BOOST Study

Participant Information Sheet

V1.3

You are being invited to take part in the BOOST study. Before you decide, it is important for you to understand why the research is being done and what it will involve. Please take time to read the following information carefully and discuss it with others, if you wish. Please ask us if there is anything that is not clear or if you would like more information. Take as much time as you need to decide whether or not you wish to take part.

Thank you for reading this information sheet.

Study title: A randomised controlled trial of a nutritional supplement (HM**B**) compared to placeb**o** (maltodextrin) to impr**o**ve muscle **st**rength and function in people with advanced liver cirrhosis: **BOOST**

What is the purpose of the study?

This study aims to test whether the dietary supplement called beta-hydroxy beta-methylbutyrate (HMB) can improve function and quality of life for people with advanced liver cirrhosis. Cirrhosis is liver scarring and people with cirrhosis can often have poorer quality of life than those with a healthy liver.

What is HMB? And how is HMB related to liver cirrhosis?

HMB is a type of protein naturally produced by the body that is available as a dietary supplement to increase muscle strength. HMB also improves the health of the gut lining. If the gut lining is not healthy, parts of bacteria can pass from the gut into the bloodstream (this is a known an as a leaky gut) and travel to the liver. This can cause inflammation and scar formation in the liver. There are currently no treatments for liver scarring or a leaky gut.

How does HMB improve the health of the gut lining?

When fibre in our diet is broken down in the digestive system, compounds called short chain fatty acids (SCFAs) are produced. SCFAs are important for gut health and without them the gut becomes leaky. HMB increases the levels of SCFAs in the gut. In this way, HMB may be beneficial for people with liver cirrhosis.

Why have I been invited to take part?

You have been identified as someone who has cirrhosis (scarring) of the liver and may be suitable to take part in the study. However, before you can be offered a place on the study, your suitability will be assessed against the following criteria:

You must meet <u>all</u> these criteria to take part:

- Must be between the ages of 18 and 85 years old.
- Cirrhosis (scarring) of the liver has been confirmed by a doctor, imaging (such as ultrasound or CT scan) or a liver biopsy.
- Liver cirrhosis is advanced; this is confirmed by blood test results (Child-Pugh score).
- There have been signs of increased pressure in the liver's blood vessels (portal hypertension) within the last 6 months.
- Willing and able to attend the study appointments (3-4 appointments over 3 months). Reasonable travel expenses will be reimbursed.
- Willing and able to give informed consent to take part in the study.

You will <u>not</u> be able to take part if any of the following apply to you:

- Have advanced liver cancer.
- Have had a liver transplant or are on the liver transplant waiting list.
- Have taken a HMB dietary supplement, or any products containing HMB, in the last 4 weeks.
- Are unable to complete the 'Liver Frailty Index' test. This involves squeezing a device that measures hand strength, standing up and sitting down from a chair several times in

a row and balancing for a short time whilst your feet are in different positions on the floor.

- Have taken part in a research study within the last 4 weeks, where you have consented to a new procedure, treatment or support.
- A history of hypersensitivity (allergic) reactions or allergy to HMB supplements or any of their ingredients.

Can I take part if I am pregnant of breastfeeding?

Yes, you will be able to take part in the study if you are pregnant or breastfeeding. This is a low-risk trial and HMB is widely available over the counter. However, there is limited information about the effect of HMB in pregnancy. If you become pregnant during your time on the study, we ask that you notify the researcher at your next study visit.

