**RESEARCH PROTOCOL**

***Full Title: Long-term abdominal drains in refractory ascites due to end stage liver disease, a pilot study***

***Short Title:*** ***Abdominal drains for ascites***

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# INTRODUCTION

Chronic liver diseases, from any aetiology, progress over time to cirrhosis if untreated. The prevalence of cirrhosis, in particular non-alcoholic steatohepatitis (NASH), is increasing and is a major cause of morbidity and mortality, creating a significant burden on the health system (1). Ascites-related readmissions are the predominant cause of hospitalisations in these patients, especially in the last few months of life (2, 3). Refractory ascites, which is characterised by either diuretic non-responsiveness or intolerance, is encountered in 10% of patients with cirrhosis and is associated with reduced survival (approximately 6 months) without liver transplantation (LT) (4). Large volume paracentesis (LVP) is the only therapeutic option in those who cannot undergo LT. LVPs are typically performed every week or two in medical day-care units (MDU) as elective procedures or as emergency hospital admissions. There are practical difficulties in organising LVPs due to bed limitations in the MDU and this often leads to emergency room presentations and hospitalisations, thus causing significant patient discomfort and economic impact. Since ascites drainage in patients unsuitable for LT is a palliative procedure, it is best done in the comfort of their homes on a regular basis. This study explores the possibility of an alternative procedure via a catheter inserted in the abdomen and repeated small-quantity drainages (simply, long-term abdominal drains or LTADs) that can be done in the comfort of a patient’s home. This type of ascites drainage with indwelling catheters is a well-accepted model of care in patients with malignant ascites and hydrothorax (5). There is preliminary evidence from the United Kingdom in favour of this procedure in cirrhotic patients with refractory ascites (6). In this study, the feasibility of patient recruitment for LTAD as a management pathway for refractory ascites will be assessed in addition to its effectiveness and safety. The real-time patient data collected will advise us of realistic outcomes to target in future trials and to assist the design of a Phase 2/3 non-inferiority randomised controlled trial (RCT) comparing LTAD with LVPs, before LTADs can become the standard of care in management of refractory ascites.

# BACKGROUND

Chronic liver disease (CLD) is an important cause of premature mortality in the Australian population (7). Common causes of CLD in Australia include hepatitis C virus (HCV) infection, alcohol misuse, and metabolic associated fatty liver disease. Ongoing chronic injury from these factors results in cirrhosis of the liver, which is an advanced stage of CLD. Progression of cirrhosis from a clinically silent compensated stage to a symptomatic decompensated stage or end-stage liver disease (ESLD) is associated with multiple complications such as gastrointestinal bleeding, ascites, renal failure, hepatic encephalopathy and hepatocellular carcinoma (2). Ascites-related readmissions are the predominant cause of hospitalisations in these patients, especially in the last few months of life (3, 4). Refractory ascites, which is characterised by either diuretic non-responsiveness or intolerance, is encountered in 10% of patients with cirrhosis and is associated with reduced survival (approximately 6 months) without liver transplantation (LT) (5). Those patients unsuitable for LT are ideally managed with best supportive care, preserving their health-related quality of life (HRQoL) while minimising health expenditure (8). In a recent British study, it has been shown that a third of patients dying of cirrhosis underwent large-volume paracentesis (LVP) in their last year of life and it was associated with significant healthcare burden (3). In the Southern Adelaide Local Health Network (SALHN), LVP is organised for patients with refractory ascites who need ascitic drainage regularly (4). This is usually required every one to two weeks and patients spend approximately 6 to 8 hours admitted to a hospital bed, wherein up to 15 litres of ascitic fluid may be removed. Intravenous albumin infusion is provided to the patient concurrently to counteract the circulatory dysfunction that can result from rapid large volume fluid removal. LVP is associated with complications such as abdominal discomfort, leakage from the puncture site, and post-paracentesis circulatory dysfunction (PPCD) in up to 30% of patients (7).

Long-term abdominal drains (LTAD) are a simple and less invasive way of draining recurrent ascites. The drain is inserted into the abdominal wall in a tunnelled fashion under ultrasound guidance in hospital. Ascites is drained in frequent small-volume drainages in the comfort of a patient’s home on a regular basis, thus avoiding the need for albumin infusion and hospitalisation. As major fluid shifts that happen in LVP are avoided, the incidence of post-paracentesis circulatory dysfunction is likely to be less with this approach.

