**ADMINISTRATIVE INFORMATION**

Title: A novel digital glycaemic monitoring tool: a pilot study

Short title: A novel digital glucose monitoring tool: a pilot study

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Study Coordinator: LL

Data Management: LL

Data Monitoring Committee: JK, RH

This study protocol follows the SPIRIT checklist (1,2).

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#

# Introduction

## Background and Rationale

There is significant potential for improvement in health outcomes for nutrition-related conditions. These conditions, chiefly diabetes and obesity, are increasing in prevalence nationally and globally (3,4). Developing tools to prevent, identify, and manage these conditions will be important in reducing their burden.

We propose the pilot testing of a novel digital glycaemic management tool. This tool is an iOS application developed by our research team that provides two key functions: (1) nutritional intake recording, and (2) continuous glucose monitoring (CGM) data display. The nutritional intake recording uses both text-based search methods as well as automated image-recognition of food items. The application displays the blood glucose recordings as measured by a continuous glucose monitor, with the data shared wirelessly. The novelty of the application is the linking of glucose data with food intake data in real-time with direct visual feedback to users. Our overall objective is to assess the effect of using the application on a participant’s blood glucose management for people with type 2 diabetes. This is achieved as the application can blind the user to the glucose readings using an administrative control only accessible to the researchers, allowing comparison of glycaemic management while using the application with only food-tracking enabled, or using the application with food-tracking and glucose-tracking enabled.

Post-prandial glycaemic responses (PPGR) are the blood glucose changes following a meal (5). There is significant inter and intra-individual variation of PPGRs to identical food items (6,7). Glycaemic responses to an individual food are predicted by metrics such as the glycaemic index, but the reported glycaemic index is specific to a food item and not the individual. Glycaemic index is altered considerably with combinations of macronutrients and when food is prepared in a different manner. Our application aims to inform individuals of their unique post-prandial glycaemic response to a food item or habitual meal they consume in a free-living setting. This is possible through the application as it allows nutritional intake tracking and displays continuous glucose monitoring data simultaneously. The primary objective and research question of this pilot study is to examine if users who can visualise their PPGRs using the application, will then adapt their diet to reduce foods with post-prandial hyperglycaemia and therefore improve their glycaemic management compared to their baseline.

## Objectives and Hypotheses

The objectives of the study are to:

1. Compare both the time-in-range and the post-prandial incremental area under curve for blood glucose over ten days using a food tracking-only application and during use of the food and glucose-tracking application in individuals with type 2 diabetes.
	1. Time-in-range is the time during a 24-hour period spent with blood glucose between 3.9 and 10mmol/L, expressed as a percentage (8).
	2. The post-prandial incremental area under curve (iAUC) is the calculated area under the blood glucose curve of a graph in the three hours from a the time a meal was recorded with blood glucose on the y-axis and time on the x-axis, with the baseline for the curve set at the pre-prandial blood glucose level. A graphic example of an incremental under curve is shown in Figure (1).
2. Assess the inter-individual and intra-individual variability of post-prandial glycaemic responses to identical food items.
	1. To assess the intra and inter-individual variability in glycaemic response participants will be given two different breakfast cereal foods, with each cereal to be consumed three times on different days during the overall study. The order of that the foods will be consumed will be randomised. The two food items are: a cup of Kellogg’s cornflakes and a cup of Kellogg’s All-Bran cereal and individual dairy milk packages to use with each. One food item will be consumed at visit 1 while fasted, and the others will be provided for consumption in a free-living setting after an overnight fast. The food item at the visit will be consumed in 12 to 15 minutes, timed by the researcher. The participant will be instructed to consume the food items in the free-living setting in 12 to 15 minutes as well. Participants will be instructed to not consume any other food or drink except water with the cereal and milk or for three hours after.
3. Assess the accuracy of the energy intake estimates from the application:
	1. The phone application provides an estimate of total energy intake by summing the energy intake of each recorded item. Total energy expenditure (TEE) can be estimated by measuring its components; resting energy expenditure (REE), activity-related energy expenditure (AEE), and diet induced thermogenesis (DIT). Resting energy expenditure is be measured by indirect calorimetry; activity-related energy expenditure is measured by accelerometery; and diet-induced thermogenesis is assumed to be 10% of total energy expenditure.
4. Explore the user experience of the application:
	1. Participants will complete a questionnaire at the end of each period of data recording to explore the user experience of the application and identify areas for improvement.



