Palliative Long-term Abdominal Drains Versus REpeated Drainage in Untreatable Ascites Due To Advanced Cirrhosis: A Randomised Controlled Trial (REDUCe 2 Study)

PARTICIPANT INFORMATION SHEET

We'd like to invite you to take part in our research study. Joining this study is entirely up to you, before you decide we would like you to understand why the research is being done and what it will involve for you. One of our team will go through this information sheet with you to help you decide whether or not you would like to take part and answer any questions you may have. Please feel free to talk to others (friends or family) about the study if you wish.

Do ask if anything is unclear. Thank you for taking the time to read this information.

Study Summary

The purpose of this research project is to assess whether a new way of managing the build-up of fluid in the abdomen due to severe liver disease (known as ascites) , is as effective and acceptable as the current standard of care. Current care involves coming into hospital for a day or two, putting a thin tube into the abdomen for a few hours and draining the fluid. This procedure, which reduces pain from the ascites, is known as hospital drainage or large volume paracentesis (LVP). We will call it hospital drain. The new method is called long-term abdominal drain (LTAD). We will call this home drain. This is currently available for people with certain conditions but is not routinely used for people with your condition.

We successfully completed previous smaller study with people with your condition using home drains. It went well with no major complications, so we are now ready to do this larger study.

You will be in the study for a total of 3 months (12 weeks), with a number of visits taking place over that time so that we can see how you are getting on and pick up on any problems.

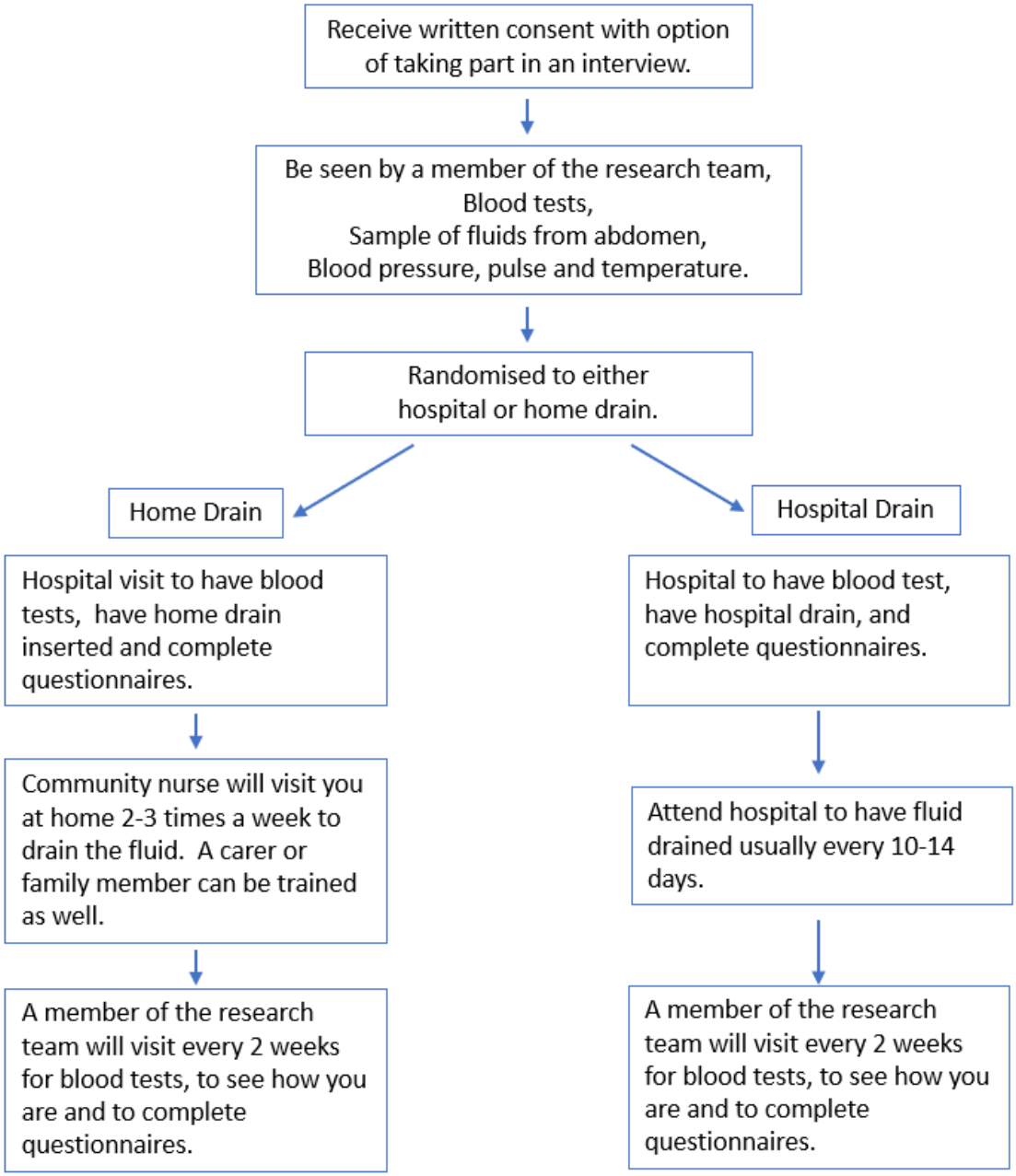
There is also the option of taking part in an interview so we can find out more about your experiences of having the home or hospital drain. You will also have the option of having an additional blood sample taken for research purposes only. This will be stored until the end of the study and then tested for proteins and chemicals associated with advanced liver disease. You can decline to take part in either the interviews or research bloods or both of these without it affecting your participation in the main study.

