

RPE in the CME sessions (figure 4.2) was similar between participants. It was also in the recommended RPE range (12-14).

*Table 4.2: mean heart rate (HR) and ratings of perceived exertion (RPE) in moderate exercise (CME) sessions.*

| Participant ID | Mean HR | Mean RPE |
|---|---|---|
| 1 | 127.8 (± 3.9) | 11.5 (± 0.7) |
| 2 | 127.3 (± 5.1) | 11.5 (± 0.7) |
| 3 | 132.3 (± 7.4) | 11(± 0) |
| 4 | 135 (± 6.4) | 11.5 (± 0.7) |

*Data is represented as mean and standard deviation*

## *4.3 Effect of exercise intensity on glucose tolerance*

### 4.3.1 The standardized meals

All participants consumed the prescribed breakfast and dinner provided by the master student. The breakfast was consumed in post-absorptive state, i.e. fasting conditions. The participants made the porridge at home by themselves, by boiling the oatmeal in water. They did not consume the meal at the exact same time each week. The dinner was prepared and eaten at NIH supervised by the master student. Due to the master student getting covid-19 in the second block (i.e., with the second group) participants 3 and 4 had unsupervised dinner in the control week. In the control week participant 4 reported eating the standardized dinner later in the evening than normal (=18:30) due to work. The participants´ mean glucose values during the intervention are represented in table 4.3.

*Table 4.3: mean glucose per participant during the three weeks intervention, with continuous glucose measuring (CGM).*

| Participant ID | Mean glucose (mmol/L) |
|---|---|
| 1 | 5.5± 0.8 |
| 2 | 5.7± 0.9 |
| 3 | 5.7± 0.8 |
| 4 | 6.2± 1.1 |

*Data is represented as mean and standard deviation*

### 4.3.2 Post-prandial glucose response following a standardized breakfast

Post-prandial glucose following the standardized breakfast is represented in figure 4.3,

as response every 30 minutes for two hours after ingestion. The mean glucose concentration increased rapidly after approx. 30 minutes in all three weeks. A non-parametric test showed a significant reduction in mean glucose concentration in CME compared to HIIE (CME= 5.8±0.9 mmol/L to HIIE= 6.5±1.0 mmol/L, *p=0.*019), but not compared to the control week. The glucose peak was higher and occurred earlier in the week with exercise of high intensity.

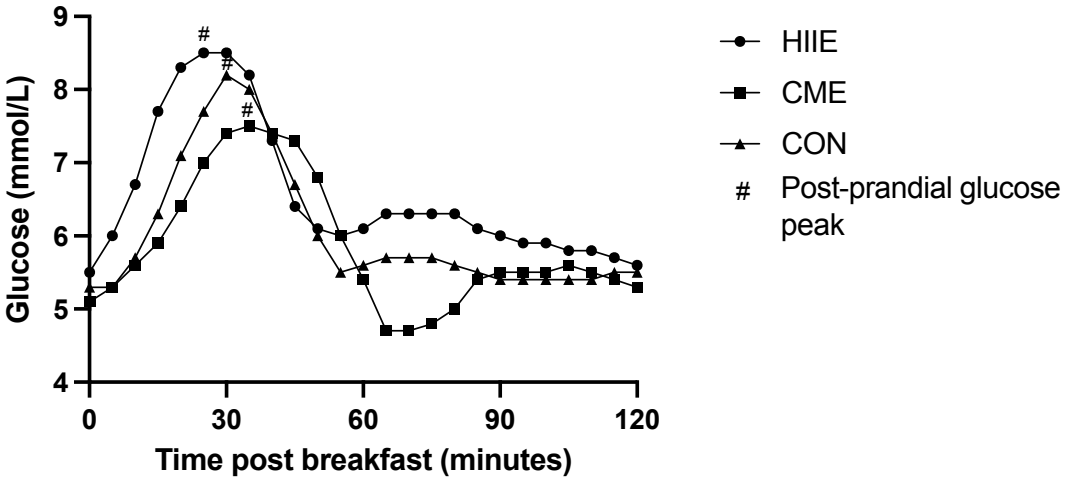


*Figure 4.3: Mean post-prandial glucose (PPG) response following a standardized breakfast the day after a day of high intensity (HIIE), a day after continuous moderate exercise (CME), and a day after a control day (CON). #, post-prandial glucose peak*

Figure 4.4 illustrates the PPG response between exercise intensities and control for each participant, individually. Both participant 3 (figure 4.4, C) and 4 (figure 4.4, D) had a higher glucose peak (#; post-prandial glucose peak) in the week of high intensity exercise. Participant 4 had higher glucose peaks value in all three weeks (figure 4.4, D: HIIE=12.3, CME=9.9, and CON=11.4) compared to the other participants. The glucose concentration increased and reached its PPG peak after 30 minutes had gone by, for all three weeks for participant 4. For participants 2 and 3, the PPG peak for both HIIE and CON was reached before 30 minutes had passed, while for participant 1 it appears that PPG peak was reached after 35 minutes after ingestion.

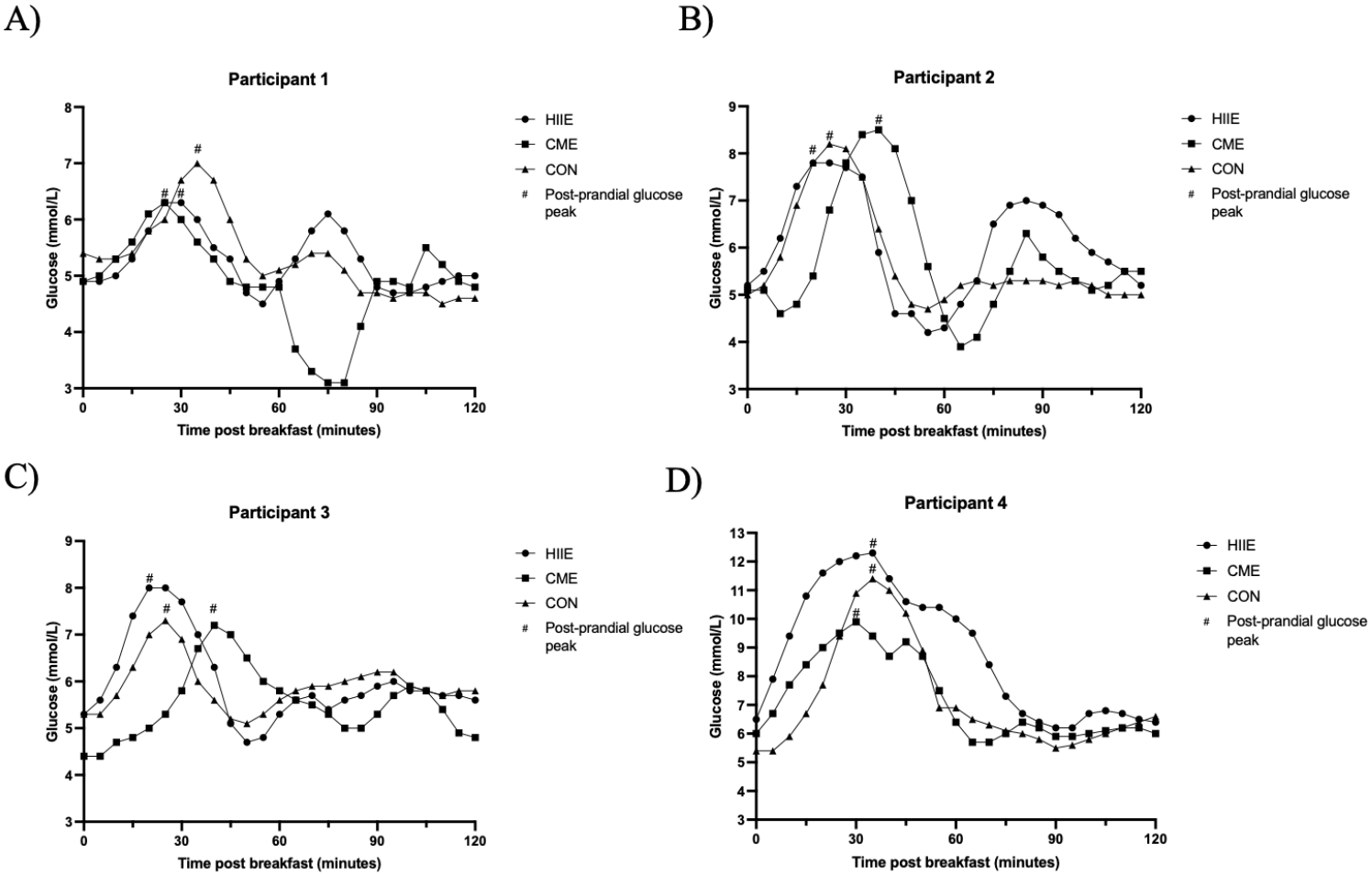


*Figure 4.4: Post-prandial glucose (PPG) response following a standardized breakfast the day after a day of high intensity (HIIE), a day after continuous moderate exercise (CME), and a day after a control day (CON). A) PPB response following a standardized breakfast for participant 1, B) PPB response following a standardized breakfast for participant 2, 3) PPG response following a standardized breakfast for participant 3, D) PPG response following a standardized breakfast for participant 4.#, post-prandial glucose peak*

### 4.3.3 Post-prandial glucose response following a standardized dinner

Figure 4.5 shows the two-hours post-prandial glucose response following a standardized dinner. A parametric test showed a significant reduction in glucose concentration in the week with HIIE compared to CME (mean HIIE=5.3±0.3 mmol/L to mean CME=5.6±0.6 mmol/L, *p=0.028*) and in the control week compared to CME (mean CON= 5.3±0.2 mmol/L to mean CME= 5.6±0.6 mmol/L, *p=0.001*).

