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| **1 Trial Details** | | | |
| **Protocol/Clinical Trial Title:** | A pilot study of telerehabilitation for people with chronic liver disease. | | |
| **Protocol Number (Version and Date):** | Version 2, 4/12/22 | | |
| **Amendment**  **(Number and Date):** | - | | |
| **Trial Start Date:** | 15/01/2023 | **Trial Finish Date:** | 31/12/2024 |
| **Coordinating Principal Investigator Name:** | Andrew Maiorana | | |
| **Coordinating Principal Investigator Contact Details:** | c/o  Advanced Heart Failure and Cardiac Transplant Service (AHFCTS)  South Metropolitan Health Service  Fiona Stanley Hospital  Ground floor, Clinic 9A, 11 Robin Warren Drive, MURDOCH WA 6150  Mob: 0433567369  Email: Andrew.Maiorana@health.wa.gov.au | | |
| **Sponsor Name (if applicable):** | NA | | |
| **Laboratory Name (if applicable):** | NA | | |

* 1. **Trial Summary**

Chronic liver disease (CLD) is an overarching term for a range of conditions that lead to liver dysfunction. Sequelae of CLD include impaired cardiorespiratory fitness and sarcopenia, the loss of muscle mass and functional strength. Preliminary research suggests that exercise is safe for people with compensated CLD and may improve health and fitness, while reducing sarcopenia.1

Previous research on the effects of exercise training in people with CLD has involved centre-based exercise programs.2-6 Centre-based exercise programs occur at locations like hospitals or community centres, such as gyms. However, these can be difficult to access for people with chronic disease. An alternate rehabilitation platform is telehealth, which involves the remote delivery and supervision of an exercise program through a video call or phone call. Telehealth exercise programs, known as telerehabilitation, have been shown to be as effective as centre-based rehabilitation for chronic cardiac and pulmonary conditions.7,8

The aim of this pilot study is to collect preliminary data on the effects of a telerehabilitation exercise program on parameters of health and fitness in people with CLD. Participants will be randomised to a control or intervention group. Intervention participants will undertake an 8-week aerobic and strength exercise program to complete at home. A few telerehabilitation appointments will be provided to monitor participants while encouraging independence. Outcome measure will be assessed before and after the intervention and control period to evaluate changes in parameters of health and fitness, and feasibility data will also be collected. These data will be used to support a fully powered RCT in the future.

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| **2 Rationale / Background** |

The liver is a complex organ with significant roles in synthesising substances such as fats, proteins and cholesterol and breaking down waste products.1 The liver is also required for metabolism and vitamin storage.1 However, the liver is at risk of diseases that affect its function and these can have severe physiological consequences. 2 One of the many consequences is sarcopenia, which is muscle atrophy and functional decline, which can finally result in frailty.9,10

Exercise programs have been found to improve the health and fitness of people with CLD. Combined aerobic and strength exercise programs have been found to reduce muscle sarcopenia and improve aerobic capacity in people with chronic liver disease.2-6 Franco et al6 observed that aerobic training can reverse liver fibrosis in people with metabolic associated fatty liver disease. Furthermore, body mass index was found to decrease in exercise participants with metabolic associated fatty liver disease. 11, 12 However, these findings have all been derived from in-person, centre-based programs, which can be difficult to access for people with chronic disease.13,14 Conversely, telehealth exercise programs (telerehabilitation) can be prescribed where participants can complete an exercise program from home with remote guidance from an exercise supervisor.15 Telerehabilitation has been shown to be safe and can offer a similar improvement in health to that of centre-based programs for people with chronic cardiac or pulmonary disease.7,8 Despite the promising evidence for telerehabilitation, this mode of exercise has not been trialled in people with CLD.

At Fiona Stanley Hospital, outpatients with CLD are given a pamphlet that guides self-management of their condition to prevent decompensation of CLD. This includes appropriate nutrition, taking prescribed medications, completing blood tests, maintaining bone health, and recommendation to complete 150 minutes of exercise a week.16 Aerobic, resistance, flexibility and balance exercises are recommended to maintain muscular strength and functional capacity, and to minimise frailty, however a structured exercise program, is not routinely provided for patients.16

The purpose of this study is to investigate if a telerehabilitation program, involving a combination of aerobic and resistance exercise training, is feasible for people with CLD and can improve their health and fitness.

