Participant ID: **Centre ID (if applicable)**

Participant Information Sheet

Anaemia & functional capacity, fatigue, daily activity, sleep and Circadian Rhythm Disruption among critical illness survivors

You are invited to take part in a research study. To help you decide whether or not to take part, it is important for you to understand why the research is being done and what it will involve. Please take time to read the following information carefully. Talk to others about the study if you wish. Contact us if there is anything that is not clear, or if you would like more information. Take time to decide whether or not you wish to take part.

What is the purpose of the study?

You were recently discharged from the intensive care unit (ICU) and are recovering from your illness. We know it can take some time for people to get back to normal after being in ICU. During this time, they can experience fatigue, feel weak, trouble sleeping, and have other symptoms that hold them back. The University of Edinburgh research team wants to find out more about people's fatigue and also measure how much moving around and exercise people can do during the period after leaving ICU.

We are particularly interested in whether anaemia (a low blood count) affects fatigue and exercise abilities, and whether treating anaemia with blood transfusions might improve fatigue, exercise ability, the activity of daily living, and quality of sleep during the weeks after leaving the ICU. Also, the cardiopulmonary exercise test that we are going to use in this study has not been used early (within 1 month) after critical illness. Thereby we want to find out not only the relation and connections between anaemia and patients' functional capacity, feeling of fatigue, daily activity, and sleep abnormalities but the practicality of the cardiopulmonary test among patients who recently come through critical illness.

Why have I been invited to take part?

We are inviting you to take part in this study for one of the following reasons:

1. You may have already agreed to take part in the 'ABC post-ICU' trial. This study is randomising people into one of two ways of managing anaemia between ICU discharge and the time you go home. One group of participants is receiving blood transfusions according to our current recommended usual care, which often means people remain quite anaemic between ICU discharge and going home. The other group of people is receiving more blood transfusions than usual to treat their anaemia and increase their blood count. The researcher speaking with you will clarify whether you are already in this study, in case you are uncertain.

2. You have been discharged from ICU and are not taking part in the 'ABC post-ICU' trial but are being invited to take part in this study.

We have an agreement that people taking part in the 'ABC post-ICU' trial can also take part in this study. This study will provide much more detailed information about fatigue, exercise capacity, the activity of daily living, and quality of sleep, which may help us understand whether using more blood transfusions to treat anaemia helps people recover.

Participant ID: **Centre ID (if applicable)**

Do I have to take part?

No, it is up to you to decide whether to take part. If you do decide to take part, you will be given this information sheet to keep and be asked to sign a consent form. If you decide to take part, you are still free to withdraw at any time and without giving a reason. Deciding not to take part or withdraw from the study will not affect the healthcare that you receive or your legal rights.

What will happen if I take part?

Participation in this study will not affect your medical care in any way. We aim to collect additional information about your recovery.

If you agree to take part, we will ask you to complete two short questionnaires, twice during the study on the day you agree to take part in the study and on the day of the cardiopulmonary exercise test, which will be explained later. The questionnaires are targeted at your perception of fatigue and how much you can currently care for yourself. Your feeling of fatigue will be assessed by the Visual Analogue Scale Fatigue (VAS-F) questionnaire based on 18 brief questions asking about your current experience of tiredness, sleepiness, exhaustion as an example. The answers to these questions should be rated on a scale from 0 to 10. While your ability to maintain common everyday activity will be assessed by an ordinal scale (Barthel Index) consisting of 10 questions regarding your ability to take food, move about, bath as an example. The answers to these questions are pre-specified and come down to whether you can do it on your own or help is required. The questionnaires usually take about 5-10 minutes each to complete, and the members of the research team will happily assist you with the questionnaires if you face difficulties while answering. Also, in case you become upset while answering the questionnaires, the research team members who are experienced doctors and nurses will provide support.

In addition, on the first day of your commitment to the study, we will ask you to wear the GENEActive accelerometer, a small device on your wrist that looks and feels like an electronic wristwatch. GeneActive device can be worn all the time (both day and night), and the technology used in it is similar to a “Smart-Watch” or a “Fitbit” with some exceptions such as the lack of both geolocation (GPS) and screen (will not display any information). This device records the frequency and amplitude of your limb movement that reflects the intensity of physical activity and is used to determine how active you are during the time it is worn. Besides, this device is equipped with light and temperature sensors that measure ambient luminosity and skin temperature, respectively. The device is water-resistant, so you can wash, shower, have a bath, or go for a swim without taking it off. In a nutshell, the device will record and store information regarding your activity intensity during the day, which will allow us to estimate how mobile you have been, and in case of wearing it during nighttime, an indirect measure of your sleep quality might be figured.

