

Netflix and Move Study protocol 2020/2021



Netflix and Move: Does interrupting streaming in the evening with short bouts of activity impact postprandial glycemia and sleep?

A randomised crossover study.

Funding Agencies: Health Research Council of New Zealand

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1. Project Summary

This study will provide important evidence around how reducing sedentary behaviour in the evening by regularly performing short bouts of resistance activity may improve postprandial metabolism and sleep, both of which are important for cardio-metabolic health. We will conduct a randomised crossover study involving 30 participants. The study will include two experimental intervention sessions each performed in the evening between 5:30 pm and 10:00 pm: 1) uninterrupted sitting; and 2) regular activity breaks, separated by a minimum six-day washout period. Blood samples will be collected intermittently across the intervention session and used to measure glucose, insulin, and triglyceride responses. Sleep duration, efficiency and onset latency will be measured via accelerometry in the 48 h after each intervention session is completed. Mixed model regression will be used to examine differences in the effect of the two interventions in these outcomes.

2. Background

Sedentary behaviour activities performed in a seated or reclining position that involve very low energy expenditure (1) is associated with increased incidence of diabetes, cardiovascular disease, some cancers and overall mortality (2-4). Results from observational studies using accelerometers as an objective measure of sedentary behaviour indicate that the *pattern* in which total sedentary time is accumulated is related to markers of cardio-metabolic health, over and above the total amount of sedentary time (5, 6). Individuals who accumulate sedentary time in long continuous bouts have higher waist circumference, body mass index (BMI), fasting glucose and triglyceride concentrations than those with a similar total sedentary time that is frequently interrupted with light physical activity (5, 6). These associations appear to be consistent across age, sex and ethnic groups (6), and occur even in those who engage in large amounts of leisure time moderate-to-vigorous physical activity (5, 6). Intervention studies have demonstrated that performing regular activity breaks (~ 2 min walking, arm cranking, or 3 min of simple resistance exercises every 20-30 min) reduces glucose and insulin concentrations by up to 39% (7-9) and may also reduce triglyceride concentrations and improve non-esterified fatty acid concentrations (10). Having higher concentrations of postprandial glucose, insulin and triglycerides promote oxidative stress, inflammation and endothelial dysfunction (11-14), all of which contribute to the development of atherosclerosis and cardiovascular disease (14, 15). Non-fasting glucose (16), insulin (17) and triglyceride concentrations (18, 19) also independently predict cardiovascular morbidity and mortality. Regular activity breaks have been shown to reduce postprandial glucose and insulin concentrations in young healthy adults (20), as well as those with obesity (21) and type 2 diabetes (7). These improvements have been shown to persist 24 h after the laboratory based intervention (22), and it is currently unknown when they dissipate. Interestingly, to date, no studies have been performed in a sample which includes participants across the spectrum of BMI categories, even though there has been some suggestion that

the effects of regular activity breaks may differ in individuals with different weight status (23).

For many individuals, the greatest accumulation of sedentary time occurs in an occupational setting. However, recent research indicates that in office workers (24), retired people (25), and those with type two diabetes, (26) the most prolonged, uninterrupted periods of sitting happen *in the evening*. In addition, the average adult also consumes ~45% of their daily energy intake in the evening (27). Elevations in postprandial glucose concentrations associated with both prolonged sitting (20) and higher energy intake may be further exacerbated by the circadian rhythm in insulin sensitivity, with poorer insulin response occurring in the evening compared to the morning (28). To date, a single small study (n=9) has found that performing regular activity breaks in the evening produces reductions in postprandial glycemia and insulinemia (29) that are similar to those observed in the morning (21). However, participants in this study were exclusively obese (29).

Uninterrupted screen time in the evenings may not only result in poorer glycemic control, but also poorer sleep (30, 31). Poor sleep is, in turn, also associated with increased risk of cardio-metabolic disease, poorer mental health and earlier mortality (32). Physical activity, on the other hand has been shown to improve sleep (33). The effects of performing regular activity breaks on sleep has not been investigated.

