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Pilot Study – The effect of an intestinal adsorbent on hydrogen and methane breath testing, in patients with abdominal and reflux symptoms, on long term proton pump inhibitor therapy

Title of Study

The effect of an intestinal adsorbent on hydrogen and methane breath testing, in patients with abdominal and reflux symptoms, on long term PPI therapy

Study Sites

The Functional Gut Clinic Manchester – 9th Floor, 73-79 King Street, Manchester, M2 4NG

Objective

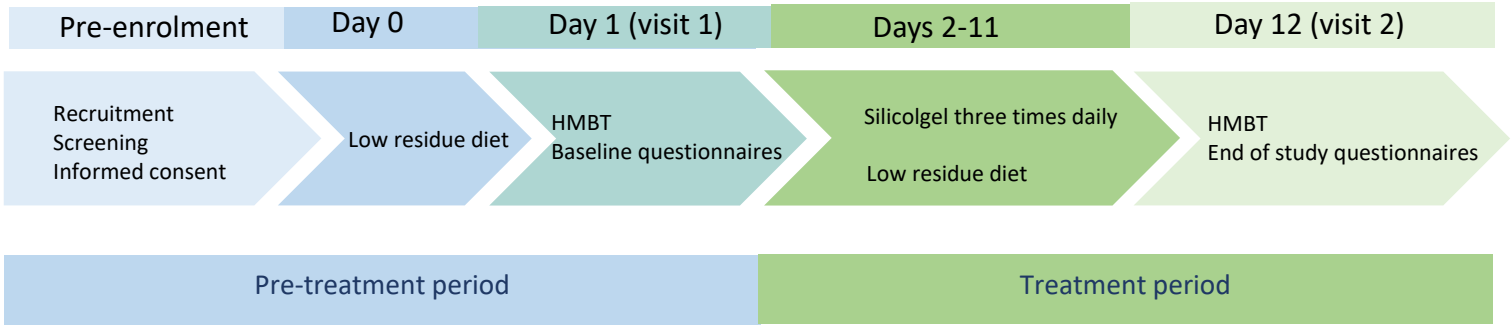
To determine the effect of Silicolgel on hydrogen and methane breath testing in patients on long term PPI therapy with reflux and abdominal symptoms.

Methodology

This protocol describes a pilot study, using an uncontrolled, open label single-armed design, consisting of two distinct periods (pre-treatment and treatment). Participants visiting a gastroenterologist at The Functional Gut Clinic or recruited through advertising on social media platforms should be eligible for the study as long as they have no concomitant exclusionary disease and meet inclusion criteria for the study.

This pilot study will be used to explore the question outlined in the objective and to determine the feasibility of carrying out a larger randomised controlled trial

Study timeline



Background

Proton pump inhibitors (PPIs) are the most commonly prescribed drugs worldwide and have shown impressive efficacy in the reduction of oesophageal mucosal damage associated with GORD and symptoms relating to GORD (1, 2). There is, however, growing evidence to show a large percentage of patients receiving long term PPI therapy, develop IBS type symptoms such as abdominal discomfort, pain, bloating, belching and altered bowel habit (3, 4). It has been proposed that the development of these symptoms may be linked to shifts in the location, concentration and species of gastrointestinal micro flora. Inhibition of gastric acid secretion, through PPI therapy, has been linked to small intestinal bacterial overgrowth in several studies (5-7). A meta-analysis interrogating the relationship between PPI use and SIBO, confirmed there was a significant relationship between PPI therapy and SIBO (8).