**Figure (1):** graphical example of incremental area under curve (iAUC), taken from Brouns et al 2005. The incremental area under the curve is the sum of the positive areas within 3 hours of the recorded meal; i.e., areas 1, 2, 3, 4, and 7 (9).

Primary hypothesis:

1. Participants will have increased time-in-range during the ten days using the food and glucose-tracking application compared to the ten days using the food tracking-only application.
2. The post-prandial incremental area under curve (iAUC) will be reduced during the ten days using the food and glucose-tracking application compared to the ten days using the food tracking-only application.

Secondary hypotheses:

1. The energy intake estimates from the application will approximate objectively measured energy expenditure.
2. Participants will have a positive user experience with the application.

## Study Design

This is a single arm intervention study with before and after comparisons within individuals. An overview of the study design is shown in Figure (1).

**Figure (2):** Overview of study design

Twenty participants will be recruited via screening—see ‘Study Population’ below for detail on inclusion and exclusion criteria—and proceed through the study as follows:

Visit 1:

* After providing written informed consent, at this visit participants will have, height measured, weight and fat-free mass recorded using bio-impedance, and resting energy expenditure measured via indirect calorimetry—please see ‘Study Procedures’ below for further detail.
* Participants will be provided with an ActiGraph GT9x accelerometer, CGM, and a food-tracking only version of the application to measure physical activity and glucose, during the ten-day recording period between Visit 1 and Visit 2. They will not be provided access to the application data and will be blinded to the CGM for the next 10 days.
* Participants will be educated on high and low glycaemic index food items. Participants will be encouraged to use this information to inform their dietary intake throughout the study.
* Participants will consume one of the cereal food items and accompanying milk in 12-15 minutes, observed by the researcher. The participant will be instructed to consume the other cereal items in the same timeframe, and to avoid any other accompanying food items. The participant will be provided with the other food cereal item and accompanying milk for consumption in the free-living setting. The order in which the cereal will be eaten, i.e., all-bran first or cornflakes first, will be randomised.
* Participants will provide a response to a Visual Analogue Scale question rating their understanding of their dietary intake and their blood glucose.

Visit 2:

* Weight and body composition measures will be repeated.
* Participants will be given access to the application with food tracking and glucose tracking enabled.
* Participants will be shown how to apply CGMs, and two CGMs will be provided, with the first applied immediately. Participants will be shown how to interpret the blood glucose readings in the application and how to identify post-prandial hyperglycaemia.
* Participants will be instructed to record for the next 20 days using the CGM and application, with full access to their glucose levels. They will be instructed on how to review and use the postprandial CGM data and use this to inform their subsequent food choices in a progressive manner over the 20 days between visits. To inform future nutritional choices, participants will be provided with and shown how to use two additional applications: FoodSwitch (The George Institute for Global Health) which provides healthy alternatives to New Zealand food items, and a mobile glycaemic index reference database. The participant will be instructed on how to use the application to review their blood glucose levels throughout the day, and how to identify the food items associated with each time-point.
* Participants will be provided with four food items: two sets of Kellogg’s cornflakes and two sets of Kellogg’s All-Bran cereal. Participants will be instructed to consume these food items and accompanying milk in the same manner as instructed in Visit 1.
* Participants will provide a response to a Visual Analogue Scale question rating their understanding of their dietary intake and their blood glucose.

Visit 3:

* Weight and body composition measures will be repeated.
* Participants will return the accelerometers.
* Participants will complete a questionnaire exploring the experience of using the application and its features, and provide a response to a Visual Analogue Scale question rating their understanding of their dietary intake and their blood glucose—please see Appendix (A) for detail.

