ReDIRECT Protocol Supplementary Material

Supplementary Material 1: ReDIRECT participant information sheet

Supplementary Material 2: ReDIRECT Consent Form

PARTICIPANT INFORMATION SHEET ReDIRECT: Remote Diet Intervention to REduce long COVID symptoms Trial	
IRAS Number: 304075	

Invitation to take part in a research study

We would like to invite you to take part in a new research study which aims to find out whether an evidence-based remote weight loss programme can help alleviate symptoms of Long COVID in people living with overweight and obesity. We hope that our results will help to improve the range of treatments available to people living with Long COVID.

This form will provide you with all the information about the study. It is important that you read and understand the study information below before deciding if you wish to participate and before giving consent to participate. Please ask any questions you may have about this study.

One of our research team will go through the information sheet with you and answer any questions you may have.

What is the aim of the study?

Around 10% of people with COVID-19 have symptoms that last for 12 weeks or longer – this is termed as having Long COVID. Long COVID symptoms are more likely to affect people with overweight/obesity compared to the rest of the population. Weight management programmes in adults with overweight/obesity can reduce symptoms such as fatigue, breathlessness and pain, however we do not know how effective intentional weight loss is on reducing Long COVID symptoms.

The aim of this project is therefore to test the effectiveness of a well-established professional weight management programme in people with Long COVID.

Why am I being invited to take part?

You are being asked to participate in this research study because you have Long COVID and may benefit from a weight management programme. Up to 200 patients across the country are expected to take part in the study.

Do I have to take part?

No. Your participation in this research study is voluntary. If you do not wish to participate this will not affect any current or future medical treatment you receive. You are free to withdraw your participation in this research study at any time without giving a reason, and without incurring any bad feelings. If you do decide to take part, you will be asked to sign a consent form stating that you understand what the research involves and that you agree to take part in the study.

Who will be suitable to take part in the study?

- People with Long COVID symptoms persisting >3months before first recruitment contact, not currently hospitalised;
- People who are aged 18 years or above;
- People with body mass index (BMI) above 27 kg/m^2 (or above 25 for people from Asian ethnicities)

Who will not be suitable to take part in the study?

- People who have had lengthy hospitalisations (>10 days) or intensive care unit (ICU) admissions related to COVID-19;
- People who are currently on insulin or anti-obesity drugs;
- People who have had a proven myocardial infarction within the last 6 months;
- People with severe mental illness (including severe depression and eating disorder);
- Women who are pregnant or considering pregnancy;
- People who have a history of substance abuse;
- People with an active illness likely to cause a change in weight;
- People who underwent bariatric surgery within the last 3 years or are planning bariatric surgery;
- People with advanced kidney problems (eGFR < 50), gallstones or pancreatitis;
- People currently participating in another clinical research trial likely to affect diet or weight change;
- People with learning disabilities;
- People who are unable to understand English (written or verbal).

What will taking part in the study involve?

This study is a randomised controlled trial. This means that you will be randomly allocated (by a computer programme) to one of two groups:

- Either immediate entry to a remote structured weight management programme, which includes an initial period of total diet replacement (soups and shakes), followed by carefully managed food reintroduction and then weight loss maintenance to enable you to manage your weight in the long term,
- Or "delayed entry", after 6 months, to the structured weight management programme described above.

Both groups will undergo the measurements described below.

If you agree to take part in the study, you will be consented and enrolled by a study researcher based in the University of Glasgow. This study is entirely "remote": there is no need to travel to a research centre or a hospital, and you can remain at home for the duration of the study. You will receive a set of scales and a blood pressure monitor (yours to keep once the study is over), and will be asked to report measurements of weight, height, blood pressure and physical activity. You will also be asked to complete questionnaires to name and rate your Long COVID symptoms, as well as questionnaires to assess your demographics, medical history, medications, health, and overall enjoyment of life.