LTADs are found to be effective from clinical and health economic aspects in the management of malignant ascites, another form of recurrent ascites (5). Drawing from the successful experience with LTADs in ascites due to malignancy, we propose performing LTADs in patients with refractory ascites due to ESLD. However, catheter-related infection is a major cause of concern in ESLD patients as they are already prone to peritonitis. It is encouraging to note the results from a recent feasibility RCT from the United Kingdom showed no increased risk of infections due to LTAD when prophylactic antibiotics were used for the study duration (6). There was significant reduction in paracentesis performed in hospital in the LTAD group without any increase in the incidence of infections. As expected, the community, hospital, and social care costs related to ascites management were lower in the LTAD group. A limitation of this study, however, was that patients were followed up for only 3 months.

In this proposed study, we plan to explore the feasibility of managing refractory ascites in ESLD patients with LTAD for the first time in Australia. The proposed study addresses a potential role of LTAD in ESLD, which is not yet a standard of care in ascites management. It explores the role of LTAD in refractory ascites due to ESLD where patients are essentially palliative but tend to live longer than those with malignant ascites (6-12 months vs 3-6 months). Currently SALHN is experiencing capacity constraints with frequent inability to admit patients to the MDU electively for LVP. This has led to increased emergency admissions and distress for patients. The problem has been escalated to relevant managers with no solution envisaged. The problem is therefore an area of critical current need and could potentially be solved by the implementation of LTADs.

# AIM OF STUDY / RESEARCH QUESTIONS

1. To evaluate the feasibility of patient recruitment in exploring the role of LTAD in the management of refractory ascites.
2. To measure the safety, efficacy and acceptability of LTAD.

# STUDY DESIGN AND LOCATION

This is a feasibility, pilot study to be conducted at the Flinders Medical Centre (FMC), within the Department of Gastroenterology and Hepatology. We plan to recruit up to 20 patients with refractory ascites due to ESLD over 2 years and with each participant followed up for six months to assess study outcomes.

# ELIGIBILITY CRITERIA

1. **Inclusion Criteria**

Patients with ESLD and ascites that satisfy the following criteria will be approached for the study:

* Age >18 years with capacity to consent for treatment
* Patient with mild cognitive impairment, at treating doctor and/or PI’s discretion
* Refractory ascites
  + - Ascites that is unresponsive to fluid and sodium restriction, and high-dose diuretic treatment (spironolactone 400 mg/day and/or furosemide 160 mg/day) with or without intolerance to diuretics
    - Ascites that recurs rapidly after LVP (requiring one or more LVP/month).
    - Considered ineligible to undergo LT and or trans jugular intrahepatic portosystemic shunts (TIPSS)

1. **Exclusion criteria:** 
   * Patients with loculated ascites
   * Patients with large exophytic liver tumours
   * Patients with chronic abdominal pain
   * Patients with extensive abdominal wall scars
   * Patients unlikely to tolerate with abdominal drains at home as judged by the treating medical team
   * Patients with active spontaneous bacterial peritonitis

# STUDY OUTCOMES

1. **Primary Outcome(s)**

* Feasibility/logistics of LTADs within SA health
* Number and rate of patient recruitment over 24 months

1. **Secondary Outcome(s)**

* Safety by measurement of adverse outcomes due to LTAD including the frequency and incidence of infections (peritonitis and infections at site of LTAD), leakage from LTAD, bleeding, and renal failure
* Efficacy as assessed by the number of hospital visits for paracentesis avoided, and the need for breakthrough hospitalisation for ascites.
* Acceptability using satisfaction surveys (patients and carers)

# STUDY PROCEDURES

1. **Recruitment of participants**

Pre-screening: A list of patients with ESLD and ascites requiring active management will be identified from the Chronic Liver Programme database, a service provided by the Hepatology Unit at Flinders Medical Centre. Under National Statement 2.3.10 a, b, d, e, f, we wish to apply for a waiver of consent to access a patient’s personal information for research purposes, in order to identify suitable participants for this research project. The study coordinator and chronic liver disease nurse will be required to access medical records to determine eligibility prior to obtaining consent from the patient. It is not feasible or appropriate to discuss screening with potential participants to access medical records. Due to the complex and involved consent process, it is imperative to establish eligibility prior to burdening patients and families with complex study information. Patients will also be identified by the Chronic Liver Programme team and referred to the chronic liver disease nurse. Formal consent will be obtained from potential participants if a patient is deemed to be eligible for this study. The study coordinator and chronic liver disease nurse in charge of pre-screening will have access to confidential patient information as part of their employment.

