TITLE OF THE STUDY

Assessment of a personalised anti-fatigue multimodal program for community-dwelling people with chronic lymphocytic leukaemia: a pilot feasibility study

SHORT STUDY TITLE / ACRONYM

LIVE-CLL

PROTOCOL VERSION NUMBER AND DATE:

0.2 13/OCT/2026

Confidentiality Statement

The Information contained in this document is the property of the University of Surrey and is provided to you in confidence as an investigator, potential investigator, or consultant for review by you, your staff and applicable regulators. It is understood that this information will not be disclosed to others without authorisation from the University of Surrey except to the extent necessary to obtain written consent from those persons who will take part in the study.

STUDY SUMMARY

Study Title	Assessment of a personalised anti-fatigue multimodal program for community-dwelling patients with chronic lymphocytic leukaemia: a pilot feasibility study
Short Title	LIVE-CLL
Planned Size of Sample (if applicable)	60
Planned Study Period	12-months
Planned Study Date	December 2026 – November 2027

FUNDING AND SUPPORT IN KIND

FUNDER(S) (Names and contact details of ALL organisations providing funding and/or support in kind for this study)	**FINANCIAL AND NON-FINANCIAL SUPPORT GIVEN**
Blood Cancer UK	

INVESTIGATORS

NAME	**Position**	**University Role**
Dr David Bartlett	Principal Investigator	Senior Lecturer of Exercise Immunology
Dr Ellie Miles	Co-Investigator	Post-Doctoral Researcher (Bartlett Lab) & ACSM Certified Clinical Exercise Physiologist
El Stratton	Co-Investigator	Post-Graduate Researcher Bartlett Lab) & Trainee Clinical Exercise Physiologist

STUDY PROTOCOL

1. Abstract

Cancer fatigue is associated with cancer therapies and low QoL. However, over 70% of treatment-naïve CLL sufferers experience debilitating fatigue, while over 75% of those who receive CLL treatments experience more severe fatigue (1). Our preliminary data suggest that CLL fatigue persists longitudinally and is increasing. Further, our data indicate that targeting CLL-specific symptoms will improve quality of life and reduce fatigue in CLL (2-5). As such, CLL fatigue is distinct and requires a focused approach rather than the cookie-cutter approaches often used for solid cancers.

This innovative, personalised, home-based, CLL-focused virtual program includes CLL-specific wellbeing, dietary, and physical assessments to determine limitations and symptom frequency/severity in 60 people with CLL experiencing fatigue. We will provide LIVE-CLL, a 12-week, 3-5 sessions-per-week aerobic and strengthening physical activity program. We will provide daily/weekly live feedback to adjust the program and ensure accurate fatigue reduction.

We hypothesise that LIVE-CLL, targeting symptoms and physical function, will improve quality of life by reducing fatigue. Upon completing this project, we will show that targeting CLL symptoms rather than adopting a 'cookie-cutter' approach can empower people with CLL to improve their QoL.

2. Background of the Project

When compared to people with solid cancer, patients with blood cancer, including CLL, experience higher levels of physical deconditioning, worse QoL and more symptoms such as severe fatigue(6). Fatigue is more severe in treated CLL, is highly prevalent in treatment-naïve patients, and is an independent predictor of poor QoL (1, 7). Although research suggests that exercise-based multimodal approaches improve fatigue in solid cancers, there is a dearth of data on CLL (and other blood cancers). Consequently, our preliminary data, in conjunction with the CLL Support Association, show that fatigue levels and severity increased from 2022 to 2024 (N=~1000 respondents) and that patients are not being referred to services that can positively impact fatigue. As such, there is a significant demand for a CLL-focused (and all blood cancer) approach that can reduce fatigue and improve quality of life.

Cancer-related fatigue is a complex phenomenon with no single aetiology. It is mostly associated with various forms of cancer treatments, including chemotherapy and targeted therapies. Targeted therapies for CLL, including BTK inhibitors (e.g., ibrutinib) and BCL2 inhibitors (venetoclax), have significant off-target effects on skeletal and cardiac muscle. Therefore, the increased severity of fatigue likely reflects muscle dysfunction, as evidenced by the increased risk of cardiac events and the prevalence of fatigue in treated CLL. However, fatigue and frailty are also more prevalent than in the general population in CLL patients who have not received any cancer therapies. Our published data suggest this phenomenon is likely due to CLL cells using essential lipid-based fuels that skeletal and cardiac muscles require to function(5). Together, our data indicate that people with CLL would benefit from multimodal approaches that target fatigue at diagnosis (prehabilitation) and at treatment initiation (rehabilitation).

This project aims to investigate the feasibility and effects of a multimodal CLL-specific program on fatigue, symptoms and QoL. Our long-term goal is to develop an online, blood-cancer-specific approach to help patients reduce symptoms. Because blood cancers differ significantly, we aim to begin with CLL, the most common chronic leukaemia.