Microsoft Teams® (MS Teams® ) will be used as a telehealth platform to connect the therapist and patient. Physitrack® will be used as an adjunct to provide a digital exercise program with pictures for the participants to follow.

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| **3 Trial Aims / Objectives / Hypotheses** |

**3.1 Aims and objectives**

To evaluate the efficacy and feasibility of a telerehabilitation program for people with chronic liver disease.

**3.2 Research question**

In tertiary hospital outpatients with compensated CLD, does an 8-week, telerehabilitation program, involving a combination of aerobic and resistance exercise, improve physiological and psychosocial measures of health and fitness, compared to a control group receiving usual care?

**3.3 Hypotheses**

Compared with usual care, a telerehabilitation program involving resistance and aerobic exercise will:

1. Increase VO2 peak and one repetition maximum strength;
2. Improve body composition and quality of life;
3. Reduce liver stiffness;
4. Be feasible.

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| **4 Trial Design** |

**4.1 Study endpoints**

Primary endpoints

* Strength: One repetition maximum chest press and leg press; handgrip dynamometry
* Aerobic capacity: VO2 peak measured during a graded treadmill test

Secondary endpoints

* Health related Quality of Life: SF-12 questionnaire;
* Anthropometry: International Society for the Advancement of Kinanthropometry (ISAK) restricted profile;
* Liver Health: Liver function blood test;
* Liver stiffness/structure: Transient elastography (Fibroscan®)
* Feasibility: integrity of study protocol, acceptability of the intervention, selection of primary outcome measure and sample size calculation

**4.2 Study design and method**

**Pilot randomised control trial**

Participants will be randomised to an exercise intervention or a usual care control group. The intervention will involve an 8-week telerehabilitation program, involving aerobic and strength components. The control group will be asked to maintain their usual activities for the 8 week study period, and will be provided with an exercise program at the conclusion of the trial. Outcome measures will be assessed before and after the study period.

***Assessments:***

Aerobic capacity will be measured during cardiopulmonary exercise testing involving a graded treadmill test (Modified Chronotropic Protocol) to volitional exhaustion, to determine peak oxygen consumption (VO2peak). During the test the participant will be continuously monitored with a 12-lead electrocardiogram, with the rating of perceived exertion (Borg Category Scale) and blood pressure measured at rest, prior to the end of each stage and at peak exercise. Consistent with standard clinical practice. Breath-by-breath indirect calorimetry will be used to determine ventilatory parameters at rest and during exercise and recovery (Vyntus CPX Jaeger, Carefusion, Germany).

Muscular strength capacity will be measured using a one repetition maximum for the upper and lower limb using machine-stack weights (Cybex equipment®). This process involves lifting progressively heavier weights until the maximum weight is found that can be lifted once only with good technique and without straining. Hand grip dynamometry will be employed to measure hand strength.

Anthropometry will be assessed using skinfold testing and girth measurements. The International Society for the Advancement of Kinanthropometry (ISAK) restricted profile will be used to measure anthropometry. This will involve the participant being weighed on a set of scales and have girth measurements of their waist and hips with a tape measure. Calipers will used on standardised parts of the body to measure participant fat percentage.

Standard of care blood biomarkers (Urea and electrolytes, full blood picture, liver and kidney function) will be measured in the PathWest laboratory using a venipuncture.

Liver stiffness/structure will be measured using transient elastography (Fibroscan®). A qualified clinician will administer this outcome measure.

Health Related Quality of Life will be measured using the SF-12 questionnaire. This questionnaire measures limitation in physical, social and occupational activities because of health problems. Furthermore, it covers bodily pain, general mental health, vitality and general health perceptions (Appendix 16.5).

Feasibility outcome measures will include investigation of the integrity of study protocol, acceptability of the intervention, selection of a primary outcome measure and sample size calculation. Participants will be asked to complete a questionnaire to document their experiences, and barriers and facilitators to participation, in the telerehabilitation program. (Appendix 16.2).

