PARTICIPANT INFORMATION SHEET (PIS) AND INFORMED CONSENT FORM (ICF)

Study title:	Digital diabetes remission trial (DIGEST)
Sponsor:	Habitual Health Ltd.
Study conducted by:	Lindus Health
Chief Investigator:	Prof Carel le Roux
Trial Contact Details:	digest@lindushealth.com

We would like to invite you to take part in a research study aiming to find out if the Habitual Remission Programme can lead to the reversal of Type 2 diabetes. The Habitual programme involves a weight loss programme together with a mobile Application (App) providing support, motivation and nutrition guidance. We are inviting you to join this trial because we understand you have Type 2 diabetes.

Before you decide whether to take part, it is important for you to understand why the research is being done and what it would involve for you. One of our team will go through the information sheet with you and answer any questions you may have. Please take time to read the following information carefully and talk to others about the study if you wish.

The information sheet is in two parts:

Part A: The Participant Information Sheet (**PIS**) provides information about the purpose of this study and what will happen to you if you take part.

Part B: The Informed Consent Form (**ICF**) gives you more detailed information about the conduct of the study, and you are required to sign this if you wish to participate.

Please ask us if there is anything that is not clear or if you would like more information. Take your time to decide whether or not you wish to take part.

Thank you for reading this.

PART A: The Participant Information Sheet (PIS)

What is the purpose of this study?

The purpose of this study is to find out if the Habitual Remission Programme is more likely to cause the reversal (also referred to as remission) of type 2 diabetes, compared to standard NHS care.

What is the Habitual Programme?

The Habitual Programme lasts for 6 months and involves using the Habitual mobile App alongside a weight loss programme.

Habitual Mobile App

The Habitual App provides psychological, emotional, and social support to guide and support you and provide useful information about nutrition and the management of your Type 2 Diabetes. The App includes incentives to help you achieve your goals. You will be required to download the App and will be asked to sign up to the App's data protection wording.

Weight loss programme

- *Months 1-3 - Total Diet Replacement*
    - Your normal meals will be replaced with the Habitual diet (porridge, shakes and soups) which will provide a complete and balanced set of nutrients.
- *Months 4-6: Gradual reintroduction to food*
    - Meals will gradually be reintroduced by one meal/day (weeks 12-15), to two meals/day (weeks 16-20) and finally three meals/day (weeks 20-24).

Please visit the Habitual webpage for more detailed information: https://www.tryhabitual.com/

What's Involved?

After consenting for the study, you will randomly be allocated to either the Habitual Programme or continue your standard diabetes care. You will remain in the same group for the duration of the study.

The study will mainly be conducted remotely, without in person visits. Those allocated to the Habitual Programme group will need to attend an initial appointment with their GP, to confirm that they are able to take part.

You will be asked to take a few measurements every other week, such as blood pressure, weight and waist circumference, using the equipment provided. You will then enter these measurements and answer a few quick questions onto the Lindus Health electronic survey using your smartphone, tablet or computer. Three or four blood samples will be collected by yourself at home, using kits and instructions provided. You will be required to send the blood samples for central processing at a central laboratory, Thriva Ltd.

Can I take part?
To take part, you need to be:

- Able and willing to give consent for the study
- Aged 18-75 years old with a diagnosis of type 2 diabetes mellitus within the last 6 years
- Have access to a smartphone or a computer
- Have a Body Mass Index (BMI) of at least 28 kg/m2
- Have had a HbA1c test within the previous 12 months of greater than 48 mmol/mol (6.5%) and less or equal to 86 mmol/mol (10%)

Before you agree to take part in the study and for your own safety, the Lindus Health team will also check the following with you:

- Not currently using insulin
- Not had a weight change of >5% in the past 3 months
- Not suffering with substance abuse
- Not have cancer
- Not had a heart attack within the previous 6 months or have severe heart failure
- Not have any learning difficulties
- Not currently on treatment with anti-obesity drugs
- Not had bariatric surgery
- Not been diagnosed with eating disorder
- Not pregnant, breastfeeding or considering pregnancy
- Not required hospitalisation for depression or taking antipsychotic drug
- Not have porphyria (a blood disorder)
- Not have a history of illnesses that could interfere with the study results
- Not have pancreatitis
- Not currently taking part in a drug trial for antidiabetic medication
- Not had an abnormal diabetic foot review

If you are taking glucose lowering medications, these will need to be stopped if you are allocated to the Habitual Programme Group. You will discuss this with your General Practitioner (GP). Your GP will also have to confirm that you are eligible to take part.

Do I have to take part?
It is up to you to decide; participation in the study is entirely voluntary. If you do decide to take part, you will be asked to read this information sheet and to sign an Informed Consent Form (ICF), found at the end of this Participant Information Sheet, to show you have agreed to take part. If you do not want to take part you continue with your management of your type 2 diabetes.

You are able to discuss the study, the Participant Information Sheet and Informed Consent Form with the study team and will be given every opportunity to ask questions. You are still free to withdraw at any time, without giving a reason, and without your medical care being affected.

What will happen to me if I take part?

If you are interested in taking part, we will ask you to complete a short online form to see if you are eligible. After completion, this Participant Information Sheet will be emailed to you, and you will be asked to book a telephone/video call with the trial Research Nurse.

Informed Consent

During the call, the Research Nurse will explain what the study involves and the potential benefits and risks of taking part and answer any questions you may have. You will be asked a few questions about your health to assess your suitability for the study. After this discussion, if you are willing and eligible, you will provide informed consent by electronically signing a consent form which will be emailed to you. The Research Nurse will also sign the consent form electronically and you will be given a fully signed copy to keep.

Randomisation

You will randomly be allocated to one of two groups using a computer-generated list:

- **Control Group**:
    - Continue to receive standard NHS diabetes care with your GP
- **Habitual Remission Programme Group**:
    - Receive the Habitual Remission Programme

You will be randomised into the study at a ratio of 2:1, which means two thirds of the participants will be allocated to the Habitual Programme Group and one third to the Control Group.

Once your GP has confirmed you are eligible to take part, you will receive a phone call from the research team letting you know which group you have been allocated to. If you have been assigned to the Habitual Programme, you will need to arrange an appointment with your GP before you can start the study. This is for your own safety as using Total Diet Replacement may cause a rapid fall in blood sugar levels and blood pressure (BP). Therefore, before taking Total Diet Replacement all medication for your diabetes will need to be stopped with your GP's approval.

If you are on the Habitual diet replacement programme you will take the Habitual Total Diet Replacement (shakes and soups) for 3 months, made of four 'meals' per day with a

total intake of 800 kcal per day. You will be supported by the Habitual mobile app during this time.

Lindus Health Electronic Survey
You will need to set-up and use the Lindus Health electronic survey and Habitual App. (if on the Habitual Programme) throughout the study. Sometimes the same information will be needed on both systems, which means you will have to enter the data twice.

At the consenting interview, the Lindus Health study team will go through the process of setting up the devices. In addition, you will be able to test out the technology during the onboarding week. The Lindus Health team and Habitual team will be available to help if any problems arise during the study. Lindus Health helpdesk telephone: 020 8609 4690.

1. Onboarding
During this time you will test the Lindus Health survey and equipment.

You will need to:

- Measure your blood pressure, weight and waist circumference using the equipment provided, and record results onto the survey.
- Answer a few brief questions in the survey.

If you are assigned to the Habitual Programme Group and have had your GP visit, you will also have a chance to sample the Total Diet Replacement products and test the Habitual mobile App. (which you will need to download).

When you are ready to start the study you can indicate this in your survey and move to the next step of taking your baseline measurements.