Consent: Eligible participants identified during pre-screening will be contacted by the chronic liver disease nurse and provided with a participant information sheet during their upcoming appointment. Those who do not have an upcoming appointment will be sent an invitation letter to consider taking part in this study, along with a copy of the participant information and consent form. If the patient agrees to taking part in the study, a clinic appointment will be made for the patient to attend the hospital to sign the consent form and book their LTAD insertion appointment. If a patient declines, they will be given the option to state that they are not approached again for this study. All responses will be recorded in our pre-screening log to ensure that participants aren’t re-approached. Patients will be given between one to two weeks to consider the consent form and they will be followed by the chronic liver disease nurse with a phone call to determine interest in participation. Potential participants will have the opportunity to contact the study team for further information during this period. The information sheet will include details about the purpose of the study, information about the LTAD, how it will be inserted, and any potential complications. Participants will have the option to withdraw from the study at any time. Consecutive patients requiring active management of cirrhotic ascites will be offered the opportunity to participate in this feasibility study with a view of recruiting up to 20 patients over a 24-month period.

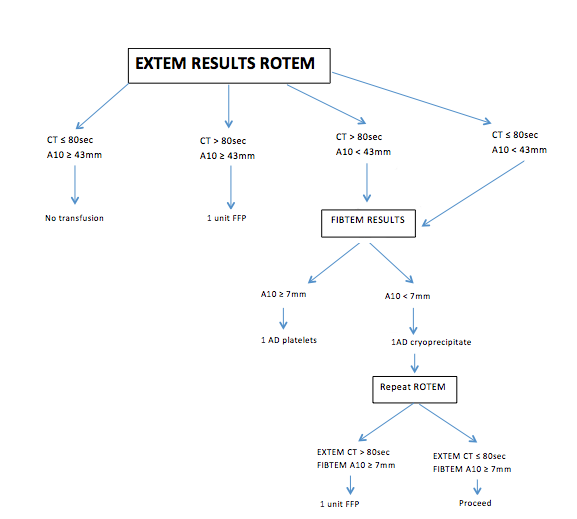
Informed consent will be obtained at a study appointment, where the potential participant will be provided with additional opportunity to ask any questions. To avoid potential coercion and feelings of obligation to participate, the PI, chronic liver disease nurses, and the patient’s own clinician will not be involved in the consent process. Only study investigators not directly involved in the potential participants treatment decisions will obtain study consent.

If hepatic encephalopathy is a recurrent condition, the investigator needs to provide an assessment for encephalopathy using a standard assessment – the West Haven Criteria. A score of 0 or 1 documented in the patient notes by the treating team or trial investigator means that the patient can be approached for consent. Patients with mild cognitive impairment may be approached and consented for the study at the treating doctor and/or PI’s discretion. If required, a third-party person responsible PISCF can be provided by the PI or study coordinator to the person responsible for the potential participant to obtain informed consent.

1. **Study design**

LTAD insertion: After signing consent*,* participantswill be admitted overnight under the liver unit*.* Rocket® LTAD catheters (Rocket Medical, Watford, UK) will be inserted in the angiography suite by interventional radiologists as is regularly done for patients with malignant ascites. The radiology team has extensive prior experience with the Rocket® LTAD catheters, as it has been used for pleural drains for many years in SALHN. Hence, they will be used for this study.

As part of standard of care within the Hepatology Unit, all participants undergoing an invasive procedure will be assessed for their risk of bleeding during admission. Based on prior standard of care bloods, INR and platelet counts will be assessed by the clinical team to determine if additional tests are required (INR≥1.5 OR Platelet count ≤50,000). If required, on the day of admission for LTAD insertion, participants will have a blood sample collected for rotational thromboelastometry (ROTEM) testing as per standard of care. ROTEM testing can predict the risk of thrombosis and bleeding in liver disease patients. This standard of care process will be explained to the participant at admission by the liver team. If an abnormal ROTEM result is present, the participant will receive blood products guided by the ROTEM algorithm (Figure 1) prior to their invasive procedure. As per the ROTEM algorithm participants will receive FFP, cryoprecipitate and/or platelets as required. Participants will undergo catheter insertion once the bleeding risk assessment has been completed by the clinical team.