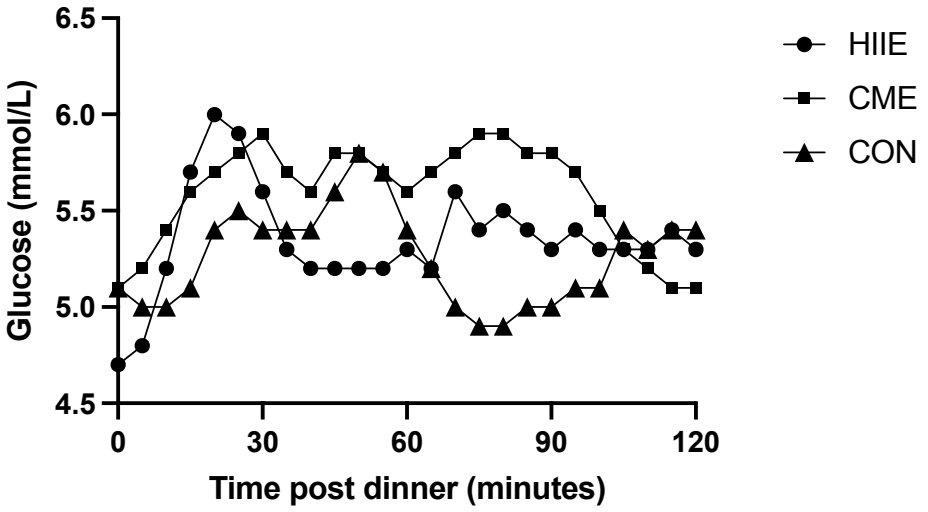


*Figure 4.5: Mean post-prandial response (PPG) following a standardized dinner on a day with single bout of high intensity interval exercise (HIIE), on a day with single bout of continuous moderate exercise (CME), and on a control day (CON).*

Figure 4.6 shows the glucose response following a standardized dinner for each participant. As mentioned above, they all seem to have normal glucose tolerance. Participant 3 (figure 4.6, C) have a decrease before the glucose concentration increases, in the control week. The post-prandial glucose peak also seems to appear later compared to HIIE week and CME week. It appears that individually, the post-prandial glucose peaks occur differently (between 30-60 minutes after ingestion). Participant 4 (figure 4.6, D) have a higher glucose concentration before the standardized dinner in the HIIE week compared to CME week and control week.

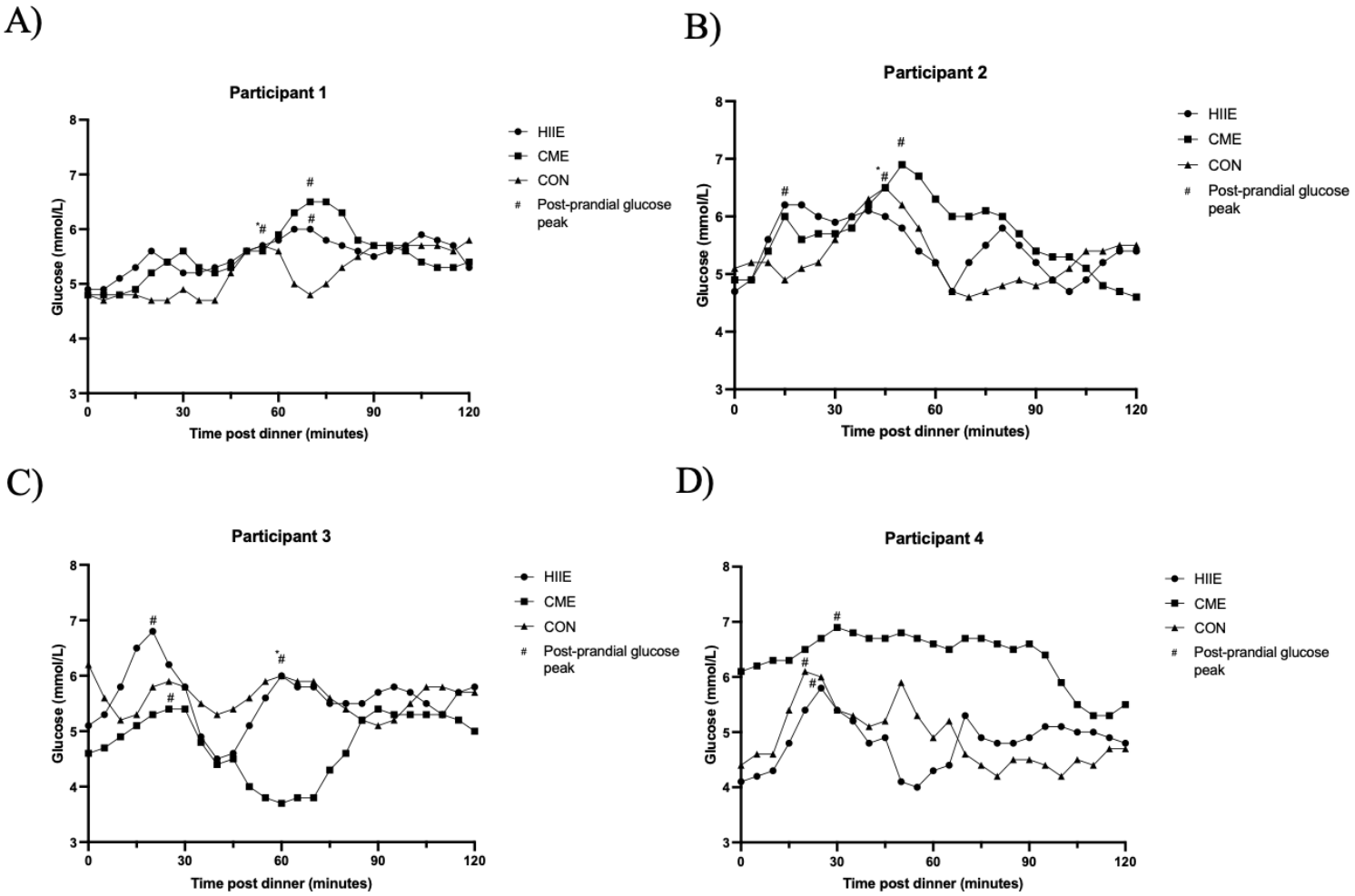


*Figure 4.6: Post-prandial glucose (PPG) response following a standardized dinner on a day with single bout of high intensity interval exercise (HIIE), on a day with single bout of continuous moderate exercise (CME), and on a control day (CON). A) PPG response following a standardized dinner for participant 1, B) PPG response following a standardized dinner for participant 2, 3) PPG response following a standardized dinner for participant 3, D) PPG response following a standardized dinner for participant 4. (*#, post-prandial peak for control week (CON), the indicated line not being visible).*

### 4.3.4 Effect of exercise on fasting blood glucose concentration

Post-prandial glucose response on FBG concentration during the night are shown in figure 4.7. Table 4.4. show the fasting glucose values during each hour (00-01, 01-02, 02-03, 03-04, 04-05, and 05-06) of the night.