3. Aim of Study

To investigate the efficacy of performing regular activity breaks during prolonged sitting in the evening as a means of improving postprandial metabolism and overall sleep quality.

4. Objectives

To compare the effects of 4 h of uninterrupted sitting to 4 h of sitting interrupted with 3 min of resistance exercises every 30 min, both during prolonged screen time in the evening, on postprandial glucose, insulin and triglyceride response and sleep duration, efficiency, and onset latency, in a sample of 30 participants across the spectrum of BMI categories.

5. Hypothesis

That performing 3 min of resistance exercise every 30 min to interrupt prolonged sitting during screen time in the evening will improve postprandial metabolism and sleep when compared to uninterrupted sitting.

6. Study Design

This study will be a randomised, crossover trial, in which each participant will complete two 4 h intervention sessions: 1) uninterrupted sitting; and 2) sitting but with a 3 min bout of simple resistance exercise every 30 min. Each intervention session will be separated by 6 days, so they are repeated on the same days of the week.

7. Study Setting/Location

This single site study will be conducted in the Department of Human Nutrition Research Clinic at the University of Otago, Dunedin.

8. Study Population

A total of 30 participants between the ages of 18 to 40 y will be recruited to participate. To provide an even distribution of participants across BMI categories: 10 participants will be normal weight (BMI 20-24.9 kg·m⁻²); 10 participants will be overweight (BMI 25 – 29.5 kg·m⁻²); and 10 will be obese (BMI ≥30 kg·m⁻²)

9. Eligibility Criteria

Participants in this study are required to be predominantly sedentary during the day, therefore we will require participants to:

- Self-report spending, on average, more than 5 h per day (at work or at home), and 2 h in the evening engaged in sedentary behaviour.

Other research indicates that smoking impacts postprandial metabolism, therefore, participants will only be included in the study if they are a non-smoker.

Because we are measuring postprandial metabolism, which can be affected by medications and dietary supplements, participants will only be included if they are not taking any medication or dietary supplements that are known to impact postprandial metabolism, including metformin and niacin.

We will also ask participants not to take part if:

- They have been told by a doctor or other medical professional (such as a physiotherapist) that they should avoid doing physical activity or any of the specific movements used in the simple resistance exercises.
- They have an intolerance or allergy to dairy or gluten as the test meal and snack will contain these foods.

Participants will be asked to gain clearance from their General Practitioner to participate in this study if their responses to the Physical Activity Readiness Questionnaire (PAR-Q) indicate that participating in physical activity may not be medically appropriate.

10. Study Outcomes

Primary Outcome:

The difference in glucose total area under the curve (tAUC) and incremental area under the curve (iAUC) measured over 4 h between the two interventions.

Secondary Outcomes

The difference in insulin total area under the curve (tAUC) and incremental area under the curve (iAUC) measured over 4 h between the two interventions.

The difference in triglyceride total area under the curve (tAUC) and incremental area under the curve (iAUC) measured over 4 h between the two interventions.

The difference in nocturnal mean and tAUC interstitial glucose in each of the two nights following the interventions.

The difference in activity patterns (sleep, physical activity, and sedentary behaviour) in the 48-h following the interventions.

The difference in sleep duration (time spent asleep) in each of the two nights following the intervention.

The difference in sleep efficiency (percentage to time spent asleep between sleep onset and sleep offset) in each of the two nights following the intervention.

The difference in sleep onset latency (the duration from the time sleep was attempted until the onset of sleep is detected) in each of the two nights following the intervention.

11. Study Procedures

Recruitment of participants

Paper and electronic copies of the recruitment flyers advertising the study will be distributed around the university campus, including on Dunedin based/focused social media. Individuals interested in participating will be asked to indicate interest by emailing activitybreaks-study@otago.ac.nz.