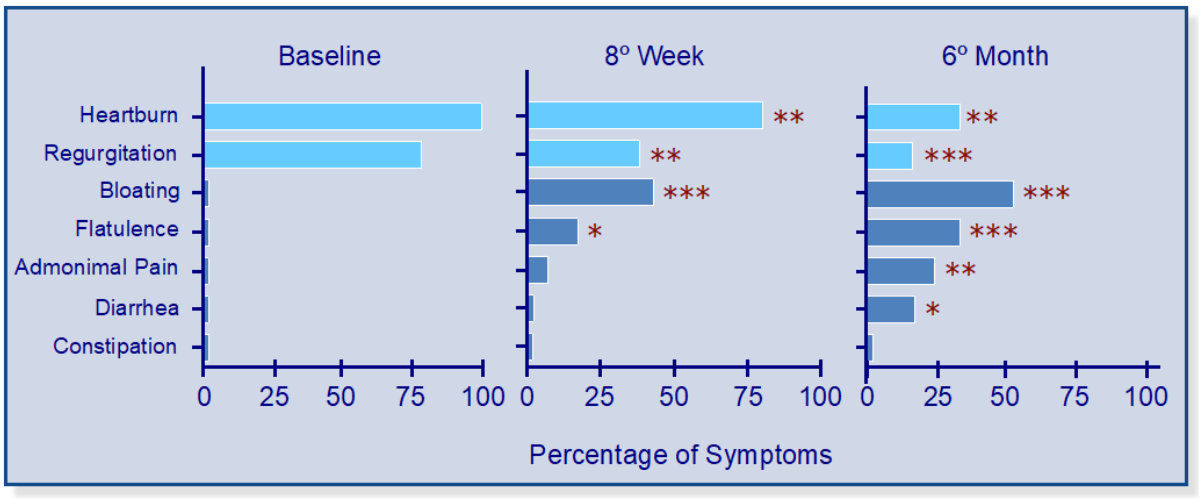


Figure 1 : Symptom pattern change in long term PPI users (*P<0.05, **p<0.01, ***p<0.001) (4).

SIBO is by definition a concentration of ≥1 × 10^5 coliform bacteria cfu per ml from a jejunal aspirate, however there is debate whether 1 × 10^3 cfu/ml may be more appropriate to define SIBO (9). Jejunal aspirate as a method of diagnosis is however expensive and highly invasive, therefore hydrogen and methane breath testing (HMBT) is most commonly used to diagnose SIBO in the clinical setting. HMBT utilises the gases produced by intestinal microflora to determine whether SIBO or dysbiosis is present in a patient. These microbiota not only produce gases during fermentation of ingested sugars, but other waste products, such as water and short chain fatty acids, which can alter conditions in the small bowel, causing troublesome abdominal symptoms (10).

Silicolgel is a liquid gel containing silicon dioxide as hydrated silicic acid in a colloidal form. The particles of polymeric Silicic acid are highly adsorptive due to large particle surface area and negatively charged surface hydroxyl groups. This allows Silicolgel, when ingested, to encompass large volumes of intestinal gases, inorganic molecules, water and organic molecules such as the waste products of bacterial fermentation. The efficacy of Silicolgel has been demonstrated in an (unpublished) study by Dr Erling Thom -Medstat Research, Lillestrom, Norway. Also an observational study of Silicea gel, a medical device with almost identical formulation to Silicolgel, demonstrated a significant reduction in both upper and lower abdominal symptoms over a 6 week treatment period (11).

This study has been designed to establish whether Silicolgel effects HMBT values and upper and lower GI symptoms, in patient's on long term PPIs, with persistent reflux and abdominal symptoms.

Proposed timeline

6-months to complete recruitment and lab analysis.

Ethical Considerations

The study will be submitted to the Greater Manchester Research Ethics Committee (REC) for approval.

Proposed budget

40 lactulose HMBT tests and analysis (£10,000); Administrative costs for writing and submitting regulatory approvals + calling patients, sending out kits and questionnaires £1000 – **Total costs - £11,000**

Statistical Methods

Sample size calculation: As this is a pilot study to determine proof of concept, a sample size of 20 will be used.

Statistical analysis:

Primary outcome: Mean change in cumulative total breath hydrogen and methane, from baseline HMBT to end of study HMBT, will be calculated statistically using 2 tailed Paired T-test.

Secondary outcomes:

- Difference between baseline and end of study IBS-SSS scores will be calculated statistically using 2 tailed Paired T-test.
- Difference between baseline and end of study reflux scores will be calculated statistically using 2 tailed Paired T-test.
- Change in bowel habit and abdominal symptoms from baseline to end of study as measured by daily bowel diaries

Study Timelines

Recruitment

Participants will be recruited through gastroenterology clinics at the Functional Gut Clinic as well as through advertisement on several social media platforms. If potential participants register interest, they will be provided with a patient information sheet and consent form to review for at least 24 hours. A screening questionnaire will be carried out to establish whether they are eligible to enter the study. If participants are eligible and have reviewed the study information, they will be enrolled into the study on giving a signature of informed consent.

Day 0

Once participants have enrolled on the study, they will arrange a date to visit the clinic to complete a hydrogen and methane breath test (HMBT), the test will be completed on day 1. The day before the trial, day 0, the participant will be required to follow a specific low residue diet as part of breath testing preparation (appendix 1).

Day 1

On day 1 of the trial, participants will visit The Functional Gut Clinic (FGC) to complete a HMBT following FGC protocol (appendix 2). Participants will also be asked to complete a Reflux questionnaire (appendix 3), IBS-SSS questionnaire (appendix 4) and Bristol stool questionnaire (appendix 5). Following completion of the HMBT and questionnaires, participants will be given a 10 day supply of the blinded product Silicolgel and provided with instructions on how to use the product (appendix 6).

Day 2-11

Participants will be asked to commence ingestion of Silicolgel on study days 2 – 11, as per instructions. Participants will take 15ml of Silicolgel three times daily, 1 hour before meals. On day 11 participants will be required to complete a low residue diet in preparation for HMBT on day 12.