In this research study we will use information from your medical records. We will only use information that we need for the research study. We will let very few people know your name or contact details, and only if they really need it for this study. Everyone involved in this study will keep your data safe and secure. We will also follow all privacy rules. At the end of the study we will save some of the data in case we need to check it. We will make sure no-one can work out who you are from the reports we write.

If you were to take part the following is a summary of what will happen to you whilst on the study. If after reading this information and you are interested in knowing more please read the more detailed information that follows.

Thank you for taking the time to read this information.

REDUCe2 Study Procedures Summary:



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Full Information of the Study.

1. Why have I been chosen?

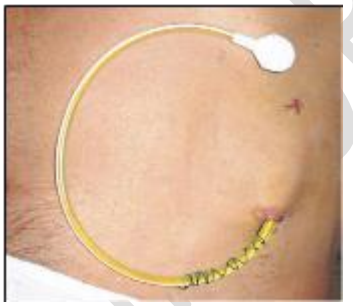
As you know, you have a liver condition called cirrhosis (scarring of the liver caused by long-term liver damage). The scar tissue prevents the liver working properly. A consequence of this is a buildup of fluid in the abdomen called ascites and this needs to be drained regularly. Draining of the fluid focuses on controlling your symptoms enabling you to have the best possible quality of life. This is known as palliative care.

2. What is the purpose of the study?

The purpose of this study is to assess a new palliative care method to manage your condition compared to the current standard of care.

Current standard of palliative care for ascites involves coming into hospital for a day or two, putting a thin tube into the abdomen for a few hours and draining the fluid. This procedure, which reduces pain from the ascites, is known as hospital drainage or large volume paracentesis (LVP). However, as the ascites builds up quickly, hospital visits for the drain are needed every 10-14 days.

When ascites is caused by certain other palliative conditions, there is an alternative called long-term abdominal drain (LTAD home drain) (see photograph below). This involves inserting a permanent drain into the abdomen. When the fluid builds up, a bag is connected to drain the fluid. This can be done regularly by community nurses or a trained family member at home, avoiding the need to come to hospital.



Currently, this is not offered as there is not enough information about whether home drainage is suitable for people with advanced liver disease.

3. Do I have to take part?

No, your participation is voluntary. You can also withdraw from the study at any time without giving a reason. Refusal to participate will not affect your current or future care.

4, What will happen to me if I take part?

Once you have had time to think about your participation, you will be seen by a member of the research team who will answer any questions or concerns you may have. They will go through this information sheet and, if you are still willing, they will ask you to sign the consent form.