***Figure 1. ROTEM algorithm to guide blood product usage****. CT, clotting time (seconds); A10, amplitude at 10 minutes (mm); EXTEM, assessment of clot formation, fibrin polymerisation and fibrinolysis via the extrinsic pathway; FIBTEM, qualitative assessment of fibrinogen status; AD, Adult Dose; FFP, fresh frozen plasma; Developed by Dr M. Sobieraj-Teague and A/Professor D Roxby, Haematology Department and Transfusion Services, Flinders Medical Centre, Adelaide, South Australia, 2019.*

LTAD ascitic drainage: After confirming successful insertion of the drain, patients will be discharged the next day with sufficient drainage kits for four weeks of drainage in the community. SALHN community nurses regularly follow-up patients with pleural and peritoneal drains after discharge from the respiratory and palliative care departments. This existing pathway will be utilised for ongoing LTAD drains via referrals to the Metropolitan Referral Unit. Community nurses will be contacted prior to study commencement and a copy of the manufacturer’s instructions (Appendix 1) will be provided to the community nurses. Community nurses are already familiar with drainage procedures using the Rocket® drainage kits as the same system is used for pleural effusions. Upon recruitment of a patient, a referral form (Appendix 2) will be provided regarding the frequency and amount of drainage to be done specific for that patient.

Participants will be followed up by community nurses on discharge and undergo ascites drainage 2–3 times per week at home (including nursing homes and/or respite care), or as clinically required. During each visit, 1–2 litres of ascites will be drained as required for the patient, as per the previously published experience with LTADs (6). The frequency of drainage will depend upon the rapidity of ascites fluid accumulation after each drainage. Drainage appointments will be organised with the participant by the community nurses. The chronic liver disease nurse, a specialist nurse who is part of the participant’s clinical care team, will have oversight over the drainage appointments and overall patient care. A diary with drainage details will be maintained by the community nurses and a copy will be kept by the patients for the study duration.

Antibiotic prophylaxis with norfloxacin 400 mg once a day or equivalent will be given to all patients if they are not already on antibiotic prophylaxis against spontaneous bacterial peritonitis throughout the duration of the LTAD being *in situ* (study duration). All other drugs, including diuretics, will be continued at the same dose as prior to study commencement.

Participants will be provided with emergency contact numbers for reporting any adverse events or need for interval drains as and when they arise. Thus, throughout the study, participants will be reviewed by community nurses on a regular basis during LTAD drainages, as well as by the chronic liver disease nurse. The PI will provide study oversight.

At the end of the study period, participants will be given the option to continue having at-home drains with the LTAD as part of their standard of care. If they agree, their care will revert to standard of care management with the LTAD, with drains to continue at home as per clinical need. If a participant declines, an inpatient appointment will be made and the LTAD will be removed by an interventional radiologist. Patients will be asked to complete a patient satisfaction survey during their 3mth and end of study appointments (Appendix 3). In the event that a patient has a carer for the duration of the study to complete a satisfaction survey during the end of study appointment (Appendix 4). If the patient has deceased prior to the end of study, the carer will be approached by the chronic liver disease nurse, with whom they already have a rapport, to complete the satisfaction survey 4 weeks after notification.

Monitoring: Patients will be regularly monitored by the community nurses during the drainage visits. The chronic liver disease nurse will make weekly phone calls to the participant throughout the study duration. As the study participants are ESLD patients followed up by the Chronic Liver Failure Programme, they will continue to be closely monitored and undergo blood tests to assess renal and liver function, as required depending on clinical status. Participants will also be booked in to attend study-specific clinic visits at Flinders Medical Centre every 4 weeks for the study duration for review by the chronic liver disease nurse. Additional, drainage kits and related consumables will be provided during these clinic visits.

Qualitative interview: Qualitative feedback will also be sort from all participants at the end of the study. Participants will be contacted approximately 4-6 weeks after the EOS appointment to obtain feedback. All semi structured interviews will be conducted over the phone. The interview will be audio-recorded and transcribed verbatim, and field notes will be taken during and after each interview. One researcher, not part of the core research team, will conduct all the interviews. The designated interviewer will be provided a set of standardised questions to ask the participants (Appendix 5) during the interview. The interviews will be open ended and carried out as a conversation to understand the participant's experience of having the LTAD. It is anticipated this session will be approximately 20 minutes.