Day 12 (end of study visit)

Participants will visit The Functional Gut Clinic (FGC) to carry out a repeat HMBT following FGC protocol (appendix 2). Participants will also be asked to repeat the Reflux questionnaire (appendix 3), IBS-SSS questionnaire (appendix 4) and bowel habit questionnaire (appendix 5). Completion of the repeat breath test and questionnaires will mark the end of the study for the patient.

Eligibility

Inclusion Criteria

1. Participant has provided written informed consent before participating in the study after being given a full description of the study and prior to any study-specific procedures being performed.
2. Patient has been taking PPI therapy for >6 months
3. Patient reports bloating ≥3 on screening questionnaire
4. Patient reports one of the following ≥3 on screening questionnaire - belching, heartburn, nausea, reflux sensation
5. Participant is a male or non-pregnant female and is age 18 years of age or above
6. Participant is able to communicate well with the Investigator and to comply with the requirements for the entire study.
7. Patient has capacity to understand written English
8. Patient agrees to follow pre-test diet for 24 hours before giving test sample (Appendix A).
9. Participant agrees to refrain from strenuous physical activity on the day of the breath test.
10. Participant agrees to refrain from smoking on the day of the breath test
11. Participant agrees to an overnight fast on the night before the breath test. Food and drink must be withheld until after all breath test samples have been taken.
12. Participant agrees to not take any probiotic for 7 days before the breath test.
13. Participant has a body mass index (BMI) between 18.5 and 34.9kg/m2 (bounds included).

Exclusion criteria

1. Participant reports using any prohibited medication, medical device or supplementation
2. Participant has taken antibiotics or undergone colonoscopy/sigmoidoscopy in the 4 weeks prior to enrolment.
3. Participant has a diagnosis of any organic gastrointestinal disease, including inflammatory bowel disease, coeliac disease and diverticulitis.
4. Participant has known mechanical obstruction of the GI tract
5. Participant has diabetes
6. Participant has any hepatic disease
7. Participant has any disease of the CNS
8. Participant is involved in this study as an Investigator, sub-Investigator, study coordinator, other study staff, or Sponsor member.
9. Participant has had previous abdominal or colorectal surgery except appendectomy, cholecystectomy, or hysterectomy.
10. Participant has previously taken Silicolgel in the past month
11. Participant has a known hypersensitivity to any of the ingredients of Silicolgel
12. Participant suffers regularly from constipation

13. Participant is involved in any other research projects either currently or during the previous month

Test Product, Planned Doses, Mode of Administration and duration of treatment

Silicolgel 15ml, oral administration. Total Participation is expected to last 12 days, with a 10-day treatment period. During the treatment period participants will take 15ml Silicolgel three times daily. Silicolgel should be taken one hour before meals. Silicolgel may be taken undiluted or diluted with water. Due to its inability to be absorbed into the blood stream and physical not pharmacological mechanism, SIlicolgel is considered a class IIa medical device according to the Medical Device Directive 93/42/EEC Annex rule 5.

The bottle must be shaken before each administration. The bottle of Silicolgel should be stored above 2^{o}C. After opening the bottle, the product should be consumed within 3 months, and it should not be used after the date given on the label.

Blinding procedure

All participants will be blinded to the study device. Silicolgel bottles will be labelled without any Silicolgel branding or product ingredients. Study participants will be made aware that the product is a CE marked medical device that works via intestinal adsorption. Any potential side effects of the product will also be disclosed to the patient.

Study Outcome Assessments

Primary outcome assessment

Mean change in cumulative total breath hydrogen and methane, will be determined from baseline HMBT to end of study HMBT. Cumulative total hydrogen and cumulative total methane will be calculated independently of one each other. Breath hydrogen and breath methane will be measured in units of parts per million (ppm). Statistical significance will be determined using a paired t-test ($p<0.05$).

Each HMBT samples will be analysed using gas chromatography analysis on the day of the breath test being carried out. Breath carbon dioxide will also be measured in order to verify the validity of each sample and apply a correction factor. A correction factor above 2.5 ($CO2 < 2\%$) is considered an invalid sample.

Secondary outcome assessment

Reflux Questionnaire (Appendix 3)

The Reflux Questionnaire is a validated questionnaire that will be used to determine severity of upper GI symptoms. The questionnaire is made up of 16 questions, each scored 0 to 5. The total of these 16 questions will be calculated to determine symptom severity. Mean difference in scores from baseline reflux questionnaire and end of study reflux questionnaire will be determined using a paired t-test, to determine significance ($p<0.05$).

