Information Sheet for Participants
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Safety and acceptability of exercise for Chronic Lymphocytic Leukaemia

We would like to invite you to participate in this research study. Please take time to read the following information carefully and contact the academic research team if anything is not clear. All research in the NHS is assessed by an independent group of people, called a Research Ethics Committee, to protect your interests. This study has been reviewed and given favourable opinion by the Dulwich Research Ethics Committee. You have been invited to take part in this study because your haematologist thinks you are physically capable and might be interested. This information sheet is divided into three parts:

Section A: information on why you should consider taking part.
Section B: a brief description of what will be required if you decide to take part.
Section C: other information about taking part

SECTION A: WHY SHOULD YOU TAKE PART?

What is the aim of the study?

This is the first study looking at how exercise might benefit people with early stage chronic lymphocytic leukaemia (CLL), monitored on a 'watch and wait' basis until treatment is needed. We want to find out how an exercise training intervention is received, and whether it has an effect on disease activity and overall health and wellbeing.

Do I have to take part?

No. It is entirely up to you whether or not to take part in this study. You are free to withdraw your participation at any time without giving a reason. If you withdraw from the study, we will keep the information about you that we have already obtained. To safeguard your rights, we will use the minimum personally-identifiable information possible.

What are the possible benefits?

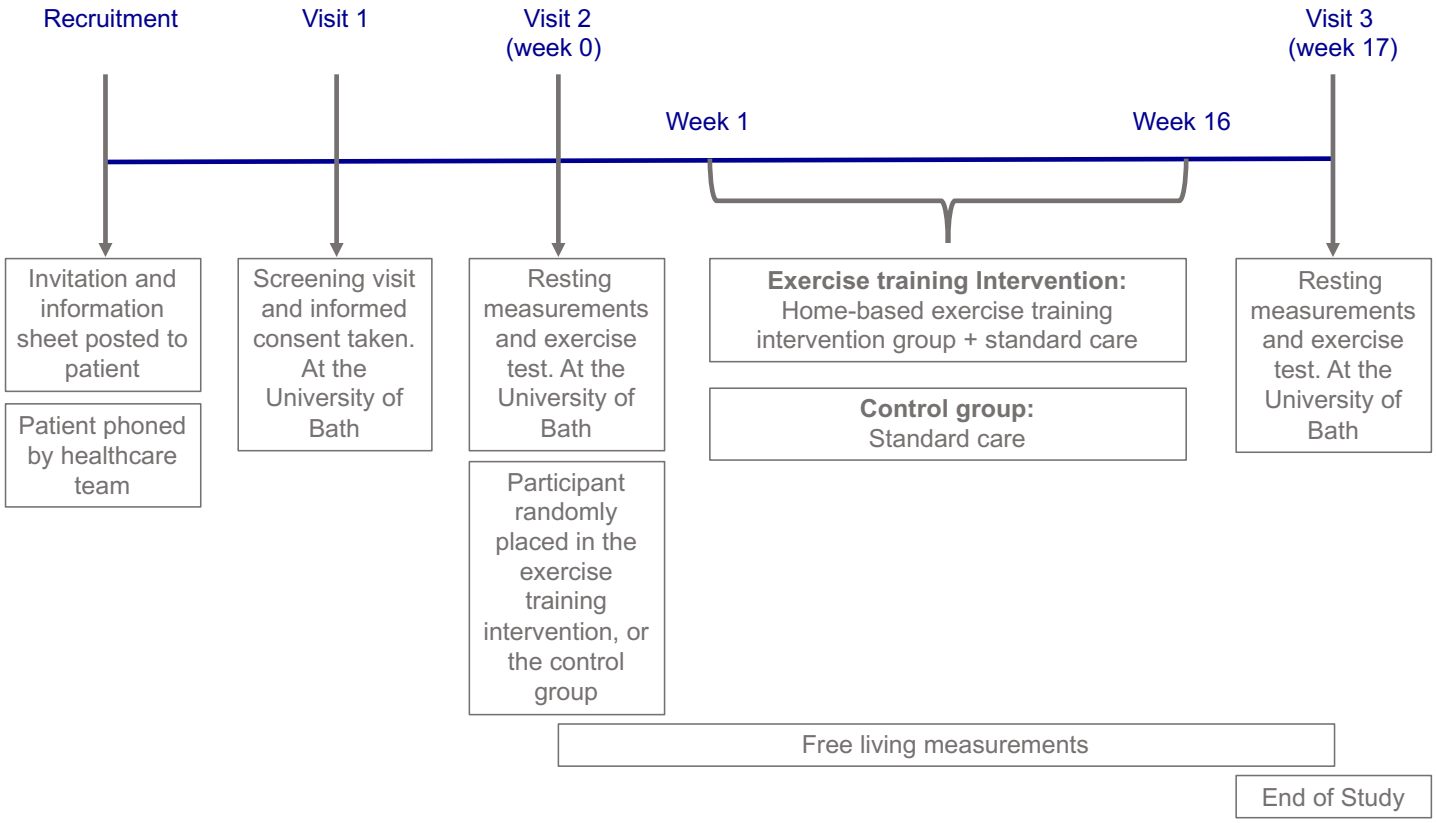
- There is no financial compensation for visits to the University of Bath, but reasonable travel expenses will be reimbursed, and parking is free of charge.