Randomisation

Participants will be block randomised (block size n=6) to complete the two interventions in 1 of 2 possible orders. Randomisation will be stratified by weight status. The randomisation sequence will be generated by MCP using Stata software and concealed electronically. The evening before each participant begins his or her first intervention session, MCP will reveal and assign the next sequential allocation. Participants will not be notified of which intervention session they are completing until they arrive at the clinic on the evening of each intervention session. However, by a process of elimination, they will obviously know what their second intervention will be as soon as they begin their first intervention session.

Study procedures

Consent and screening

The postgraduate research students/research assistant or the PI (MCP) will respond to email enquiries providing the information sheet and a link to the REDCap consent and demographic questionnaire. Once the participants have completed the consent and demographic questionnaire, the responses to the PAR-Q will be checked. If medical clearance is required, the participant will be emailed and asked to contact their GP to gain clearance to participate in the study. Once medical clearance is obtained, or if it is not required, participants will be scheduled to attend an initial introductory session.

At this introductory session, the participant will be asked if they have any further questions about the study. Once any questions have been addressed, they will have their height, weight, and blood pressure (in triplicate 1 min apart; after 15-min seated rest) measured. If blood pressure is greater than 140/90 mmHg and participants have not already obtained medical clearance, then they will be asked to contact their GP to gain clearance to participate in the study. Participants will then be shown a video of the exercises they will be asked to perform in the regular activity breaks intervention and asked to practise these movements with the investigator. Technique will be corrected as necessary. To assess the usual sleep and activity patterns of participants before they start the intervention, participants will be fitted with an ActiGraph or AX3 accelerometer (depending on availability – all participants will be fitted with the same model), at the end of this session, which they will be asked to wear for a seven-day period (24 h a day). Participants will also be asked to complete a sleep and wear time diary over this time.

Standardisation of prior physical activity and diet

The afternoon prior to each intervention session, participants will collect food for their breakfast, morning tea and lunch for the following day. Participants will also be fitted with both an ActiGraph (worn at the wrist to measure sleep and physical activity) and a continuous glucose monitor which they will continue to wear through the intervention session and for the following 48 h. They will also be provided with a sleep and wear-time diary, which they are to complete (by recording times of accelerometer removal and bed and attempted sleep times each day). To minimise the influence of previous activity on outcome measures, participants will be required to avoid all intentional moderate-to-vigorous intensity physical activity and be largely sedentary for 24 h prior to each intervention.

Providing food to participants ensures their food intake is standardised before arriving at the clinic. The breakfast, morning tea and lunch together will provide 55% of each participant's estimated energy requirements (Schofield equation (34), using a physical activity factor of 1.5), with a macronutrient profile of 55% carbohydrate, 15% protein, and 30% fat. Participants will be asked to ensure that all provided food is consumed prior to 2 pm, and to replicate the timing of consumption prior to both intervention sessions. Following 2 pm, participants will refrain from eating until they arrive at the clinic.

Intervention sessions

Uninterrupted sitting intervention: Participants will arrive at the clinic at 5:30 pm. A cannula will be inserted into a forearm vein to allow collection of multiple blood samples. The participant will then rest comfortably for at least 15 min before a baseline sample will be collected. At ~6:00 pm participants will be fed a standardised dinner providing 35% of their estimated energy requirements, with a macronutrient profile of 55% carbohydrate, 15% protein and 30% fat. Participants will be required to consume this meal in 15 min. A snack/dessert will be provided at 8:00 pm, providing the final 10% of the participant's estimated energy intake. Blood samples will be collected hourly for 4 h with additional samples collected 30 and 45 min after each feeding. A total of nine blood samples will be collected (Figure One). During the postprandial period, participants will be required to remain as sedentary as possible, only leaving their chair to use the bathroom when required (timing and duration of bathroom breaks will be recorded by an investigator). Upon completion of the intervention session, participants will return home by car (taxi will be arranged and paid for those who do not have their own transport). Participants will continue to wear the continuous glucose monitor and accelerometers for 48 h. Participants will also be asked to record the times they went to bed, started trying to go to sleep and got up for the day for the two nights directly following each intervention session in the sleep and wear-time diary they will be provided with.