Irritable Bowel Syndrome Symptom Severity Score (IBS-SSS) (Appendix 4)

The IBS-SSS is a validated questionnaire that will be used to determine severity of abdominal and bowel symptoms. The questionnaire is comprised of 7 questions, 5 of which are scored from 0 to 10. The total of these 5 questions will be calculated and multiplied by 10 to determine symptom severity. Mean difference in scores from baseline IBS-SSS and end of study IBS-SSS will be determined using a paired t-test, to determine significance ($p<0.05$).

Bristol stool chart (Appendix 5)

The Bristol stool chart will be used by participants stool frequency and consistency. Participants will be asked to identify their stool type during the past 7 days using the chart and describe their stool frequency. Mean difference in stool frequency and consistency from baseline and end of study will be determined using a paired t-test, to determine significance ($p<0.05$).

Safety Outcome Assessments

Definitions

Types of AEs associated with medical devices and applicable for this study are defined in accordance with the European Commission guidelines on medical devices.

Adverse events

Any untoward medical occurrence, unintended disease or injury or any untoward clinical signs (including an abnormal laboratory finding) in subjects, users or other persons whether or not related to the investigational medical device.

NOTE 1: This includes events related to the procedures involved (any procedure in the clinical investigation plan).
NOTE2: For users or other persons this is restricted to events related to the investigational medical device.

Adverse Device Effect (ADE)

AE related to the use of an investigational medical device.
NOTE 1: This includes any AE resulting from insufficiencies or inadequacies in the instructions for use, the deployment, the implantation, the installation, the operation, or any malfunction of the investigational medical device.
NOTE 2: This includes any event that is a result of a use error or intentional misuse

Serious Adverse Device Effect (SADE)

Adverse device effect that has resulted in any of the consequences characteristic of a serious AE.

Serious Adverse Event

AE that:
a) led to a death,
b) led to a serious deterioration in health that either:
1. resulted in a life-threatening illness or injury, or
2. resulted in a permanent impairment of a body structure or a body function, or
3. required in-patient hospitalisation or prolongation of existing hospitalisation, or
4. resulted in medical or surgical intervention to prevent life threatening illness or injury or permanent impairment to a body structure or a body function.
c) led to foetal distress, foetal death or a congenital abnormality or birth defect.

NOTE 1: This includes device deficiencies that might have led to a SAE if a) suitable action had not been taken or b) intervention had not been made or c) if circumstances had been less fortunate. These are handled under the SAE reporting system.
NOTE 2: A planned hospitalisation for pre-existing condition, or a procedure required by the Clinical Investigation Plan, without a serious deterioration in health, is not considered to be a SAE.

Unanticipated Serious Adverse Device Effect (USADE)

Serious adverse device effect which by its nature, incidence, severity or outcome has not been identified in the current version of the risk analysis report or product safety information.

NOTE: Anticipated: an effect which by its nature, incidence, severity or outcome has been previously identified in the risk analysis report

Expected Adverse Events and Adverse Events of Special Interest

According to the standard Package Information Leaflet, SIlicolgel does not have any known side effects or adverse events.

Reporting and reporting of adverse events

Investigational procedures and treatment

AEs will be collected throughout the study from screening visit until week 24. If an AE is reported by the patient, the relationship of the event to the study treatment or procedures should be assessed by the local PI, or a delegated sub-PI or nurse. The following information will be recorded for all AEs:

- Medical term of the AE (SNOMED CT terminology)
- Start date and date of resolution
- Seriousness
- Severity
- Study treatment action
- Outcome
- Relationship with the study treatment
- Expectedness

SADEs, SAEs, and USADEs should always be recorded in the CRF and reported to the Sponsor using the Sponsor's SAE reporting form. Any SAEs that occur during the screening period that resulted from the administration of any study procedures and are unexpected, should also be reported. The form should be emailed to enquiries@fwmedical.co.uk (Jill Stuart) within 24 hours of the site team becoming aware of the event, and the Principle Investigator should be copied in this email (anthony@thefunctionalgutclinic.com). If the site does not receive an acknowledgement of the receipt of the report within 24 hours, they should immediately contact the Principle investigator.

The Sponsor should also report all serious adverse events, whether initially considered to be device related or not, immediately to the MHRA

Concomitant medication, medical device or supplementation

Restrictions regarding concomitant medicines are described below. All concomitant medicines taken from the time of informed consent at the Screening Visit through the End of Treatment Visit will be recorded on the appropriate concomitant medicine page of the participant's CRF.

28 days prior to Visit 1

1) Participants must have not taken any oral or parenteral antibiotic medication at least 28 days prior to visit 1. Participants must not commence any antibiotic therapy from signature of informed consent until after the end of study visit or have withdrawn participation
2) Participants must not have used Silicolgel at least 28 days prior to visit 1.