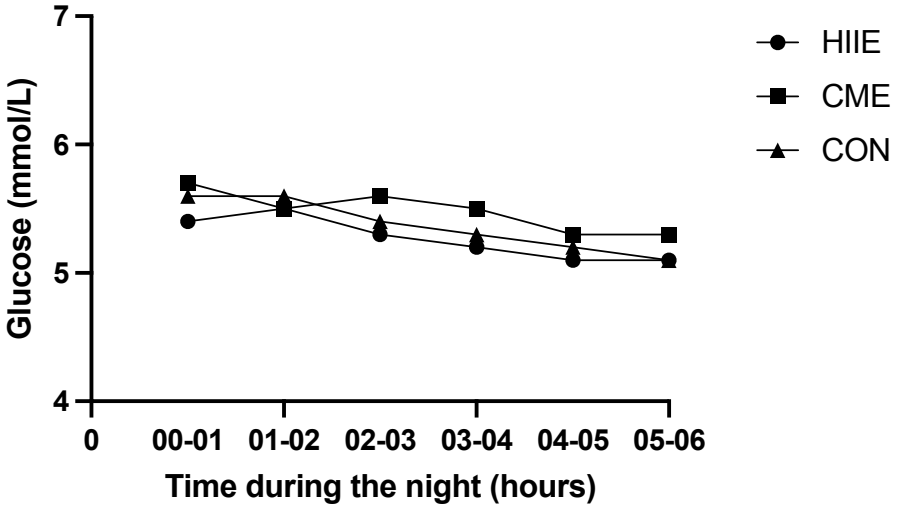


*Figure 4.7: Mean post-prandial glucose (PPG) response following a standardized dinner during midnight until 6:00 after a day with single bout of high intensity interval exercise (HIIE), on a day with single bout of continuous moderate exercise (CME), and on a control day (CON).*

The difference between the FBG appear small and do not differ too much between the three weeks. A non-parametric test showed that FBG did not significantly differ between HIIE, CME, and CON, H(2) = 1.212, *p=0.546*, neither for the entire night nor per hour.

*Table 4.4: Mean fasting blood glucose values during the night.*

| **Time during the night** | **HIIE (glucose value in mmol/L)** | **CME (glucose value in mmol/L)** | **CON (glucose value in mmol/L)** |
|---|---|---|---|
| **00-01** | 5.4 | 5.7 | 5.6 |
| **01-02** | 5.5 | 5.5 | 5.6 |
| **02-03** | 5.3 | 5.6 | 5.4 |
| **03-04** | 5.2 | 5.5 | 5.3 |
| **04-05** | 5.1 | 5.3 | 5.2 |
| **05-06** | 5.1 | 5.3 | 5.1 |

High intensity interval exercise showed a seemingly small reduction in FBG compared to CME and CON (table 4.4) while this reduction was not significant. All participants had a slightly reduced FBG value (figure 4.8) when comparing any exercise intensity on the control week (figure 4.7), except for participant 4 (HIIE=5.5 mmol/L, CME=6.5 mmol/L, CON=5.1 mmol/L).

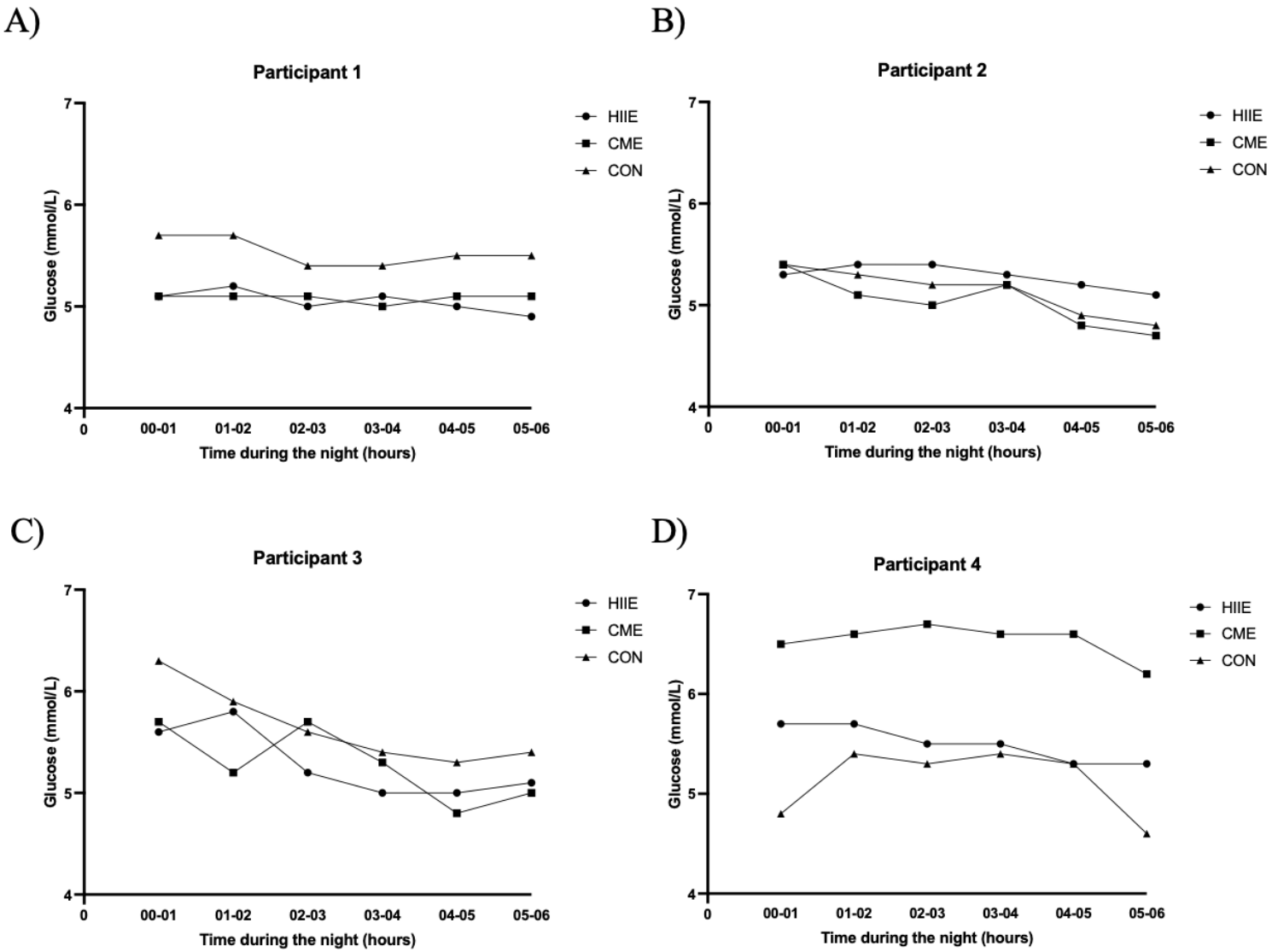


*Figure 4.8: Fasting blood glucose (FBG) response during midnight until 6:00 post standardized dinner, the night after a day with single bout of high intensity interval exercise (HIIE), on a day with single bout of continuous moderate exercise (CME), and on a control day (CON). A) FBG during the night for participant 1, B) FBG during the night for participant 2, C) FBG during the night for participant 3, D) FBG during the night for participant 4.*

# 5. Discussion

## 5.1 Main findings

The primary objective of this present study was to investigate if there was a significant difference in glucose tolerance between high intensity interval exercise and continuous moderate exercise compared to a control week. The secondary objective was to investigate if there were any changes in fasting blood glucose concentration from exercise. Due to other researchers claiming exercise of high intensity is superior to exercise of lower intensities, it was interesting to investigate if this is supported by the present study.

This present study showed a significant reduction in glucose concentration after breakfast, after exercise of high intensity interval exercise compared to continuous moderate exercise and control week with no exercise. Continuous moderate exercise had a significant reduction in glucose concentration after dinner, compared to high intensity interval exercise and control week. There were no significant reductions in FBG during the night among any of the intensities or the control week.

## 5.2 Characteristics of the exercise sessions

Unsurprisingly, the mean HR was higher in the HIIE sessions compared to CME. Figure 4.1 and figure 4.2 show that the HR peak was at its highest at the end of each minute of each interval as well as at the last interval of the exercise session. This is supportive by other research conducted on HR in 4x4 minutes intervals (Acala et al., 2020).

## 5.3 Effect of exercise intensity on glucose tolerance

### 5.3.1 Post-prandial glucose response on glucose tolerance following a standardized breakfast

The standardized breakfast was large, flaked oatmeal boiled in water, with a banana. Cooked oatmeal often has a GI of 60 (Tosh & Chu, 2015) which is considered to be a mid-range GI (Zhang et al., 2021). A mature banana normally has a GI of approx. 52 (Diabetesforbundet, 2022), which is considered a low-range GI (Zhang et al., 2021). Research has shown that food of low GI has a preventive effect on development of T2DM and can even be an important tool in cases of impaired glucose tolerance and T2DM (Barclay et al., 2008). The food of low GI generates a post-prandial glucose

concentration with smoother PPG peaks and reduce the duration of these speaks (Zhang et al., 2021). The glucose response from the standardized breakfast ingested in the post-absorptive state in this present study, can be compared to the response given from an OGTT. Valsdottir et al. (2019) report that OGTT performed 10-24 hours after a single bout of exercise increased glucose tolerance. The standardized breakfast was not ingested at the same period of time in the morning for all participants, but they reported eating it within 13-16 hours after the exercise at NIH. This could explain why the present study observed a significant reduction in glucose concentration within 2 hours post breakfast, in the week with continuous moderate exercise.

