The effectiveness and sustainability of health outcomes from an advanced GLP-1-supported digital weight-loss programme in the UK: A randomized controlled trial

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Introduction

You have been invited to take part in a clinical research study. This is because you have been deemed eligible by a UK doctor for GLP-1 RA-supported weight-loss therapy and have expressed an interest to enroll in the Juniper program. Participants in the study will all receive the same GLP-1 RA treatment as standard Juniper patients but will be divided into one of two health coaching groups. This will allow researchers to achieve their objective of comparing the outcomes of the two different health coaching approaches.

The study design is a randomized controlled trial, meaning that you will be randomly allocated (like flipping a coin) into either a control or intervention group to assess the relative effectiveness of the trial's novel health coaching intervention. Irrespective of which group you are allocated to, you will receive the same GLP-1 RA (Mounjaro) treatment as standard Juniper patients. This will allow the study's investigators to reliably compare the effectiveness of the different health coaching approaches in the control and intervention groups. You will not be told which group you have been allocated to.

This participant Information Sheet and Consent Form tells you about the research project. It explains the purpose of the research, procedures and risks involved. It also describes information about you that will be obtained, how that information will be used and with whom it will be shared. Knowing what is involved will help you decide if you want to take part in the research. Please read this information carefully. Ask questions about anything that you don't understand or want to know more about. Before deciding whether or not to take part, you might want to talk about it with a relative, friend or your local doctor. Participation in this research is voluntary. If you don't wish to take part, you don't have to. You will receive the best possible Juniper care whether or not you participate in the study. If you decide you want to take part in the research project, you will be asked to sign the Consent Form.

You will be given a signed and dated copy of this participant information sheet and consent form to keep.

Purpose of the study

You are invited to participate in a research study, which is being conducted in order to compare the effectiveness and sustainability of two GLP-1 RA-supported health coaching interventions for weight loss. The study will run for 12 months.

Study procedures

After consenting to trial participation, you will provide weight, body composition and strength measurements at a designated health clinic. Body composition measurements will be obtained via a DEXA machine; weight measurements via a standard set of scales; and strength measurements through three isometric exercises performed on force plates, including an isometric squat, push up, and mid-thigh pull. You will then receive 6 months of GLP-1 RA (Mounjaro) therapy and a form of health coaching.

Baseline measurements will be retested at 6 months (end of intervention) and 12 months (6 months post-intervention) to compare the effectiveness and sustainability of two health coaching approaches. In total, you will be required to make 3 appearances at your designated health clinic to provide weight, body composition and strength measurements. Each session should take approximately 30 minutes.

The difference between the two health coaching groups is the nature of communication, i.e., communication frequency and the level of personalization. These two dimensions of Juniper health coaching (communication frequency and personalization) will be more systematic (stricter coaching rules) in both study arms than the coaching provided in the standard Juniper weight-loss program. One of the study arms (health coaching groups) will have a higher level of communication frequency and personalization than the other.

As a participant of this trial, you will be expected to adopt certain lifestyle changes, including dietary and exercise modifications. Irrespective of which group you are allocated to, you will have significant input into the nature of these changes, however all exercise programs will include various resistance exercises. Gym attendance may be encouraged but will not be a program requirement. You will be expected to complete 4 30-minute exercise sessions per week and dedicate a further 10 minutes per week (minimum) to health coach communication and lifestyle tracking. As is the case with the standard Juniper weight-loss program, all health coaching content will be delivered to you through the program app, including health coach messaging, learning resources, and health data

tracking. Similarly, you will use the program app to communicate with other members of your multidisciplinary care team (MDT), to report any adverse events, and to access all materials related to your GLP-1 RA (Mounjaro) treatment.

You will be excluded from the trial if you fail to provide all baseline measurements (scans, blood tests and strength measurements) within three weeks of consenting to trial participation. If you are excluded, you will still have the option of proceeding with a standard Juniper weight-loss program subscription.