The timeline of outcome measure assessment and the intervention period is explained by *(figure 1.1)*

Invitation of participants to partake in the trial

Participants that give informed consent, meet inclusion criteria and do not meet the exclusion criteria are recruited

Participants undertake initial outcome measure assessment

Randomisation to the control and intervention group through opaque envelopes

8-week Intervention group (staggered & identical intervention)

Control group

Randomisation to intervention group 1 or 2 via opaque envelopes

Intervention group 2

Intervention group 1

Final outcome measure assessment

Data analysis

*Figure 1.1: Trial Design*

***Exercise intervention:***

Exercise prescription will involve aerobic training 3 times a week and strength training 2 times a week for participants to complete at home *(Figure 1.2).*

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| --- | --- | --- | --- | --- | --- | --- | --- |
| Exercise | Monday | Tuesday | Wednesday | Thursday | Friday | Saturday | Sunday |
| Aerobic |  | ☐ | Rest day | ☐ |  | ☐ | Rest day |
| Strength | ☐ |  |  | ☐ |  |

*Figure 1.2: Exercise program schedule*

Participants will be encouraged to complete all exercise sessions as described in *(Figure 1.2)* Telerehabilitation appointments will be provided to monitor participant exercise form. Exercises will be tailored to individual participant’s level of fitness as evaluated during the baseline assessments. The intervention group will be split into two groups of 5 participants each, which will complete the exercise program in a staggered manner. One intervention group will begin the exercise program one week before the other group to ensure timely outcome measure assessment post-intervention. Participants will be given a training log to monitor compliance (Appendix 16.4). Participants will be taught the exercise program in person at FSH on the same day as initial outcome measure testing or can elect to attend FSH another day to learn the exercise program.

The aerobic training component will involve a walking program, which will be over and above any current walking they are doing for exercise. Participants will begin with a moderate intensity 15-minute walk every aerobic training session for the first week of the intervention. For the first 4 weeks (week 1-4), walking duration will increase by 5 minutes every week until the participants are walking 30 minutes per session i.e. week 1 walks will be 15 minutes in duration, week 2 walks 20 minutes in duration, week 3 walks 25 minutes in duration and week 4 walks 30 minutes in duration. For the last 4 weeks of the program (week 5-8), high intensity walking intervals will be progressively added each week, until the participant is walking 30 minutes at a high intensity. *(Figure 1.3)* describes how higher intensity intervals will be progressively added to the aerobic walking program. Walking intensity will be relative to participants’ baseline aerobic fitness and will be prescribed based on heart rate and rating of perceived exertion. Participants will be loaned polar monitors® to check their heart rate when completing aerobic training to ensure they are exercising at a moderate intensity. Furthermore, they will be instructed to use the Borg Rating of Perceived Exertion (Borg RPE) 6-20 scale for subjective intensity of exercise.

This aims to confer an improvement in aerobic capacity through progressive overload.

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| --- | --- | --- | --- | --- | --- | --- | --- |
|  | Time | 0-5min | 5-10min | 10-15min | 15-20min | 20-25min | 25-30min |
| Intensity | Week 5 | Moderate | High | Moderate | High | Moderate | Moderate |
| Week 6 | Moderate | High | Moderate | High | Moderate | High |
| Week 7 | High | High | Moderate | High | Moderate | High |
| Week 8 | High | High | High | High | High | High |

*Figure 1.3: Progressed aerobic interval training program (week 5-8)*

The strength training program will consist of a whole-body exercise program *(Figure 1.4)*. Exercises will be completed using body weight and a resistance band/gymstick®. Participants will be loaned a gymstick® if they prefer or will be provided a resistance band for the exercises requiring a resistance band. For the first 4 weeks (week 1-4), easier exercises will be completed which include: standing up from a chair, resistance band rows in a long sitting position, mini squats, wall push ups, double leg calf raises, and leg raises with flexed knees in a supine position. The exercises will be completed in a circuit format with a 5-minute rest between sets. The 5-minute rest will be active recovery, where participants walk at low intensity.