All participants seem to have normal glucose tolerance in most weeks, except for participant 4 who may have a slightly impaired glucose tolerance. Her mean PPG peak after breakfast (11.4±1.2 mmol/L) is above what is recommended for people with NGT (<7.8 mmol/L) (Ceriello & Colagiuri, 2008). It is worth noticing that mean PPG peaks in HIIE (8.5±2.4 mmol/L) and in CON (8.2±1.9 mmol/L) are also above what is recommended for people with NGT. A high post-prandial glucose peak can be an increased risk not only for T2DM, but also for cardiovascular disease (CVD) (Hanssen et al., 2020). Hanssen et al. (2020) report that the biggest risk comes from the duration outside the "normal range", and it seems that the glucose concentration for participant 4 was reduced 20 min after the observed post-prandial glucose peak, and then remained normal. For individuals with impaired glucose tolerance, as well as individuals with T2DM, food of low glycaemic index is recommended. This present study included breakfast in the low- to mid-range GI as the participants were young and healthy women. The results show that participant 4 has high post-prandial glucose peaks after ingestion of breakfast, despite her moderate activity level and normal BMI, and she could therefore possibly benefit from food of low-range GI, such as steel cut oatmeal (Tosh & Chu, 2015). Figure 4.4 showed that all participants had at least one PPG peaks occurring after 30 minutes had passed, after ingestion, in the intervention. The participants ate their standardized breakfast at home unsupervised, which mean that it is a possible error in the entry logs from breakfast. The practical implication of this is that it is possible that the PPG peak could occur earlier.

### 5.3.2 Post-prandial glucose response on glucose tolerance following a standardized dinner

The present study showed a significant reduction in post-prandial glucose concentration in the week with high intensity interval exercise compared to the week with continuous moderate exercise, observed after the standardized dinner. Little et al. (2014) using CGM, also reported a slight reduction in two-hour post-prandial glucose concentration due to high intensity interval exercise, although not significant. Manders et al. (2010) also using CGM, overserved the opposite, where the significant reduction in glucose concentration after dinner was a result of continuous moderate exercise. The disadvantage of comparing the result of the present study with these studies is that the population was either obese (Little et al., 2014) or diabetic (Manders et al., 2010). The research conducted on people with higher risk of T2DM, such as high BMI, seem to have a better effect of exercise on glucose uptake, and it appears that well trained endurance athletes have an impaired glucose tolerance due to excessive high intensity exercise (Flockhart et al., 2021).

The post-prandial glucose response following the standardized dinner (figure 4.5) show smoother post-prandial glucose peak compared to the response after the standardized breakfast (figure 4.3). Neither participant had a glucose peak above 7.8 mmol/L from the standardized dinner (recommended for people with NGT, Ceriello & Colagiuri, 2008) which is not surprising as they are young and healthy. Although participant 4 had a glucose peak above what is recommended for NGT, as a response from the breakfast, figure 4.6. D, shows that this response is not observed for participant 4 with the standardized dinner. This can be explained by the glycaemic response were decreased by implementing fat and protein with a meal rich in carbohydrates (Wolever, 2017).

In this present study, we conducted a pre-prandial exercise prescription, i.e. the ingestion of a meal occurred after exercise, when analysing the effect of exercise on a meal. Borrror et al. (2018) suggest that post-prandial exercise, i.e. exercise occurring after ingestion of a meal, have a better effect on managing post-prandial hyperglycaemia (i.e. high blood glucose levels after a meal) because of the increased glucose uptake into the skeletal muscle. In addition, in post-prandial exercise, the exercise-induced glucose uptake may be complemented by the endogenous insulin secretion stimulated by the meal (Borror et al., 2018). One other thing to consider when

analysing the glucose response after the dinner, is that all the exercise sessions started at 17:00 each week but finished at different times. The CME sessions lasted longer than the HIIE, and therefore it was more time to rest before dinner after completing the HIIE session. This means that recovery processes (increased glucose uptake for example) may have started earlier, before dinner even were consumed.

### 5.3.3 Effect of exercise intensity on fasting blood glucose concentration

There was no significant difference between FGB during the night and exercise at any intensity in this present study. These findings have also been found by others (Norton et al., 2012; Ross et al., 2012; Slentz et al., 2009; Valsdottir et al., 2019). The observation done on each participant individually showed that high intensity exercise and continuous moderate exercise were 8.7% lower in FBG compared to control week for participant 1. Slentz et al. (2009) reported that even though the FBG levels did not change for the exercise group, they observed an increase in fasting glucose for the control group. In the present study it was observed that ¼ of the sample included, had a higher FBG value in the control week. It would be interesting to investigate if there would be a similar difference such as the one observed in Slentz et al. (2009), with a bigger sample size than of the present study. Elevated FBG can often be strongly correlated to hepatic insulin resistance rather than skeletal muscle insulin resistance, which can be a partial explanation to why exercise does not seem to reduce FBG (Bird & Hawley, 2016; Nathan et al., 2009).

## *5.4 High intensity intervals as a superior choice to continuous moderate intensity*

Lastly, one of the research questions was: do high intensity interval exercise have a superior effect over continuous moderate exercise? The reason as to why this is interesting is that the majority of the population seems not to fulfil the World Health Organization recommendations of 150-300 minutes per week of moderate physical activity or 75-150 of vigorous PA (WHO, 2022). In Norway 68% of the population is reported not to meet the minimum recommendations (Helsedirektoratet, 2016). The data on the topic of high intensity interval exercise vs. continuous moderate exercise varies in the present study. CME had a significant reduction in glucose concentration from the breakfast compared to HIIE, while the opposite was observed in glucose response from the dinner. This is interesting to investigate because it is possible that exercise in the

form of high intensity interval training can save time and therefore be the preferred form of exercise for many people due to time commitment barriers (Babraj et al., 2009; Little et al., 2014).

Several studies have concluded that exercise of high intensity with short duration has the superior effect on post-prandial glucose concentration and hyperglycaemia (Babraj et al., 2009; Little et al., 2014; Sandvei et al., 2012) although some conclude that it is more effective with continuous moderate exercise (Borror, et al., 2018; Manders et al., 2010). Most studies conclude that exercise itself has a positive effect on post-prandial glucose concentration (Bonen et al., 1998; Cockcroft et al., 2014; Little et al., 2014) regardless of exercise comes before meal or after (Borror et al., 2018). It has also been suggested that a greater duration of exercise may be more important than intensity.

A possible explanation behind why exercise improves glucose tolerance is the increased glucose uptake into skeletal muscle after exercise, via expression of GLUT4 translocation (Houmard et al., 1993). The increase in GLUT4 translocation occur both as an acute effect of exercise and as a chronic effect of exercise (Borghouts and Keizer, 2000). Muscle contraction will increase $Ca^{2+}$ and also lead to increased level of AMP to ATP which will activate AMPK, which will lead to increased GLUT4 translocation and therefore increased glucose uptake. The effect of exercise has also proven to increase the insulin sensitivity (Babraj et al., 2009; Borghouts and Keizer, 2000). The insulin-dependent GLUT4 translocation is more understood than the one of glucose uptake via GLUT4 from contraction, yet there are similarities between the two. The proteins TBC1D1 and TBC1D4 (the latter also known as AS160, see figure 2.2) inhibits GLUT4 translocation at rest by converting target Rab-GTPase-activating protein (GAP) to an inactive GDP-bound form. With both contraction and increased plasma insulin, the GAP is reduced resulting in increased GLUT4 translocation to the membrane (Frøsig et al., 2010).

It is important to note that these studies have conducted more statistical analysis on more outcomes to conclude the overall effect on glucose tolerance from exercise and differences observed between the exercise intensities, than the present study have. Another important factor to consider when discussing the results of this present study is the limitations due to the small sample size compared to larger sample size in the

research mentioned above. This is further discussed below.

## 5.5 Strength and weaknesses

The main strength to this present study is the use of CGM to analyse and investigate the effect of exercise on glucose tolerance. A continuous glucose measurement device increases the quantity glucose measurements and gives the opportunity to analyse glucose metabolism across 24 hours. It might also feel less painful when comparing to blood samples after an OGTT (Klonoff et al. 2017). Another strength could be the chosen study design. Cross-sectional study design gives the benefit of having fewer participants as they are their own control. On the other hand, with few participants the consequence of drop-out is more severe as opposed to larger groups (>20) in randomized control trials (RCT) which is normally the golden standard. The participants were also encouraged to refrain from caffeine before and until after three hours post standardized breakfast. Neither participant reported drinking caffeine after 12:00 the day of standardized dinner, with or without exercise. This is a strength to the present study because research has shown that caffeine can have a negative effect on glucose tolerance. A review article from Shearer and Graham (2014), report that regardless of what metabolic state one is in (i.e. young and healthy but overweight, pregnant or T2DM), caffeine reduces glucose uptake. Therefore, the likelihood of caffeine affecting aspects of glucose metabolism in the present study, are small, on the bases of what the participants reported.