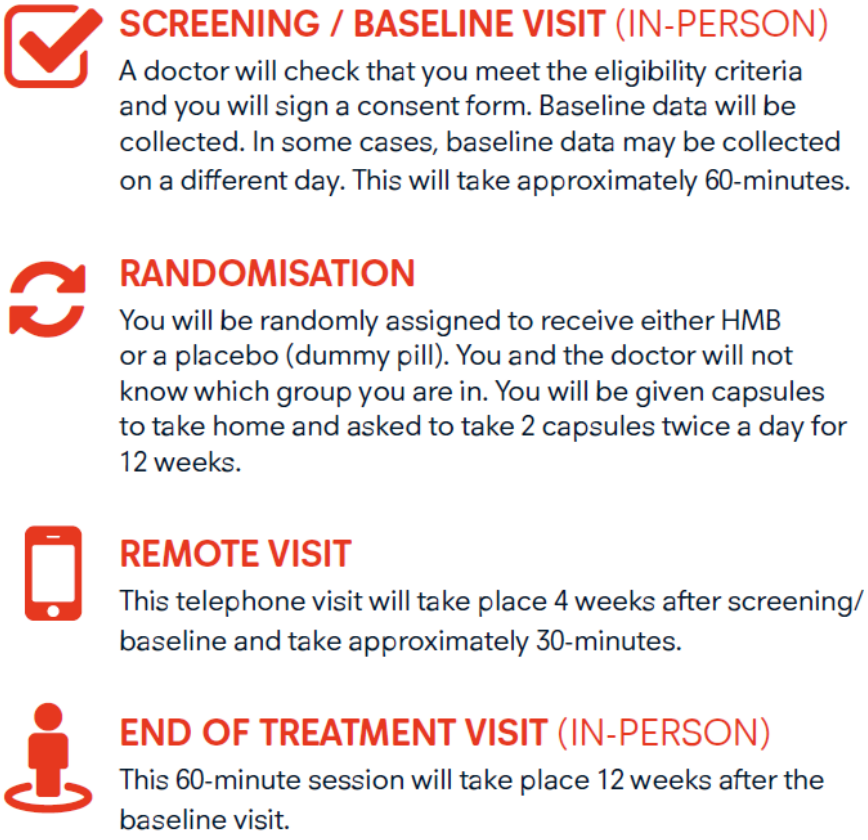
Do I have to take part?

No, it is up to you to decide whether or not to take part. If you do decide to take part, you will be asked to sign a consent form. During the study, you are free to withdraw at any time without giving a reason. If you decide to withdraw or decide that you don't want to take part, the usual care you receive will not be affected.

What will happen if I take part?

If you would like to take part, you will attend your local participating hospital for study visits over a 3-month period. You will attend 2 or 3 in-person visits and one remote visit on the telephone.

In addition to these study visits, we will contact you (by text or email) at the beginning and part-way through the study to remind you about your next study visit. A summary of the study visits you would attend can be seen on the following page.



BOOST study visits

If you decide you would like to take part, you can **contact the research team** by telephone or e-mail using the details found at the end of this information sheet. Alternatively, you may **inform the clinician who provided you with this information sheet** that you are happy for a member of the research team to call you. You can also **complete a self-referral form** on the BOOST website:

www.plymouth.ac.uk/boost

After receiving confirmation of your interest, a researcher will contact you by telephone to discuss the study and see whether the study may be right for you.

If you are likely to be eligible and you wish to take part, you will be invited to attend a face-to-face **screening appointment** at your local hospital, and your suitability for the study will be assessed by a member of the research team. This appointment will take around **15 minutes** and will consist of:

- Confirming that you have read and understood this Participant Information Sheet. Answering any questions you may have.
- Checking your medical history to determine your suitability for the study. The researcher will use routine results from previous imaging, laboratory results and medical notes to check that you meet the eligibility criteria. No specific test will be carried out at this visit.
- If you are eligible, and you are willing to take part in the study, you will be asked to:
    - Complete and sign a consent form.
    - Book an appointment for your baseline visit. This will take place within the next month but, if appropriate, **the baseline visit can be carried out immediately after the screening appointment.**

The next appointment, known as the **baseline assessment**, will take approximately **45 minutes**. The assessment will consist of:

- Collecting some information about your medical history and medications.
- Asking you about your food and drink intake over the last 24-hours.
- Asking about alcohol consumption over the last 7 days.
- Measuring your brain function by asking you to name as many different animals as you can in 1 minute.
- Complete two questionnaires about your wellbeing, mood and quality of life. These are called the Short Form 36 questionnaire and the Warwick-Edinburgh Mental Wellbeing questionnaire.
- Measure your weight and height to calculate your Body Mass Index (BMI).
- Measuring the width of your lower leg to show muscle mass.
- Three short tests known as the Liver Frailty Index:
    - Measuring your hand strength by asking you to squeeze a small device, called a dynamometer, as hard as you can and holding it for a few seconds.