Regular Activity Breaks Intervention: This intervention will follow the same protocol as for the prolonged sitting intervention. However, in addition, participants will perform 3 min of simple resistance exercises every 30 min. Simple resistance exercises will consist of calf raises, half squats, knee raises, and straight leg hip extensions. These exercises will be performed in time with a prepared video with technique cuing commentary. In addition, the investigator will accompany the participant in the activity breaks to provide support and monitor safe technique.

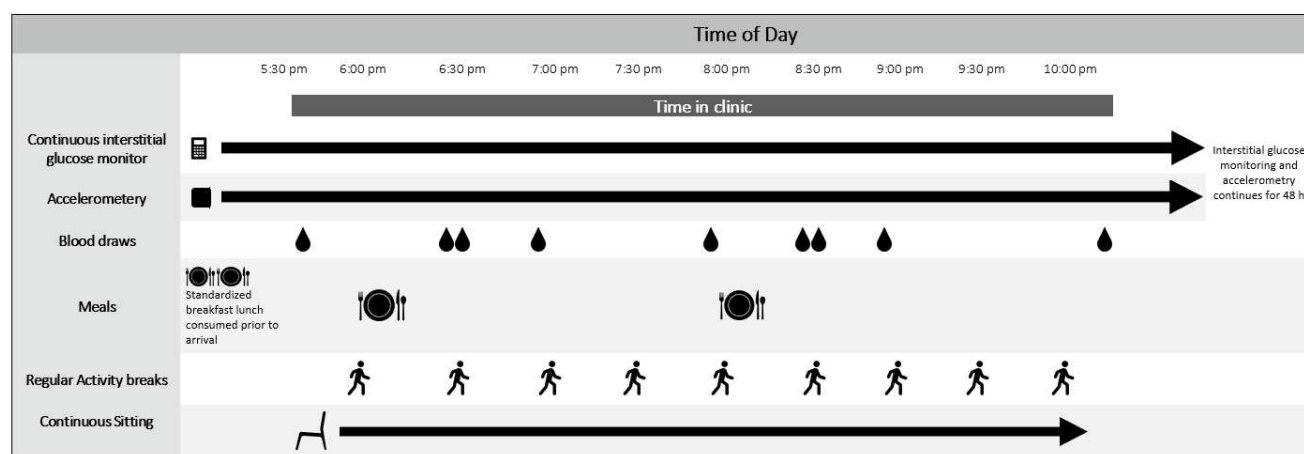


Figure 1: Intervention Day timeline

Analytical Methods

Blood samples collected for the analysis of glucose, insulin and triglycerides will be centrifuged within an hour of collection and plasma stored at -80°C until analysis. Insulin analysis will be carried out using the Electrochemiluminescent Immunoassay (1010 Immunoassay System, Roche Diagnostic Elecsys[®], Mannheim, Germany). Blood glucose, and triglycerides will be determined using enzymatic colorimetric methods (Roche diagnostics). All analysis will be carried out in the Department of Human Nutrition Diabetes and Lipid Laboratory at the University of Otago. The individual conducting the analysis will be blinded to intervention.

Accelerometer data processing

Usual activity patterns - From the 7-day wear period prior to completing the intervention sessions, an estimate of habitual time spent sedentary, and in light and moderate-to-vigorous physical activity and asleep will be calculated. These variables will be used to describe the baseline characteristics of the population and investigated as moderators in exploratory analysis, as it is possible that baseline physical activity status impacts the effects of regular activity breaks on glycemic control (35).