Following this, you will be randomly allocated to receive 12-months treatment on the Counterweight-Plus/DiRECT diet weight management programme, which is delivered online by Counterweight Ltd with personal video/telephone support contact. Around 100 participants will start the programme immediately following their first appointment, with the remaining 100 participants being offered access to the programme after a 6-month delay. If you are allocated to the "delayed entry" arm, you will still follow the visit schedule shown below in the blue diagram. You will have an additional two visits compared to someone who is allocated to the "immediate entry" arm.

When you start the weight management programme, you will be asked to do two things:

1. stop eating your usual food and meals and instead start a Total Diet Replacement Plan of porridge, soups, and shakes for 12 weeks, with the aim of achieving your maximum potential weight loss. The porridge, soups, and shakes will be provided for you free of charge as part of the study. These come in sachets that will require you to add either cold water or hot water from a kettle to make them into a meal.
2. stop taking your antihypertensive and diabetes tablets, if you usually take any. This is following a well-established protocol and is necessary because your blood pressure and blood glucose will fall during active weight loss. We will inform your GP of this change and can discuss any concerns that you or your GP have about this.

You will be provided with the Counterweight app, for recording measurements, e.g. weight, blood pressure etc, and provided with weekly educational content. During this 12-week period you will also be supported and given advice by a specialist Counterweight dietitian, with monthly online/telephone appointments. There will also be an option of additional support via an app, through a chat function.

After 12 weeks on the soups and shakes, you will be helped to reintroduce normal foods into your diet gradually over the next 8 weeks. During this time, you will continue to record measurements, and be provided with weekly educational content. You will also continue to have monthly online/telephone appointments with your specialist Counterweight dietitian. There will also still be an option of additional support via an app, through a chat function.

The initial 2 phases of the programme aim to achieve at least 15-20 kg (2-3 stones) weight loss. Once the food re-introduction phase is completed, you will enter the weight loss maintenance programme to learn how to maintain your new lower weight while enjoying a variety of foods. You will continue to be supported by your specialist Counterweight dietitian and offered monthly online/telephone appointments up to 12 months. You will continue to be provided with educational content/advice to help maintain your weight loss which will include goal setting, self-monitoring, physical activity, relapse prevention if your weight tends to rise again, and nutrition education.

Review appointments with the dietitian will take place online or over the telephone; your measurements (diet, weight, blood pressure, and other lab measurements you may have received from your GP, such as blood glucose or glycated haemoglobin) and your medication will be reviewed and any changes to this recorded. In some cases, your prescribed medication may need to be updated or changed to ensure that it is safe for you to participate in the weight management programme, as any rapid weight loss may impact upon how your medications work. The study dietitians will liaise with your GP about changes to your prescribed medications if these are required, and no changes to your medications will be made without your permission.

Independently, measurements will be taken on a maximum of 7 occasions **at study visits held online or on the phone**.

For both groups:

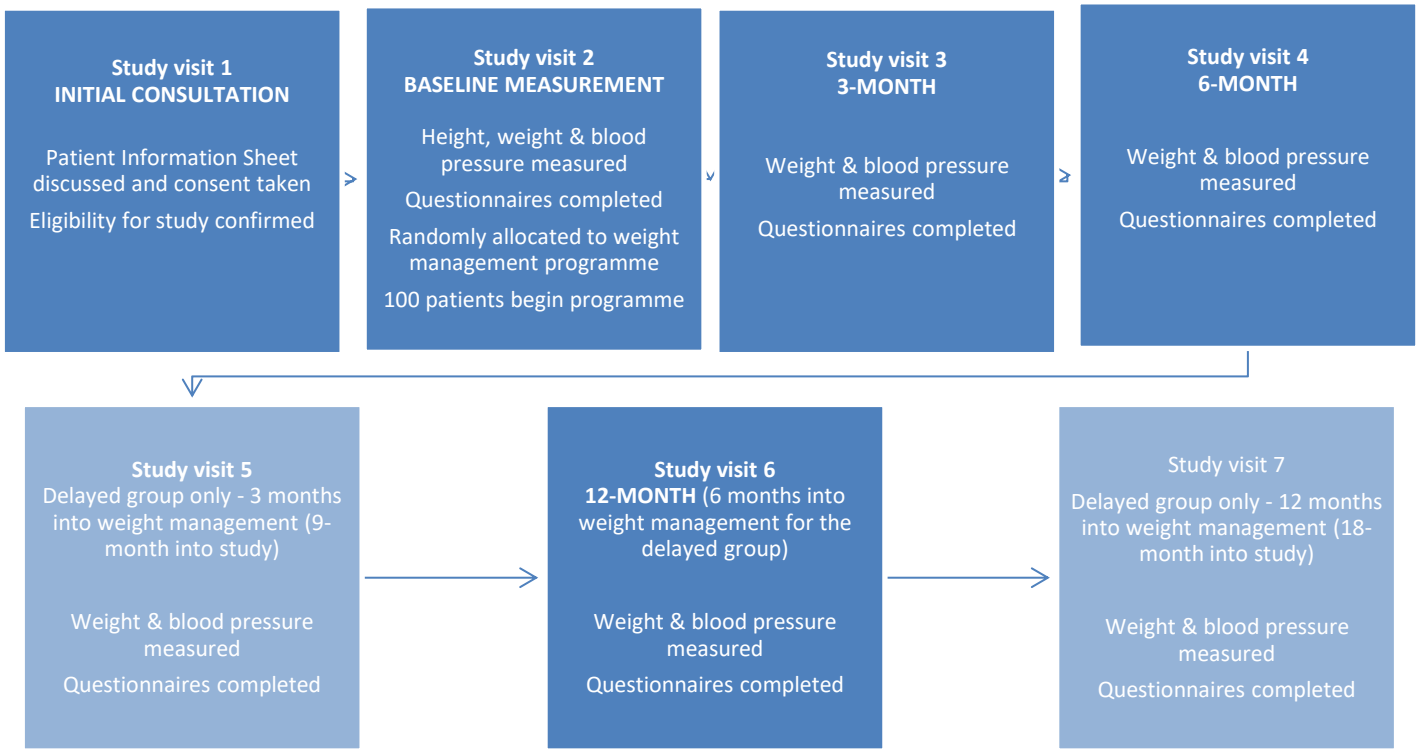
1. an initial consultation,
2. measurements at the start of the study,
3. 3-months after enrolment
4. 6-months after enrolment
5. 12-months visit at the end of the weight management programme.

For people in the delayed entry group

6. measurements at 3 months into the weight management programme (9-months after enrolment).
7. measurements at 6 months into the weight management programme (12-months after enrolment).

Your participation in the study would therefore last either 12-months, if you enter the weight management programme immediately (with 5 visits) or, 18-months, if you enter the programme after a 6-month delay (with 7 visits). We do not collect any blood or urine samples in this study.

The diagram below details what will happen at each of the study visits throughout the study:



Is there any long-term follow-up?

We would like to ask your permission to obtain information on your future health and wellbeing after the study has ended to determine the longer-term effects of this treatment. We can obtain this information by linking to records held by the Government (e.g. Registrar General) or NHS (e.g. health records, NHS Digital, eDRIS). We would also like to obtain information on your medication and any new

medical diagnoses/hospital admissions or new medical conditions that you may have been diagnosed with in the future, i.e., at 5- and 10 years, and potentially again up to 20 years, and again we can obtain this information through confidential electronic record linkage. This would not require us to contact you directly, so you would not be contacted for this after the end of the study. To do this we would have to retain some personal identifiers e.g., your name, date of birth, address, and postcode, as well as your NHS number.

You may also be asked to be interviewed about your views and experience of your treatment, including any difficulties you may have encountered. These interviews will happen three times: once the study has started, after 6-months, and after 12-months. There is a separate consent form and information sheet about these interviews, for those who are interested.

Will I be paid to take part in the study?
No. Participants will take part in the study on a voluntary basis. The total replacement diet sachets (containing your soups and shakes) will be provided free of charge. If you are happy to be interviewed about your experience of being involved in the study, you will be offered a £20 voucher for your time.