*Study Synopsis:*

|  |  |
| --- | --- |
| **Participants** | Wellington-based individuals with type 2 diabetes. |
| **Intervention** | Food and glucose-tracking digital health application. |
| **Primary Outcome(s)** | Time-in-range (%) during the ten days with the food tracking-only application compared to time-in-range in the last ten days of using the food and glucose-tracking application. Post-prandial incremental area under curve (iAUC) during the ten days with the food tracking-only application comapred to time-in-range in the last ten days of using the food and glucose-tracking application.  |
| **Planned Sample Size** | 20 |
| **Study Duration** | 30 days per participant.  |

# Methods

## Participants, Interventions and Outcomes

### Study Setting

This study will be conducted at the Centre for Clinical Research (CRC) in the University of Otago, Wellington and at the Centre for Endocrine, Diabetes, and Obesity Research (CEDOR) in the Wellington Regional Hospital. Both sites are located on the same grounds. The CRC contains the indirect calorimeter and the accelerometer equipment and will only be used for Visit 1. CEDOR contains the bio-impedance scale and will be the site for all subsequent visits. Both sites are in Wellington, New Zealand.

### Eligibility Criteria

Inclusion criteria:

* Aged ≥18 years
* Type 2 diabetes with an HbA1c 65-90 mmol/mol on any hypoglycaemic therapeutic regimen other than insulin.
	+ If the individual has a high baseline time-in-range, the potential improvements will be difficult to detect at smaller sample sizes, which necessitates selecting for those who have the greatest potential for benefit. Participants with an HbA1c >90 mmol/mol should have additional therapy initiated and will therefore be ineligible for this trial.
* Speaks and reads English
	+ Due to scope limitations, the application has only been developed in English
* Owns an iOS device capable of running iOS 16 and above
	+ These are the technical specifications required to use the application
* Able to consume dairy milk and gluten

Exclusion criteria:

* Type 1 diabetes or forms of diabetes other than type 2.
* Changes to diabetes-related medications or dosing in the last three months
* Insulin or intention to initiate insulin therapy during the trial
	+ Although this application may have future benefit to people living with diabetes who require insulin therapy, the use of insulin will make it difficult to assess the isolated effect of dietary change on glycaemic management.
* Intention to change dosage of anti-hyperglycaemic agents or initiate continuous glucose monitoring during the trial
* Pregnancy
* Participation in another trial requiring a prescriptive nutritional intake.
	+ As this study is examining the effect of changing nutritional intake informed by the application, the participant must be able to change their intake at will, which would contradict the other trial.

### Intervention

Both the food tracking-only and the food and glucose-tracking applications exist on the same platform. The different functionalities of the application; the ability to record and review nutritional intake, and the ability to track glucose levels via the CGM, can be independently activated or inactivated through an administrative option that is not accessible to the participants, and is controlled from the Firestore database that is username and password protected.

The food-tracking functionality is shown in Figure (2):

**Figure (3):** Food-tracking functionalities of the application: dashboard screen to review intake (left), text-based input (centre), and automated image-based input (right).

The food-tracking functionality has three primary features. The first is the ability to review recorded nutritional intake using a ‘home’ or dashboard screen. This shows a sum of the energy (in kilocalories or kilojoules per user preference), carbohydrates (grams), protein (grams), and fat (grams), among a list of micro-nutrients. Per participant preference, the energy ring and numeric summary can be disabled. Recording nutritional intake is achieved using text-based input; searching an integrated database, and automated image-based input; where machine-learning algorithms recognise the food items in the camera view. The navigation bar at the bottom of the screen allows users to switch between viewing the dashboard, text-based input, and image-based input. The text-based and image-based input uses the Passio Inc. Nutrition AI Software Development Kit, provided as in-kind funding from Passio Inc. (California, United States).

The glucose tracking functionality is shown in Figure (3).

**Figure (4).** Glucose-tracking functionality of the application.



The glucose-tracking shows participants a graph of their blood glucose level recorded by the continuous glucose monitor over time. The current daily average blood glucose level and last recorded blood glucose are shown above this graph. Indicators for recorded food items during the day will be shown but are not displayed in Figure (3).

Shown in the left-most image of Figure (2) and in Figure (3) is the Food/Glucose tab-bar. This allows the user to switch between viewing the food-tracking and glucose-tracking. This tab-bar will only be enabled in the food and glucose-tracking application. In the food-tracking application, the user will not see the tab-bar and be unable to access the glucose functionality. At Visit 2 the blood glucose levels and trends from the previous 10 days of blinded recording will be un-blinded to identify food items that have induced post-prandial hyperglycaemia, and the participant will be encouraged to avoid these food items and choose a lower glycaemic index or lower carbohydrate alternative. Identifying food items that result in post-prandial hyperglycaemia will involve assessing the absolute rise in blood glucose after the meal, ideally avoiding any foods that raise blood glucose by more than 3 mmol/L. This review process also functions as an example of how to review and apply the application feedback.