7 days prior to visit 1

1) Participants must not have used laxative therapy at least 7 days prior to visit 1 and not use any laxative therapy for the duration of the study.
2) Participants must not have taken a probiotic product at least 7 days prior to visit 1 and must refrain from using any probiotics until after the end of study visit or have withdrawn participation.

From Day 0 to end study

All medicines, medical devices and supplementation listed in this section are excluded from day 0 for the duration of the study.

1) Any investigational drugs.
2) All narcotics either alone or in combination (e.g., tramadol, codeine, morphine, propoxyphene, loperamide, diphenoxylate, and paregoric).
3) Any medicine that is known to cause diarrhoea
4) Any over-the-counter or prescription laxative, suppository, or enema.
5) Any anti-spasmodic medication
6) Any other medical advice with adsorptive properties
7) Any medical device affecting gastrointestinal motility
8) Antidepressants unless the participant has been on a stable dose for at least 1 month before visit 1 and there is no plan to change dose during the investigation.

Study Operations

Good Clinical Practice

This study will be conducted according to the protocol and in compliance with ICH GCP, the ethical principles stated in the Declaration of Helsinki, and other applicable regulatory requirements.

The Investigator confirms the above by signing the protocol.

Termination of Participants

Participants will be informed that they have the right to withdraw from the study at any time for any reason, without prejudice to their medical care. The Investigator will make reasonable efforts to keep each participant in the study. However, if the Investigator removes a participant from the study or if the participant declines further participation, the evaluations required at the end of study visit should be performed if possible. All evaluations and observations, together with the description of the reason(s) for study withdrawal, must be recorded on the appropriate page of the participant's CRF.

The following are justifiable reasons for the Investigator to withdraw a participant from the study:
• The occurrence of an AE;
• Withdrawal of consent;
• Unforeseen events: any event that, based on the Investigator's judgement, makes further treatment inadvisable;
• Serious violation of the study (including persistent participant attendance failure and non-compliance).

An effort must be made to determine why a participant fails to return for the necessary visits or is dropped from the study. Regardless of the reason for termination, all data available for the participant at the time of discontinuation of follow-up should be recorded where applicable on the CRF. All reasons for discontinuation of treatment should be documented.

Financial Disclosure

Relevant financial disclosures will be included in the submission to the ethical committee.

Essential Documents

1) Current, signed curricula vitae of the Investigator and all sub-Investigators;
2) Copy of current medical license of the Investigator and all sub-Investigators (as applicable);
3) Copy of Research Ethics Committee (REC) approved Participant information sheet;
4) Evidence of Sponsor insurance or indemnity;
5) Copy of the REC approval letter for the protocol and informed consent;
6) Copy of the REC-approved informed consent document to be used;
7) Copy of the REC approval of recruitment advertising (if applicable);
8) A list of REC members and their qualifications, and a description of the committee's working procedures.

During the study, the Investigator must maintain the following essential/administrative documents related to the study:

1) Copy of the signed Protocol Signature Page
2) Copy of financial disclosure form(s) for the Investigator and all sub-Investigators
3) Curricula vitae of any new Investigator(s) and/or sub-Investigators involved in the study
4) Adverse Event Reports
5) Updates of laboratory/technical procedures/tests
    a. Normal value(s)/range(s)
    b. Certification
    c. Accreditation
    d. Established quality control and/or external quality assessment
    e. Other validation (where required)
6) Responsibility Log
7) Other logs (screening, enrolment, etc.)
8) Signed ICFs
9) Validated questionnaires
10) CRFs

Case Report Forms and data management

All data relating to the study will be recorded in the participant's CRF. The CRFs are to be completed at the time of the participant's visit, except for results of tests performed outside the Investigator's office. CRF data should indicate the participant's participation in the study and should document the dates and details of study procedures, AEs, all observations, and participant status. The Investigator is responsible for verifying that all data entries on the CRFs are accurate and correct and ensure that all data are entered in a timely manner, as soon as possible after information is collected. An explanation should be provided for all missing data. The Investigator must provide his or her formal approval of all the information on the CRFs and changes to the CRFs to endorse the final submitted data for the participants for which he or she is responsible.

The CRFs will be in the form of paper and will be stored initially in locked filing cabinets in the Functional Gut Clinic and subsequently archived.

A record of participant screen failures will be maintained for participants who do not qualify for enrolment, including the reason for the failure

Reference List

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Appendix 1 – Patient Information sheet for HMBT and patient preparation

Hydrogen & Methane Breath Test - Small Intestinal Bacterial Overgrowth (SIBO)

What is a Hydrogen & Methane Breath Test?

Breath testing is used to detect abnormal growth of bacteria within the small intestine, or small intestinal bacterial overgrowth (SIBO). SIBO can cause a variety of symptoms including diarrhoea, nausea, bloating, gas and abdominal cramps.