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| --- | --- | --- | --- | --- | --- | --- | --- |
| Exercise | Sit to stand | Resistance band rows (long sitting position) | Mini-squats | Wall push ups | Calf raises on flat ground | Leg raises (flexed knees) | Rest |
| Body Part | Lower limb | Upper  limb | Lower  limb | Upper  limb | Lower  limb | Abdominals | 5 minutes |
| Repetitions | 10 | 10 | 10 | 10 | 10 | 10 |
| Sets | 2 | 2 | 2 | 2 | 2 | 2 |

*Figure 1.4: Generic Initial strength circuit program (week 1-4)*

For the last 4 weeks (week 5-8), participants will partake in more difficult exercises as outlined by *(figure 1.5)*, which include standing up from a lower seat (or any other stable and lower surface), resistance band rows in a bent over standing position, lunges to ½ range, kneeling/ normal push-ups, single leg calf raises, and abdominal crunches. A circuit format and a 5-minute walking active recovery will be used again. By increasing the intensity of the exercise program halfway through the intervention, it is anticipated that participants will have an improvement in strength due to progressive overload.

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| --- | --- | --- | --- | --- | --- | --- | --- |
| Exercise | Sit to stand (lower seat) | Resistance band rows (bent over standing position) | ½ range Lunges  (bilaterally) | Kneeling/ normal push ups | Single leg calf raises (bilaterally) | Abdominal crunches | Rest |
| Body part | Lower limb | Upper limb | Lower  limb | Upper  limb | Lower  limb | Abdominals | 5 minutes |
| Repetitions | 10 | 10 | 10 | 10 | 10 | 10 |
| Sets | 2 | 2 | 2 | 2 | 2 | 2 |

*Figure 1.5: Progressed strength circuit program (week 5-8)*

Telerehabilitation appointments on MS Teams® will be provided in small groups (2-3 participants). Participants will complete their strength exercise program with supervision. These telerehabilitation programs will be scheduled once per week in week 1, 3 and 5 to observe participants and ensure participants are maintaining good form. In week 7, a catch-up session will be scheduled where participants can ask questions and motivation will be provided by the exercise supervisor. A catch-up session will be provided instead of a monitored strength session to promote participant independence post-intervention. Furthermore, intervention participants can elect to join a Facebook messenger® group chat where they can interact with each other and the intervention supervisor regarding the intervention. This will allow participant questions to be addressed in a timely manner instead of having to always wait for the telerehabilitation appointment.

**4.3 Bias**

Allocation bias will be avoided by allocating participants to the control and intervention group using opaque, sealed envelopes. Intention to treat will be used when reporting results from the study to reflect a realistic telerehabilitation program. However, participants and exercise program personnel will not be blinded. Outcome measure assessment personnel will also not be blinded.

**4.4 Randomisation, de-identification and re-identification of participants**

Participants will be randomised using opaque envelopes. After randomisation, participants will be deidentified and assigned a participant code. The participant identification information will be stored on a password protected computer at Fiona Stanley Hospital.

When required, the study coordinator will log into the password protected computer and re-identify the participant by associating the participant with their code.

**4.5 Trial termination**

Individual participants will be withdrawn from the trial if they meet any of the following criteria:

* Withdraw informed consent and elect to terminate their participation in the study
* If a participant’s health changes and they develop a condition outlined in the study exclusion criteria once beginning the trial.

Parts of the trial will be terminated if any of the following criteria are met:

* No access to outcome measure equipment (Fiona Stanley Hospital enters a state of emergency and no access to equipment at other institutions such as Curtin University)

The entire trial will be terminated if the following criteria are met:

* Australia/ WA enters a state of emergency for an extended period

**4.6 Data identification**

Data collected from the study will be deidentified and stored on the R:Drive at Curtin University on a password protected computer with a lock-out period of 5 minutes. Participant identification codes will be stored at Fiona Stanley Hospital on a separate computer to the data, only accessible to Professor Maiorana and Nikil Redipali and will be password protected. Data will be stored for 7 years after which time it will be deleted. Any hard copies of data will be stored in a locked filing cabinet in a locked room at Fiona Stanley Hospital.

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| **5 Source and Selection of Participants** |

**5.1 Source of Participants**

Participants with compensated chronic liver disease will be recruited from the Fiona Stanley Hospital Gastroenterology Outpatients service. Out-patients will be mailed an information form regarding the study from Professor Maiorana and advised that Nikil Redipali will contact them by phone to answer any questions they have about the study and ascertain their interest in participating. The sample will consist of 20 individuals. There will be 10 participants in the control group and 10 participants in the intervention group.