After we have received your consent to participate in this research

a. Screening visit. The research team member will ask some brief questions about your health and liver condition and check your vital signs: pulse, blood pressure and temperature. A blood sample of about 4 teaspoons (20 ml) will be taken for routine clinical tests. A routine sample of ascitic fluid (fluid in your abdomen) of 4 teaspoons (20ml) will be examined to ensure there is no infection present. If infection is found, you will receive antibiotic treatment for five days. We will proceed with the study once this infection has resolved.

c. After this, a computer programme will be used to randomise (like flipping a coin) participants into two groups: home drain (group 1 or intervention group) or hospital drain (group 2 routine hospital drainage). There will be an equal chance of being allocated to either group but neither you nor your doctor will be able to choose which treatment you have. Within 10 days of the screening visit, we will call you to let you know which group you are in.

Depending on which group you are in, slightly different things will occur.

If you are in the home drain group

a. Baseline visit. An additional visit will be arranged for drain insertion within 10 days of the screening visit. The research doctor will ask brief questions about your health and liver condition and check your vital signs. About 4 teaspoons (20 ml) of blood will be taken for routine clinical tests. With your consent, an additional 20 ml of blood will be taken for research purposes, though this is optional. You will be reimbursed for your travel costs to attend this visit. You will be asked to fill in four questionnaires to assess your symptoms, quality of life and use of health/hospital services. These will take less than an hour to complete. The questionnaires can be completed online via a smartphone or computer. If you are unable to do this online then your caregiver or research nurse/doctor can help you.

b. Experienced doctors will then insert the drain using a local anesthetic and ultrasound to ensure that the drain is inserted in the best site with minimal pain and discomfort. The research doctor will explain to you how to look after your drain. As part of routine care, you will receive an antibiotic, one tablet a day, to reduce the risk of infection in the ascites. You can go home later that day and you will be able to continue with your usual daily activities.

c. The Research Doctor will arrange for a community nurse to support you at home when drainage is needed. This will be 2-3 times a week and takes around 30 minutes for each visit. Around 1-2 litres of fluid may be drained at a time and will be painless. Your caregiver, if they wish, can take over draining the fluid. They will be given the necessary training from the research doctor/nurse and community nurses. Community nurses will use a drainage diary to record the drainage and any concerns about the home drain. The

research doctor/nurse will collect this information from you every two weeks during the home visits.

d. An appointment will be arranged for the research doctor/nurse to visit you at home every two weeks at home for up to three months. Each visit will take up to one hour. About 4 teaspoons (20) ml of blood will be taken for routine testing and information from the drainage diary collected. You will also have the opportunity to discuss any concerns about the home drain. Every two weeks, you will be asked to complete three of the four questionnaires online (looking at symptoms, health outcomes and use of health services); the remaining quality of life questionnaire will be completed every 4 weeks. These should take under an hour to complete. If you are unable to do this online then your caregiver or research nurse/doctor can help you. Alternatively, if you prefer, the questionnaires can be answered over the phone within three days of the home visit, just let the research doctor/nurse know.

If you are in the hospital drainage group

a. Baseline visit. A visit will be arranged for drain insertion as part of routine clinical care. The research doctor will ask brief questions about your health and liver condition and check your vital signs. About 4 teaspoons (20 ml) of blood will be taken for routine clinical tests. With your consent, an additional 4 teaspoons (20 ml) of blood will be taken and stored for research purposes, though this is optional. You will be asked to fill in four questionnaires to assess your symptoms, quality of life and use of health/hospital services. These will take less than an hour to complete. The questionnaires can be completed online via a smartphone or computer. If you are unable to do this online then your caregiver or research nurse/doctor can help you.

b. You will continue to receive current routine clinical care involving hospital visits to drain your fluid and you will have blood taken for routine testing, usually every 10-14 days. As part of routine care, you will receive an antibiotic, one tablet once a day, to reduce risk of infection in the ascitic fluid. The research doctor/nurse will collect information about the amount of fluid drained.

c. An appointment will be arranged for a member of the research team to visit you at home every two weeks at home for up to three months. Each visit will take up to one hour. About 4 teaspoons (20 ml) of blood will be taken for routine clinical testing. Every two weeks, you will be asked to complete three of the four questionnaires online (looking at symptoms, health outcomes and use of health services); the remaining quality of life questionnaire will be completed every 4 weeks. These should take under an hour to complete. If you are unable to do this online then your caregiver or research nurse/doctor can help you. Alternatively, if you prefer, the questionnaires can be answered over the phone within three days of the home visit, just let the research doctor/nurse know.