2. Baseline Measurements
You will need to:

- Measure your blood pressure, weight and waist circumference and record the measurements in the survey.
- Collect a blood sample for HbA1c (glycated haemoglobin) to help us monitor your diabetes, using the kits provided and then send the sample in the pre-paid envelope for central processing. You will be asked to collect about 6-7 drops of blood (approximately 250uL), for each blood test.
- Answer a few brief questions in the survey.

3. Blood Pressure Monitoring in the Intervention Group

If allocated to the Habitual Programme Group, you will receive a phone call from the Research Nurse, 4 weeks after starting your Total Diet Replacement, to discuss any potential issues you may have relating to your blood pressure.

4. Fortnightly Survey (weeks 2, 4, 6, 8, 10, 14, 16, 18, 20 and 22)

You will need to record in your online survey:

- If you have experienced any side effects or any change in medication.
- Your blood pressure (BP), weight, waist circumference.

5. Month 3 (week 12)

You will need to complete the activities described in the ***fortnightly survey*** described above, and in addition, collect a HbA1c blood sample to help us monitor your diabetes. Please use the kits provided, and then send the sample for central processing in the pre-paid envelope.

For those in the Habitual Programme Group, food will gradually be reintroduced at this stage. You will be supported by the Habitual App. At week 12 - 15 you will have one meal per day (shakes/soups for the rest of meals), at weeks 16 - 20 you will have two meals, and weeks 20 - 24 three meals.

6. Month 6 (week 24)

You will need to complete the activities described in the ***fortnightly survey*** above, and in addition, collect a HbA1c blood sample to help us monitor your diabetes. Please use the kits provided, and then send the sample for central processing in the pre-paid envelope. You will also receive a link to an end of study survey.

7. Months 6-12 - Observational phase (Habitual Programme Group only)

On month 9 and month 12, if you are in the Habitual Programme Group only, you will need to:

- Complete the activities described in the fortnightly survey above.
- Collect a final HbA1c blood sample to help us monitor your diabetes using the kits provided, and then send the sample for central processing (month 12 only).
- On month 12, complete an end of study survey about your experience on the trial.

Expenses and payments
You will not be paid for taking part in this study. The study is conducted remotely so no other expenses are anticipated.

All blood sample kits, measuring equipment, courier costs and Total Diet Replacement products will be paid for by the Sponsor and provided to you to keep. For those allocated to the Control Group, you will also be offered the Habitual Programme, including Total Diet Replacement products at the end of the trial for free.

What are the possible disadvantages and risks of taking part?
There are a number of side-effects associated with the Habitual's Total Diet Replacement product including: bad breath, abdominal pain, diarrhoea, headache, hair loss, dry skin, mood changes, feeling cold, tiredness/fatigue. However, the Habitual meals are formulated to provide complete nutrition and meet strictly regulated requirements (EU legislation - Regulation on Foods for Specific Groups 609/2013/EU).

If you are randomised to the Habitual programme, all diabetic medication will need to be stopped the day the trial begins. This is for your own safety as Total Diet Replacement use can cause a rapid fall in blood sugar levels. The withdrawal of these medications is conducted following your GP's approval, and the research team will continue to monitor you.
You will need to collect blood samples at home using the kits provided, which may cause mild discomfort and bruising. The devices provided have been selected to minimise the discomfort, bruising and allow easy blood collection. The HbA1c result from your sample, will allow us to monitor your diabetes carefully and allow us to see if the Habitual Remission Progress is able to reverse diabetes.

How will I know if I have any abnormal results?
The research team will monitor your blood pressure readings, any potential side-effects and your HbA1c results during the trial. If any of the results are clinically significant we will contact you and/or your GP.

What are the possible benefits of taking part?
Taking part in this study may not have any direct benefits, but it may help you better manage your diabetes. If you are in the Habitual Programme you may be able to put your diabetes in remission and/or reduce the medication taken previously, however this is not guaranteed.

In addition, information gathered from this study can be used to improve the management and treatment of type 2 diabetes in the future.