**5.2 Participant inclusion criteria**

Eligible participants must have the following characteristics:

* Diagnosis of compensated chronic liver disease
* Outpatient from Fiona Stanley Hospital
* Access to appropriate technology for telehealth appointments which may include a computer/smart phone/tablet that can download the MS Teams app® .

**5.3 Participant exclusion criteria**

Characteristics that would exclude candidates from participation are:

* De-compensation of CLD
* The American College of Sports Medicine’s contraindications to completing an exercise program17
* Musculoskeletal conditions that will make the exercise program painful (including severe rheumatoid arthritis, severe low back pain and acute injuries such as ligament sprains)

**5.4 Participant withdrawal criteria**

1. When participant withdraw or trial termination criteria are met, participants will immediately be removed from the study. Participants can notify one of the researchers to withdraw from the study if they wish to. They can verbally withdraw from the study or withdraw in writing if they wish.
2. Intention to treat analysis will be used on the collected data. If participants choose to withdraw from the study at any point, they will be included in data analysis with their written permission.
3. Participants that withdraw will be replaced if possible.
4. When withdrawing from the study, participants will be asked for the reason they wish to withdraw if they choose to disclose that information, as this will be valuable for informing feasibility. They will be thanked for their contribution and if they elect to receive them, they will be notified of the results of the study at its conclusion.

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| **6 Treatment of Participants** |

**6.1 Description of the treatment method**

The treatment will consist of an 8-week aerobic and circuit-based strength telerehabilitation program. Telerehabilitation appointments will be provided for the strength training program on week 1, 3 and 5 to ensure participants are completing the exercises correctly. In week 7, a telerehabilitation appointment will be provided to participants as an opportunity to ask questions and maintain motivation for the last part of the intervention period. Participants can elect to join a Facebook Messenger® group chat to communicate about intervention related concerns. A description of the exercise program can be found under the subheading: Trial Design (4).

**6.2 Justification of the treatment method**

Previous research highlights that an exercise program is safe and may be effective in improving the health of people with chronic liver disease.2-6 The effect of telerehabilitation on the health of people with chronic liver disease has not been researched, however, telerehabilitation has been shown to be safe and effective in improving the health of those with chronic cardiac and pulmonary disease.7,8

An 8-week exercise program will be completed as this duration facilitates progressive overload and has previously been shown to be associated with improvements in participant health and fitness.5

Aerobic training will be completed 3 times a week and a strength circuit program will be completed 2 times a week to aim for reduction in sarcopenia and improvement in general health. Strength training will consist of a whole-body exercise program and aerobic training will consist of a walking program. This may facilitate maintenance of whole-body muscle mass and may improve functional mobility.

Participants will complete a moderate intensity exercise program at a Borg rating of perceived exertion (RPE) Scale of 11-13 (fairly light to somewhat hard) and a heart rate equivalent to 60-75% of the maximum measured heart rate during baseline exercise testing.

Aerobic training will initially be 15 minutes in duration per session, however, participants will be progressively overloaded to complete 30 minutes of walking per session by the end of the exercise program to facilitate aerobic adaptation.

**6.3 Permitted medications/treatments**

Participants are to continue taking all prescribed medication. Rescue medication and first aid will be provided if required at any point during the study. Appropriate medical intervention will not be withheld if required.

**6.4 Monitoring of participant compliance**

Participants will be provided with an activity diary for each week, where they can tick off a day if they have completed the exercise program in its entirety.

During weekly telerehabilitation appointments, the exercise supervisor can discuss compliance with participants and provide motivation if participants are non-compliant.

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| **7 Assessment of Efficacy** |

**7.1 Outcome measures**

Outcomes investigated are:

* Health related Quality of Life: SF-12 questionnaire
* Aerobic capacity: VO2 peak graded treadmill test
* Strength: One repetition maximum chest press and leg press7; hand dynamometry
* Anthropometry: International Society for the Advancement of Kinanthropometry (ISAK) restricted profile
* Liver Health: Liver function blood test
* Liver stiffness/structure: Transient elastography (Fibroscan®)
* Feasibility: integrity of study protocol, uptake, compliance and acceptability of the intervention

**7.2 Efficacy assessment**

Outcome measures to evaluate efficacy of the program will be assessed pre- and post- the study period. Results will be deidentified and stored in a excel spreadsheet on a computer at Fiona Stanley Hospital. All outcome measure assessment will occur during normal working hours. SPSS Statistics® will be used for data analysis. A Shapiro-wilk test will be used to determine the normality of the scores. A paired samples t-test will be used to compare changes in outcomes over time if normally distributed. A Wilcoxson signed rank test will be used to compare changes in outcomes over time if not normally distributed. Statistical significance will be set at P<0.05.

