Protocol

The effects of a fasted versus fed remote walking-based training programme on glycaemic control in overweight individuals

Short title: Can fasted exercise enhance glycaemic control in overweight individuals?

Investigators:

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Background and rational:

According to recent statistics, 64.3% of the UK adult population are now classified as overweight or obese. People who are overweight or obese have high levels of fat in their muscle, which is linked to insulin resistance and ultimately the development of type 2 diabetes. Interestingly, healthy people also have high levels of muscle fat, but they are highly insulin sensitive. This is because healthy people are able to burn this fat to generate energy during exercise, resulting in a reduction in the amount of fat in the muscle that can then be replaced with a meal. Healthy people who regularly breakdown these stores during exercise, and rebuild them following exercise, have a high turnover of their fat stores. However, people who are overweight or obese have difficulty using muscle fat during exercise. Fasted exercise has been shown to increase the reliance on muscle fat stores during exercise and is well utilised in trained individuals to improve their capacity to burn fat. Whether this type of exercise has the potential to be beneficial in less healthy individuals is less well known. Most importantly, whether this simple exercise-nutrition strategy can be implemented into the daily lives of less healthy individuals to improve glycaemic control and reduce type 2 diabetes risk now requires investigation.

Aim: To determine whether a remote 12-week fasted walking-based intervention can increase glycaemic control compared to a fed group.

Participants: N = 34

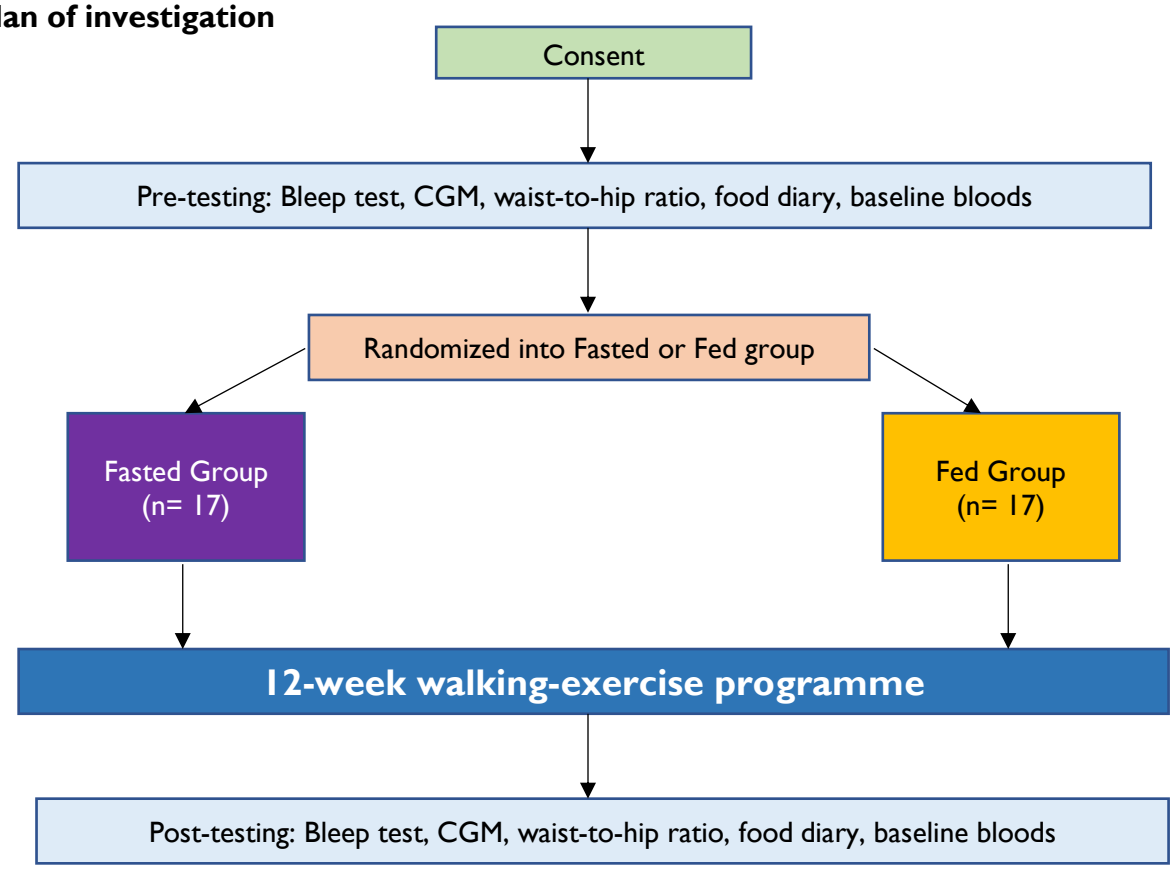
Inclusion criteria
You are likely to be eligible for this study if you fulfil the following criteria:

- Aged 20-60 years
- BMI >28 $kg.m^{-2}$
- Not currently using any anti-diabetes medication
- Physically inactive (performing less than two 30 min structured exercise sessions per week for the last year)
- Not pregnant or currently breast feeding
- Pre-menopausal or peri-menopausal
- Not currently involved in a weight loss programme or using weight loss medication

Exclusion Criteria
(Meeting any of the following criteria will prevent you from participating in the study)

- Involved in regular exercise (engaged in more than 3 sessions of structured exercise of >30 min per week)
- Currently using anti-diabetes medication (e.g. insulin, metformin)
- Pregnant or breast feeding
- Currently engaged in active weight loss programme or using weight loss medication
- Diagnosed with chronic kidney disease
- Post-menopausal

Plan of investigation



Consent and pre-screening:

Participants will be sent a participant information sheet after expressing interest via email and will have the opportunity to contact with any questions about the study before providing consent via email.

Questionnaire: Participants will complete a Readiness to Exercise questionnaire and send via email to ensure they are fit to undertake exercise as part of the study.

Pre-testing:

Waist-to-hip ratio and weight: Participants will be provided with a tape measure and instructions on how to measure waist circumference and hip circumference. From this, waist-to-hip ratio will be calculated. Additionally, participants will be asked to use their own scales to provide their weight (if they don't have any they will be provided).

Blood pressure: (pending Matts suggestion for this)

Baseline blood sample: Participants will receive blood sample kits containing (Thriva) full instructions that will be used to measure fasting insulin, glucose, lipid profile, HbA1c, cholesterol (includes triglycerides), liver enzymes (ALT usually elevated in people with NAFLD). A researcher will be available to video call if needed while these are being completed.

CGM: Participants will receive a continuous blood glucose monitor that contains full instructions to fit and use. These will be worn for two weeks – 1 week before the intervention and during the first week of the intervention (see Fig. 1).

Diet: Participants will receive a food diary to record their habitual dietary intake for three days (24 hours after the CGM is fitted). During the first week on the intervention they will also be asked to write down what they eat for lunch on the days they exercise.

Fitness test: Participants will receive a polar beat heart rate monitor and instructions on how to download an app containing a bleep test protocol. They will be asked to complete the bleep test wearing the HR monitor at least 48 hours before they begin the intervention.

Exercise intervention:

Pairs of participants from each group (matched for gender, age, BMI and) will be randomized to undertake 12 weeks of steady walking in either a fasted state (before breakfast each day) or a fed state (after breakfast each day). They will be asked to eat the same breakfast on each day they complete the exercise, whether it is before or after.
Walking sessions will be 4 times per week and will be two continuous sessions (~50% HR max) and two interval sessions (3 minutes at 40% HR max, 3 minutes 80% HR max) monitored by the polar beat app. Participants will initially walk for 30 minute sessions in week 1 and this will increase by 5 minutes each week until they are completing 4x 60 minute sessions per week (see table.1).

A CGM will be in place during week 1 to measure the glycaemic response to exercise. And a second CGM will be inserted at the beginning of week 12 to see the changes in glycaemic control on exercise days and will remain in place for post-intervention CGM monitoring.

Post-testing:

The post intervention assessments will be identical in all aspects to the pre-intervention assessments and will begin ≥72 hours after the final training session.

Proposed analysis:

Adherence: From the training data, we will monitor adherence to the study intervention since this is remotely ran. We will also monitor whether participants hit their target HR zones during each exercise bout.

Blood samples: All blood samples will be analysed by Thriva.

CGM: The 24 h glycaemic profile obtained during the CGM period will be used to determine average glucose levels, and the prevalence of hyperglycaemia and hypoglycaemia. Based on the ADA/EASD guidelines, the prevalence of hyperglycaemia and hypoglycaemia will be defined as the total time during which glucose concentrations are >10 mmol.L^{-1} or <3.9 mmol.L^{-1}, respectively. The primary outcome from the CGM data will be the time spent in range (3.9 – 10 mmol.L^{-1}).