What are the potential risks from taking part in this research study?
There are very few health risks from following this weight management programme. Some people may experience some of the symptoms listed below during weight loss. These are usually temporary and go away once body weight is stable at a lower level.

- Constipation (we advise taking Fybogel to overcome this)
- Dizziness is possible when standing up suddenly. This is due to the body adjusting to a healthier, lower blood pressure and happens mainly in those who are taking medication to control their blood pressure. If this occurs, take more time standing up, and aim to remain well hydrated by drinking plenty of water.
- Gallstones – this is unusual and is most often a consequence of existing gallstones. The diet we are using contains some fat, which further minimises the risk of gallstone problems.
- Taking part will involve change in lifestyle and substantial time commitment. The weight management programme is challenging but you will be given full support throughout the study.

What are the potential benefits from this research study?
While we anticipate that participants in the study will lose weight, there is no guarantee of improvement in your health or success of the intervention. Others living with Long COVID and overweight/obesity in the future, but who are not participating in this study, may benefit from the results of this study.

What will happen to the results of this research study?
The study will provide valuable information to help inform future best support and treatment for people living with overweight/obesity who also have Long COVID and the results will be presented at national and international scientific conferences and published in scientific journals. You are welcome to contact the research team for a copy of the study results once they are published.

Who is funding the research?
The study is being funded by the UK National Institute of Health Research who will reimburse the University of Glasgow for the procedures to undertake the study. Neither the study researchers nor your own doctor are being paid for including you in the study.

Who has reviewed the study?
The study has been reviewed by and received a favourable opinion from the South East Scotland Research Ethics Committee 01.

What if I want to make a complaint?
If you have a concern about any aspect of the study then you should speak to the researchers in the first instance. If you remain unhappy and wish to complain formally you can do this through the NHS Complaints Procedure - ***complaints@ggc.scot.nhs.uk***

What if something goes wrong?
In the unlikely event, you are harmed from your participation in this study, medical treatment will be available to you. If this is due to someone's negligence then you may have grounds for a legal action for compensation against the study Sponsors, Greater Glasgow and Clyde Health Board, but you may have to pay your legal costs. The Sponsors have taken out insurance to cover this eventuality, and the normal complaints mechanisms will still be available to you.

Confidentiality and Data Protection
NHS Greater Glasgow and Clyde (NHS GG&C) are the sponsors for this study based in the United Kingdom. NHS Greater Glasgow and Clyde and the University of Glasgow will be using information from you and your medical records in order to undertake this study and will act as joint data controllers for this study. This means that we are responsible for looking after your information and using it properly. The University of Glasgow and NHS Greater Glasgow and Clyde Health Board will keep identifiable information about you for up to 20 years after the study has finished.

Your rights to access, change or move your information are limited, as we need to manage your information in specific ways in order for the research to be reliable and accurate. If you withdraw from the study, we will keep the information about you that we have already obtained. To safeguard your rights, we will use the minimum personally-identifiable information possible. You can find out more about how we use your information at https://www.hra.nhs.uk/information-about-patients, or by contacting your study team (details are provided below).

All information that is collected about you during the course of the research will be kept strictly confidential and will be processed in accordance with the EU General Data Protection Regulation (GDPR) (2018). This information will include your name, address, phone number, email address, NHS or CHI number, and your date of birth. Your personal information and all study data will be kept on file and securely stored in the University of Glasgow, with relevant data provided to Counterweight Ltd for the purpose of study procedures only. Counterweight Ltd will specifically have access to your contact details and address, in order to contact you to start the Counterweight-Plus programme. Counterweight Ltd also needs this information to send your meal replacement sachets and provide you with access to the App. Dietitians at Counterweight Ltd will also see restricted information about any health condition or medication relevant to the diet, in order to tailor their approach. Project managers at the NHS will be able to see your name and address to dispatch your study material (scales and blood pressure monitor). People who do not need to know who you are will not be able to see your name or contact details. Your signed consent form for this study will be scanned and uploaded to a separate secure database within the University of Glasgow.