1. **Methods of data collection**

Multiple demographic (age, gender) and clinical (aetiology of disease, MELD score, Child-Pugh score, treatment experience) variables will be obtained from medical records (hardcopy and electronic). Patient acceptability of LTAD insertion will be assessed by patient satisfaction survey completed at 3mths and at end of study, as well as the end of study qualitative interview. In the event that a patient has a carer for the duration of the study, the carer will also be approached to complete a satisfaction survey at the end of the study.

Clinical data collected:

* Biochemistry before and end the study follow-up
* Number of ascitic drains (both LVP and LTAD) performed after study commencement
* Number of ascitic drains (LVP) performed 3 months prior to study commencement
* Use of diuretics
* Assessment of LTAD insertion site
* Hospitalisation related and unrelated to LVP
* Any adverse or serious adverse events related and unrelated to LTAD will be recorded.

1. **Adverse events**

Participants will be assessed for adverse events weekly by the chronic liver disease nurse, via phone calls during the six-month follow-up period after LTAD insertion. Any adverse event related to LTAD such as leakage from drain site, redness, discomfort, or fever will be informed to the study team by the participant and/or community nurse. If clinically indicated by the presence of abdominal pain, fever, redness, and pain around the LTAD site, patients will be advised to contact the chronic liver disease nurse immediately, or present to the emergency department at Flinders Medical Centre (after-hours and on weekends). The adverse events will be discussed with the medical team. Patients will be provided with the contact details of the study team, and after-hour contact numbers for emergencies.

Adverse events related to LTAD, as listed below, requiring hospitalisation will be classified as serious adverse events (SAE):

1. Leakage from the drainage site
2. Redness and swelling around the drain insertion site
3. Fever
4. Bleeding
5. Spontaneous bacterial peritonitis
6. Severe pain

These events will be recorded in the study proforma and reported to the SAC HREC within 24 hrs. All other adverse events deemed related to LTAD by the PI will be listed and informed to the SAC HREC within 72 hrs.

Management of serious adverse events specific to LTAD

*Pain and discomfort:* Discomfort during the insertion of the drain may occur. Participants will be given injections to numb the pain during the procedure. If needed, analgesics will be prescribed for a few days after procedure at the time of discharge from hospital.

*Infection*: If infection at the insertion site is suspected, a swab will be sent for analysis from the insertion site. Upon confirmation, the infection will be managed as per standard of practice with antibiotics.

*Bleeding*: Bleeding around the site is a very rare complication. If bleeding around the site occurs, it can be managed with a pressure dressing at the insertion site. If bleeding persists, patients will be advised to contact the chronic liver disease nurse immediately, or present to the emergency department at Flinders Medical Centre (after-hours and on weekends). Patients will be managed according to standard practice guidelines with blood products.

*Leakage*: Leakage of the ascitic fluid is another rare complication and it reduces as ascites drainage continues.

*Fever and abdominal pain* due to an infection of abdominal fluid may also occur. When these symptoms occur, patients will be advised to contact the chronic liver disease nurse immediately, or present to the emergency department at Flinders Medical Centre (after-hours and on weekends). If infection is confirmed, patients will be admitted to hospital and appropriate treatment will be organised as per current treatment guidelines.

Community nurses who visit participants periodically to drain the abdominal fluid will inspect the drain insertion site. They are trained to address these complications. The nurses will make a note of these adverse events and inform the study team. They will also refer participants to hospital if any of the complications are persistent and severe.

If there is persistent infection at the insertion site or recurrent infection of the ascitic fluid attributable to LTAD, participants will be admitted to hospital and the drain will be removed. Participant care will revert back to standard of care with regular LVPs in the MDU.

Adverse events related and unrelated to the study in ESLD patients include:

* 1. Spontaneous bacterial peritonitis
  2. Hepatic encephalopathy
  3. Renal failure, electrolyte disturbances
  4. Variceal bleeding
  5. Non variceal bleeding
  6. Hepatocellular carcinoma
  7. Liver failure
  8. Multiorgan failure and death

These events will be managed as per current standard of practice guidelines. The PI and study team will determine if any of these events are related to the intervention. If not, the event will not be reported to the HREC.