What happens when the research study stops?
When the study ends you will continue to be reviewed by your GP under standard routine care.

For those allocated to the Control Group, you will be offered the Habitual Programme, including Total Diet Replacement, at the end of the trial for free, for 6 months. Within the App, you will be advised to see your GP prior to undergoing the programme. If you are taking certain medications, your GP will need to provide written confirmation of a medication plan. You will have finished the trial at this stage and so will not be followed up by the research team.

All participants will be offered lifetime access to the Habitual App to allow you to continue making behavioural changes to help manage your diabetes. Total diet replacement products will not be provided following the end of the trial, but you can purchase these commercially if you would like to use them to help with weight maintenance.
After the end of the trial, we will not collect any trial data via the App. The data the App will collect is outlined in Part B 'How will we use information about you?'.

What happens if there is a problem?
Any complaint about the way you have been dealt with during the study or any possible harm you might suffer will be addressed. The detailed information on this is given in Part B.

Will my taking part in the study be kept confidential?
Yes. We will follow ethical and legal practice and all information about you will be handled in confidence. The details are included in Part B.

If you still have further questions, please see the FAQ's in Part C or email digest@lindushealth.com.

If the information in Part A has interested you and you are considering participation, please read the additional information in Part B before making any decision

PART B - Informed Consent Form (ICF)

What if relevant new information becomes available?

Sometimes new information becomes available about the product used in this study. If new information becomes available, we will notify you. The relevant regulatory authorities will also be informed and the study may be stopped or changed if appropriate. If the information sheet is changed significantly, you will be asked to read the updated information sheet and sign another consent form. You will be given the opportunity to discuss this with the Lindus Health team and have any questions answered. You will be able to withdraw from the study at any stage.

What will happen if I don't want to carry on with the study?

You can withdraw from the study at any time, without giving a reason, and this would not affect either the standard of care you receive, or your legal rights. If you withdraw from the study, and it is considered to be in your best interest, you are advised to contact your GP.

If you decide to withdraw or lose capacity to consent, we will need to use all the data collected up to the time of your withdrawal. This means that all the samples that you give will be analysed.

What if there is a problem?

Complaints

If you have a concern about any aspect of this study, you can contact meri@lindushealth.com, and any complaint about the way you have been dealt with during the study or any possible harm you might suffer will be addressed.

Am I covered by Insurance?

This study should not affect your health, but in case you have private insurance you should check with the company before agreeing to take part in the study. You will need to do this to ensure that your participation will not affect your medical insurance.

In the unlikely event that you become ill or are injured as a result of taking part in this study you will be covered by insurance held by the Sponsor. Compensation will be provided for any injury caused by taking part in this study in accordance with the guidelines of the Association of the British Pharmaceutical Industry (ABPI). We will pay compensation where the injury probably resulted from:

- A product being administered as part of the trial protocol; or
- Any test or procedure you received as part of the trial.

Any payment would be without legal commitment (please ask if you would like more information on this). The Sponsor would not be bound by these guidelines to pay compensation where:

- The injury resulted from a drug or procedure outside the study; or
- The study procedures were not followed.

In the event that something does go wrong and you are harmed during the research and this is due to someone's negligence, then you may have grounds for a legal action for compensation, but you may have to pay your legal costs. If you wish to make a claim against this insurance you should talk to the Lindus Health team.

How will we use information about you?

We will need to use information from you, your medical records and your GP for this research project.

This information will include your

- Initials
- Name
- Contact details
- HbA1c results
- Medical history

People will use this information to do the research or to check your records to make sure that the research is being done properly.

People who do not need to know who you are will not be able to see your name or contact details. Your data will have a code number instead. We will keep all information about you safe and secure.

Once we have finished the study, we will keep some of the data so we can check the results. We will write our reports in a way that no-one can work out that you took part in the study.

The Habitual App collects identifiable information (medical history, medications, behavioural data, body measurements and usage data). This information is not shared outside of the Habitual team, and access to this data is limited to those that require it (product, and customer support). Please see the Habitual Privacy Policy for further details: https://www.tryhabitual.com/privacy-policy.