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| **8 Assessment of Safety** |

**8.1 Risks and benefits of an exercise program for those with chronic liver disease**

**Risks**

The risk of adverse events resulting from exercise testing or training are exceedingly low.3,7,8 For example, even in patients with established cardiovascular disease, the risk of complications serious enough to require hospitalisation associated with a maximal exercise test is 1-3 per 10,000 tests, while the risk of death is estimated to be 2-5 per 100,000 tests.19 These risks will be reduced by the study’s strict exclusion criteria and close monitoring of participants.19 Other minor risks associated with exercise include the possibility of muscle soreness when commencing new exercises. This usally resolves within 48 hours and is reduced with subsequent exercise sessions.There is a low likelihood of participants suffering musculoskeletal injuries from an exercise program. Physically de-conditioned individuals are predisposed to musculoskeletal injuries with a high intensity exercise program that over-exerts them. This can be prevented by prescribing an exercise program to match a participant’s baseline fitness and encourage adaptation through progressive overload.

**Benefits**

Previous research has highlighted the potential benefits associated with an exercise program in people with CLD. Franco et al6 proposes that aerobic training may reverse liver fibrosis in people with metabolic associated fatty liver disease. Body mass index was found to decrease in exercise participants with metabolic associated fatty liver disease.6,18 Combined aerobic and strength exercise programs have previously been found to reduce muscle sarcopenia and improve aerobic capacity in people with chronic liver disease.2-6

**8.2 Risks and benefits of a telerehabilitation program for people with chronic disease**

**Risks**

The incidence of adverse events with a telerehabilitation program for people with chronic disease has not been found to be increased compared with ‘in-person’ exercise.7,8 Furthermore, safety is optimised by excluding patients at increased risk of adverse exercise responses, based on established contraindications to exercise.7,8

**Benefits**

A telerehabilitation program for people with pulmonary or cardiac disease has been shown to offer similar benefits when compared to centre-based rehabilitation program. A systematic review by Cox et al7 found that aerobic capacity, dyspnoea and quality of life improved to a similar extent in participants undertaking centre-based pulmonary rehabilitation compared with pulmonary telerehabilitation. A systematic review by Ramachandran et al8 found that cardiac telerehabilitation and centre based cardiac rehabilitation offered a similar improvement in aerobic capacity, quality of life and depression, while cardiac telerehabilitation may foster better physical activity behaviours.

**8.3 Safety**

Should a participant safety event occur, the SMHS Ethics Committee will be notified and any factors contributing to the event will be reviewed with necessary changes made to the study protocol.

In the unlikely event of a serious adverse event, data collection will be ceased until any future risk to the participants is resolved.

**8.4 Adverse event reporting**

The CPI Maiorana will assess any adverse events, and if deemed serious, refer the patient to AI Ayonrinde for his review. Detailed records of all reported adverse events (AEs) will be recorded in BOSSnet. We will report all significant safety issues (SSIs) that meet the definition of an Urgent Safety Measure (USM) within 72 hours of becoming aware of the issue. We will also submit details of the SSI to HREC without undue delay and if an amendment to the protocol is deemed appropriate, this will be submitted with 15 calendar days.

**8.5 Follow-up of Adverse Events**

Any participant experiencing a serious adverse event will be reviewed at the earliest opportunity by a doctor from FSH. In a case where the event occurs in hospital and the the participant returns home after the event, they will be followed-up within 24 hours to review their recovery from the event. They will then be encouraged to contact the research team if the effects of the event don’t resolve over the ensuing days.

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| **9 Data Management, Statistical Analysis and Record Keeping** |

**9.1 Statistics and Interim Analysis**

Descriptive statistics of patients will include age, sex, medical history including chronic liver disease history and medication.

A Shapiro-wilk test will be used to determine the normality of the scores. A paired samples t-test will be used to compare changes in outcomes over time if normally distributed. A Wilcoxson signed rank test will be used to compare changes in outcomes over time if not normally distributed. The statistical significance will be set at P<0.05.