3. Patient/Participant involvement

In 2022, we conducted a Patient Focus Group and online questionnaire with patients with CLL to discuss 1) motivations and barriers to exercise, 2) preferences for exercise interventions, 3) the role of diet and nutrition, and 4) research directions where lifestyle interventions may develop new understandings of CLL disease pathology and manage symptomology (8). Based on the focus groups, we designed and initiated a large 6-month exercise trial to understand exercise, immunity, and frailty development (paper currently under review). We have asked the patients who completed the study (N = 60) about the project's design and its relevance to people with CLL. The responses indicated that, alongside exercise, there is a greater desire to understand how lifestyle approaches can influence symptoms such as fatigue and how to incorporate them into the community.

4. Aims and objectives

1) **Objective 1. Determine the feasibility of a personalised CLL symptom-focused virtual physical activity-based program (LIVE-CLL)**. In 60 people with CLL (30 treatment-naïve and 30 on treatment), we will assess the feasibility of LIVE-CLL.

2) **Objective 2. Evaluate the effects and relationships of 12-weeks of LIVE-CLL on fatigue, all symptoms and QoL.** From those in Objective 1, we will evaluate changes in fatigue, symptomology, and QoL using validated questionnaires, along with related changes in physical and wellbeing program targets.

Similar to other hematologic malignancies (9), there are currently no specific health and lifestyle guidelines for people with CLL. This partly contributes to the higher risks of premature frailty and poor quality of life. As such, the benefits of this study are numerous. Specifically, we will demonstrate that exercise and a balanced diet can play a crucial role in the health and QoL of individuals with CLL. This will lead to the development of guidelines for the thousands of people living with CLL. Additionally, study participants will directly benefit from the interventions and from the knowledge gained from the assessments and feedback provided.

5. Recruitment Methods

We have developed a growing database of ~250 people with CLL willing to participate in our research studies. We will recruit directly from this database and through word-of-mouth referrals. In our exercise trial, we recruited 20 participants in year 1 and 40 participants in year 2, where the more extensive assessment days limited us to 2-4 participants per month. Here, we can recruit 6-10 participants per 4-week period, and thus the recruitment of 60 participants is achievable within the 37-week recruitment window.

Participant Inclusion Criteria

- Confirmed diagnosis of CLL (including small lymphocytic leukaemia) as per the International Workshop on CLL Guidelines [7].
- ≥ 18 years of age
- FACIT-Fatigue Total Score <34 (10)

Participant Exclusion Criteria:

- Lack of access to digital platforms used to assess and deliver the program.
- Absolute contraindications to physical activity: Self-reported recent (<6 months) acute cardiac event, unstable angina, uncontrolled dysrhythmias causing symptoms or hemodynamic compromise, symptomatic aortic stenosis, uncontrolled symptomatic heart failure, acute pulmonary embolus, acute myocarditis or pericarditis, suspected or known dissecting aneurysm, and acute systemic infection.

If we find a participant ineligible for the study, their screening questionnaire will be destroyed because it contains sensitive information.

6. Adverse Publicity

As this is a lifestyle health intervention in a population of people with chronic cancer, we do not expect any adverse publicity. In fact, we expect positive publicity. As mentioned previously, there is strong interest in understanding how exercise can influence symptoms such as fatigue and incorporating it into the community. In the unlikely event of adverse publicity, we will meet with the University Communications Teams to develop an appropriate public response.

7. Informed Consent and Withdrawal of Consent

Informed consent

All participants will provide written informed consent for their participation and for the use and retention of study data. The Consent Form will be provided online via Qualtrics and signed and dated by the participant before they enter the study. Prior to signing the consent form, the research team will explain the details of the research and provide a Participant Information Sheet, ensuring that the participant has sufficient time to consider participating or not. Additionally, the research team will address any questions the participant may have regarding study participation. We will collect informed consent from each participant before undergoing any assessments. The participant will retain one copy, and the research team will retain one. Those incapable of providing valid consent will not be recruited. In addition, participants under 18 will not be recruited.

Participant Withdrawal

During the consenting process, all participants will be notified that they may withdraw from the trial at any time, without providing a reason. Participants will be removed from the trial by the Principal Investigator if:

1. The participant develops a medical condition before entering the study or during the study, which may adversely affect the study's outcome or ability to participate.
2. If the participant suffers a serious adverse event.

Before starting this study, a favourable ethical opinion will be obtained from the university ethics committee (UEC). In addition, all applicants will receive information about the procedures, risks, inconveniences, and benefits of participation, as well as how their data will be processed in accordance with the University of Surrey's Data Protection Policy.