The breath test detects hydrogen and methane, which are gases produced by intestinal bacteria. Bacteria normally found in the large intestine produce these gases through fermentation of carbohydrates or sugars. Some of the gas produced by bacteria is absorbed by the intestine whereby it enters the blood and is transported to the lungs. The gases are then exhaled via the lungs through breathing and can be collected in a tube for analysis.

In SIBO, the small intestinal bacteria ferment the sugars before the body has had chance to digest them and this produces an early rise in gas, detected in the breath.

What are the benefits of having this test?

This test will help your doctor understand whether SIBO is causing your symptoms and aid them in determining what treatment is best suited to you.

Are there any risks associated with this test?

There are no real risks associated with this test. You may experience some of your usual symptoms throughout the test, this is normal.

What preparation is required for this test?

For four weeks before the test—

Do not take any antibiotics

For one week before the test—

Do not take any:

- Laxatives or Stool Softeners – Movicol, Dulcolax, Senna etc
- Stool Bulking Agents – Metamucil, Citrucel etc
- Motility Agents – Prucalopride, Linaclotide etc
- Probiotics – VSL#3, Actimel, Yakult etc
- Intestinal adsorbants

You can continue taking any other essential medicines.

Additionally, there must be a period of one week between any tests which require cleansing of the bowel e.g. colonoscopy, barium enema, before having a breath test.

The day before the test—

You must follow the 'white food diet' which consists of **only** the following foods and drinks:

- Plain white bread
- Plain white rice
- White potatoes (no skin)
- Baked/Grilled white meat or white fish (no oily fish)
- Maximum of 2 eggs
- Water
- Non-flavoured black coffee (no milk)
- Non-flavoured black tea (no milk and no herbal teas)
- 1tbsp butter/margarine/oil
- Salt to flavour food

Do not eat or drink anything else, eating prohibited foods could give false results for the test.

For 12 hours before the test—

Apart from water you must stop eating and drinking and fast for 12 hours before the test.

The day of your test—

Apart from up to 500ml/1 pint of water you should **not** eat or drink anything in the morning before your test.

Do **not** smoke or chew gum on the morning of the test.

You may take your essential medications with a small amount of water but do not take anything that could affect your bowel (see previous list).

You may brush your teeth, but please try not to swallow any toothpaste.

If you are diabetic requiring insulin or diabetes medicine, please contact us for information about adjusting your morning dose.

What happens during the test?

At your appointment the physiologist will explain how the test works, what SIBO is and ask you to describe your symptoms. Please feel free to ask any questions you may have about the test procedure at this stage.

You will then be asked to give a baseline breath sample by blowing into a test tube through a straw.

The test substrate, which is a non-digestible sugar, will be mixed with water and given to you to drink.

Breath samples will then be collected every 15 minutes. During this time, you will be invited to sit in our waiting room which has wi-fi and television. Please do not eat, chew gum, smoke, sleep or exercise during your test. Throughout the test the physiologist will note any symptoms that occur.

The test will last 2 hours and 15 minutes.

You may return to your usual diet and activity after the test

Appendix 2

HYDROGEN & METHANE BREATH TEST PROTOCOL

PURPOSE
To provide guidelines for all staff assisting with or performing this procedure.

POLICY
Hydrogen & Methane Breath Testing

PROCEDURE

INDICATIONS:
1. Investigation of Small Intestinal Bacterial Overgrowth
2. Investigation of Colonic Dysbiosis

ABSOLUTE CONTRAINDICATIONS
1. Post-prandial hypoglycaemia
2. Failure to give consent

RELATIVE CONTRAINDICATIONS

1. Failure of patient to follow pre-study diet
2. Non-adherence to cessation of smoking
3. Failure of patient to fast for 12 hours prior to the study
4. Antibiotic therapy in the previous 4 weeks

EQUIPMENT

- Functional Gut Diagnostics Breath Test Kit containing
    - 10 collection tubes
    - 10 collection tube labels
    - 1 straw
    - 1 substrate sachet (lactulose/glucose/lactose/fructose)
    - 2 bubble wrap pouches
    - Symptoms score sheet
- Consent form and clinical history sheet
- Plastic cups
- Drinking water

Before the procedure

- Check the patient details including a contact telephone number

- Obtain the patients history using the clinical history sheet. This should include: symptoms, duration, previous medical and surgical history, medication, previous treatments/diagnostic procedures and any known allergies
- Confirm the patient has stopped required medication, followed the pre-study diet and fasted for the past 12 hours.
- Explain the test procedure, benefits and risk of the test and obtain written consent using the consent form.