Lindus Health collaborates with Thriva Ltd (https://www.thriva.co.uk), to provide you with your blood test results. Lindus Health and Thriva are independent data controllers that share your personal data to perform the blood test and provide you with the blood test results and associated services. You will be asked to provide consent for Thriva to process your blood test results and provide the results to Lindus Health.

What are your choices about how your information is used?
You can stop being part of the study at any time, without giving a reason, but we will keep information about you that we already have.

If you choose to stop taking part in the study, we would like to continue collecting information about your health from your GP. If you do not want this to happen, tell us and we will stop.

We need to manage your records in specific ways for the research to be reliable. This means that we won't be able to let you see or change the data we hold about you.

Where can you find out more about how your information is used?
You can find out more about how we use your information

- at www.hra.nhs.uk/information-about-patients/
- our leaflet available from www.hra.nhs.uk/patientdataandresearch
- by asking one of the research team
- by sending an email to digest@lindushealth.com or
- by ringing us on 020 8609 4690.

Other information about your data
Our procedures for handling, processing, storage and destruction of data comply with the Data Protection Act of 2018. We will keep identifiable information about you for up to twelve months after the trial has finished. This excludes any research documents with personal information, such as consent forms, which will be held securely for 10 years after the end of the study.

Lindus Health may also retain personal data for business improvement purposes. For example, use of behavioural data to make feature improvements to the Electronic Data Capture platform.

Involvement of the General Practitioner/Family doctor (GP)
Your GP will be informed about your participation in the study and will need to confirm that you are eligible to take part. Your GP is contacted as a safety precaution, and it is in your best interests if you go to your GP with a medical problem during or shortly after the study period. We may also ask your GP for confirmation of your medical history. It is important for the Lindus Health team to know about your medical history so that you are not put at unnecessary risk.

If you have been assigned to the Habitual Programme you will need to arrange a visit with your GP to discuss the study and stopping your diabetic medication, before starting the study.

What will happen to any samples I give?
You will have to collect blood HbA1c samples at home every 3 months to help us monitor your diabetes. These will be sent to a central laboratory by you for processing.

No samples will be kept in storage. Once processed and results reported, the samples will be destroyed.

Your samples and laboratory results will be identified with a unique participant identification number only.

Will any genetic testing be done?

No genetic testing will be conducted as part of this study.

What will happen to the results of the research study?

The results and findings may be published in scientific papers and presented at meetings. Your identity will not be disclosed in any of these. If you wish, we can notify you if an article based on the results of this study is published.

Who is organising and funding the research?

This study is sponsored and organised by Habitual and conducted by Lindus Health. The Chief Investigator is Professor Carel Le Roux.

Who has reviewed the study?

This research study was reviewed and approved by an independent group called a Research Ethics Committee to protect your safety, rights, wellbeing, and dignity. This study was given a favourable ethical opinion for conduct by the London Bridge Research Ethics Committee Research Ethics Committee (REC reference: **22/LO/0664**).

Further information and contact details

If you require further information about being in a clinical study, the following link may assist you. It provides information about how clinical trials are run and what to expect if you take part in a trial. http://www.nhs.uk/conditions/Clinical-trials/Pages/Introduction.aspx

If you would like to know more about this study, you can contact the study team who will explain more about the study and discuss any questions that you have.

Study team contact details:

- **Email**: digest@lindushealth.com
- **Phone**: 020 8609 4690

If you would like advice about whether you should participate in the study, you may want to contact your GP surgery or the study team. It is often useful to discuss the study with your friends and family.

Thank you once again for reading this information sheet, and for considering participation in the research.