Sleep - Accelerometer data, including data from the sleep and wear time diaries will be used to investigate the acute effects of uninterrupted sitting and regular activity breaks on sleep duration (time spent asleep), sleep efficiency (ratio of total time spent asleep compared to the total amount of time spent in bed, between sleep onset and sleep offset) and sleep onset latency (the duration from the onset of self-reported attempted sleep time, to the onset of sleep) for two nights after the intervention.

Qualitative Assessment of Practicality of Performing Regular Activity Breaks in the Evening

Participants who complete the intervention study will be invited to participate in focus group discussions or individual interviews to investigate their experiences of performing regular activity breaks in the evening in a laboratory setting and their opinions about how transferable this behavior would be to real life. They will also be encouraged to identify barriers and facilitators that they foresee to performing regular activity breaks in the evening. Consent to participate in these focus groups will be obtained separately from the intervention study. Each focus group will include a maximum of 6 people and would likely last 45-60 min. The discussions will be scheduled at times that suit participants. Where participants completing the study cannot be scheduled into a focus group at a convenient time, individual interviews may be conducted. Focus groups/interviews will be recorded, and transcripts analyzed using inductive thematic analysis (36).

Data Monitoring and Quality Control

No formal data monitoring will take place.

Quality control will be ensured by developing standard operating procedures for all data collection, including:

- The introductory session (anthropometry and blood pressure measurements)
- Procedures around standardisation of diet and exercise prior to each intervention
- All measurements conducted during each of the two intervention sessions (meal preparation and timing of administration, timing of blood collection, timing of activity breaks)
- Biological specimen management and analysis (tube labelling, centrifuging, separating of serum for storage in freezer, analysis of glucose and insulin concentrations)

All student researchers/research assistants involved in the research will be thoroughly trained in all operating procedures and the PI (MP) will perform periodic checks throughout data collection to ensure protocols are being adhered to.

12. Statistical Considerations and Data Analysis

Sample size and statistical power

Using variances calculated for the first four hours of our previous study (20), a sample size of 30 participants will give 80% power to the 5% significance level to detect a difference of 0.4 standard deviations. A sample of this size will also allow us to detect differences in the secondary outcomes in the order of 0.4 standard deviations of insulin and triglyceride AUC, and 20 min of sleep duration.

Statistical methods

Statistical analysis will be performed using Stata version 16. As a crossover design, each person will be compared to themselves and the mean difference between the uninterrupted sitting and regular activity breaks interventions for the whole group is determined. The mean difference in outcome variables between the two interventions will be estimated, along with 95% confidence intervals, using mixed effects regression models, with intervention condition as the exposure variable, participant ID as a random effect, and controlling for randomisation order.

Exploration of effect moderation by weight status and by sedentary and physical activity patterns will be undertaken by running the mixed effects regression models stratified by these moderating variables. While not powered to detect significant differences in these smaller groups, effect sizes will be compared to see if moderation is indicated.

13. Ethical Considerations

The study will be conducted in full conformance with the most current revision of the Declaration of Helsinki, the International Conference for Harmonization of Good Clinical Practice Regulations and Guidelines and the laws and regulations of New Zealand.

Quality assurance

This research will be conducted by researchers who are skilled in the technical aspects of this research study. Students/research assistants working on the research project will be carefully trained and overseen by the named investigators. Standard operating procedures will be developed and adhered to at all times.

Risks/safety considerations

Cannula insertion and blood collection.

There is a risk of discomfort, pain and bruising from the cannula insertion. Participants will be informed of the risks. An experienced nurse or phlebotomist will insert the cannula and ensure strict aseptic technique is followed during blood collection from the cannula to minimise any risk of infection.

While most participants tolerate blood collection from a cannula very well, there are a small percentage of participants who may feel faint during and after collection. All blood samples will be collected with the participant sitting in a recliner, which allows for the participant to be reclined with feet elevated should they feel unwell during cannula insertion or blood collection.