1. **COVID-19 Management plan**

All patients admitted to SA community care will have a COVID-19 screen prior to all visits, in line with SA Health and National CDMA guidelines. If a patient becomes positive with COVID-19, then a care plan review will occur. If the patient is stable enough for care to be continued in the community then care related to the study will continue with the appropriate precautions.

# DATA ANALYSIS

In view of the small number of study subjects, the data obtained will be described in detail using descriptive statistics.

Qualitative: Recordings of interviews will be allocated a unique study ID prior to being sent for transcription. All data will be assigned a unique study ID and will be stored securely, in a password protected computer and only FMC study investigators will have access to the data. Hardcopies of the transcriptions will be kept in a secure locked filing cabinet in the Hepatology Department research office at FMC. Participants will be given the option of requesting the transcript to check their answers.

A qualitative approach will be used to analyse the collected data as described in grounded theory. This approach for content analysis is interpretive in nature and used to describe or illuminate a phenomenon through identification of manifest (the obvious) and latent (underlying meaning) content in a text. This will involve: (1) reading of the text several times to become familiar with it and reflect upon the content, (2) identification in the text of meaning units that describe the phenomenon, (3) meaning units condensed and essential content is abstracted and labelled with a code, and (4) codes compared based on similarities and differences sorted into themes. Coding and sorting of themes will be assisted using the analysis tool NVivo (QSR Software, 2021).

# DATA HANDLING AND RECORD KEEPING

1. **Data Collection and Management Responsibilities**

Data collection is the responsibility of the research staff of FMC under the supervision of the Principal Investigator. The Principal Investigator is responsible for ensuring the accuracy, completeness, legibility, and timeliness of the data reported. Custodianship for the data will commence when it is accessed and downloaded by the research team. All electronic data will be stored on secure servers and computers in accordance with Australian legislation. Only the researchers involved in this project will have access to this data.

1. **Study Records Retention**

Study participant data will be de-identified and be labelled with a unique study number. De-identified study data will be entered into an Excel spreadsheet and stored in a secure, password protected computer. A separate password protected spreadsheet will be created to link study ID to patient identifying information, which will only be accessed by the chronic liver disease nurse. Only study investigators will have access to the de-identified study data. Data will be stored for a maximum of 15 years as per NHMRC guidelines, and after this time it will be erased/destroyed.

1. **Protocol Deviations**

A protocol deviation is any noncompliance with the study protocol, GCP, or HREC requirements. The noncompliance may be either on the part of the participant, the investigator, or the study site staff. As a result of deviations, corrective actions are to be implemented promptly.

The principal investigator will use continuous vigilance to identify and report deviations within 72 hours of identification of the protocol deviation. All deviations must be addressed in study source documents, reported to the approving HREC(s) and site Research Governance Officer(s).

# STUDY TIMELINE

The study is expected to commence in August 2022, upon ethics and governance approvals and completion anticipated by April 2025. Recruitment is expected to take place over 2 years, with a 6-month follow-up period of each enrolled patient. Data collection is anticipated to be completed by April 2025, with data collation and analysis expected to take a further four months.

# ETHICAL CONSIDERATIONS

1. **Confidentiality**

Electronic de-identified data will be stored on SA Health servers in secure folders accessible to only investigators of the Hepatology Unit at Flinders Medical Centre. All computers will be two-level password protected. Confidentiality will be maintained beyond study parameters.

1. **Risks and benefits of the study**

Risks: LTAD has been shown to be safe, effective, and acceptable to patients with malignant ascites in a small-scale study in cirrhotic patients (6). The adverse effects due to LTAD were self-limiting (leakage from LTAD site, cellulitis and bleeding) and did not require hospitalisation in a recent RCT. If participants develop any of the expected complications such as leakage from LTAD site, blocked drainage, swelling, pain, fever, and generalised abdominal pain, they will be asked to contact the chronic liver disease nurse, the emergency contact person for the study, during work hours. During weekends and out of office hours, patients will be asked to present to the emergency department at Flinders Medical Centre. Depending on the severity of complication, participants will either be reviewed by the community nurses or be asked to present to the emergency department at Flinders Medical Centre. Thus, any adverse effect will be attended to as early as possible. If the situation demands removal of the LTAD catheter, the participant will have the option of having the catheter removed and withdrawing from the study, and will return to LVPs (SOC). The incidence of infections, either at the insertion site or intraperitoneally, should be less with the prophylactic antibiotics administered throughout the duration of LTAD. Potential risks related to LTAD insertion are detailed clearly in the participant information sheet and participants will be given the option to ask questions before consent is obtained.