Throughout the trial, you will follow a normal Mounjaro treatment schedule (and the standard titration escalation plan), unless you have to lower dosage due to discomfort. The schedule is as follows:

- 0.25mg of Mounjaro for weeks 1-4;
- 0.5mg of Mounjaro for weeks 5-8;
- 1mg of Mounjaro from week 9 to end of intervention (6 months)

Medication will be sent to you on a monthly basis to self-administer, along with return labels to allow trial investigators to monitor treatment adherence via drug vial return.

Risks and discomforts

This study's focus is on the impact of varying features of the Juniper health coaching intervention. Rapid and significant weight loss associated with this intervention could lead to nutritional deficiencies and increase the risk of gallstone formation[1][2]. Several studies have also found that patients who lose a large amount of weight often experience disproportionate reductions in vital fat-free mass[3][4]. The physical demands of your prescribed exercise program may also increase your risk of musculoskeletal injury and/or

[1] Calton, J. Prevalence of micronutrient deficiency in popular diet plans. J Int Soc Sports Nut, 2010;7(24)
[2] Weinsier, R., & Ullmann, D. Gallstone formation and weight loss. Obesity research, 1993;1(1):51-56
[3] Vink, R., Roumans, N., Arkenbosch, L., et al. The effect of rate of weight loss on long-term weight regain in adults with overweight and obesity. Obesity, 2016;24(2):321-327.
[4] McCarthy, D., & Berg, A. Weight loss strategies and the risk of skeletal muscle mass loss. Nutrients, 2021;13(7): 2473.

your level of psychological stress. In general, significant dietary and exercise modifications bring about varying levels of physical discomfort.

If you consent to participating in this study and experience any form of discomfort, you will need to inform your MDT who will provide appropriate guidance for managing the adverse event. In cases of severe side effects, you should ring 999 immediately and seek emergency medical assistance.

You will be counselled by your assigned doctor during your pre study evaluation if blood screening is to be performed for Hepatitis B, Hepatitis C and/or HIV. If you test positive for any of these conditions, your doctor is required by law to report the information to Government Health Authorities.

Although the study has set up robust protocols to anonymize all patient data in perpetuity, there is always a small risk that privacy standards are breached.

If you do become pregnant whilst participating in the research project, you should advise your MDT immediately. Your assigned doctor will withdraw you from the research project and advise on further medical attention should this be necessary. You must not continue in the research if you become pregnant.

The effects of Mounjaro on the unborn child and on the newborn baby are not known. Because of this, participants must not participate in the research if pregnant, trying to become pregnant, breastfeeding, or planning ovum donation.

In the event you do become pregnant the Sponsor will request that you sign a separate consent form to allow monitoring of your pregnancy and the birth and the health of your child up to 4 years of age.

Ionising radiation

This research study involves exposure to ionizing radiation. You will have 3 full-body DEXA scans. These procedures are additional to those you would have received if you were not in this study.

As part of everyday living, everyone is exposed to naturally occurring background radiation and receives a dose of about 2 to 3 millisieverts (mSv) each year. The effective dose from this study is, according to an external assessment of our measurement site[5], about 0.03 mSv.

At dose levels less than 2 mSv, no harmful effects of radiation have been demonstrated and the risk is negligible.

Possible benefits

Participation in this study could possibly result in significant health benefits, including weight loss and body composition. A recent study revealed that a cohort of people with overweight or obesity who adhered to the Juniper weight-loss program for 5 months lost, on average, over 10% of their baseline weight [6]. Despite this, it is possible that you will receive no benefit from participating in the trial. The study is being undertaken to reliably establish whether the Eucalyptus program delivers health benefits.

Alternatives to participation

If you do not wish to participate is study, you are free to proceed with the Juniper weight-loss therapy you are currently receiving and your relationship with your current MDT and the Eucalyptus organization will not be impacted in any way. You are also free to explore other digital or face-to-face weight-loss programs, such as My Weight Loss Clinic or services provided at your local medical center.

Tissue samples and data

OBLIGATORY:

Blood tests to determine fasting glucose, fasting insulin, HbA1c and fasting lipid levels. These samples will need to be provided via a certified UK pathology clinic (e.g., Nationwide pathology, Spire Healthcare) in the three-week period between participation confirmation and study commencement. Inability to provide this sample within the specified period will result in exclusion from the trial.