- You will be given a report of your test results, so you know more about your blood pressure, body composition (body mass index (BMI), fat, muscle and bone density), diet, physical activity level and fitness level, in comparison to the general public.

SECTION B: WHAT WILL BE REQUIRED IF YOU TAKE PART

What is involved if I do take part?

There will be three visits to the University of Bath, a screening visit (Visit 1), an initial measurement visit (Visit 2) and a final measurement visit (Visit 3). Visits 2 and 3 will involve an exercise test. After Visit 2, you be randomly placed in either the exercise training intervention group, or the control group. The exercise training intervention group will take part in 4 months of exercise sessions (at home). The control group will continue without an exercise intervention. And after 4 months both the exercise training intervention and control groups will complete Visit 3. You should be prepared to commit this time to the study if you decide to take part.



What will happen at the screening (visit 1)?

This will happen at the University of Bath with a member of the research team. You will have an opportunity to ask any questions, the researcher will check you are suitable to take part and then they will ask for your written informed consent (signature). The researchers will measure your heart and other heart-related measurements by conducting a resting electrocardiogram (ECG) on you. You will be fitted with an electrocardiogram (ECG) where 10 stickers will be placed on your chest and abdomen, and you will remain in a seated position for 5 minutes while the ECG records your resting heart activity. This is to make sure that it is safe for you to perform difficult exercise during the following visits.

Free-living measures pre trial:
You will be given a physical activity monitor, that is like a standard wristwatch, which measures your activity for 9 days and a food diary to record your food intake for 3 days.

We will then agree a time for you to come in for visit 2.

What will happen at visit 2?

This visit is at the University of Bath and will take roughly 90 minutes. This visit will be on a weekday morning and at a convenient time for you.

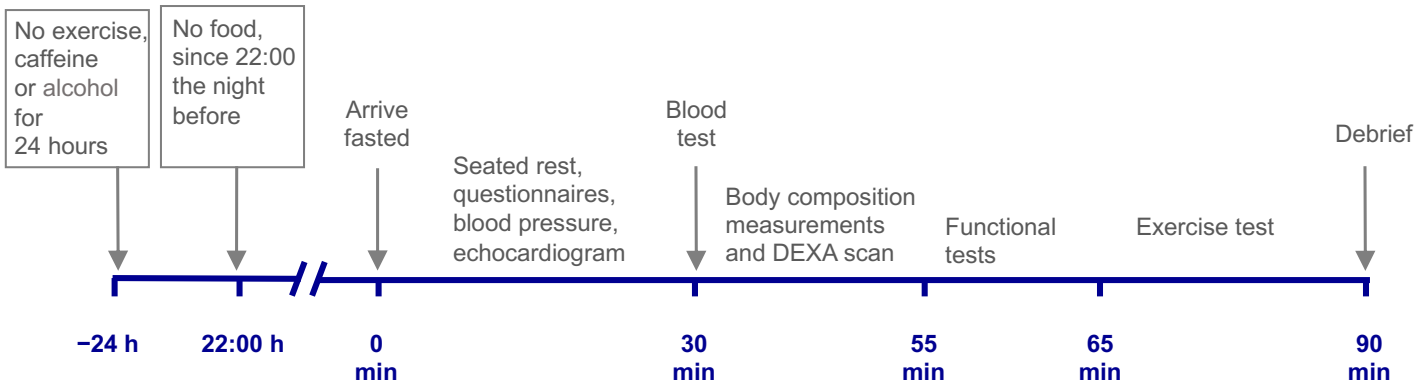
What we will ask you to do in the 24 hours before your visit:

1) Please do not exercise.
2) Please do not have caffeine-containing products (e.g., tea, coffee, chocolate, sports or energy drinks).
3) Please do not drink any alcohol.
4) Please eat your last meal before 22:00 the night before (you may drink water on the morning of your visit)

5) Please arrive at the University wearing light clothing suitable for exercise during this visit (ideally shorts, t-shirt/sports top and supportive shoes).