Participants may withdraw from the study at any time for any reason. If they withdraw from the study, the research team may use the anonymised data already collected, as indicated in the Participant Information Sheet and Consent Form, and will delete personal information.

Withdrawal timeframe. Participants can withdraw from the study at any point up to and including their post-intervention assessment. Participants can also ask for the data collected about them to be withdrawn and destroyed up until 2 weeks after their final (post-intervention) assessment, or 2 weeks after the date they withdraw if they leave the study early. At this point, the link between the participant's identity and their study ID code is removed, the data become anonymised, and it is no longer possible to identify and remove an individual's data. When a participant withdraws, the research team will ask whether they are happy for the data collected up to that point to be retained; if not, and the request is made within the 2-week window, their data will be deleted. Withdrawal does not affect the participant's medical care.

8. Experimental Design, Data Collection and Methods

This study is a prospective, single-arm, pretest-post-test feasibility study. In addition to receiving standard care, individuals with CLL who experience fatigue will participate in a semi-supervised 12-week virtual physical activity-based program.

Participants. We will recruit 60 people with a confirmed diagnosis of CLL (11) who are unlikely to change their current pathway (e.g., moving from treatment-naïve to treatment or finishing treatments such as venetoclax). Because this project is online, we will consider all participants, and we have provisions to translate documents into relevant languages. No translated documents have been prepared at this stage. If translation is required, the translated Participant Information Sheet and Consent Form will be submitted to the University Ethics Committee as an amendment and will not be used until a favourable ethical opinion has been given.

Power Calculation. As this is a pilot study designed to generate estimates to power a larger trial, we did not conduct formal power calculations and instead used the standard 30 people per group estimate for feasibility (12).

Screening & Consent (~1 hour)

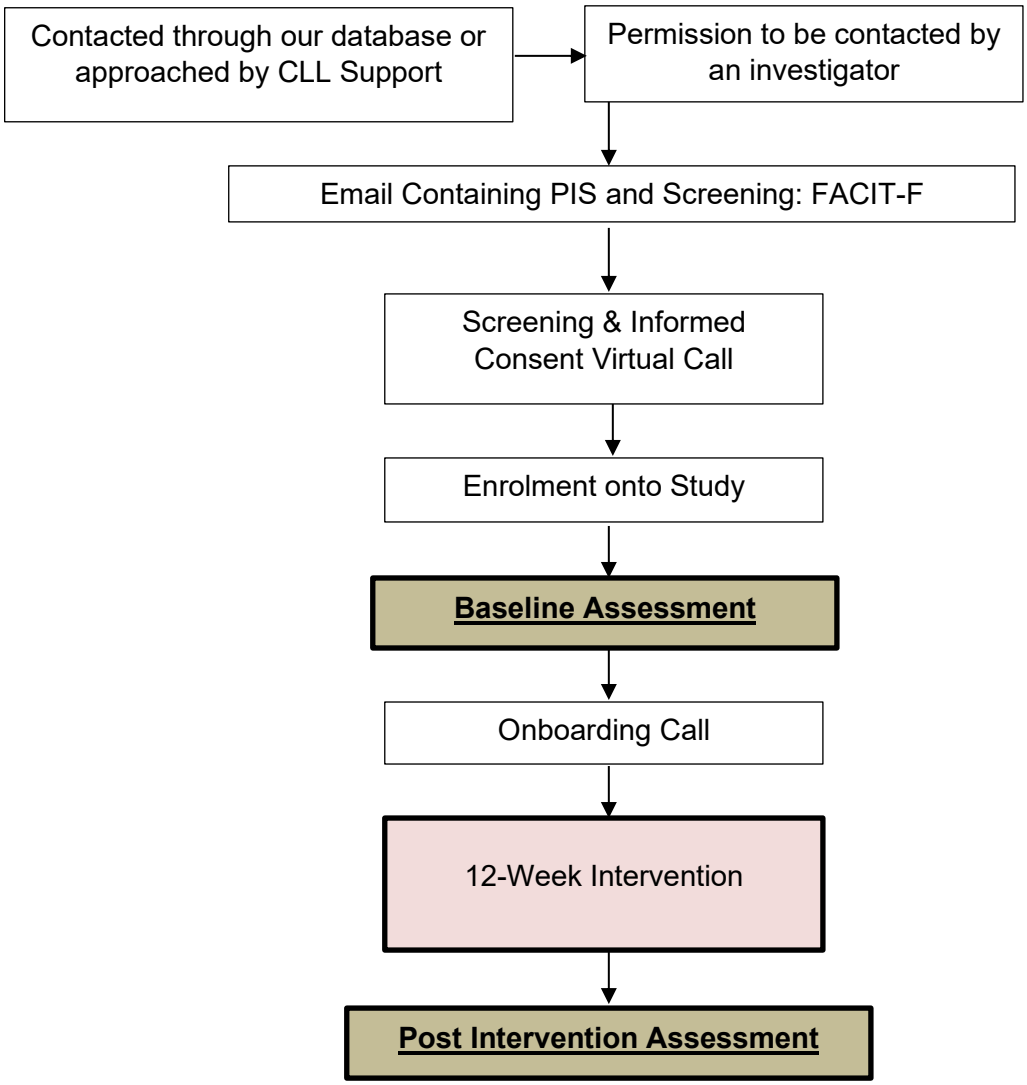
Once participants have expressed interest in participating in the study and have given permission to be contacted by an investigator, they will be sent the information sheet and asked to complete an online version of the FACIT-Fatigue Questionnaire. If participants have a FACIT-Fatigue score of greater than 34, they are not deemed to be experiencing clinical fatigue and will be excluded from the study (10). They will, however, be signposted to Macmillan's general physical activity guidelines (https://www.macmillan.org.uk/cancer-information-and-support/treatment/preparing-for-treatment/physical-activity-and-cancer).