We are interested in these findings as a way of finding out how you are recovering. We would ideally like you to wear the device for 2 months as this is the longest time the internal battery could run on a single charge (you do not need to recharge the battery). However, if for any reason you do not want to wear the device, you are free to take it off, either temporarily or permanently. If you decided not to wear the device or have any problems with it, we would ask that you let us know and we will try to resolve the problem or set up the returning process. We might contact you during the study to get to know how you are getting on, and close to the end of the study, you will be contacted by us to arrange the device return by either posting you a pre-paid envelope or arranging a courier.

Participant ID: **Centre ID (if applicable)**

The last investigation we would ask you to undertake as part of the study is a cardiopulmonary exercise test or CPET. Cardiopulmonary exercise testing is used mostly in hospital settings and has a prominent prognostic and diagnostic value. It measures people's physical fitness and shows how your lungs, heart, and muscles react and interact together when you exercise. This test has to be undertaken only once, later during your recovery, when you feel physically able to try it, which is likely to be just before you are going to be discharged home from the hospital. This test will provide really important information about how the body works after a critical illness, but if you prefer, you can still take part in the study without having this test.

The test involves exercising for around 8-12 minutes on an exercise bike in the sitting position that takes place in the hospital's cardiopulmonary exercise testing laboratory. The idea is to gradually raise the pedal resistance until you are exerting as intensely as you feel able to. During the resting, active, and recovery phase of the exercise test, physiological measurements such as your exhaled gas content, heart rate, blood pressure, oxygen saturation, and electric cardiogram will be recorded. The whole test visit takes approximately 45 - 60 minutes from beginning to the end, which includes a pre-test check-up, introduction to the test procedure, placing all necessary monitoring equipment, but as was mentioned earlier the active exercise part is only 8-12 minutes long.

The cardiopulmonary exercise testing specialist will evaluate your suitability for the test, and we will let you know the exact timing of your exercise test in advance. We will take you for the exercise test from the hospital ward. During the test, you will be under the supervision of at least 2 expert staff doctors and nurses who are qualified to conduct the test and have extensively trained in providing both basic and advanced life support. The real-time monitoring throughout the test will include heart rate, cardiogram, blood pressure, transdermal blood oxygen content (oxygen saturation), and exhaled gas content via a tightly fitted face mask. During the active phase of the test, the test supervisors will encourage you to pedal as long as you can. The test will be immediately stopped if the supervisors have any concerns about you. You also can stop the test anytime if you feel unwell, do not feel able to carry on, or need to do so. The exercise testing laboratory has everything in place to deal with emergencies that might happen during the test and the supervising staff are fully prepared to address any issue properly.

Although we hope participants will all be able to do the cardiopulmonary exercise test, you could decide not to undertake the test when it was due if you did not feel able to. This would not affect your medical treatment in any way, and you can remain in the study for the other measurements.

Over the study, we will also gather some details about you from your medical health records, we are interested in, for example, what happened in ICU and how your health was before your current illness, how severely you were ill, and your laboratory test results such as haemoglobin concentration (the substance which transports oxygen), inflammatory markers. The complete list of information that will be collected from your medical records is discussed later in the confidentiality section.

Taking part in the study will not change your treatment in any other ways, and we do not need to take any additional blood tests. All the information we collect will be kept secure and will be anonymised before any analysis, which means that all data leading to your identity will be erased, providing complete anonymity.

Participant ID: **Centre ID (if applicable)**

Is there anything I need to do or avoid?

You will wear the wrist-worn accelerometer device by GENEActiv for the next 2 months. On the day of the cardiopulmonary exercise test, if you are willing and feeling able to undertake it, avoid having solid food and smoking for 2 and 8 hours before the test, respectively. Apart from the above, there is nothing you need to avoid because of taking part in this study.

What are the possible benefits of taking part?