Procedure Method

- Collect a baseline breath sample by asking the patient to insert the straw halfway into the tube and breath through the straw until they see condensation. They can then remove the straw and replace the cap.
- Ensure to fill out all the information on the collection tube label and adhere to each tube after sample collection.
- Ask the patient if they are experiencing any symptoms (specifically bloating, nausea or abdominal pain) at the beginning of the test. Ask them to rate each symptom on a scale of 0 – 10 (with 0 being no symptoms and 10 being severe symptoms) and record the results on the symptom score sheet.
- Mix the substrate sachet with 200ml drinking water and instruct the patient to drink it.
- Continue to take samples and note symptoms every 15 minutes until 10 samples have been collected (full test duration is 2 hours and 15 minutes). Invite the patient to sit in the waiting room for the rest of their test.
- When collecting the 10^{th} sample, invite the patient back into the clinic room and explain that results will be sent out electronically to the referring doctor in 48 hours.
- Ask if they have any questions

After the procedure

- Ensure all 10 collection tubes are labelled correctly and pack them into the bubble wrap pouches. Put the pouches and the symptom sheet back into the kit box and post back to Functional Gut Diagnostics.
- Dispose of the plastic cup and straw.

Reporting the results

- Once the Functional Gut Diagnostics technical report is uploaded to DGL, an TFGC cover letter will be written using the report template. This will be saved and sent as a PDF file.
- Templates are available on each TFGC laptop/ computer on the desktop and have been emailed to each member of staff at TFGC.

Clinic risk assessment

- A clinical risk assessment has been made regarding this procedure which is available as a hard copy in the Clinic Registry folder and has been emailed to each member of staff at TFGC.

How the results will be communicated?

- If the patient consents, during the consent process, to allowing TFGC to email reports to the referring consultant then this will be the only option.

- If the referrer or patient requests another method then the use of fax will be used.
- TFGC is a diagnostic clinic and all reports/results will be sent to the referring consultant.

Appendix 3 – Reflux Questionnaire

Reflux Questionnaire

Patient Name: **Date:**

GERD-HRQL Questionnaire

□ On PPIs □ Off PPIs If off, for how long? _____ days/weeks/months

Scale:
0 = No symptom
1 = Symptoms noticeable but not bothersome
2 = Symptoms noticeable but not bothersome everyday
3 = Symptoms bothersome everyday
4 = Symptoms affect daily activity
5 = Symptoms are incapacitating

Please check the box to the right of each question to best describe your experience over the past 2 weeks;

1.	How bad is the heartburn?	□0 □1 □2 □3 □4 □5
2.	How is the heartburn when lying down?	□0 □1 □2 □3 □4 □5
3.	How bad is the heartburn when standing up?	□0 □1 □2 □3 □4 □5
4.	Heartburn after meals?	□0 □1 □2 □3 □4 □5
5.	Does heartburn change your diet?	□0 □1 □2 □3 □4 □5
6.	Does heartburn wake you from sleep?	□0 □1 □2 □3 □4 □5

Heartburn score = ☐

7.	How bad is the regurgitation?	□0 □1 □2 □3 □4 □5
8.	Regurgitation when lying down?	□0 □1 □2 □3 □4 □5
9.	Regurgitation when standing up?	□0 □1 □2 □3 □4 □5
10.	Regurgitation after meals?	□0 □1 □2 □3 □4 □5
11.	Does regurgitation change your diet?	□0 □1 □2 □3 □4 □5
12.	Does regurgitation wake you from sleep?	□0 □1 □2 □3 □4 □5

Regurgitation score = ☐

13.	Do you have difficulty swallowing?	□0 □1 □2 □3 □4 □5
		□0 □1 □2 □3 □4 □5
		□0 □1 □2 □3 □4 □5

14. Do you have pain with swallowing?
15. If you take medication, does this affect your daily life?
16. How satisfied are you with your present condition?

□ Satisfied □ Neutral □ Dissatisfied

Total score (inc. heartburn and regurgitation scores) = ☐

Appendix 4 – Irritable Bowel Syndrome Symptom Severity Score (IBS-SSS)

IRRITABLE BOWEL SYNDROME SYMPTOM SEVERITY SCORE (IBS-SSS)

1. A. Do you currently (in the last month) suffer from abdominal (tummy) pain?

☐ Yes
☐ No

B. If yes, how severe is your abdominal (tummy) pain? Please indicate a number from 0 to 10, with 0 meaning "no pain" and 10 meaning "very severe."

no pain 0 1 2 3 4 5 6 7 8 9 10 very severe

C. Please enter the number of times that you get the pain every 10 days. For example, if you choose 4 it means that you get pain 4 out of 10 days. If you get pain every day enter 10.

no days with pain 0 1 2 3 4 5 6 7 8 9 10 10 days with pain

2. A. Do you currently suffer from abdominal distention *(bloating, swollen or tight tummy)? *Women, please ignore distention related to your period.