We are asking you not to exercise, eat, drink caffeine or alcohol before the visit because we know that exercise, caffeine, alcohol and certain foods may affect some of the results that we are measuring during this visit. We will provide a snack for you to eat after the measurements have been taken.

During the visit…
Please see the schematic diagram below that summarises what will happen during visit 2 and the accompanying text below:



1) Questionnaires: while resting in a seated position, you will be asked to answer questions on your wellbeing, physical activity level, sleep, fatigue, ability to conduct daily activities independently, stress levels and general health **(20 minutes).**

2) Blood pressure (BP): three measures will be taken by a cuff squeezing your arm.

3) Echocardiogram: a trained researcher will conduct a non-invasive (skin is not pierced) test called an echocardiogram to show how your heart muscle and valves are working. This test uses an ultrasound scan, which means a small ultrasound probe is used to send out high-frequency sound waves that generate pictures of your heart. When you are lying down, a lubricating gel will be applied to your chest or directly to the ultrasound probe, it will feel cold. You will be asked to lie on your left side and the probe will be moved across your chest.

4) Blood test (50 millilitres or 3 tablespoons): a trained phlebotomist will use a small needle (smaller than if donating blood) to take blood from a vein in your forearm, much like having a blood test at the hospital or doctor's surgery.

   From this blood test we will be measuring how many cells you have in your blood. We will then see how many immune and CLL cells are in the blood at rest. We are interested in seeing how the exercise training intervention will impact the number of these immune and CLL cells. We will also store some of the liquid non-cellular part of your blood in a freezer to make other measurements in the future **(5 minutes).**

5) Body composition: your waist and hip size and height will be measured with a tape measure. Your weight will be measured with scales **(10 minutes).**

6) Dual-energy x-ray absorptiometry (DEXA) scan: you will lie still on a bed while a low-dose x-ray scanner measures your body fat, muscle and bone density **(10 minutes).**

7) Functional tests: you will perform a number of simple tests that mimic normal daily activities, such as getting out of a chair, walking a short distance, reaching towards your toes and scratching your back. These measure your strength, balance and flexibility **(10 minutes).**

8) Exercise test: this will be performed on a static exercise bike. The test starts with 3 minutes of rest, followed by 3 minutes of easy cycling. The test will then get harder every minute; this will feel like you are cycling up hill. The test will carry on until the researcher stops it.

   Before the test starts, you will be fitted with an electrocardiogram (ECG) where 13 stickers will be placed on your chest and abdomen. You will also wear a blood pressure cuff on your arm, oxygen saturation clip on your finger and a facemask which covers your nose and mouth to measure the air you breathe. During the test a small capillary blood sample (less than 50 microlitres) will be collected from your ear lobe at the end of every 1 minute stage. These measurements are taken to safely and accurately measure your fitness. It also allows us to set a personalised exercise training intervention for you **(20 minutes).**

9) Debrief: we will explain the results of some of the measurements so you can find out more about your health and fitness **(5 minutes).**

Randomisation

You will then be randomly placed in either the exercise training intervention group, or the control group (no exercise). This method of allocation is performed using a web-based platform and based on chance alone. The researchers will not know which group you will be allocated before the randomisation is carried out.

Free-living physical activity measures during trial (both groups)

At four times during the trial period (weeks 2, 6, 10 and 14), you will be sent a physical activity monitor and a pre-paid envelope. You will be asked to wear the monitor for 9 days (to capture 7 full days) for measurement of free-living physical activity. The monitor is worn on the wrist and records acceleration and skin temperature continuously. No identifiable data is collected by the monitor. You will be provided with instructions on how to use the monitor, these instructions will emphasise the importance of wearing the monitor continuously, the monitor is waterproof so can be worn during waterborne activities (e.g. showering/swimming). At the end of the 9 days, you will be asked to return the monitor in the pre-paid envelope.