For both groups:

Optional interviews

We would also like to do an interview with a group of 30 participants to find out more about their experiences of the drainage. You do not have to consent to this as interviews are optional, but it will help us understand more about patient views. The research doctor or nurse will ask your permission to share your contact details with the interview researchers. If

you agree for your contact information to be passed on, the interview researchers will contact you at a convenient time to answer any questions or concerns you may have. Verbal consent for the interview will be taken over the phone at the time of interview.

The purpose of the interviews is to find out what you think, so there are no right or wrong answers. We are interested in hearing your views and experiences. If there any questions that you do not want to answer, just tell the researcher and they will move on to the next topic.

The interview will last between 15-45 minutes, at a date and time that is convenient for you. Breaks will be allowed. We will ask for your permission to audio-record the interview, but you can ask for the recorder to be switched off at any point. The audio recording will be typed up by a professional company. Our agreement with them ensures that the content of the interviews will be kept completely confidential. This company will have no access to any of your personal information and will not know your name, only your study identification number. Once we receive the transcript back, we will ensure any identifiable details are removed and we will destroy the audio file. Transcripts and audio files will be stored securely.

Optional research blood samples

An additional 4 teaspoons (20ml) of blood will be taken for research purposes and tested at the end of the study (see section 13).

5. **What happens if I lose my capacity during the study**

England and Wales
We will identify a Consultee who can either be your caregiver or an independent medical consultant who is not associated with the study. In case you lose your capacity during the study, we will approach your Consultee who will advise if it is in your best interest to continue in the study.

Scotland
If you lose your capacity during the study, your previous consent will still be valid. When you sign your consent form we will however ask you how you wish proceed in case you lose capacity during the study: you can either give consent to continue in the study or choose to withdraw from the study. We will also ask your consent to keep and use any data that we have collected so far.

6. What are the side effects, risks and implications of taking part in the study?

It is possible that talking about your health may raise topics that you find upsetting or difficult. Should this happen, please contact the study team who will provide additional support and advice. You will also need to take time to complete the questionnaires and have home visits. These are to ensure all is going well and any questions you have can be answered.

During our earlier smaller study the following risks were observed with the home drain:

- Inability to insert home drain (fewer than 6 in 100 people)
- Leaking of fluid and inflammation of skin around the drain (about 40 in 100 people) - mild in all cases and settles in a couple of days without need for hospitalisation. Draining ascites to dryness in hospital after insertion of home drain, can reduce leakage and this is now our standard practice

- Infection of the ascites fluid (peritonitis) (fewer than 6 in 100 people)
- Pain, bleeding or drain blockage needing hospitalisation were not identified in any patient. Kidney function and protein level (albumin) remained stable

You will be closely monitored by the community nursing teams and the research teams during home visits, so if any complications do occur, they will be promptly identified and acted upon. However, you do not need to wait for the home visits to seek medical attention. In case you feel unwell in between the home visits and for any out of hours emergency, please contact your GP or if needed attend your nearest A&E department.

The complications observed in the home drain group were similar to that seen in the hospital drain group, except leakage and inflammation around drain site were higher in the home drain group (about 40 in 100 people versus about 11 in 100 people)

7. What are the possible benefits of taking part?
You may not benefit directly from taking part in this research study. Information collected about you and others taking part in this study will help us determine whether home drains are a suitable option for people with cirrhosis and if so, whether they improve quality of life.

8. What happens when the research study stops?
The study will last for 3 months, after which you will continue to receive routine clinical care by your usual hospital consultant and GP. At the end of the study, for those in the hospital drain group your care will not change. You will continue with ascites drainage in hospital. Participants with a home drain will have the option to either carry on using the drain or have it removed. If you elect to have it removed this will be done in hospital and then you will revert back to having ascites drainage in hospital If you elect to continue using the home drain you will be closely monitored by your hospital consultant.