The main limitation to this present study has already been mentioned above, which is the small sample size. A small sample size made the comparison with other published reference material on this population challenging. The main reason behind the small sample size was the late start-up of the data collection. The data collection was initially planned to start in September/October 2021 but got delayed due to the ethical committee application (appendix 3) submitted August 19$^{th}$, 2021, was not approved until October 2021. It was further delayed due to expired CGM equipment, where new sensors were not available until the December 2021. Another factor affecting sample size was the global pandemic of Covid-19. When data collection started in January 2022, there were increased number of Covid-19 cases in the Norwegian population which lasted throughout March 2022 (FHI, 2020, last updated: 05.23.2022) and onwards. This led to more people withdrawing their interest to participate and to delays

and changes in the planned schedule.

The small sample size decreases the internal validation and therefore decreases the external validation (Patino & Ferreira, 2018). This increases the risk of type 2 error, and by retaining $H_0$ we could wrongly conclude that there is not a difference when there might have been one with a larger sample size. Due to the sample size and only women included, the result cannot be representative to a larger population. It was not just the small sample size alone that decreased the statistical power. Both parametric and non-parametric tests were performed due to non-normal distributed data. Even though it is possible to run parametric tests on non-normal distributed data, it requires a larger sample size to be more valid. Assumed normality in a test done on small sample sizes may not detect deviation from the equal variance assumption (Morgan, 2017).

The sample of the present study only included women may be a limitation, not only due to the degree of external validity, but also because of the menstrual cycle. Valsdottir et al. (2019) who found an effect of exercise on glucose tolerance also conducted the exercise on moderately active, healthy women. It has been proven that the menstrual cycle can affect glucose metabolism, and therefore it might be a factor worth noticing. Research has shown that the female body has better glucose uptake in the follicular phase, i.e. from the start of the menstruation to mid ovulation and it is impaired in the luteal phase (Diamond et al., 1989). In the present study, it was not known where the women were in their menstrual cycle and therefore, we can not conclude what effect the menstrual cycle had on glucose metabolism in this case. The training status may also influence the acute effect from a single bout of exercise can have on glucose tolerance. Steenberg et al. (2019) observed that the insulin-stimulated glucose uptake after an acute exercise session is reduced in trained state, although after the 12 week of training intervention they did observe increased insulin-stimulated glucose uptake. This could be a possible explanation as to why both this present study and Valsdottir et al. (2019) found a positive effect of exercise on moderate trained individuals.

Individual differences may also affect the outcome. The participants did not vary too much in age, weight, or height. The inclusion criteria for this present study was that the participants had to be moderately active. The participants included had different training experience. One of them was a spinning instructor while the other did not have much

experience on a bicycle. The mode of exercise may therefore influence the effect of the exercise sessions. A person who is used to cycling may have a higher efficiency compared to a person who is not (Hopker et al., 2007). It does not appear that this has affected the PPG response for either the standardized breakfast or dinner in the present study. The intensity measurements used in the present study were percentage of $HR_{max}$ and RPE. Percentage of $HR_{max}$ are relative measurement and RPE is a subjective way of determining intensity of exercise (Maclntosh et al., 2021). If the intensity was determined by for example power output in watts, it might increase the internal validation. Another weakness was that the $HR_{max}$ used to calculate the intensity of the exercises, was the one that each participant reached in the $VO_{2max}$ test. There was one exception. One participant reached a significant lower HR in the $VO_{2max}$ test, compared to what her age-predicted $HR_{max}$ was. This was apparent during the first exercise where she reached the HR from $VO_{2max}$ test within 2 minutes of the first interval. Therefore, her age-predicted $HR_{max}$ was used to calculate the intensity of the exercise sessions, both HIIE and CME.

We did not have full control of what the participants did on their spare time when it came to dietary intake and physical activity. On the other hand, I talked to the participants the days they were supposed to change the CGM sensors, and in advance of the days with attendance at NIH. I was also available for them to contact me when they had problems with the CGM and questions about what to report the 24 hours before attendance. It is also important to note that, we had no control over what the participants did prior to the intervention. Therefore, it is possible that potential physical activity the week prior to the intervention had an effect on the first week of participation, as opposed to the third one as the latter follows a control week.

## *5.6 Further research*

This present study only included women. This was initially to make the sample homogenic along with inclusions criteria such as moderately active and age between 18-45. The possible practical implications of menstrual cycle and glucose metabolism was previously described in section 5.3.2. It might be necessary to conduct a similar study on women in the follicular phase to compare the results with men in matched age, weight, and training status. Due to the small sample size and only one gender included, the result of the present study cannot be represented to a larger and more heterogenic

population. It would therefore be interesting to conduct a similar study on both men and women with a larger sample size. If we would have performed a longer intervention and post-tests, we could potentially say more about the superior effect that exercise with high intensity could have compared to more continuous moderate exercise. It would be interesting to investigate this possible effect, not only for the overall glucose control, but for other parameters such as maximal oxygen (Helgerud et al., 2007) as well.

The intention behind this present study was to get a better understanding on the effect exercise and exercise intensities have on glucose tolerance, on healthy women, using CGM. Exercise of high intensity, often compounded as intervals, has the benefit of being time saving and possibly having a superior physiological effect. Therefore, it was interesting to investigate the effect of exercise intensities on glucose tolerance. The majority of the research seems to have been conducted on individuals with either risk of T2DM (obesity, inactivity, etc.) or diabetes itself. The use of CGM gives the benefit of analysing multiple glucose parameters, other than the 2h post meal and 6 hours FBG analysed in this present study. It would be interesting to further investigate the 24-hour glucose response of exercise. CGM gives the opportunity to investigate both the acute and the chronic effects of exercise.

# 6. Conclusion

This present study concludes that both exercise of high intensity intervals and continuous moderate exercise reduces PPG and therefore improves glucose tolerance. Continuous moderate exercise improves glucose tolerance after standardized breakfast while high intensity interval exercise improves glucose tolerance after standardized dinner. Neither exercise intensities have a superior effect on fasting glucose concentration, but it appears that the FBG was higher in the control week than of the exercise weeks. This present study contained a very small sample size, and it is therefore important to note that it decreased the statistical power for this study and may therefore be hard to generalize to a larger population.

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# Table overview

# Figure overview

*Figure 4.5: Mean post-prandial response (PPG) following a standardized dinner on a day with single bout of high intensity interval exercise (HIIE), on a day with single bout of continuous moderate exercise (CME), and on a control day (CON).*

*Figure 4.6: Post-prandial glucose (PPG) response following a standardized dinner on a day with single bout of high intensity interval exercise (HIIE), on a day with single bout of continuous moderate exercise (CME), and on a control day (CON). A) PPG response following a standardized dinner for participant 1, B) PPG response following a standardized dinner for participant 2, 3) PPG response following a standardized dinner for participant 3, D) PPG response following a standardized dinner for participant 4. (*#, post-prandial peak for control week (CON), the indicated line not being visible).*

*Figure 4.7: Mean post-prandial glucose (PPG) response following a standardized dinner during midnight until 6:00 after a day with single bout of high intensity interval exercise (HIIE), on a day with single bout of continuous moderate exercise (CME), and on a control day (CON).*

*Figure 4.8: Fasting blood glucose (FBG) response during midnight until 6:00 post standardized dinner, the night after a day with single bout of high intensity interval exercise (HIIE), on a day with single bout of continuous moderate exercise (CME), and on a control day (CON). A) FBG during the night for participant 1, B) FBG during the night for participant 2, C) FBG during the night for participant 3, D) FBG during the night for participant 4.*

# Abbreviations

| | |
|---|---|
| T2DM | Type 2 diabetes mellitus |
| PA | Physical activity |
| HIIT | High intensity interval training |
| EE | Endurance exercise |
| OGTT | Oral glucose tolerance test |
| CMG | Continuous glucose measurement |
| HIIE | High intensity interval exercise |
| CME | Continuous moderate exercise |
| CON | Control week |
| NEFA | Non-esterified fatty acid |
| GT | Glucose tolerance |
| NGT | Normal glucose tolerance |
| IGT | Impaired glucose tolerance |
| BMI | Body mass index |
| WHO | World Health Organization |
| FBG | Fasting blood glucose |
| RPE | Rating of perceived exhaustion |
| $VO2_{max}$ | Maximal oxygen uptake |
| HK | Hexokinase |
| AMP | Adenosine monophosphate |
| ATP | Adenosine triphosphate |
| ADP | Adenosine diphosphate |
| BM | Body mass |
| NIH | Norwegian School of Sport´s Science |
| HR | Heart rate |

| | |
|---|---|
| $HR_{max}$ | Maximal heart rate |
| Kcal | Kilocalorie |
| RPM | Revolutions per minute |
| W | Watt |
| RER | Respiratory exchange ratio |
| BPM | Beats per minute |
| GI | Glycaemic index |
| RCT | Randomized control trial |