Exercise training intervention group

Exercise classes: alongside standard care, participants allocated to the exercise training intervention group will take part in two home-based exercise classes each week for 4 months. These classes are home-based and will be observed by a member of the Research Team via the Microsoft Teams video communication platform, each class will have a small number of participants, you will be given the choice of whether you would like to see other members of the class on the screen, at the same time, or not. These classes will last about 1 hour and will include cycling on a static exercise bike (delivered to your home at the start of the study), exercises to strengthen your muscles and stretches to improve your flexibility. At the beginning of each week, during the trial period, you will be emailed a link to the Microsoft Teams video communication platform. This link will enable you to attend the exercise training sessions observed by a member of the Research team. We will discuss the best time for your sessions at the beginning of the study. If you can't make a class at short notice, that is fine. There will be extra classes each week to make up any missed sessions. Each person's exercise programme is designed specifically for them to make it achievable, but it will be challenging as the cycling will build up to 'vigorous intensity'…you will get sweaty!

Unsupervised exercise at home: to meet exercise guidelines for good health, we would like you to do extra exercise in your own time once a week – a Sunday walk in the park, for example. We will also give you balance and mobility exercises which are important for reducing the risk of falls and fractures.

Exercise monitoring: the observed exercise classes and the unsupervised exercise will both be monitored using a Polar A370 fitness monitor. The Polar A370 fitness monitor is a wrist worn device that measures heart rate continuously. You will not be required to wear this monitor for the duration of the trial, you will only be required to wear the monitor during the observed and the unsupervised sessions. You will be provided with instructions on how to use the Polar A370, you will be asked to press a button on the face of the fitness monitor, at the start of each observed training session, and at the start of each unsupervised walking session, to record all of the sessions. Once a week, you will be asked to upload the data from the monitor and the monitor will be returned after Visit 3.

Control group

Participants allocated to the control group will continue with their standard care for 4 months. You will not take part in an exercise training intervention, but you will be offered exercise advice after the 4 month period (see end of the study section below).

Your free-living physical activity level will be monitored at four times during the trial period (weeks 2, 6, 10 and 14) during this 4 month trial period please do not vary your routine. To maintain scientific accuracy, we need to capture a true reflection of your usual free-living physical activity level.

What will happen at visit 3?

After 4 months, participants in both groups will be asked back to the University of Bath for visit 3.

Free-living measures:
You will be given another physical activity monitor and a food diary before visit 3.

Visit 3:

Repeat of visit 2 – at the University of Bath, at a similar time to when you attended visit 2. Please refer back to section “What will happen at visit 2” for detailed information.

The end of the study (both groups)

At the end of the study participants in both the exercise training intervention and the control group will be given a report of your test results, so you know more about your blood pressure, body composition (body mass index (BMI), fat, muscle and bone density), diet, physical activity level and fitness level, in comparison to the general public. In addition, you will be given an information sheet with recommendations on staying active upon completion of this study. This will include a home-exercise programme and resistance bands provided free of charge, and information on local exercise referral schemes.

What other data will be collected?

Information about your CLL, other relevant medical conditions and medications you take will be accessed from your medical notes by a member of your healthcare team and shared with the researchers.

SECTION C: OTHER INFORMATION ABOUT TAKING PART

What are the risks?

Blood sampling: carries risks including slight pain, bleeding, bruising, and infection. A trained phlebotomist will take your blood, much like in the doctor’s surgery, following best practice so these risks are minimised.

Radiation: the DEXA scan involves a very small dose of radiation, which is considered safe and is an equivalent

amount of radiation that you would be exposed to if taking a short flight from London to Paris.

Exercise test and exercise classes: exercise will make you feel sweaty and out of breath. There is also a chance that you might get injured, and during exercise your risk of having a cardiac event (e.g. heart attack) is slightly higher than normal. However, we will assess your risk of these complications before you enter the study and take all possible measures to minimise this risk, including taking time to ask your haematologist about any health concerns you have, and discussing any new health problems if they arise during the project. In the long-term, exercise reduces the risk of injuries associated with falling, cardiovascular diseases, and other diseases.

Questionnaires: some of the questions you will be asked to answer are to assess your mental health and anxiety levels. These may be uncomfortable questions. If you are worried about your mental health, you should contact your GP or health care team. If appropriate, these health care professionals may refer you to a clinical psychologist. The research team based at the University of Bath will not refer you to a clinical psychologist.

Activity monitoring: wearing activity monitors may, in some cases, result in some minor skin irritation, but this should be minimal if guidance is followed. We will show you how to use the monitors and give you some instructions to take away with you to reduce this risk.

What will happen to my data?