If participants are classified as fatigued, then a screening session will take place virtually using MS Teams. During the screening, we will ask questions related to:

- General Medical History Questionnaire*
- Cancer History*
- Emergency Contact Details*
- Location during online assessments/exercise*

- Completion of the physical activity readiness questionnaire (PAR-Q+). The PAR-Q+ is the international standard for pre-participation screening. Coupled with our screening for exclusion criteria, this questionnaire will identify participants unable to complete the proposed program due to medical limitations. We have used this questionnaire before and found that most people with CLL are cleared for exercise. However, it will identify those with additional comorbidities requiring medical clearance. In that case, they will complete the ePARmed-X+ form, and we will ask the participant to seek medical clearance from their healthcare provider. Their healthcare provider will inform us of their recommendation for exercise intensity. We will then admit the participant and modify the exercise prescription based on the medical recommendations. If their healthcare provider does not provide medical clearance, participants will be excluded from the study.
- The PAR-Q also indicates the safe intensities of physical activity that can be achieved. For example, almost all people are safely able to complete low-intensity physical activity. The PAR-Q aids in identifying other safe zones of physical activity intensity (e.g., moderate- or vigorous-intensity). In certain situations, we may require the participant to seek approval from their GP to exercise. *Collected using a screening form

Figure 1. Study Design



Medical Summary Form. Once screening is complete, the clinical exercise physiologist will complete a medical summary form. This will be used during fitness assessments and delivery of the exercise intervention, ensuring exercise professionals have ready access to participants' medical information, emergency contact details, and exercise considerations.

Baseline Assessments (Online) (~30 minutes)

Before completing online physical assessments, the research team will determine the participant's environment and available equipment. These will include, but are not limited to, understanding the space in their home, the availability of chairs, and the availability and use of exercise equipment (e.g., resistance bands). From this, an appropriate set of assessments will be completed. Part of the feasibility assessment is determining our ability to complete assessments. Inability to complete any assessment does not exclude the participant. Once screening is complete and consent has been obtained, participants are deemed eligible to participate in the study. We will then organise an online assessment (via MS Teams) with trained exercise professionals. The primary assessor will lead the assessment and serve as the participant's main point of contact. The secondary assessor will be present during the assessments to record assessment results and, if necessary, support safety and emergency procedures.

Body Composition: Participants will self-report height and weight during the online assessment. If participants take their own weight using their own scales, they must do so on a flat surface, with all heavy clothing, items, and jewellery removed (e.g., shoes, jumpers). Alternatively, participants can provide height and weight measurements from their most recent doctor's appointment, ideally from within the last 30 days.

Resting Values: To measure resting heart rate and blood pressure, participants will either need a device that measures both pulse rate and pressure (e.g., an automated blood pressure cuff), pulse rate alone (e.g., a wrist-worn accelerometer with pulse rate capabilities), or to manually palpate their radial or carotid pulse with support from the assessor. We may provide participants with a wrist-worn smartwatch that tracks heart rate and physical activity. If this occurs, watches and instructions for use will be posted to participants and returned to the study team at the end using pre-paid return envelopes.

Physical Performance: Standardised protocols will assess physical performance during online assessments (13). These tests include, but are not limited to, shoulder flexion range of motion, chair sit-to-reach, 30-second sit-to-stand, 2-minute step test, single-leg stance test.

Questionnaires (these can be completed in their own time, online and returned to the research team) will take around 30 minutes:

- Fatigue: Fatigue Assessment Scale (FAS) & Fatigue Severity Scale (FSS), FACIT-Fatigue
- Quality of Life and Wellbeing: EORTC QLQ-30, EORTC QLQ-CLL17, FACT-Lym, HADS, FACT-Cog, Pittsburgh Sleep Quality, Geriatric-8
- Physical Activity/Function: Godin Leisure Time, Stanford Brief Physical Activity Questionnaire.
- Dietary Analysis: 7-day food diary and short-form food frequency questionnaire (SFFFQ)(14)
- Comorbidities: CLL Comorbidities Index (15)

All online forms and questionnaires used for screening and assessment will be collected using Qualtrics. Data will be downloaded from Qualtrics to the UoS system within 2 weeks of the questionnaire being submitted and then deleted off Qualtrics.