# Appendix 1 – Recruitment poster

NORGES IDRETTSHØGSKOLE

## Vil du være med på en spennende studie?

**HENSIKTEN med studiet er å undersøke effekten av ulike treningsintensiteter på kroppens evne til å normalisere blodsukkernivået etter et måltid, samt effekten på fastende glukosenivå ved å bruke en kontinuerlig glukosemåler.**

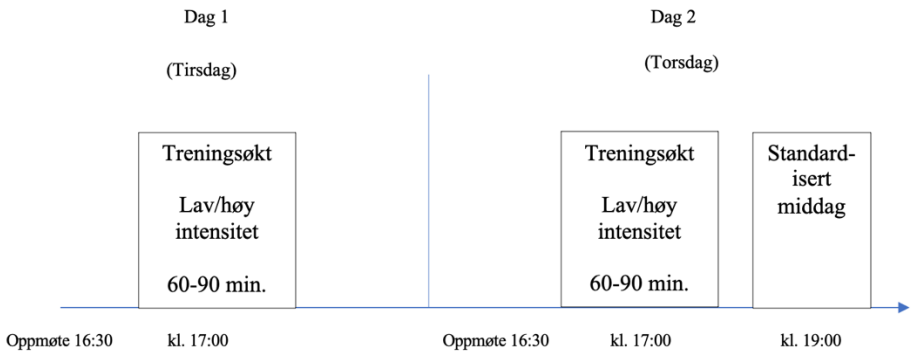
Gratis $VO_{2max}$ test!!

Hvem kan delta?

- Kvinner
- 18-45 år
- Frisk, ingen kjente sykdommer
- Moderat utholdenhetstrent (1-2 økter de siste 6 mnd.)

### Når foregår dette?

Datainnsamlingen starter i januar og avsluttes i februar. Du vil enten være med i januar eller februar. Deltakelsen innebærer kun 3 uker pluss tilvenningsøkter og VO2max test før start.




For mer informasjon ta kontakt med Silje Løyning Sævareid på e-post

silje.saevareid@gmail.com

# Appendix 2 – Health examination questionnaire

## Egenerklæring for forsøkspersoner

| | |
|---|---|
| Etternavn: | Fornavn: |
| Fødselsdato: | |
| E-post: | |
| Tlf.: | |
| Idrettsbakgrunn (angi omtrent hvor mange timer du trener per uke): | |

Takk for at du vurderer å delta som forsøksperson ved Norges idrettshøgskole! Før du kan delta, må vi imidlertid kartlegge om din deltakelse kan medføre noen form for helserisiko. Vær snill å lese gjennom alle spørsmålene nøye og svar ærlig ved å krysse av for JA eller NEI. Hvis du er i tvil, bør du be om å få snakke med legen som er ansvarlig for forsøket.

Hvis du krysser av for JA på ett eller flere av disse spørsmålene, må du gjennomgå en legeundersøkelse før forsøksstart.

| Spørsmål | JA | NEI |
|---|---|---|
| 1. Kjenner du til at du har en hjertesjukdom? | | |
| 2. Hender det du får brystsmerter i hvile eller i forbindelse med fysisk aktivitet? | | |
| 3. Kjenner du til at du har høyt blodtrykk? | | |
| 4. Bruker du for tiden medisiner for høyt blodtrykk eller hjertesjukdom? (f.eks. vanndrivende midler)? | | |
| 5. Har noen av dine foreldre, søsken eller barn fått hjerteinfarkt eller dødd plutselig (før fylte 55 år for menn og 65 år for kvinner)? | | |
| 6. Røyker du? | | |
| 7. Har du besvimt i løpet av de siste seks månedene? | | |
| 8. Hender det du mister balansen på grunn av svimmelhet? | | |
| 9. Har du sukkersjuke (diabetes)? | | |
| 10. Får du allergiske eller hypersensitive reaksjoner av bedøvelse? | | |
| 11. Kjenner du til noen annen grunn til at din deltakelse i prosjektet kan medføre helse- eller skaderisiko? | | |

Gi beskjed straks dersom din helsesituasjon forandrer seg fra nå og til undersøkelsen er ferdig, f.eks. ved at du blir forkjølet eller får feber.

_____

Sted – dato

_____

Underskrift

# Appendix 3 – Application to NSD and approval from NIH Ethics committee

# Vedlegg 3 Søknad NSD

NSD NORSK SENTER FOR FORSKNINGSDATA

**Meldeskjema 843956**

**Sist oppdatert**

18.08.2021

**Hvilke personopplysninger skal du behandle?**

---

- Navn (også ved signatur/samtykke)
- Fødselsdato
- Adresse eller telefonnummer
- E-postadresse, IP-adresse eller annen nettidentifikator
- Bilder eller videoopptak av personer

**Type opplysninger**

---

**Skal du behandle særlige kategorier personopplysninger eller personopplysninger om straffedommer eller lovovertredelser?**

- Helseopplysninger

**Prosjektinformasjon**

---

**Prosjekttittel**

Effekten av treningsintensitet på glukosetoleransen

**Prosjektbeskrivelse**

Det er blitt utført noe forskning på trening og glukosetoleranse ved bruk av kontinuerlig glukosemåling (CGM). Mye av forskningen er blitt utført på utsatte individer som for eks. individer med overvekt og fedme, og diabetes mellitius. Resultatene har gitt lite svar på om det har særlig effekt. Det vises at trening av høyere intensitet gir bedre effekt enn trening av lav intensitet. Hovedresultatet i dette prosjektet vil altså være om høy intensitet eller lav intensitet gir best effekt på glukosetoleransen hos kvinner.

**Begrunn behovet for å behandle personopplysningene**

Behandling av personopplysninger, spesielt helsedata, er nødvendig for å svare på forskningsspørsmålene. Bruken av dem vil imidlertid være begrenset og begrenset til minimumsnivået.

**Ekstern finansiering**

**Type prosjekt**

Forskerprosjekt

**Behandlingsansvar**

---

**Behandlingsansvarlig institusjon**

Norges idrettshøgskole / Institutt for fysisk prestasjonsevne

**Prosjektansvarlig (vitenskapelig ansatt/veileder eller stipendiat)**

Jørgen Jensen, jorgenj@nih.no, tlf: 98869223

**Skal behandlingsansvaret deles med andre institusjoner (felles behandlingsansvarlige)?**

Nei

**Utvalg 1**

---

**Beskriv utvalget**

Utvalget er friske kvinner som karakteriseresmoderat fysisk aktive (trener ca.2 ganger i uken). De må være normalvektige, ikke-røyker og ingen kjente sykdommer.

**Rekruttering eller trekking av utvalget**

Rekruttering vil skje via universitetets nedsider og ulike treningssenter.

**Alder**

18 - 45

**Inngår det voksne (18 år +) i utvalget som ikke kan samtykke selv?**

Nei

**Personopplysninger for utvalg 1**

- Navn (også ved signatur/samtykke)
- Fødselsdato
- Adresse eller telefonnummer
- E-postadresse, IP-adresse eller annen nettidentifikator
- Bilder eller videoopptak av personer
- Helseopplysninger

**Hvordan samler du inn data fra utvalg 1?**

**Medisinsk undersøkelse og/eller fysiske tester**

**Grunnlag for å behandle alminnelige kategorier av personopplysninger**

Samtykke (art. 6 nr. 1 bokstav a)

**Grunnlag for å behandle særlige kategorier av personopplysninger**

Uttrykkelig samtykke (art. 9 nr. 2 bokstav a)

**Redegjør for valget av behandlingsgrunnlag**

**Humant biologisk materiale**

**Grunnlag for å behandle alminnelige kategorier av personopplysninger**

Samtykke (art. 6 nr. 1 bokstav a)

**Grunnlag for å behandle særlige kategorier av personopplysninger**

Uttrykkelig samtykke (art. 9 nr. 2 bokstav a)

**Redegjør for valget av behandlingsgrunnlag**

**Informasjon for utvalg 1**

**Informerer du utvalget om behandlingen av opplysningene?**

Ja

**Hvordan?**

Skriftlig informasjon (papir eller elektronisk)

**Tredjepersoner**

---

**Skal du behandle personopplysninger om tredjepersoner?**

Nei

**Dokumentasjon**

---

**Hvordan dokumenteres samtykkene?**

- Manuelt (papir)