[5] Review conducted by DOSEL Australasia

[6] Talay, L., Vickers, M. Effectiveness and care continuity in an app-based, glucagon-like peptide-1 receptor agonist-supported weight-loss service for women with overweight and obesity in the UK: A real-world retrospective cohort analysis. Diabetes, Obesity and Metabolism.

Study investigators will not have access to the physical blood samples, which will be collected and stored according to the laboratory's polices, (determined by the Royal College of Pathologists). Study investigators will simply record the blood sample results reported from the pathology clinic.

Voluntary participation/right to refuse or withdraw

There is no obligation for you to be involved in this study. If you do not participate your normal treatment plan will be followed. If you decide to participate in the study and later feel that you no longer wish to be part of it, you may withdraw from the study at any time without prejudice to any current or future medical treatment. If you decide to participate and then later withdraw from the study, all information collected prior to your withdrawal will remain part of the study database to ensure the scientific validity of the research and will be included in the final analysis.

Confidentiality

This study will gather certain personal information about you. This information will be held by Eucalyptus (Juniper parent company) and its authorized representatives and will only be re-identifiable under strict legal or medical conditions by one member of the Eucalyptus organization – namely in the context of a relevant criminal investigation sanctioned by UK law, or upon request from a qualified doctor for an urgent health-related issue. In accordance with UK Medical Research Council guidelines, your deidentified data will be stored in the Eucalyptus central data repository for 20 years whose access is restricted to the Eucalyptus analytics team and study investigators. Data will be kept for this period to allow researchers and institutions with a reasonable interest to access it under appropriate circumstances. At the end of this storage period, your data will be destroyed. Study investigators and parties who access study data upon reasonable request will only be able to see your allocated study number rather than your name. No third parties will be able to access your personal data during the trial period.

All personal information will be used only for the purpose of administering your participation in this study and in accordance with the laws governing the protection and privacy of personal information under UK privacy legislation. Your trial MDT will not be able

to contact the study's investigators and reveal your identity to them. If you have any questions about this, direct them to the Principal Investigator.

By signing the attached consent form, you authorise the release of/or access to this confidential information to the relevant study personnel and regulatory authorities as noted above.

In most cases, you have the right to access personal information collected from you in connection with the study and request corrections of any such personal information that is incorrect.

Your records relating to this study and any other information received will be kept strictly confidential. However, staff participating in your care, the sponsor and other agencies authorised by law, may inspect the records related to the study. In the event you are admitted to hospital as a result of an adverse event resulting from this study, your treating doctor may require access to your study records. Your identity will not be revealed, and your confidentiality will be protected in any reviews and reports of this study which may be published. However, results may be suppressed for commercial reasons as the sponsor of the project retains the rights to the data. Your treating Doctor/s will be notified of your participation in this study and of any clinically relevant information noted by the trial doctor in the conduct of the trial.

Costs

All costs related to the provision of the study's measurements will be covered by Eucalyptus. This includes the consultation, travel and parking costs incurred in your journey to your closest available pathology clinic and health clinic. Receipts will need to be provided where applicable. In the case of car travel, reimbursement will be determined by petrol costs and kilometres travelled.

All other direct costs associated of your trial weight-loss program will be covered by Eucalyptus, including your medication (Mounjaro), health coaching, access to your MDT, and your use of the program app.

You will be responsible for any costs associated with dietary and/or exercise modifications, e.g., gym membership, different groceries.

Illness or injury

If, as a result of being in this study, you become ill, injured, or experience any kind of discomfort, please immediately contact your MDT via the program application. She or he will then give you all necessary information and treatment and will inform the trial sponsor. In the case of a serious and rapidly escalating adverse reaction contact emergency services on 999. Ensure that you have your emergency card with you so the study doctor can be contacted as necessary. A dedicated Data and Safety Monitoring Board has been set up for this trial to maximise the speed at which your MDT responds to any adverse events you experience. In the event of a serious adverse event, emergency clinicians may require access to your medical records.

Compensation for injury

If you are injured as a result of your participation in this investigation you may be entitled to compensation through the UK legal system.

It is the recommendation of the independent ethics committee responsible for the review of this investigation that you seek independent legal advice before taking any steps towards compensation for injury.