**9.2 Sample Size**

Twenty (20) participants will be enrolled. There will be 10 individuals assigned to the control group and 10 individuals assigned to the intervention group. A sample size of 20 participants will be recruited to obtain preliminary data and establish feasibility of a full powered RCT in the future. This study is likely to not have the power to establish a statistically significant difference.

**9.3 Study Power and Significance**

Study power will not be calculated for this pilot study. Statistical significance will be set at P<0.05.

**9.4 Statistical plan deviations**

N/A

**9.5 Selection of participants for analyses**

All randomised participants that have not withdrawn consent to use outcome measure data will be included in the analyses. Intention-to-treat data analysis will be used for the primary outcome meaures.

**9.6 Data management**

Data collected during the study will be stored on a password protected computer at Fiona Stanley Hospital, accessible only to the research team

Upon completion of the study, data will be de-identified and transferred to Curtin University via the Curtin Research (R):Drive. Data at Curtin will be stored on a password protected computer with a lock-out period of 5 minutes. Participant identification codes will be kept separate to the data on a password protected computer at Fiona Stanley Hospital. This will only be accessible to Professor Maiorana and student Nikil Redipali. Data will be stored for at least 7 years post-publication, and then deleted.

**9.7 Procedures for missing, unused and spurious data**

N/A

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| **10 Monitoring / Audit** |

**10.1 Monitoring, Audit and Regulatory Inspections Statement**

We, the project investigators will permit project-related monitoring, audits, and regulatory inspections, providing direct access to source data/documents. This may include, but not limited to, Human Research Ethics Committees and institutional governance review bodies.

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| **11 Quality Control and Quality Assurance** |

**11.1 Compliance statement**

This trial will be conducted in compliance with the protocol, Good Clinical Practice and the application regulatory requirements.

**11.2 Quality control**

The quality of data will be reviewed frequently throughout the study to ensure quality control.

Quality control & quality assurance measures to ensure quality of data.

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| **12 Ethics** |

**12.1 Ethical considerations**

Ethical considerations regarding this project are centred around the time burden to patients, privacy of information, travelling for outcome measure assessment and duty of care.

Completing the exercise program, follow up sessions and outcome measure testing will take participants’ time. To limit time burden on participants, participants will only have to attend FSH for outcome measures before and after the exercise program and to be taught the exercise program in-person.

During the study, Professor Andrew Maiorana will have the ethical responsibility to direct participants to receive appropriate help for example if they report signs of mental health issues, reduced quality of life or if they sustain a physical injury during the intervention or outcome measures.

Data collected from the study will be deidentified and stored on the R:Drive at Curtin University on a password protected computer with a lock-out period of 5 minutes. Participant identification codes will be kept in a separate location to the data, only accessible to Professor Maiorana and Nikil Redipali and will be password protected. Data will be stored for 7 years after which time it will be deleted.

Participants will be provided with an information and consent form to read before deciding whether to partake in the study. They will be encouraged to ask questions and to only sign the form if they consent and completely understand the information provided.

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| **13 Budget, Financing, Indemnity and Insurance** |

**13. 1 Budget**

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| Item | Estimated cost | Source of Funding |
| Blood testing for liver health | - | Standard of care testing |
| Transient elastography (Fibroscan®) | - | Provided ‘in-kind’ Gastroenterology Department |
| Participant parking reimbursement | $180 | Curtin Honours student allowance |
| Resistance bands | $20 | Curtin Honours student allowance |
| Gymsticks® | - | Provided ‘in-kind’ Gastroenterology Department |

*Figure 1.8: Budget*

**13.2 Insurance and indemnity**

Professor Andrew Maiorana will be insured by Curtin University for the purpose of the study.

Dr Koya Ayonrinde will be insured by Fiona Stanley Hospital

Nikil Redipali will be insured by Curtin University.

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| **14 Publication** |

Results will be published in a student thesis. The manuscript will be submitted to a scientific journal and a presentation will be made at a conference

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| **15 References** |

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| **16 Appendices** |

**16.1 Participant information and consent form**

**16.2 Barriers and facilitators questionnaire**

**16.3 Participant invitation letter**

**16.4 Telerehabilitation training log**

**16.5 SF-12 Questionnaire**