Study data, images, and results may be provided to experts out with your NHS Board/Trust, government agencies, and published in medical literature or conferences; however, no information will be released through which you could be identified. Certain individuals from NHS Greater Glasgow and Clyde and regulatory organisations may look at your medical and research records to check that the research study is being carried out to an appropriate standard. The people who analyse the data and information generated by the study will not be able to identify you and will not be able to find out your name, NHS/CHI number, or contact details. The data generated by this study may also be utilised in future research projects which would be subject to funding and regulatory approvals. You have a right to privacy and the doctors involved in this research study will take all reasonable measures to protect the confidentiality of your records. 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.

Your GP will be informed of your participation in this study. By signing the consent form you will be agreeing that your GP can be notified and advised of any clinically relevant information obtained during the course of the trial.

If you choose to consent to long-term follow-up about your future wellbeing by data linkage, the University of Glasgow will provide your personal information to NHS departments to allow them to provide information on your health status. We would also like to let you know about other research studies that may be of interest to you and will ask for your permission to contact you about them. These studies would be subject to funding and regulatory approvals, and your consent for this is optional. If you choose to consent to be contacted about future research studies, your personal information will be used by the University of Glasgow to facilitate this. Any personal information provided for long-term record linkage or for contact about future research studies will be stored securely and kept strictly confidential.

Questions?

If you need additional information regarding this research study, your rights as a research patient, or in the event you develop a research-related problem, contact a member of the ReDIRECT Trial research team at ReDIRECT-study@glasgow.ac.uk

Contact for further information

If you wish to speak to someone not connected with the project, you can contact Professor Frances Mair. Email: Frances.Mair@glasgow.ac.uk

NHS Greater Glasgow and Clyde

ReDIRECT
Remote Diet Intervention to REduce long COVID symptoms Trial

University of Glasgow

PARTICIPANT INFORMED CONSENT FORM

ReDIRECT: Remote Diet Intervention to REduce long COVID symptoms Trial

Please Initial Boxes

1. I confirm that I have read and understood the patient information sheet version ___, dated _____, and that I have had any questions I have about the study answered. ☐
2. I understand that my participation is voluntary and that I am free to withdraw at any time, without giving any reason, and without my medical care or legal rights being affected. If I decide to stop participating in this study, I understand that any data already collected about me will be retained and used by the research team. ☐
3. I understand that relevant sections of my medical notes and data collected during the study may be looked at by authorised individuals from the study Sponsor, Counterweight Ltd, and from regulatory authorities where it is relevant to my taking part in this research. I give permission for these individuals to have access to my records. ☐
4. I understand that my GP will be informed of my participation in the study. ☐
5. I agree to my GP being contacted of any relevant information identified during the course of the trial ☐
6. I agree that my personal details can be retained by the study team at the University of Glasgow and Counterweight Ltd for use in relation to study procedures. ☐
7. I agree to my data being held on servers located within and out with the UK, including at the University of Glasgow, for research purposes. Access to data will be managed by the sponsor and the University of Glasgow in line with Data Protection Legislation. I understand that this form will be uploaded and saved to a secure server at the University of Glasgow. ☐
8. I understand that there is no formal program for compensating participants for any medical complications (e.g. gallstones) arising from this research. Medical treatment will be provided for complications as per routine care pathways. ☐
9. I agree that my de-identified data relating to the study may be retained for use in future research. ☐
10. I agree to take part in this study. ☐

	YES	NO
11. *OPTIONAL: I agree to be contacted and asked to participate in interviews about my views and experience of the study.*	☐	☐
12. *OPTIONAL: I agree to long term follow-up information by record linkage being collected on my future wellbeing and treatment from NHS and Government health records, and that my identifiable information will be retained for this purpose.*	☐	☐
13. *OPTIONAL: I agree to be contacted about future ethically approved research studies.*	☐	☐

_____	_____	_____
Patient Name (Print)	**Patient Signature**	**Date**
_____	_____	_____
Person Obtaining Consent (Print)	**Signature**	**Date**