Benefits: Since the study will be conducted only in patients for whom no other treatment modalities such as liver transplantation or TIPSS can be safely offered, we foresee no ethical implications. In this study, the feasibility of caring forthese patients at home using LTAD will be explored, and the safety and efficacy of this pathway will be studied. ESLD patients with refractory ascites have a poor quality of life and high symptom burden. Drainage of ascites with LTAD in the comfort of their home, without hospitalisation or albumin infusion, is likely to be seen as the best form of supportive care. In the only available RCT that compared LVP and LTAD, there was no increase in incidence of serious adverse events (6). Thus participants could potentially avoid presenting to hospital every week for ascitic fluid removal and the associated discomfort if a hospital bed is not immediately available. If successful, this study will be the first of its kind to provide feasibility data and help us plan large scale RCTs to establish the role of LTAD in ESLD.

1. **Ethical Review**

The study will be conducted in full conformance with principles of the “Declaration of Helsinki”, Good Clinical Practice (GCP), the National Statement on Ethical Conduct in Human Research (NHMRC, 2007), Australian Code for the Responsible Conduct of Research (2007) and within the laws and regulations Australia.

Ethical approval from the following HRECs will be obtained:

* Southern Adelaide Clinical Human Research Ethics Committee (SAC HREC)

Any future use of the data collected in this study for a new research purpose will be subjected to HREC approval.

1. **Site/Governance Review**

In accordance with the *SA Health Research Governance Policy Directive,* Site Specific Assessment (SSA) Approval will be sought from individual public health sites where the project is being conducted, including:

* Flinders Medical Centre, SA

1. **Consumer Engagement**

Consumers with prior experience in repeat LVPs were engaged to provide feedback on the study design, the potential benefit of LTADs, the participant information, and any other feedback. The overwhelming response from consumers was that they believed LTADs would be beneficial to patients with ESLD. The ability to be in the comfort of their homes and spend more time with family, while freeing hospital resources was a reason cited for the benefit of the LTAD. Another reason was the reduction in travel time as some stated that the in-hospital drains could be extremely tiresome requiring two to three days to recover. Of note, it was highlighted that the at-home drains may be difficult for patients outside of the metro area with access to community nurses and time constraints. This has been noted for consideration in future study designs should the study progress beyond this pilot, feasibility study. It was also highlighted that some patients may require some verbal explanation of the study requirements. This has been factored into the time patients get to consider the PISCF, with patients provided numbers to contact the study team with questions. The consenting team will discuss the study further with the patients prior to obtaining informed consent. All consumers were happy with the current study design and noted that the participant information sheet was clear and comprehensive about the requirements for potential participants.

# STUDY OUTCOMES AND SIGNIFICANCE

Ambulance ramping, overcrowding of emergency rooms, and increased demand for hospital beds are major problems faced in SALHN on a day-to-day basis. Based on a departmental audit, it was evident that 15 to 25 LVPs occurred every month in the year 2021 for patients with cirrhosis, and LVPs for refractory ascites contribute to at least 50% of this burden. These procedures are booked in the MDU, which is shared with the entire hospital and can offer only two slots, thrice a week. Our clinical demand often exceeds this, and as a result these palliative patients present to emergency rooms and occupy hospital beds. Therefore, in this study we are examining the feasibility of caring forthese patients at home using LTAD, as well as assessing the safety and efficacy of this pathway.

We anticipate that conducting ascitic drains in the comfort of a patient’s home will help to mitigate the bed shortage crisis and emergency room presentations. In addition, this pathway has the potential to significantly reduce costs in terms of saved hospital beds and albumin infusions. We also anticipate the use of LTADs will be associated with patient acceptability and improved quality of life (QoL) with timely abdominal drainage without hospital stay.

If successful, SALHN will be a pioneer in advocating this model of care in Australia. Well-planned RCTs that evaluate the efficacy of LTAD in comparison to standard of care LVP are needed before LTAD can become an integral part of ESLD care. Results from this study will be used to inform the design of a multicentre, phase 2/3 non-inferiority RCT. Hence, the planned study will inform us of the feasibility of conducting further RCTs in this area of growing need in clinical medicine.

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