- Asking you to stand from a seated position in a chair, without using your hands to push yourself up, 5 times in a row. This will only be done if you feel safe enough to do so.
- Assessing your balance by asking you to stand with your feet in three different positions for 10 seconds each. You will be asked to stand with your feet side by side, one slightly in front of the other and one foot fully in front of the other. Please see the image below to show how your feet will be placed.



Figure 2. Foot positions for the balance check.

- Taking blood samples (15ml which is around 3 teaspoons) to check liver and gut function.

After the baseline assessment has been completed, you will be assigned to either Group 1 (placebo 'dummy pill' with usual care) or Group 2 (HMB with usual care). This is done using a computer system that chooses a group at random; the clinicians, researchers and you are not involved in this choice in any way. This is a 'double-blind' study, which means that you, and the clinicians will not know whether you are taking the placebo or the HMB. Both groups will attend the study visits and have the same tests.

At the end of the baseline appointment, you will be given a 12-week supply of capsules – these will be capsules of placebo or HMB depending on the Group that you have been placed in.

- You will be asked to take **2 capsules twice a day (4 capsules every day) for 12 weeks**. The capsules contain 750 mg of HMB or placebo. The placebo is maltodextrin, a type of carbohydrate that is commonly added to food.

Four weeks after the baseline appointment, you will have a **Week 4 Telephone/Video Call** with the researcher. This will take approximately **30 minutes** and will consist of:

- Checking any medication changes.
- Asking about alcohol consumption over the last 7-days.
- Checking if you have had any hospital admissions/attendances or infections.
- Recording any adverse health events you have experienced since the baseline visits.
- Checking if you have taken the capsules given to you (HMB or placebo).
- Checking if you have knowingly or possibly taken HMB from another source.

You will attend one more in-person visit. This will take place around **3 months** after your first baseline visits. This visit will be like the baseline visit, with the addition of:

- Recording any adverse health events you have experienced since the last visit.
- Checking if you have taken the HMB/placebo capsules.
- Check if you have taken HMB outside of the study

In addition to the study visits, you will receive an email or text message during Week 2 and Week 8, to remind you about your next study visit and how to contact us if you have any queries.

Optional Interviews

If you are willing, a researcher from the University of Plymouth might contact you to find out what you thought about the study. Depending on your preference, the interview will take place over the telephone, online via video call, or in person at a convenient location (where possible). You can decide when you are completing your consent form whether you would like to be considered to take part in these interviews. There will be a separate information sheet relating to these interviews, which the researcher will provide you with if you are contacted about participating in this part of the study. The interviews will be carried out with a small number of people, so you may not be contacted about this.

What facilities does your department have?

Some visits may take place in a community setting, such as your GP surgery. The facilities in these settings may differ from the department facilities above.

If English is not your first language, you are asked to bring an English-speaking relative or friend to your appointments to assist with translation.

What are the possible disadvantages and risks of taking part?

Blood samples

Risks associated with taking blood are very low, but in some instances, people may experience discomfort, bruising, redness, or swelling at the site where the needle goes in, fainting or vein puncture.

HMB

HMB is a supplement that is currently available over the counter and is generally safe and well tolerated, with minimal side effects. When taking any supplement, there is a risk of side effects. This will be monitored closely by the research team.

Maltodextrin (placebo)

Maltodextrin is a commonly used as a placebo in studies and is considered safe. If consumed in large amounts, it may cause an increase in blood sugar levels. The amounts used in this study are very low.

What are the possible benefits of taking part?

If you are allocated to the HMB group you might experience an improvement in your physical wellbeing, but you might not. If you are in the placebo group, or do not benefit directly, your participation will help us learn more about HMB as a treatment for liver cirrhosis. In this way, your participation (whichever group you are in) may benefit people with advanced cirrhosis, in the future.