The food-tracking functionality will be enabled throughout the study. Food-tracking is significantly affected by under-reporting, a well-recognised issue in dietary assessment. Our previous work has shown that prompts to record dietary intake improve the reporting rate for image-based dietary assessment, especially if those prompts are sent at time-points close to the participants meal-times. Adherence to the food-tracking functionality is particularly important to this study as we examine post-prandial hyperglycaemia, which can only be assessed if the meal timing is known. We have developed a novel algorithm to determine the timing of these prompts, shown below in Figure (4).

**Figure (5).** Overview of novel energy-weighted prompt algorithm.

*Each food item recorded in the food log has an associated time and energy value. Each food item is categorised into a meal-time as a breakfast, lunch, or dinner item by time. Within each meal-time label, the time and energy value of each food item is used to calculate an energy-weighted time average. If the user reports to the application during set-up that they regularly eat breakfast, lunch, or dinner, they will receive a prompt at the energy-weighted mean time-point.*

This energy-weighted prompt algorithm will be active while the participant uses the application. This is algorithm is intended to increase adherence to the food-tracking functionality of the baseline and intervention periods.

Inter- and intra-individual variability of post-prandial hyperglycaemic responses will be assessed using two identical meals; Kellogg’s cornflakes and Kellogg’s All-Bran cereal and individual dairy milk packages. These items were selected for their high and low glycaemic indices, respectively.

### Concomitant care and co-interventions

Concomitant care will remain with the usual primary care team and will be unaffected during this trial. Participants will be asked to monitor their blood sugar as they normally do between Visit 1 and 2.

### Outcomes

1. Time-in-range (TIR%):
	1. The time during a 24-hour period spent with blood glucose between 3.9 and 10mmol/L, expressed as a percentage.
	2. The TIR% of Day 1 to 10 after Visit 1 (Visit 1 being V1 Day 0), and Day 11-20 after Visit 2 (Visit 2 being V2 Day 0) will be included in analysis.
	3. These will be compared using a paired t-test.
2. Post-prandial incremental area under curve (iAUC):
	1. The area under the glucose curve in the three hours after a recorded meal, with the baseline set at the most recent pre-prandial blood glucose.
	2. The post-prandial iAUC of Day 1 to 10 after Visit 1 (Visit 1 being V1 Day 0) and Day 11-20 after Visit 2 (Visit 2 being V2 Day) will be included in analysis
	3. These will be compared using a paired t-test
3. Duration of post-prandial hyper-glycaemia:
	1. The total time during the three hours after each recorded meal spent with blood glucose above 10 mmol/L, expressed as a percentage.
	2. A meal is defined as any number of food items recorded within 1 hour of each other.
	3. The post-prandial hyperglycaemia of Day 1 to 10 after Visit 1, and Day 11-30 (the 20 days following Visit 2) after Visit 2 will be included in analysis.
	4. These will be compared using a paired t-test.
4. Intra-individual and inter-individual variability:
	1. Intra-individual: standard deviations in the post-prandial iAUC in the three hours following consumption of the provided meals, resulting in two standard deviations for the high and low glycaemic index food items per participant.
	2. Inter-individual: standard deviations in the post-prandial iAUC in the three hours following consumption of the provided meals, resulting in two standard deviations for the high and low glycaemic index food items for the participant cohort.
5. Agreement between energy intake recorded by the application and objectively measured energy expenditure:
	1. Energy intake is reported by the application directly. Energy expenditure will be calculated by summing resting energy expenditure (measured via indirect calorimetry), activity-related energy expenditure (measured via accelerometery), and diet-induced thermogenesis (assumed to be 10% of total).
	2. Day 1 to 10 after Visit 1 and Days 11-30 (the 20 days following Visit 2) will be included in analysis.
	3. Agreement will be assessed using Bland-Altman analysis.
6. Qualitative user experience of the application:
	1. Qualitative experience will be assessed at Visit 3 with a short questionnaire.
	2. At Visit 1 and 2 participants will provide a response to a Visual Analogue Scale rating their understanding of the relationship between their dietary intake and their blood glucose.