Post-Intervention Assessments (Online)

Post-intervention assessments will be conducted in the same manner as the baseline assessments, in the same order.

Onboarding Call. Once the personalised programme is created, participants will receive an additional call to guide them on how to log in to the online system (see below), view the programme, and complete the forms.

Physical Activity Interventions. The screening platforms of the PARQ+ and medical history screening allows for all participants to engage in a safe and intensity-appropriate physical activity programme as suggested by the UK Chief Medical Officer (16). We will use an established framework for prescribing exercise training in cancer and cancer-related fatigue. This framework integrates resistance exercises with aerobic exercises in a safe intensity-appropriate manner, providing the basis for the current proposed program (17). For some this will be low-intensity physical activity (e.g., walking) and for others this will be moderate-intensity physical activity (e.g., jogging). The team will prescribe a specific program that safely targets the limitations identified in the online assessment, utilising achievable aerobic and resistance exercises. This will involve using ratings of perceived exertion (Borg Scale, 6-20 or Borg CR-10 Scale) to determine intensities, using equipment available to participants, our online workout classes, and modifying the exercise environment (e.g., using weighted shopping bags for resistance). Programs will vary but aim to involve 3-5 sessions per week (participant-dependent) and are designed to improve limitations and overall fitness within 12 weeks. All programmes will follow the ACSM exercise guidelines and prescription recommendations and be created by a Clinical Exercise Physiologist. Optional live online group classes will take place during study team working hours (9:00 a.m. to 5:00 p.m., Monday to Friday) and will be led by a Clinical Exercise Physiologist with a second member of the study team present on the call, so that one team member can manage any emergency while the other remains with the rest of the group.

The programme will be prescribed via a web-based and mobile application online exercise prescription platform (Physitrack, London). Over 60 NHS trusts use Physitrack to improve patient outcomes, including in the geriatric population and complex chronic conditions (18). This online platform gives participants easy access to their programme and provides messaging access to a member of the study team from 9:00 a.m. to 5:00 p.m., Monday to Friday. The study team monitor the platform and respond to messages only during these hours; messages sent at other times will be answered on the next working day. Each day, before each session, participants will complete a form about their readiness to exercise, including any new injuries and fatigue levels. If daily fatigue levels exceed 7/10 (where 0 indicates no fatigue and 10 indicates debilitating fatigue), participants will be offered an alternative exercise session.

Additionally, if participants report symptoms that contradict exercising, they will be signposted to contact a member of the research team immediately and not proceed without advice. Participants will complete a more in-depth form at the end of the week to assess their physical and mental wellbeing, providing the exercise physiologist with information to guide exercise regression/progression. If there is concern about a participant's wellbeing, a video or phone call with the research team will be organised.

Format of delivery and out-of-hours support. The programme is predominantly self-directed: participants can open their programme in Physitrack and complete their sessions at a time that suits

them, including evenings and weekends. The study team does not have to observe self-directed sessions in real time and cannot therefore recognise a medical event as it happens. Support from the study team (messaging, review of readiness and weekly forms, and calls) is available from 9:00 a.m. to 5:00 p.m., Monday to Friday, excluding bank holidays and University closure days. Live contact with the study team (online assessments, the onboarding call and optional live classes) only takes place during these hours.

To manage the risk of an event occurring during self-directed sessions or out of hours, the following procedures apply: (1) at onboarding, and in written guidance within Physitrack, participants are told that the platform is not monitored in real time or outside working hours and is not an emergency service; (2) participants are advised to stop exercising and call 999 in an emergency (e.g., chest pain, severe breathlessness, fainting or a fall with injury), and to contact NHS 111, their GP or their haematology team for urgent but non-emergency concerns; (3) participants are asked to tell a friend, neighbour or family member when they plan to exercise and to keep a phone within reach; (4) participants are encouraged to schedule sessions within study team hours where possible, particularly during the first weeks of the programme; (5) if the pre-session readiness form indicates new symptoms, injury or fatigue above 7/10, the participant is advised within the platform not to proceed with the planned session (or to complete the alternative low-intensity session) and to contact the team, who will follow up on the next working day; and (6) participants whose physical function is deemed weak or frail at baseline will be asked to have a friend or family member present during all exercise sessions and will be supervised by the research team rather than self-directed. Participants are asked to report any adverse event to the study team at the earliest opportunity, and these will be recorded and reported as described under Safety Monitoring and Reporting.