Are there any alternatives for treatment?

Currently, no treatments have been established for liver cirrhosis. This is currently the only study registered in the United Kingdom assessing HMB for liver cirrhosis. There are other studies of other dietary supplements (which contain HMB) ongoing in Italy.

What happens to any samples that I give?

Any blood samples collected as part of the study will be transferred, stored, and analysed at your local hospital and the University of Southampton safely and securely. Once the study is complete, with your consent, samples will be transferred to the Inflammatory Liver Disease Biobank at the University of Plymouth for use in approved future research. All samples will have personal identifiers removed so it will not be possible to identify you. If you agree to this, there will be an option for you to tell us on the consent form.

What if new information becomes available?

Sometimes during the course of a research study, new information becomes available about the treatment that is being studied. If this happens, we will tell you about it and discuss with you whether you want to continue in the study. If you decide to withdraw, your usual clinical care will not be affected. If you decide to continue in the study, you may be asked to sign an updated consent form.

Will my General Practitioner (GP) be informed that I am taking part in this study?

Yes, we do this just in case they see you during your involvement in the study. If you do start the study and there is any new information from your doctor, other healthcare professional or one of the researchers that could affect your participation, we may ask you to withdraw from the study. If this happens, we will discuss it fully with you, and always consider your best interests, before making a decision.

Will I have my expenses reimbursed?

Reasonable travel costs for the study visits will be reimbursed. Your local research team will be able to give you information on how to claim these back.

What happens when the research study stops?

At the end of your time on the study, your usual care will continue as normal.

What happens if I take HMB from another source during the study?

If you take part in this study, you will be provided with a 12-week supply of HMB or placebo. It is important that you don’t knowingly take any other supplement or dietary product containing HMB during your participation in the study. This applies to all participants, regardless of whether you are in the HMB group or placebo group. If you do take

supplements containing HMB during the study, please let the researcher know at your study visits; you will still be able to continue in the study and it will not affect your care.

What if something goes wrong?

Whilst it is something we hope will not happen, if you experience any problems or have any concerns during your involvement in the study, please speak to the research team using the contact details at the end of this information sheet.

Alternatively, you may wish to contact:

University Hospitals Plymouth NHS Trust (UHP)
Research and Development,
17 Research Way,
Plymouth Science Park,
Plymouth,
PL6 8BT
Email: plh-tr.rdgovernance@nhs.net
Phone: 01752 432195

If you are harmed by taking part in this study, there are no special compensation arrangements. If you are harmed due to someone's negligence, then you may have grounds for a legal action, but you may have to pay your legal costs. Regardless of this, if you wish to complain, or have any concerns about any aspect of the way you have been approached or treated during the course of this study, the normal National Health Service complaints mechanisms will be available to you.

If you would prefer to speak with someone who is not linked to this research study and can act as an independent source of information, you can contact the hospital's Patient Advice and Liaison Service (PALS) or equivalent. PALS offers support, information and assistance to patients, relatives and visitors and will:

- Provide information about hospital services.
- Offer advice on where to go to get health information.
- Help with problems that you haven't been about to sort out with staff in a clinic.
- If you want to make a complaint – advise you how to do so.
- Tell you about independent organisations that can help you with a complaint.
- Listen to your views on how we can improve our services and pass this on to the appropriate people for action.

What will happen to the results of the research study?

We aim to complete this research by May 2027 and a report will be submitted to the National Institute of Health Research (NIHR), which is funding this work. Findings may also be published in scientific and medical journals, at conferences and research interest groups and at training days for clinicians. Confidentiality and patient anonymity will always be maintained. A summary of the results will be available to read on the Peninsula Clinical Trials Unit website (www.plymouth.ac.uk/penctu), and you will receive a notification via email (if provided) when the results are available.

Can I find out what group I was allocated to?

Yes, once the study has ended we will offer you a summary of the results and let you know who you can contact to find out which group you were in, if you wish.

Who is funding and organising the research?