### Participant Timeline

The study schedule is as follows:

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  | **Enrolment** | **Visit 1** | **Visit 2** | **Visit 3** |
| **TIMEPOINT** | **0** | **1** | **2** | **3** |
| **Eligibility screen** | X |  |  |  |
| **Informed consent**  | X |  |  |  |
|  | X |  |  |  |
| **INTERVENTIONS:** |  |  |  |  |
| **CGM recording** |  |  |  |  |
| **Food tracking enabled for participant** |  |  |  |  |
| **Glucose tracking enabled for participant** |  |  |  |  |
| **Low and High GI Food Items** |  | X | X |  |
| **ASSESSMENTS:** |  |  |  |  |
| **Height** | X |  |  |  |
| **Bioelectrical impedance** | X | X | X | X |
| **Indirect calorimetry** |  | X |  |  |
| **Accelerometery** |  |  |  |  |
| **Qualitative questionnaire** |  | X | X | X |

### Sample Size

For a sample size of twenty participants, this gives a projected a 95% CI of +/- 12.8% time-in-range. A change of 10% in time-in-range has been shown to reflect a change of 9 mmol/L HbA1c (10). A change of 5-10 mmol/L in HbA1c is generally considered to be clinically relevant. A larger sample size, informed by this pilot study, will be able to examine a smaller effect size.

### Recruitment

Recruitment will be multi-modal. Posters will be circulated on social media such as Facebook and Instagram, Wellington Regional Hospital staff-wide mailing lists, through diabetes clinics at CEDOR, and information will be circulated via word-of-mouth. The participant information and consent form will be circulated through a CEDOR participant list of people with type 2 diabetes who have expressed interest in participating in studies.

## Data Collection, Management and Analysis

### Data Collection Methods

Data collection methods are as follows:

* Height
	+ Measured using a calibrated wall-mounted stadiometer. Height will be measured three times to the nearest centimetre and the mean will be recorded as height.
* Weight and body composition metrics
	+ Measured using a two-electrode foot-to-foot bioelectrical impedance scale, the TBF-400 (Tanita Corporation, Arlington Heights, IL). The scale passes a weak electrical current through the body, with the voltage measured to calculate the impedance (electrical resistance) of the body, with impedance used to estimate body composition (i.e., muscle mass, fat mass, free-water mass, bone mass etc.). Weight will be measured to the nearest tenth of a kilogram. Results will be recorded digitally and the print-off will be kept in physical files. The print-off will be scanned and re-printed to avoid data loss by ink-fade. Weight and body composition metrics will be used to assess if differences in energy intake recorded via the application and objectively measured energy expenditure are due to misreporting or changes in energy stores.
* Novel glycaemic monitoring application.
	+ Participants will be instructed to record all dietary intake and view blood glucose data for 30 days total using the application. This is currently an iOS-only app that allows for both image-based and text-based input. The image-based method uses the on-device camera and the Passio Nutrition AI Software Development Kit (Passio Inc., California) to identify and quantify food items through automated recognition software. Both the image-based and text-based methods use the Passio nutrition database for food item names, energy, and macronutrient information. The application displays total energy intake and macronutrient data from the foods consumed that day, with the option of this being turned off. The application pairs with the AiDEX Continuous Glucose Monitor and displays the blood glucose information using a custom display.
* Continuous glucose monitoring (CGM)
	+ The CGMs are AiDEX CGM’s (Microtech Medical, Beijing, China). These record blood glucose levels every five minutes that are transmitted to the application via Bluetooth (approximate range of ten metres) and do not require Near Field Communication (NFC) to record on the application and can communicate at a range of approximately ten metres. Each sensor is accompanied by a transmitter that facilitates the Bluetooth transmission. This transmitter will be re-used between sensors. Participants will be provided with a single CGM sensor at Visit 1, and provided with two CGM sensors at Visit 2. Participants are to wear the CGM for ten continuous days between Visit 1 and 2. After Visit 2, participants will wear the first CGM for ten continuous days, discard of the CGM, and immediately apply the other CGM for another ten continuous days.
* Accelerometery
	+ Participants will be provided an ActiGraph GT9X (ActiGraph Corporation, Pensacola, FL), a tri-axial accelerometer, and accompanying wrist-strap at Visit 1. Participants will be instructed to wear it continuously until Visit 2, except when showering or swimming for more than 30 minutes. Participants will be encouraged to continue with normal activity, and only the time-keeping feature will be displayed to the participant. Data generated from the ActiGraph will be processed using GGIR (2.10-1) using the thresholds stated in Hildebrand et al (11,12). Accelerometery is used to estimate total energy intake: we can first estimate total energy expenditure by measuring its components; resting energy expenditure, activity-related energy expenditure, and diet-induced thermogenesis (assumed to be 10% of total). Accelerometery using the ActiGraph GT9X provides measurement of activity-related energy expenditure.
* Indirect calorimetry
	+ Calorimetry will be carried out by trained investigators only, who have demonstrated competence at conducting nitrogen gas validation by obtaining a score of 98-102% of target O2 retrieval.
	+ Calorimetry recordings must all include the date of calibration for CO2, O2 and WVP sensors, the operator name, the participant ID, and the raw data file-name as a minimum data set. Prior to completing a visit the calorimetry raw data will be checked across all channels for baselining errors, significant artefact or other errors that may require a repeat recording. Once the raw data has been checked it should be immediately backed up and the file-name recorded in the participants file.
	+ Participants will be recorded reclining at 30-45° for the duration of the recording. Participants will be monitored visually during all recordings. Any movement occurring during a calorimetry recording will be recorded along with the sample numbers over which the movement occurred. In the event of artefact, the signal processing technique used to correct the artefact will be noted, e.g. smoothing, rolling averages etc.
	+ Recorded visit data will have pre-specified ranges or drop down menus to reduce operator error. Data checking will occur separate to data entry and prior to statistical analysis. A data checking log will be kept that details any errors identified, any changes to the data set made, the reasons for this and by whom. Indirect calorimetry allows measurement of resting energy expenditure, which will be used to calculate total energy expenditure, and therefore total energy intake under the assumption of body mass stability
* Qualitative questionnaire
	+ Participants will complete a questionnaire hosted on REDCap (Vanderbilt University) at Visit 3, with a sub-set question delivered at Visit 1 and 2, exploring their perspective on the usability of the application. The questionnaire will use both Likert scales and free-text. Please see Appendix A for the questionnaire. The questionnaire is used to identify points of improvement for the application we must understand the qualitative experience. Once these areas for improvement are known we can make changes for further iterations of the application

### Retention

Participants are free to withdraw from the study at any point. The energy-weighted algorithm will assist in retention during the study. If a participant chooses to withdraw they will be invited to fill out the qualitative questionnaire at that point. If the participant has completed ten days of food tracking this data will be used to assess the accuracy of the energy intake estimates from the application. If the participant completes at least ten days the food and glucose-tracking component, these data will be included in a sub-analyses of the primary outcome.

### Data Management

Standard clinical and research practice for continuous glucose monitoring data management is to be sent to a secure cloud storage database. This study shall adhere to standard practice, and all data recorded via the application including continuous glucose monitoring data is stored in Firestore, a secure cloud database (Alphabet Inc., US). An ad-hoc cleaning and exporting algorithm will convert these data into a csv. file for analysis in R (R Foundation, Vienna, Austria). All data stored in this database is de-identified, and will only contain Study ID, height, weight, and self-reported metrics such as physical activity level and regular mealtimes. Anthropometric, body composition, indirect calorimetry will be stored in a secure REDCap database (Vanderbilt University). This REDCap database will only contain de-identified data. Accelerometery data can only be processed through proprietary ActiLife software (ActiGraph Corporation, Pensacola, FL), after which the data will be transcribed to the exported csv. Firestore file and deleted from ActiLife. The Firestore database will be deleted after ten years. A physical copy of all baseline measurements will be stored in a locked cabinet in CEDOR to prevent data loss and will be archived at the end of the study and destroyed after ten years.

### Statistical Methods

Statistical analysis will be performed with R 4.2 (R Foundation, Vienna, Austria).