Physitrack and data protection. Physitrack is an external company. However, no personal information is stored in the app or the companies database. All participants have a unique ID login provided by the study team that is linked to our study email and not the participants.

Table 1. Schedule of Events

Procedures	**Visits (insert visit numbers as appropriate)**		
	Screening	**Baseline**	**Post-Intervention**
Informed consent	x		
Demographics	x	x	
Medical History	x	x	
Body Composition		x	x
Physical Fitness Assessment		x	x
Questionnaires		x	x

Safety Monitoring and Reporting

The Principal Investigator (PI) is responsible for identifying and documenting adverse events (AEs) and serious adverse events (SAEs). At each study visit, the PI or trained designee will assess, through non-suggestive inquiries of the subject or evaluation of study assessments, whether an AE or SAE has

occurred. For this study, physical testing and physical activity AEs and SAEs will be collected in real-time or shortly after.

Adverse Events (AEs). An adverse event (AE) is any untoward medical occurrence in a participant receiving exercise testing or exercise training. All adverse events that are related to exercise testing or training will be collected from the time of first exercise testing and training until the last exercise testing and training. Anticipated (expected) side effects associated with exercise testing and training include fatigue, muscle soreness, joint pain, lower back pain, and leg cramps. We will not collect expected side effects. Unanticipated side effects associated with exercise testing and training include falls, sprains, strains, light-headedness, and fainting. To minimise the risk of anticipated and unanticipated AEs, the Exercise Physiologist is a Level 4 Cancer Rehabilitation Specialist. All participants will be made aware of the safety protocols before each session. These include filling out a form before each session, answering questions about any injuries, feeling unwell and fatigue levels before commencing, ensuring the participant has informed a neighbour, friend or family member of the days and times they are completing the session, and ensuring that the participant's address and emergency contact details are at hand. During live sessions (online assessments and live classes, which take place between 9:00 a.m. and 5:00 p.m., Monday to Friday), emergency procedures include the Exercise Physiologist stopping the session and remaining on the call with the participant while the second team member calls an ambulance to the participant's address and contacts their emergency contact and/or GP, or insisting the participant call one of these. Exercise Physiologists will therefore not be lone working when managing an adverse event during a live session. During self-directed sessions, no member of the study team is present; participants follow the emergency guidance given at onboarding and within Physitrack (stop exercising and call 999), as described under Format of delivery and out-of-hours support.

AEs will be recorded in the adverse events case report form found in the participant's study folder. AEs will be assessed according to the Common Terminology Criteria for Adverse Events (CTCAE), version 5.0. If CTCAE grading does not exist for an AE, the severity of the AE will be graded as mild (1), moderate (2), severe (3), life-threatening (4), or fatal (5).

Attribution of AEs will be indicated as follows:

- Related: The AE is related to the exercise training, exercise testing or study procedure.
- Unrelated: The AE is NOT related to exercise training, exercise testing, or study procedure.

In the unlikely event that a Serious AE (SAEs) occurs (i.e., fatal, life threatening, a medically significant condition (defined as an event that compromises subject safety or may require medical or surgical intervention to prevent one of the outcomes above), requires inpatient hospitalisation, or results in persistent or significant incapacity or substantial disruption to conduct normal life functions) the PI will report these to the University Ethics Committee within 24 hours of becoming aware of the event.

Statistical Analysis

We will report study population characteristics using descriptive statistics, such as mean ± standard deviation (SD) or median and interquartile range, depending on data normality. To assess our primary outcome, we will determine feasibility based on our ability to recruit, whether participants achieve>85% adherence to the prescribed sessions/week, whether >80% comply with the prescribed exercise intensities/durations, and whether <15% of participants drop out of the study. To evaluate changes in fatigue, symptoms, and QoL across the intervention, continuous data (e.g., QoL Scores) will be assessed using a linear mixed model ANOVA. If data are not normally distributed, a non-parametric Kruskal-Wallis Test will be used. Categorical data (e.g., physical activity levels of low,

moderate and high) will be assessed using a Pearson Chi-square Test. All statistical tests will be considered significant at $p \leq 0.05$. Trends for significance will be suggested if $p \leq 0.10$.