INFORMED CONSENT FORM (ICF)

Title of Protocol: Digital Diabetes Remission Trial (DIGEST)

Protocol Name: DIGEST

Participant Information Sheet (version/ date): **V2.1, 02 Nov 2022**

Participant Identification Number:

Please initial each statement if you agree

I confirm that I have read and understand the current patient information sheet for the above study. I have had the opportunity to ask questions and had these answered satisfactorily.

I understand that my participation is voluntary and that I am free to withdraw at any time, without giving any reason, without my medical care or legal rights being affected.

I understand that clinical research data collected about me may be shared by Lindus Health in an anonymised format for commercial use.

I understand that if I choose to withdraw or lose capacity to consent, data already collected will continue to be used.

I consent to my GP being informed of my participation in the study and I understand that the trial team may contact my GP about my ongoing participation in the trial.

I consent to provide blood samples which will be used for this research study only. I understand I will not gain any direct personal or financial benefit from them.

I understand that my name and contact details will be shared with third parties where required for the delivery of the trial, (eg. supply of equipment).

I understand that sections of any of my medical notes may be looked at by responsible individuals from Lindus Health, Habitual or companies working on their behalf or from regulatory authorities where it is relevant to my taking part in research. I give permission for these individuals to have access to my records.

INFORMED CONSENT FORM (ICF)

I agree to take part in the above study.

Participant name	Date & time	Signature

Study Nurse	Date & time	Signature

PART C – FAQs

When will I receive the next survey?

You will receive surveys every 2 weeks, on the same day of the week and time of day.

What if I start to experience side effects or a medical event?

Please complete the scheduled survey where you can report the side effect. You can also contact us to report any information you think we should be aware of.

Please call 999 if you are having a medical or mental health emergency.

What will happen to the results of the research study?

The results and findings may be published in scientific papers and presented at meetings. Your identity will not be disclosed in any of these.

What should I do if I haven't received all of my equipment?

If you're missing any of the equipment, please let us know by emailing digest@lindushealth.com or calling us on 020 8609 4690.

Where can I download the Habitual App?

The Habitual App is available to download for free for all plan participants from the Apple and Play stores.

When do I stop taking my diabetic medications?

These should be stopped on the day you start your new total diet replacement meals. You must obtain approval from your GP before stopping your diabetes medication.

What if I fail to fully adhere to the Habitual Total Diet Replacement?

The Habitual App will guide and support you to adhere to the programme by using techniques which will help to change the way you think about nutrition, mood, and motivation.

However, if you do have a meal which is not in the Habitual Programme, you can continue with the trial (completing surveys, inputting measurements etc). If you are finding the programme challenging, please open the Habitual App and chat to someone on the patient care team.

What shall I do if I run out of the Habitual meal kits?

A month's supply of meal kits (chosen by you) will be delivered at the start of each month. When your box is shipped, you will receive tracking information via email. If you're having any issues tracking your delivery, please reach out to us at hello@tryhabitual.com with details of your order including your name and address.

Will I be hungry?

You may be a bit peckish during the first few days, while your body is adjusting to the reduced calorie intake, but after that you will feel surprisingly full!

This is because during total diet replacement, your body goes into a state of mild ketosis. Which has an effect which makes you feel full. There is also research that an all-liquid diet increases satiety, meaning that you will feel fuller than if you were eating the same amount of solid food.

What if I forget to check my blood pressure/weight/waist circumference?
You will receive email reminders on the day your surveys are due to remind you to take your measurements.

What do I do if I think my blood pressure is high or low?
If you are in the Habitual programme group, you should have been emailed a blood pressure traffic light system which guides you on your blood pressure readings and informs you of what actions to take. If you cannot find this guide, please email digest@lindushealth.com to request a new guide.

If you are ever worried about your blood pressure, you can always contact us.

Further information and contact details
If you require further information about being in a clinical study, the following link may assist you. It provides information about how clinical trials are run and what to expect if you take part in a trial http://www.nhs.uk/conditions/Clinical-trials/Pages/Introduction.aspx

If you would like to know more about this study, you can contact the study team who will explain more about the study and discuss any questions that you have.

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