Paired t-tests will be used to compare the primary outcome of time-in-range and duration of post-prandial hyperglycaemia. Standard deviations will be used to compare inter-individual and intra-individual variability of post-prandial glycaemic responses to the provided food items. Bland-Altman analysis using the blandr package in R 4.2 will be used to assess the accuracy of the energy intake measurements from the application (13,14). For significance tests, alpha level will be set at 0.05 (two tailed).

## Monitoring

### Study Committee

A Study Committee will meet fortnightly to monitor recruitment, sample size assumptions, completeness of data acquisition, and evidence for group differences in the main efficacy and safety outcome measures (harms).

*The Study Committee comprises: Professor Jeremy Krebs, Dr Rosemary Hall, Lachlan Lee.*

### Interim analysis

There will be no interim analysis.

### Harms

The following Serious Adverse Events will be reported to the Study Committee:

* Death
* Hospital admission

### Auditing

Auditing of trial conduct and documentation completeness will be undertaken monthly by the site principal investigator. All previously un-audited hard-copy and digital records will be examined for errors.

# Ethics and Dissemination

## Research Ethics Approval

Ethics approval is being sought through the Health and Disability Ethics Committee.

## Locality Approval

Locality approval is being sought through Te Whatu Ora Wellington and the University of Otago Wellington.

## Protocol Amendments

All amendments to the final version of this protocol will require review and approval of the Steering Committee, and will be submitted to HDEC and local Te Whatu Ora Research Offices, as appropriate. All amendments, including approval date, will be recorded with this protocol (appendix 4.6).

## Consent / Assent

Informed consent will be obtained at the screening visit. The protocol of the study will be explained and the participant will have the opportunity to ask questions at any point. Informed consent will be documented using a dated hard-copy PISCF that contains the participant’s first and last name, signature, and a researcher name and signature.

### Ancillary studies

No ancillary studies are planned for this study.

## Confidentiality

Electronic databases will be stored on secure servers and access will be controlled by unique user ID, with full electronic tracking log. Data will be identifiable only by study ID and DOB. Forms will not contain identifiable information such as names, address, or NHI. Extracted data files will contain DOB, as this is necessary for analysis, but participant initials will be removed. Contact and personal information will be stored separately from study data. Hard copy PISCFs, which contain first and last names, will be stored in a locked cabinet. Study reports will contain only summary data and individual participant data will not be reported. Identifiable data will not be released to any third party. Research staff will be certified in best practice for clinical trials.

At the completion of the study, all electronic data will be deleted after ten years and accessible only to the study investigators. All hard copy records that have been digitally scanned will be added to the archive, and then destroyed. Remaining hard copy records will be stored in a locked cabinet in a secure office, and will be accessible only to the study investigators. Records will be retained for 10 years after the study is complete, and will then be destroyed.

## Declaration of Interests

Investigators will declare any financial, intellectual, or other potential conflicts of interest, as outlined by the ICMJE (15).

## Access to Data

The investigators will have access to the full dataset and oversee analysis, interpretation and reporting of results. Approval will be sought from the investigators prior to publication of study data. Care will be taken to avoid duplication in reporting of results.

## Ancillary and Post-trial Care

No compensation will be provided through the study. Any compensation for accidents will be sought through the Accident Compensation Corporation. No ancillary or post-trial care is specifically provided.

## Dissemination Policy

The results from this study will be submitted for publication in peer reviewed journals and be included in LL’s doctoral thesis.

### Authorship policy

All named investigators in this protocol (JK, RH, LL) will be authors in future publications. Additional authorship will be at the discretion of the investigators based on contribution to the study.

# Appendices

## Participant Documents

The following participant documents are to accompany this protocol:

|  |  |  |
| --- | --- | --- |
| Title | Version | Date |
| Participant Information Sheet and Consent | 1.0 | 15 August 2023 |
| User experience questionnaire | 1.0 | 15 August 2023 |

## Biological Specimens

Biological specimens involved in this study are the HbA1c point-of-care test discs and the continuous glucose monitors. These specimens are to be disposed of immediately after use into sharps containers. Participants will return the CGMs within the sharps containers at Visit 2 and Visit 3 for disposal by the researcher. No biological specimens will be stored.

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