9. Risk Assessment

1. Identified Risks	2. Likelihood	3. Potential Impact/ Outcome	4. Potential Severity of Outcome	5. Risk Management/Mitigating Factors	
Underlying medical condition, unsuitable to participate	Possible	Participant	Low	• Screening of participants using a health questionnaire, and exclusion from the investigation.	N/A
Cardiopulmonary event or musculoskeletal injury during exercise	Unlikely	Participant • Physical injury • Medical care	Low	• A clinical exercise physiologist (Ellie Miles) will programme an adequate warm-up implemented before physical assessments and exercise sessions. The study investigators have >12 years of experience in clinical exercise both virtually and in-person. • Participants will be instructed to provide the research team with contact details of friends or family who can assist them if required. We will encourage participants to have a friend or family be present during sessions. If the participant's physiological condition is deemed weak or frail (based on the physical function test), a friend or family member will be asked to be present during sessions and will not be allowed to complete self-directed sessions. Participants will be informed of emergency procedures before each session. These include calling their GP or an ambulance for them, or asking	TRA-786 Acute Exercise Responses TRA-348 Use of Treadmills TRA-346 Use of Exercise Bikes

1. Identified Risks	2. Likelihood	3. Potential Impact/ Outcome	4. Potential Severity of Outcome	5. Risk Management/Mitigating Factors	
				them to call their GP or an ambulance if an emergency occurs.	
Risk of Data Loss	Unlikely	Participant • Contribution wasted Researcher • Stress due to imperilment of research	Low	• Data will be stored on a secure University server, and paper copies will be scanned and uploaded to the server.	NA

10. **Data Management**

Study Data

Monitoring of study data shall include confirmation of informed consent prior to inclusion; data storage and data transfer procedures; local quality control checks and procedures, including QA scans, and backup of any local databases. A nominated designee of the study team shall carry out monitoring of study data as an ongoing activity.

Data Handling

The Principal Investigator will act as custodian for the trial data. The following guidelines will be strictly adhered to:

- Consent forms, screening forms and questionnaires will be completed electronically via Qualtrics; no paper forms are planned. Data will be downloaded from Qualtrics to the University's secure server within 2 weeks of submission and then deleted from Qualtrics. Identifiable data (consent forms, contact and emergency contact details, screening and medical summary forms) will be stored separately from the pseudonymised research data in a restricted-access folder that only the immediate research team can access. In the unlikely event that a paper record is produced (e.g., a participant requests a posted form), it will be kept in locked storage managed by Dr Bartlett, scanned to the secure server and the paper copy destroyed.
- The storage location for identifiable special category data will be on the secure University OneDrive folder, only accessible by the research team.
- Participant's data will be pseudonymised
- All data will be stored in a secure location on the University’s servers and on a password-protected computer. These will align with best practices recommended by the University of Surrey Research and Information Governance policies.
- All trial data will be stored and archived as indicated by The Medicines for Human Use (Clinical Trials) Amended Regulations 2006.
- When a participant does not meet the inclusion criteria, all questionnaires and collected data will be destroyed.

Record retention and archiving

In compliance with the ICH/GCP guidelines and regulations and in accordance with the University of Surrey Code of Research Conduct and Research Ethics, the Chief or local Principal Investigator will maintain all records and documents regarding the conduct of the study. These will be retained for at least ten years or longer if required. If the responsible Investigator can no longer maintain the study records, a second person will be nominated to take over this responsibility.

Statement of confidentiality

Medical or personal information obtained from participants as a result of this study is considered confidential, and disclosure to third parties is prohibited with the exceptions noted above. The medical information provided by participants may be given to any medical personnel involved in the study if required for purposes related to the safety or health of that participant. Data generated as a result of this study will be available for inspection on request by authorised representatives of the University of Surrey for monitoring and audit purposes. With the participant's consent (a required item on the Consent Form), the research team may contact the participant's GP, and share relevant information, only where

this is needed for the participant's safety (e.g., to obtain medical clearance to exercise, or following an adverse event). As participants are recruited from the University's research database and by word of mouth, and not through the NHS, NHS REC and local R&D review are not required for this study.

Given the potential interest and value of this project's results for other researchers investigating aspects of cancer-related fatigue, we will also ask participants for explicit permission to share anonymised data and findings with current and/or future research partners.

11. Ethical considerations

Ethical considerations include anxiety about low levels of physical activity or a want for guidance on physical activity levels if participants do not meet the inclusion criteria of <34 points on the FACIT-F Questionnaire. If participants express concerns about their activity levels, we will signpost them to general physical activity guidelines provided by Macmillan (https://www.macmillan.org.uk/cancer-information-and-support/treatment/preparing-for-treatment/physical-activity-and-cancer). We will also offer to discuss processes/habits that they can change/add to their everyday life to improve or increase activity participation.

Ethical considerations also include the potential identification of participants with significant wellbeing issues in certain instances. In these cases, we will refer them to the Macmillan Wellbeing services (online and by phone).

12. Dissemination

The study results will be reported and disseminated to the scientific community via peer-reviewed journals and international conferences. The research team also aims to hold a feedback event open to all participants and members of the CLL Support Association. The general public will be engaged by releasing results to local and national media, relevant charities, and community networks, and by hosting an invited talk at the University.