☐ Yes
☐ No

B. If yes, how severe is your abdominal distention/tightness? Please indicate a number from 0 to 10, with 0 meaning "no distention" and 10 meaning "very severe."

no distention 0 1 2 3 4 5 6 7 8 9 10 very severe

3. How dissatisfied are you with your bowel habits? Please indicate a number from 0 to 10, with 0 meaning "very happy" and 10 meaning "very unhappy."

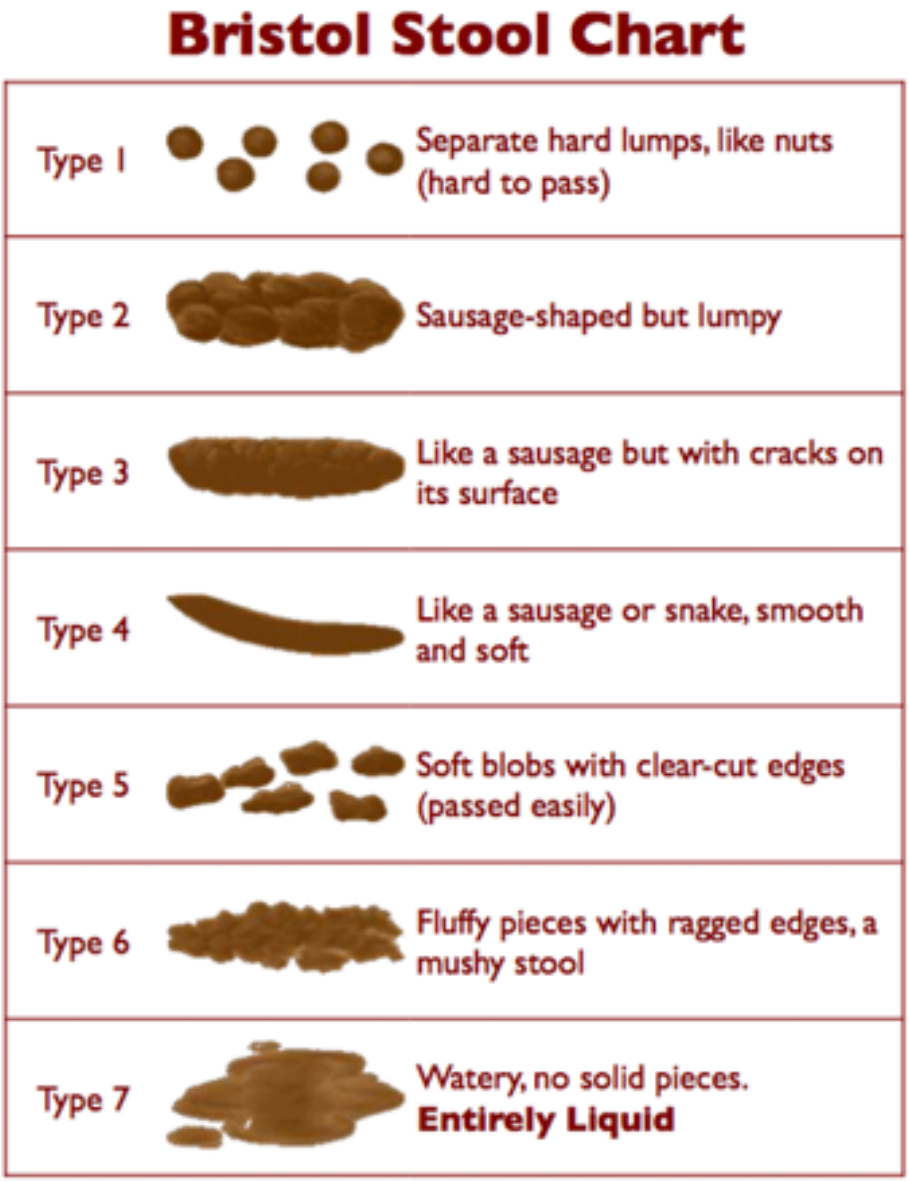
very happy 0 1 2 3 4 5 6 7 8 9 10 very unhappy

4. Please indicate how much abdominal pain or discomfort or altered bowel habits are affecting or interfering with your life in general. Please indicate a number from 0 to 10, with 0 meaning "not at all" and 10 meaning "completely."

not at all 0 1 2 3 4 5 6 7 8 9 10 completely

Total x10 = Score = ☐

Appendix 5 – Bristol Stool Questionnaire



1) Over the last 7 days, how would you describe the frequency of your bowel movements?

- ☐ More than 3 a day
- ☐ 1-3 a day
- ☐ 3-6 a week
- ☐ Less than 3 a week

2) Using the Bristol Stool Chart above, how would you describe your average bowel movement over the last 7 days?

☐ Type 1 ☐ Type 2 ☐ Type 3 ☐ Type 4 ☐ Type 5 ☐ Type 6 ☐ Type 7