Termination of the study

This research project may be stopped for a variety of reasons. These may include the following:

- Unacceptable side effects,
- the study sponsor enduring a major financial setback,
- additional information coming to light

When the trial is stopped, your treating doctor will discuss ongoing care with you, however there may be no further treatment options available to you.

Investigators benefits

All clinicians and investigators who are involved in this study are being remunerated under their existing Eucalyptus salaries. They will not allow a conflict of interest to compromise their position or this research study. Their conflict of interest will be clearly declared to the journal they attempt to publish study results in.

New information arising during the project

During the research project, new information about the risks and benefits of the project may become known to the researchers. If this occurs, you will be told about this new information. This new information may mean that you can no longer participate in this research. If this occurs, the person(s) supervising the research will stop your participation. In all cases, you will be offered all available care to suit your needs and medical condition.

Results of project

You will be emailed the results of the study as soon as the analysis has been peer-reviewed and submitted for publication.

Consent

This form has provided you with all information regarding the nature and purpose of the research study, its risks and benefits, and the possibility of alternative treatment. It must be stated that you are free to withdraw anytime and that if you do not participate you will not suffer any prejudice and will be free to access the Eucalyptus weight-loss program as a normal (non-trial) patient. If you withdraw at any stage of the trial, all your study-related data will be transferred to your Eucalyptus profile on the company's encrypted central data repository, where your original program data is held. All information collected prior to your withdrawal will remain part of the study database to ensure the scientific validity of the research (even if not used in the analysis).

Advice and information

If you have any further questions regarding this study, please do not hesitate to contact Dr. Louis Talay at louis.talay@sydney.edu.au

The Bellberry Human Research Ethics Committee has reviewed and approved this study in accordance with the National Statement on Ethical Conduct in Human Research (2024). This Statement has been developed to protect the interests of people who agree to participate in human research studies. Should you wish to discuss the study or view a copy of the Complaint procedure with someone not directly involved, particularly in relation to

matters concerning policies, information or complaints about the conduct of the study or your rights as a participant, you may contact the Director of HREC Operations, Bellberry Limited on +61 08 8361 3222.

Consent Form

Protocol Title: Prospective study of the sustainability of health outcomes from a digital real-world weight-loss programme that combines behavioural and pharmacological treatments.

Project Sponsor: Eucalyptus

Principal investigator: Dr. Louis Talay

Location: United Kingdom

Declaration by Participant

I _____ , the undersigned hereby voluntarily consent to my involvement in the research project titled:

_____

_____

I understand the purposes, procedures and risks of the research described in the project. Specifically, the details of the procedure(s) proposed and the anticipated length of time it will take, the frequency with which the procedure(s) will be performed and an indication of any discomfort that may be expected have been explained to me.

- I freely agree to participate in this research project according to the conditions in the Participant Information Sheet which I confirm has been provided to me.
- I understand that my involvement in this study may not be of any direct benefit to me.
- I understand the purposes, procedures and risks of the research described in the information sheet.
- I have been told that no information regarding my medical history will be divulged to unauthorised third parties and the results of any tests involving me will not be published so as to reveal my identity.
- I understand that access may be required to my medical records in the event of a serious adverse event and I consent to this access.
- I understand that I am free to withdraw from the study at any stage without prejudice to future treatment. If I decide to withdraw from the study, I agree that the

information collected about me up to the point when I withdraw may continue to be processed.
- I am 18 years of age or over.
- I consent to my treating Doctor/s being notified of my participation in this study and of any clinically relevant information noted by the trial doctor in the conduct of the trial.
- I declare that all my questions have been answered to my satisfaction.
- I have read, or have had read to me, and I understand the Participant Information Sheet, dated _____.

I understand that I will be given a signed copy of this document to keep for myself.

Name of Participant (Please print) _____

Signature of Participant _____ Date _____

Declaration by Principal Investigator (PI) or Co-Investigator (CI):

A written explanation of the research project, its procedures and risks has been given to the participant and I believe that the participant has understood that explanation.

Name of PI or CI:

Signature of PI or CI: _____ Date:

The Principal Investigator or Co-Investigator must provide the explanation and provision of information concerning the research project.