13. References

1. Shanafelt TD, Bowen D, Venkat C, Slager SL, Zent CS, Kay NE, et al. Quality of life in chronic lymphocytic leukemia: an international survey of 1482 patients. Br J Haematol. 2007;139(2):255-64.
2. Artese AL, Sitlinger A, MacDonald G, Deal MA, Hanson ED, Pieper CF, et al. Effects of high-intensity interval training on health-related quality of life in chronic lymphocytic leukemia: A pilot study. Journal of geriatric oncology. 2023;14(1):101373.
3. MacDonald G, Sitlinger A, Deal MA, Hanson ED, Ferraro S, Pieper CF, et al. A pilot study of high-intensity interval training in older adults with treatment naïve chronic lymphocytic leukemia. Scientific reports. 2021;11(1):23137.
4. Sitlinger A, Deal M, Thompson D, Stewart T, Weinberg JB, Bartlett D, et al., editors. Assessing physical fitness in treatment-naive and ibrutinib-treated chronic lymphocytic leukemia (CLL) patients. LEUKEMIA & LYMPHOMA; 2020: TAYLOR & FRANCIS LTD 2-4 PARK SQUARE, MILTON PARK, ABINGDON OR14 4RN, OXON ….
5. Sitlinger A, Deal MA, Garcia E, Connelly M, Thompson D, Stewart T, et al. Associations of clinical and circulating metabolic biomarkers with low physical fitness and function in adults with chronic lymphocytic leukemia. Frontiers in Oncology. 2022;12.

6. Cristian A, Ruiz M. Comparison of Function, Fatigue, Frailty in Patients with Malignant Hematology, Pre-Bone Marrow Transplant and Solid Tumors. Biology of Blood and Marrow Transplantation. 2020;26(3):S362.
7. Shanafelt TD, Bowen DA, Venkat C, Slager SL, Zent CS, Kay NE, et al. The physician-patient relationship and quality of life: lessons from chronic lymphocytic leukemia. Leuk Res. 2009;33(2):263-70.
8. Miles EE, Nicol JL, Fowler H, Roberts A, Hulton AT, Jeary C, et al. Physical Activity, Symptoms, Quality of Life and Exercise Program Preferences in People With Chronic Lymphocytic Leukaemia. EJHaem. 2025;6(4):e70100.
9. Nicol JL, Woodrow C, Burton NW, Mollee P, Nicol AJ, Hill MM, et al. Physical Activity in People with Multiple Myeloma: Associated Factors and Exercise Program Preferences. J Clin Med. 2020;9(10).
10. Eek D, Ivanescu C, Corredoira L, Meyers O, Cella D. Content validity and psychometric evaluation of the Functional Assessment of Chronic Illness Therapy-Fatigue scale in patients with chronic lymphocytic leukemia. Journal of patient-reported outcomes. 2021;5(1):27.
11. Hallek M, Cheson BD, Catovsky D, Caligaris-Cappio F, Dighiero G, Dohner H, et al. Guidelines for diagnosis, indications for treatment, response assessment and supportive management of chronic lymphocytic leukemia. Blood. 2018.
12. Kunselman AR. A brief overview of pilot studies and their sample size justification. Fertility and Sterility. 2024;121(6):899-901.
13. Daun JT, Wagoner CW, Dreger J, Williamson T, Danyluk J, Capozzi LC, et al. Conducting online fitness assessments in exercise oncology. ACSM's Health & Fitness Journal. 2024;28(4):21-30.
14. Cleghorn CL, Harrison RA, Ransley JK, Wilkinson S, Thomas J, Cade JE. Can a dietary quality score derived from a short-form FFQ assess dietary quality in UK adult population surveys? Public health nutrition. 2016;19(16):2915-23.
15. Gordon MJ, Kaempf A, Sitlinger A, Shouse G, Mei M, Brander DM, et al. The Chronic Lymphocytic Leukemia Comorbidity Index (CLL-CI): A Three-Factor Comorbidity Model. Clin Cancer Res. 2021;27(17):4814-24.
16. UK Chief Medical Officer. Physical activity guidelines: Guidance from the Chief Medical Officers in the UK on the amount and type of physical activity people should be doing to improve their health. 2023 [Available from: https://www.gov.uk/government/collections/physical-activity-guidelines.
17. Sasso JP, Eves ND, Christensen JF, Koelwyn GJ, Scott J, Jones LW. A framework for prescription in exercise-oncology research. Journal of cachexia, sarcopenia and muscle. 2015;6(2):115-24.
18. Brown RC, Keating SE, Jegatheesan DK, Mayr HL, Barnett A, Conley MM, et al. Utilizing technology for diet and exercise change in complex chronic conditions across diverse environments (U-DECIDE): feasibility randomised controlled trial. BMC Health Services Research. 2024;24(1):935.

Amendment History

Amendment No.	Protocol version no.	Date issued	Author(s) of changes	Details of changes made