At the end of the study if the home drain is found to be beneficial, then patients in the hospital drain group can have the option to have the home drain inserted as part of standard of care.

9. What about my data and confidentiality?
The University of Sussex is sponsoring this study and will act as data controller; we will be responsible for maintaining and safeguarding your information. We will only use information that we need to carry out this research. All information collected about you will be kept strictly confidential to ensure compliance with data protection legislation that researchers follow.

How will we use information about you?
We will need to use information from your medical records for this research project. This information will include your name/ NHS number/contact details. 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 anonymised research data will be stored electronically, for analysis, publication, and audit and retained in line with University of Sussex records retention policy, which can be accessed here:
http://www.sussex.ac.uk/ogs/policies/information/recordsmanagementguidance

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. 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/
The university's privacy notice can also be found here: https://www.sussex.ac.uk/about/website/privacy-and-cookies/privacy All personal and research data will be stored and processed according to the UK Data Protection Act (2018).

However, if you tell us about serious risk of harm to yourself or others, we will need to break confidentiality, which means letting your GP know.

10. What if relevant new information becomes available?
Sometimes, during a research project, new information becomes available about the intervention being studied. If this happens, your research doctor/nurse will tell you about it and discuss whether you want to, or should, continue in the study. If you decide not to carry on, your research doctor/nurse will make arrangements for your routine clinical care to continue. If you decide to continue in the study, you will be given an updated patient information sheet to read and asked to sign an updated consent form.

11. What will happen if I don't want to carry on with the study?
Should you wish, you can withdraw from the study at **ANY** time, without giving a reason and without this affecting your future routine clinical care. If you have been fitted with a home drain you can choose to continue with drainage at home. Alternatively, you can have the home drain removed under local anaesthetic and return to attending hospital to have the ascites drained.

12. Complaints
If you have a concern about any aspect of this study, you should ask to speak with the research doctor or nurse at your local hospital. If you remain unhappy you can contact the University of Sussex at researchsponsorship@sussex.ac.uk

13. Will my GP be informed
We will inform your GP if you decide to take part in this study.

14. What will happen to any samples I give?
All routine blood samples you give will be analysed at the same time. Research blood samples will be labelled with your study number, no other personal identifiers being used. They will be stored at study sites and then sent to University Hospitals Sussex NHS Foundation Trust at the end of the study. The research bloods will be analysed for proteins and chemicals associated with ascites and to help predict who is more likely to develop an infection with the home drain. It may also include genetic testing. You will not be provided with any results of these tests as they are for research purposes only. Any surplus research blood samples will be destroyed at the end of the study in accordance with the hospital procedures.

15. What will happen to the results of the research study?
The results of the research study will be written up and published in scientific journals and discussed at medical conferences. Your personal information will not be identifiable in any way. A lay summary of the results will be available for patient groups.

If you/your caregiver would like to be sent or emailed a copy, please request this on your consent form.

16. Who is organising the research?
The University of Sussex are overseeing the conduct of the study, alongside the Chief Investigator and the Brighton and Sussex Clinical Trials Unit (BSCTU). The universities of Brighton and Sussex have insurance for any liabilities arising from this research. The questionnaire and interview component of the study is being led by researchers from the Sussex Health Outcomes Research and Education in Cancer (SHORE-C) at the University of Sussex. The study is funded by a grant from the Department of Health (National Institute for Health Research). Your doctor or the researchers will not receive any personal financial payment if you take part.

17. Who has reviewed the study?
To protect your interests, all research in the NHS is looked at by an independent group of people, called a Research Ethics Committee. This study has been reviewed and approved by the Oxford REC Committee (REC reference number 22/SC/0164).

18. Contact for further information
If you, for family caregivers have any questions or concerns about the study, now or in the future, please contact:

Dr Yaz Haddadin, Clinical Research Fellow
Tel: 07881 326775

Please insert local site details here:

For further information about the interviews you can contact SHORE-C at:
Brighton and Sussex Medical School University of
Sussex Science Park Road, Falmer, Brighton, BN1 9RX
Phone: 01273 873019
Email: shorec-reduce2@sussex.ac.uk

Thank you for taking the time to read this information sheet and for considering taking part in this research study