**Hvordan kan samtykket trekkes tilbake?**

Elektronisk (e-post, e-skjema, digital signatur), manuelt (på papir) og muntlig

**Hvordan kan de registrerte få innsyn, rettet eller slettet opplysninger om seg selv?**

Elektronisk (e-post, e-skjema, digital signatur), manuelt (på papir) og muntlig

**Totalt antall registrerte i prosjektet**

1-99

**Tillatelser**

---

**Skal du innhente følgende godkjenninger eller tillatelser for prosjektet?**

- Biobank
- Annen godkjenning

**Annen godkjenning**

Etisk godkjenning fra NIHs etiske komiteen

**Behandling**

---

**Hvor behandles opplysningene?**

- Maskinvare tilhørende behandlingsansvarlig institusjon

**Hvem behandler/har tilgang til opplysningene?**

- Prosjektansvarlig
- Student (studentprosjekt)
- Eksterne medarbeidere/samarbeidspartnere innenfor EU/EØS

**Tilgjengeliggjøres opplysningene utenfor EU/EØS til en tredjestat eller internasjonal organisasjon?**

Nei

**Sikkerhet**

---

**Oppbevares personopplysningene atskilt fra øvrige data (koblingsnøkkel)?**

Ja

**Hvilke tekniske og fysiske tiltak sikrer personopplysningene?**

- opplysningene krypteres under lagring
- Adgangsbegrensning
- Andre sikkerhetstiltak

**Hvilke**

Kodenøkkel innlåst i safe med begrenset tilgang

**Varighet**

---

**Prosjektperiode**

01.09.2021 - 01.09.2031

**Skal data med personopplysninger oppbevares utover prosjektperioden?**

Ja, data med personopplysninger oppbevares til: 01.09.2036

**Til hvilket formål skal opplysningene oppbevares?**

Dokumentasjonshensyn eller vilkår fra Regionale komiteer for medisinsk og helsefaglig forskningsetikk

**Hvor oppbevares opplysningene?**

Internt ved behandlingsansvarlig institusjon

**Vil de registrerte kunne identifiseres (direkte eller indirekte) i oppgave/avhandling/øvrige publikasjoner fra prosjektet?**

Nei

**Tilleggsopplysninger**

---

Jørgen Jensen
Institutt for fysisk prestasjon

OSLO 05. september 2021

# Søknad 198-020921 – Effekten av treningsintensitet på glukosetoleransen

Vi viser til søknad, prosjektbeskrivelse, informasjonsskriv og innsendt melding til NSD.

I henhold til retningslinjer for behandling av søknad til etisk komite for idrettsvitenskapelig forskning på mennesker, ble det i komiteens møte av 2. september 2021 konkludert med følgende:

**Vurdering**

I søknaden fremgår det at det skal brukes et helseundersøkelsesskjema som ledd i screening og inklusjon av forskningsdeltakerne. Komiteen forstår det slik at informasjon i dette skjemaet ikke inngår i datagrunnlaget for prosjektet og derav ikke skal lagres. Komiteen anbefaler imidlertid at det i samtykkeskrivet til deltakerne redegjøres for formålet med skjemaet samt hva som skjer med informasjonen som samles inn.

Komiteen godkjenner opprettelse av en prosjektspesifikk biobank for prosjektet. Komiteen ber imidlertid prosjektleder vurdere nødvendigheten av å opprette en biobank i lys av prosjektets formål. I dette ligger at dersom det ikke er behov for å lagre materiale etter analyser er foretatt, så er det ikke grunnlag for en egen biobank. Da kan materiale destrueres etter analyser og at det opplyses om dette i informasjonsskrivet. Gitt behov for lagring av materiale også etter gjennomførte analyser, så legger komiteen til grunn at tidspunkt for destruering av materialet er det samme som sletting av øvrige personopplysninger (1. september 2031).

Komiteen finner også grunn til å påpeke at forskningsspørsmålet – hypotesen – ikke fremstår som klart formulert i prosjektbeskrivelsen. Uten å stille vilkår knyttet til dette, anbefaler komiteen om at prosjektleder vurderer om forskningsspørsmålet kan formuleres tydeligere.

**Vedtak**

*På bakgrunn av forelagte dokumentasjon finner komiteen at prosjektet er forsvarlig. Komiteen godkjenner opprettelse av en prosjektspesifikk biobank. Til vedtaket har komiteen lagt følgende forutsetning til grunn:*

- *At vilkår fra NSD følges*

- *At prosjektleder sender en redegjørelse for behovet for å opprette en biobank. Redegjørelsen sendes komiteen til orientering innen 13. september*
- *At informasjonsskrivet justeres i tråd med komiteens merknad og sendes komiteen til orientering*
- *At det inngås avtaler med samarbeidene institusjoner*
- *At det biologiske materialet destrueres innen oppgitt sluttdato og at retningslinjer for innsamling, bruk og lagring av humant biologisk materiale ved NIH følges*

**Vedtak**

*På bakgrunn av forelagte dokumentasjon finner komiteen at prosjektet er forsvarlig. Komiteen godkjenner opprettelse av en prosjektspesifikk biobank. Til vedtaket har komiteen lagt følgende forutsetning til grunn:*

- *At vilkår fra NSD følges*
- *At det inngås avtaler med samarbeidene institusjoner*
- *At det biologiske materialet destrueres innen oppgitt sluttdato og at retningslinjer for innsamling, bruk og lagring av humant biologisk materiale ved NIH følges*

Komiteen gjør oppmerksom på at vedtaket er avgrenset i tråd med fremlagte dokumentasjon. Dersom det gjøres vesentlige endringer i prosjektet som kan ha betydning for deltakernes helse og sikkerhet, skal dette legges fram for komiteen før eventuelle endringer kan iverksettes. Komiteen gjør oppmerksom på at vedtaket er avgrenset i tråd med fremlagte dokumentasjon. Dersom det gjøres vesentlige endringer i prosjektet som kan ha betydning for deltakernes helse og sikkerhet, skal dette legges fram for komiteen før eventuelle endringer kan iverksettes.

Komiteen forutsetter videre at prosjektet gjennomføres på en forsvarlig måte i tråd med de til enhver tid gjeldende tiltak ifbm Covid-19 pandemien.

Med vennlig hilsen

Anne Marte Pensgaard

Professor Anne Marte Pensgaard
Leder, Etisk komite, Norges idrettshøgskole

# Appendix 4 – Information and consent form

NORGES IDRETTSHØGSKOLE

## FORESPØRSEL OM DELTAKELSE I FORSKNINGSPROSJEKTET

# EFFEKTEN AV TRENINGSINTENSITET PÅ GLUKOSETOLERANSEN

Dette er et spørsmål for deg som ønsker å delta i et forskningsprosjekt som undersøker effekten av ulike treningsintensiteter på regulering av glukosemetabolisme. Trening kan redusere risikoen for metabolsk syndrom, og en akutt treningsøkt øker glukosetoleransen samt øker insulinsensitiviteten. Kontroll på glukosenivået er viktig og da insulinresistens og vedvarende høyt nivå av glukose i blodet kan føre til diabetes type 2, kan det hjelpe å forstå mekanismen rundt glukosetoleranse. Vi ønsker dermed å undersøke effekten av to ulike intensiteter av trening på glukosetoleransen. Deltakerne vil utføre to treningsøkter med lav intensitet og to treningsøkter med høy intensitet i løpet av 2 uker, samt en kontrolluke.

Vi søker friske kvinner i alderen 18-45 år, som karakteriseres som moderat fysisk aktive (trener 2-3 ganger i uken). Du må være frisk, normalvektig og ikke-røyker.

Ytterlige informasjon finnes i skrivet. Om du har lest denne informasjonen og ønsker å være forsøksperson, ber vi deg om å skrive under og returnere den siste siden på dette skrivet til oss. Du kan når som helst trekke deg fra studien uten å oppgi en grunn.

Ansvarlig for studien er Norges idrettshøgskole, og prosjektleder er professor Jørgen Jensen. Masterstudent Silje Løyning Sævareid (45461292, silje.saevareid@gmail.com) vil ha det praktiske ansvaret for den daglige driften underveis i studien.