The University of Bath is the sponsor for this study based in the United Kingdom. We will be using information from you and your medical records in order to undertake this study and will act as the data controller for this study. This means that we are responsible for looking after your information and using it properly. Your rights to access, change or move your information are limited, as we need to manage your information in specific ways in order for the research to be reliable and accurate. If you withdraw from the study, we will keep the information about you that we have already obtained. To safeguard your rights, we will use the minimum personally-identifiable information possible.

The Royal United Hospitals Bath NHS Foundation Trust will keep your name, date of birth, contact details and next of kin details confidential and will not pass this information to the sponsor (University of Bath). The researchers will access this information as needed, contact you about the research study, and make sure that relevant information about the study is recorded for your care, and to oversee the quality of the study. In particular personal addresses will be used to contact you initially and may be used to update you on new information that becomes available during the study which may affect your involvement. You will be contacted by telephone to gauge interest, complete a screening phone call and book in trial visits. You may also be reminded of trial visits via text message, or email.

Certain individuals from University of Bath and regulatory organisations may look at your medical and research records to check the accuracy of the research study. University of Bath will only receive information without any identifying information. The people who analyse the information will not be able to identify you and will not be able to find out your name, date of birth, contact details and next of kin details.

The Royal United Hospital will keep identifiable information about you from this study until the final study contact has been made. The University of Bath will keep study data (without identifying information) for 10 years in line with the University of Bath research data policy.

When you agree to take part in a research study, the information about your health and care may be provided to researchers running other research studies in this organisation and in other organisations. These organisations may be universities, NHS organisations or companies involved in health and care research in this country or abroad. Your information will only be used by organisations and researchers to conduct research in accordance with the UK Policy Framework for Health and Social Care Research. This information will not identify you and will not be combined with other information in a way that could identify you. The information will only be used for the purpose of health and care research, and cannot be used to contact you or to affect your care. It will not be used to make decisions about future services available to you, such as insurance.

What will happen to my blood samples?

The blood samples will be processed in a laboratory at the University of Bath and stored in secure freezers until they are analysed. Blood will be separated into the liquid components (called serum and plasma) and white blood cells. In plasma we will measure metabolic health, and in serum and white blood cells we will measure inflammation, molecular biomarkers, immunity and the genetic features (including DNA) of the immune and cancer cells. Your clinicians and health care providers will not be informed of any blood test results as the measurements are only validated for research (and not clinical) use.
Your samples will be labelled with a unique study ID number, that will not contain any personal identifiers such as initials or date of birth. The researchers are able to identify your samples by accessing a spreadsheet which links your personal data to the unique study ID number. This is stored separately at the Royal United Hospital, and access is limited to the research team. When your personal data are deleted from this spreadsheet (at the end of the study) the link to your personal data will be broken and your samples will be fully anonymised. However, your DNA is unique to you so it can never be completely anonymous.
We will keep your samples for 10 years in secure freezers so we are able to perform more analysis in future to answer other related research questions, or if new biomarkers or methods are discovered that can help advance understanding. This analysis will only be done by researchers from the Department for Health at the University of Bath. After 10 years, your samples will be destroyed in line with the Human Tissue Act.

What should I do if I want to take part?

You will be telephoned within 7-10 days of receiving this information to arrange a time for your screening visit if you are interested in taking part. If you are undecided at the time of the phone call, please arrange another time to be called back. If you are worried that you have not received a phone call or have questions, please contact the researcher (Frankie Brown: 01225 385761, email f.brown@bath.ac.uk).

What happens if there is a problem?

If you have any concerns about this study, please speak with the Chief Investigator Dr John Campbell (Tel: 01225 385495 or Email: j.campbell@bath.ac.uk) who will do his best to answer your questions. If you remain unhappy or wish to speak with someone outside of the research team, please contact Lisa Austin – the Research Manager for Bath Research and Development at the University of Bath. Her contact number is: 01225 386575. Alternatively, you can contact the RUH Patient Advice and Liaison Service (PALS) Telephone: 01225 825656 / 826319 or Email: ruh-tr.pals@nhs.net Further information about PALS can be found at: https://www.ruh.nhs.uk/patients/advice_and_support/pals/index.asp?menu_id=5
Indemnity insurance cover for this study is provided by the University of Bath http://www.bath.ac.uk/insurance-services/liability-covers/index.html.

You have come to the end of this information sheet, thank you for reading it through! You will be contacted within 7-10 days, so please use this time to reflect and think of any questions you would like to ask.