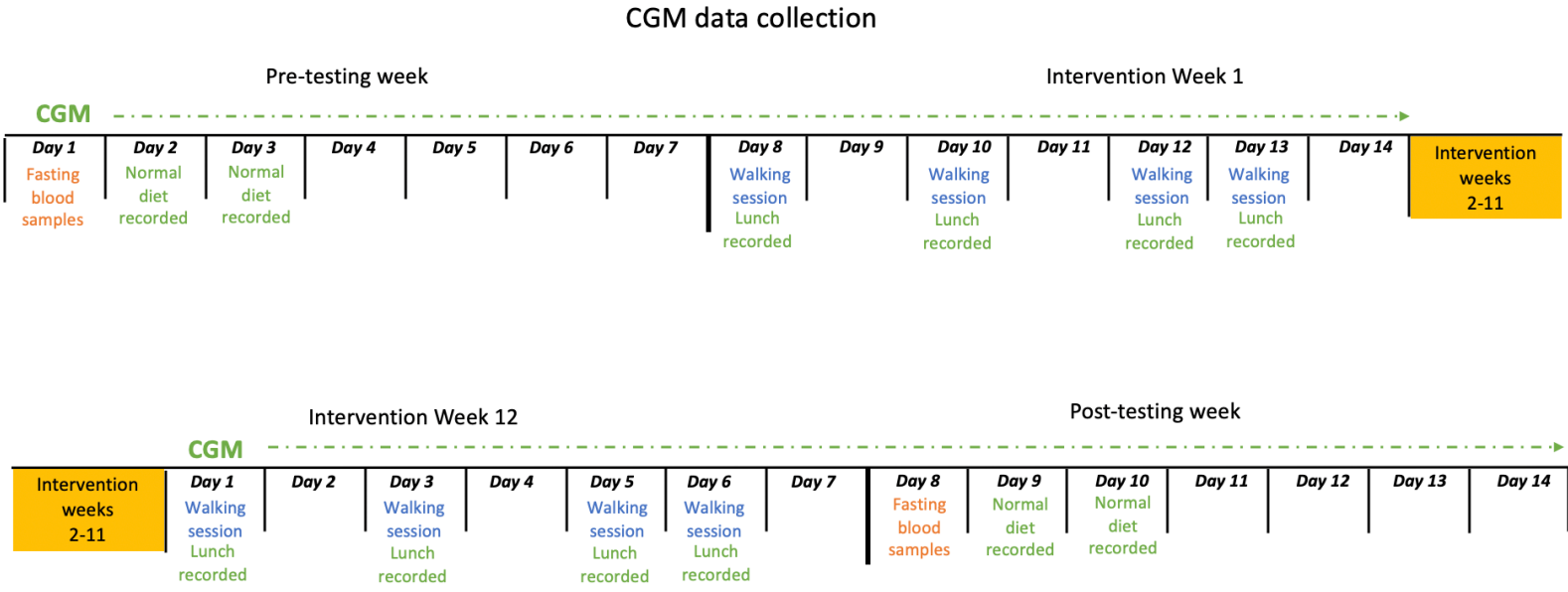


Figure 1. Plan of CGM data collection. Participants will wear a CGM at two time points; once at the beginning of the study and once at the end. Each CGM time point will measure one resting week and one intervention week.

Table 1. An outline of the walking-based exercise programme. All participants will follow the same intervention make up of 4 sessions per week; 2 continuous walking sessions and 2 interval walking sessions.

Week 1 & 2		**Week 7 & 8:**	
Session 1: continuous	30 min	Session 1: continuous	45 min
Session 2: Interval	30 min	Session 2: Interval	48 min
Session 3: continuous	30 min	Session 3: continuous	45 min
Session 4: Interval	30 min	Session 4: Interval	48 min
Week 3 & 4:		**Week 9 & 10**	
Session 1: continuous	35 min	Session 1: continuous	50 min
Session 2: Interval	36 min	Session 2: Interval	54 min
Session 3: continuous	35 min	Session 3: continuous	50 min
Session 4: Interval	36 min	Session 4: Interval	54 min
Week 5 & 6:		**Week 11 & 12**	
Session 1: continuous	40 min	Session 1: continuous	60 min
Session 2: Interval	42 min	Session 2: Interval	60 min
Session 3: continuous	40 min	Session 3: continuous	60 min
Session 4: Interval	42 min	Session 4: Interval	60 min