## HVA INNEBÆRER STUDIEN?

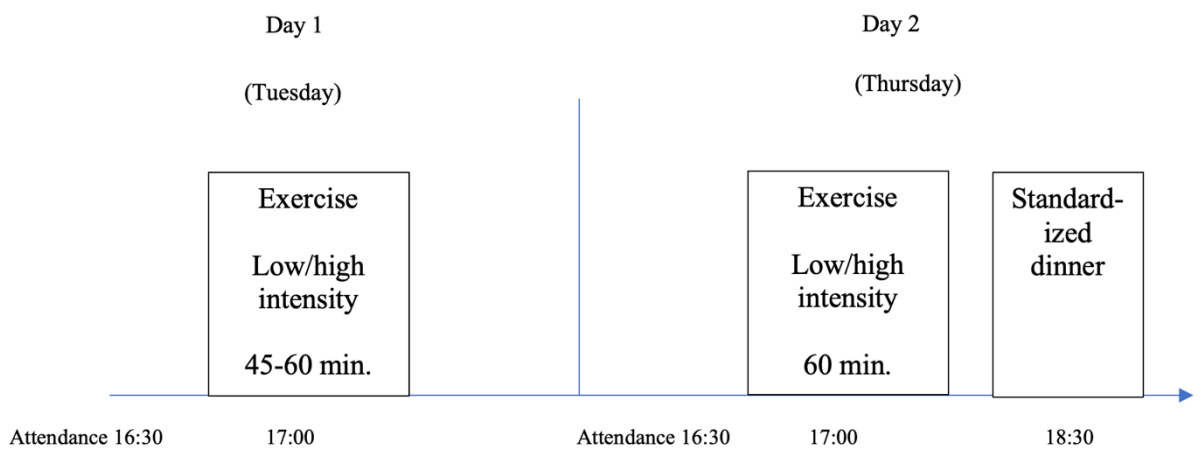
Dersom du ønsker å delta kreves det at du følger prosjektets retningslinjer som inneholder to hovedtestdager i 2 uker, samt 1 kontrolluke uten trening. I løpet av disse ukene vil du også måtte gå med en kontinuerlig glukosemåler (CGM) som måler blodsukkernivået via en probe festet på magen.

Under de to hovedtestdagene må du møte kl. 16:30 på NIH. Du vil bli tilfeldig plassert i uke hvor man starter enten med treningsøkter med lav, høy intensitet eller kontrolluke. Deltakerne vil også spise en standardisert middag etter endt treningsøkt på Norges idrettshøgskole på dag 2 i de to treningsukene, og på tilsvarende dag i kontrolluken.

Det vil også utføres pre-tester før ukene nevnt ovenfor starter. Disse testene vil være $VO_{2max}$ og vekt og høyde. Her vil det også utføres tilvenningsøkter. Se figur 1 for oversikt over ukene. Figur 2 viser oversikt over ukene som inneholder treningsøkter og standardisert middag på NIH.

| | | | | |
|---|---|---|---|---|
| **$VO_{2max}$** | ⬇ | | | |
| **CGM** | | ⬇ | ⬇ | ⬇ |
| **Standardisert middag på NIH** | | ⬇ | ⬇ | ⬇ |
| **Standardiserte treningsøkter på NIH** | | ⬇ | | ⬇ |
| **Uke** | 0 | 1 | 2 | 3 |

*Figur 1: Oversikt over perioden.*



*Figur 2: Oversikt over protokollen i treningsukene.*

## MULIGE FORDELER OG ULEMPER

Trening kan føre til stølhet og utmattelse som kan føre til midlertidige ulemper. Ved invasive prøver, som CGM er den viss risiko for infeksjoner, men dette vil reduseres ved at prøvene utføres i sterile forhold og godt trent personell. Det vil derimot være flere fordeler ved å delta. Deltakerne får teste sitt maksimale oksygenopptak gratis som ellers ville vært veldig dyrt å teste. Dette vil føre til en god pekepinn på deres fysiske form og helse, og gi et innblikk i hvordan forskning foregår.

## FRIVILLIG DELTAKELSE OG MULIGHET FOR Å TREKKE SITT SAMTYKKE

Det er frivillig å delta i prosjektet. Dersom du ønsker å delta signerer du vedlagt samtykkeskjema. Du kan når som helst trekke deg fra studien uten å oppgi noen grunn. Det vil ikke få noen konsekvenser for deg hvis du ikke vil delta eller senere velger å trekke deg.

Dersom du trekker deg fra prosjektet, kan du kreve å få slettet innsamlede prøver og opplysninger, med mindre opplysningene allerede er inngått i analyser eller brukt i vitenskapelige publikasjoner.

Dersom du senere ønsker å trekke deg eller har spørsmål til studien, kan du kontakte Silje Løyning Sævareid (silje.saevareid@gmail.com) eller Jørgen Jensen (jorgenj@nih.no).

## DITT PERSONVERN – HVORDAN VI OPPBEVARER OG BRUKER DINE OPPLYSNINGER

Vi vil bare bruke opplysningene om deg til formålene vi har nevnt i dette skrivet. Vi behandler opplysningene konfidensielt og i samsvar med personvernregelverket. Du som deltaker har rett til å få innsyn i hvilke personopplysninger som er registrert om deg.

Spørreundersøkelsesskjemaet om helsestatus skal kun brukes i rekruttering av forsøkspersoner, ikke i datagrunnlaget. Dette betyr at denne informasjonen blir ikke lagret etter dataen er analysert.

Informasjonen som registreres vil bli behandlet uten navn og fødselsnummer, eller andre direkte gjenkjennende opplysninger. Det vil brukes nummererte koder i stedet for navn. Alle data vil bli behandlet avidentifisert og ingen, bortsett fra deg og testleder, kan knytte dataene tilbake til deg. Det vil derfor ikke være mulig å identifisere resultatene dine i studien du har deltatt i når disse senere publiseres.

Professor Jørgen Jensen er daglig ansvarlig for prosjektet, og Norges idrettshøgskole ved administrerende direktør er databehandlingsansvarlig. Prosjektleder har ansvar for at opplysninger om deg blir behandlet på en sikker måte.

## FORSIKRING

Norges idrettshøgskole er en statlig vitenskapelig høgskole, og staten er selvassurandør.

## DINE RETTIGHETER

Så lenge du kan identifiseres i datamaterialet, har du rett til:

- Innsyn i hvilke personopplysninger som er registrert om deg,
- Å få rettet personopplysninger om deg,
- Få slettet personopplysninger om deg,
- Få utlevert en kopi av dine personopplysninger (dataportabilitet),
- Å sende klage til personvernombudet eller Datatilsynet om behandlingen av dine personopplysninger.

## HVA SKJER MED OPPLYSNINGENE DINE NÅR VI AVSLUTTER FORSKNINGSARBEIDET?

Prosjektet skal etter planen avsluttes 2031. Dataen vil lagres frem til 2036 av dokumentasjonshensyn. Det vil ikke være mulig å identifisere resultatene dine i studien du har deltatt i.

## HVA GIR OSS RETT TIL Å BEHANDLE PERSONOPPLYSNINGER OM DEG?

Vi behandler opplysninger om deg basert på ditt samtykke. På oppdrag fra Norges idrettshøgskole har NSD – Norsk senter for forskningsdata AS vurdert at behandlingen av personopplysninger i dette prosjektet er i samsvar med personvernregelverket.

## HVOR KAN JEG FINNE UT MER?

Hvis du har spørsmål til studien, eller ønsker å benytte deg av dine rettigheter, ta kontakt med:

- Norges idrettshøgskole ved prosjektansvarlig Jørgen Jensen (telefon 98 86 92 23, eller på epost jorgenj@nih.no), doktorgradsstudent Silje Løyning Sævareid (telefon 45 46 12 92, eller på epost silje.saevareid@gmail.com).
- Vårt personvernombud: NIHs etiske komite, på epost (personvernombud@nih.no)
- NSD – Norsk senter for forskningsdata AS, på epost (personverntjenester@nsd.no) eller telefon: 55 58 21 17.

## GODKJENNING

Studien er godkjent av intern etisk komite ved Norges idrettshøgskole (saksnummer: 198_02092).

# Samtykke til deltakelse i studien

Jeg har mottatt og forstått informasjon om prosjektet *«effekten av treningsintensitet på glukosetoleransen»*, og har fått anledning til å stille spørsmål. Jeg samtykker til:

- ☐ å delta i dette vitenskapelige forsøket
- ☐ at mine personopplysninger lagres i 5 år etter prosjektslutt for etterprøvbarhet og kontroll

Jeg samtykker til at mine opplysninger behandles frem til prosjektet er avsluttet, 1. september 2036.

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Sted og dato

Deltakers signatur

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Deltakers navn med trykte bokstaver

# Appendix 5 – Registration of food and beverage intake 24 hours prior to testing

**Måltidsregistrering og fysisk aktivitet**

FPnr: _____ Uke____

**Registrering av måltider og fysisk aktivitet siste 24 timer før første oppmøtedag (standardisert treningsdag + middag på NIH):**

| | |
|---|---|
| Fysisk aktivitet (dagen før): | |
| Middag, kveldsmat + drikke (dagen før): | |
| Frokost + drikke: | |
| Lunsj + drikke: | |
| Eventuelt mellommåltid: | |
| Standardisert treningsøkt + standardisert måltid/ standardisert måltid. | Fra kl.17.00 → |

**NB: dette skal gjentas før hver oppmøte torsdager i hver uke. FP skal innta det samme kostholdet og gjennomføre samme form for fysisk aktivitet.**