Performing Regular Activity Breaks

There is a small risk of loss of balance when performing exercises which require participants to balance on one leg (such as the knee raises and hip extensions). Participants will be encouraged to perform these exercises within arm's reach of the back of their chair, so they have something to grab onto if they do lose their balance (although most will simply be able to place both feet on the floor to regain their balance).

Over the course of the regular activity breaks intervention, participants will perform upwards of 200 repetitions of each exercise. If they are not used to performing these movements, they may experience a small amount of delayed onset muscle soreness in the days immediately following the intervention. This type of muscle soreness is common after the initiation of any new activity programme, is unlikely to be severe, and should only last for a few days.

Participants will be free to withdraw from the study at any time without any disadvantage to them.

Potential Benefits

Very little is understood about how performing regular activity breaks in the evening will affect postprandial metabolism and sleep. This study will provide high quality experimental evidence around the effects of interrupting sedentary behaviour with short bouts of resistance activity on glucose and lipid metabolism and sleep. This will inform the development of future public health and physical activity guidelines.

Informed Consent

Individuals who have indicated they are interested in participating will be emailed an information sheet and an online consent, screening, and demographic questionnaire. Participants will be asked to read the information sheet before completing online consent. Participants will be encouraged to contact the study investigators at any time if they have any questions about the study.

Online informed consent will be collected from the participant before the begin any screening procedures.

Consent information will be stored electronically on REDCap.

Participant Confidentiality

Upon enrolment, the participant will be assigned a unique identifying code consisting of "NET" at the beginning, followed by 2 numbers (e.g., NET01). To preserve confidentiality during data-collection, all data will be recorded against this ID number. Any information linking the participant's identity to the ID number will be kept in a password-protected computer file.

Responses to questionnaires will be electronically linked to study ID number, as will accelerometry data. Study ID numbers will also be written on all biological sample tubes, sleep and wear time diaries and the recording sheets for anthropometry and blood pressure.

Participant Follow-up

Once the data from the study have been analysed, the participants will be provided with an overall summary of the results. Participants are also free to request a copy of their individual data once the summary of results has been provided to them. Any participant who is identified as having a blood pressure above 140/90 or a baseline (non-fasting) glucose concentration above $7.8 \text{ mmol}\cdot\text{L}^{-1}$ during the study will be provided a written copy of these results and advised to see their general practitioner to discuss their results.

Data Management

Data will be collected as per Standard Operating Procedures and cleaned as per standard data entry procedures. Data quality checks will be run on all entered data to check for accuracy, consistency, and completeness.

In the database that contains the results of the study, each participant will be represented by an ID number. This database will be stored on the investigators' computers, all of which are password-protected. A backup copy may also be stored on the University's shared server space, but only the PI (MCP) will have the password that will enable access to the data stored on the server.

The file linking participants to their ID number will be stored in a separate password-protected file that only the PI (MCP) will have access to. The only reason this information will be accessed once the study is completed is if the participant requests their individual results. This file will be destroyed once all participants have been given the opportunity to request individual information. The deidentified information collected as part of this research will be retained for at least 10 years in secure storage.

14. Outcomes and Significance

Completion of study proposed here will provide important high-quality evidence around how reducing sedentary behaviour by performing short bouts of regularly performed activity may facilitate improvements in both postprandial metabolism and sleep, both of which are established risk factors for cardio-metabolic disease.

The USA 2018 Physical Activity Guidelines Advisory Committee have recently highlighted the lack of high-quality evidence currently available around the interactions between sedentary behaviour and light- and moderate- intensity physical activity on health (37). This research clearly fills a gap in the literature that is of high importance to policy makers. In addition, similar research has recently been used to inform the development of the Canadian 24 h movement guidelines for adults (38). It is, therefore, anticipated that the outcomes of this research will help to inform public health messages and physical activity guidelines both in New Zealand and internationally.

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