The study is funded by the NIHR as part of their Research for Patient Benefit (RfPB) funding stream. The money is to cover research expenses associated with the study, including part of the salaries of the research staff. No payment is made to your referring doctor.

Doctors and researchers at the University of Plymouth, University Hospitals Plymouth NHS Foundation trust, University of Southampton and Imperial College London are leading this research. The Chief Investigator is Professor Ashwin Dhanda (University of Plymouth).

Who has reviewed the study?

This study and information sheet were prepared in consultation with the BOOST Patient Advisory Group. All research in the NHS is looked at by an independent Research Ethics Committee to protect your safety, rights, wellbeing, and dignity. This study has been reviewed and given favourable opinion by North East - Newcastle & North Tyneside 1 Research Ethics Committee.

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 name, NHS number, date of birth, and contact details, including your telephone number and email address. 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.

University Hospitals Plymouth NHS Trust is the Sponsor of this research and is responsible for looking after your information. All information about you will remain strictly confidential and will be kept safe and secure. All data will be collected, processed, and stored in accordance with the UK General Data Protection Regulation (UK GDPR) and the Data Protection Act 2018.

International transfers of research data

There is a possibility that in the future, we may share the study data outside of the UK. The data we share about you outside the UK would only be for research-related purposes to further investigate liver disease.

If this happens, we will only share the data that is needed. We will also make sure you can't be identified from the data that is shared. If your data is shared outside the UK, it will be with organisations such as other health and academic institutions that carry out health research.

We will make sure your data is protected. Anyone who accesses your data outside the UK must do what we tell them so that your data has a similar level of protection as it does under UK law. We will make sure your data is safe outside the UK by doing the following:

- (some of) the countries your data may be shared with have an adequacy decision in place. This means that we know their laws offer a similar level of protection to data protection laws in the UK, for example, member states of the European Union.
- For other countries we use specific contracts approved for use in the UK, which give personal data the same level of protection it has in the UK. For further details, visit the Information Commissioner's Office (ICO) website International data transfer agreement and guidance | ICO.

- We do not allow those who access your data outside the UK to use it for anything other than what our written contract with them says.
- We need other organisations to have appropriate security measures to protect your data that are consistent with the data security and confidentiality obligations we have in the UK. This includes having appropriate measures to protect your data against accidental loss and unauthorised access, use, changes, or sharing.
- We have procedures in place to deal with any suspected personal data breach. We will tell you and applicable regulators when there has been a breach of your personal data when we legally have to. For further details about UK breach reporting rules, visit the Information Commissioner's Office (ICO) website Personal data breaches: a guide | ICO.

How will we use information about you after the study ends?

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.

We will keep your study data for a minimum of 5 years. The study data will then be fully anonymised and securely archived or destroyed.

Please note, if any information from your participation in the research study leads to any test or treatment that might make money for the Sponsor and/or Funder, you will not share in any profits that they might receive from such commercialisation. You will not be paid for the use of your information.

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 the 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 central NHS records, your hospital, and your GP. If you do not want this to happen, tell us, and we will stop.

You have the right to ask us to remove, change, or delete data we hold about you for the purposes of the study. We might not always be able to do this if it means we cannot use your data to do the research. If so, we will tell you why we cannot do this.

We may wish to contact you about participating in future research studies. If you agree to this, there will be an option for you to tell us on the consent form.

Where can you find out more information about how your information is used?
You can find out more about how we use your information, including the specific mechanism used by us when transferring your personal data out of the UK.

- our leaflet by visiting www.hra.nhs.uk/patientdataandresearch.
- by asking one of the research team,
- by sending an email to the Sponsor Data Protection Officer: informationgovernancepht@nhs.net

If you are still concerned after speaking to the Data Protection Officer and believe we are processing your personal data in a way that is not lawful, you can complain to the **Information Commissioner's Office** (ICO) https://ico.org.uk/make-a-complaint/

Contact for further information
If you need further information about the study, or would like to speak to the research team about taking part, please contact your local research team.

Thank you for taking the time to read this information sheet and considering this study.