There are no direct benefits for you from taking part in this study. The information we gather in this study may help us understand more about recovering from being in ICU and whether anaemia (a low blood count) and other individual and illness-related factors relate to people's ability to be active during recovery.

What are the possible disadvantages of taking part?

There are no apparent disadvantages in taking part in the study. However, you should know that an exercise test could carry some risks. The cardiopulmonary exercise test is a safe procedure, but adverse events during or shortly after the test occur. Adverse events are categorised into major and minor. The major adverse events lead to additional hospital admission or extend a current treatment course while the minors are self-limiting and disappear on their own with no consequences. For example, minor adverse events might manifest as breathlessness, significantly increased heart rate, rise or fall of the blood pressure above or below recommended values, and major events could manifest as heart attack, cardiac arrhythmias, loss of consciousness, serious orthopaedic injuries, and even death. Fortunately, the major adverse events are exceptionally rare and are akin to adverse events happening during any physical exercise at moderate to vigorous intensity. For safety reasons, you will be closely monitored for any signs of developing adverse events to make sure that we find out about any problems quickly and treat them appropriately.

What if there are any problems?

If you have a concern about any aspect of this study please contact Prof Timothy Walsh, Professor of Anaesthesia, Critical Care and Pain Medicine, Consultant Critical Care. Email timothy.walsh@ed.ac.uk or telephone 0131 242 6395, who will do their best to answer your questions.
In the unlikely event that something goes wrong and you are harmed during the research and this is due to someone's negligence then you may have grounds for a legal action for compensation against NHS Lothian but you may have to pay your legal costs. The normal National Health Service complaints mechanisms will still be available to you (if appropriate).

What will happen if I don't want to carry on with the study

You are free to withdraw your consent to take part at any time, without giving a reason, and any study procedure, along with any data collection, will be stopped. This would not affect the standard of care you receive in any other way or your legal rights. If you choose to withdraw from the study, we will ask you to complete a withdrawal form. On the form, you will have two options for your withdrawal:

- You can withdraw from the study completely; in this circumstance, you would no longer be followed up by the research team and all data already collected would be removed from the analysis.

Participant ID: **Centre ID (if applicable)**

- You can withdraw from any further study activity/data collection, in this case, you are happy for us to use the information collected up to the point of withdrawal, but we cannot collect any new data.

- In case you lose competence throughout the study, you will be withdrawn from the study together with all collected data. We will seek consent from your legal representative to include previously collected data in the study.

What happens when the study is finished?

Your participation in the study will be finished when you are asked to take the wrist-worn accelerometer device off and return it, whereas the study will be deemed over when the required data from all participants will be collected. This will be followed by the data analysis process. We plan to present and publish the results of the study in the doctoral dissertation and through medical publications. Individual participants and personal data will not be identifiable to any published results.

During the study, research-generated identifiable (personal) information will be stored on the secure NHS computer/server and at the end of the study, all identifiable/personal information will be completely wiped out, leaving unidentifiable study data alone, which is known as the anonymisation process. It is worth recounting that only anonymised research-generated data will be analysed and further subjected to publication. For the anonymised data analysis and storage, the protected University of Edinburgh computer and server will be used, respectively. The data file will be accessed via a VPN service provided by the University of Edinburgh.

Considering that we are not collecting blood or any other biological samples, the data generated by the study might only be useful in the subsequent different analysis types or might be merged with the alike data from the other studies. The study data will neither be used nor shared with commercial, pharmaceutical entities.

Will my taking part be kept confidential?

All information we collect in the study's course will remain confidential and there are strict laws to guarantee patient privacy at every stage.

We will inform your GP of your taking part in the study and if any concerning findings, the cardiopulmonary exercise test will reveal, GP will be notified as well.

Initially, electronic identifiable participants' information will be stored on computers managed by the NHS in a password-locked Microsoft Excel / Access database whereas a study generated paper-based information sources will be stored in the lockable cupboard, within the room accessible only for the members of the University of Edinburgh Intensive care Research Team at the Royal Infirmary Edinburgh hospital. At the end of the research period, the collected research data will be anonymised (removal of personal information or links that could lead to personal identification). Further, only non-identifiable information will be analysed, and the results will subsequently be used in the thesis and publications in scientific journals. Only unidentifiable data will be subjected to long-time storage at The University of Edinburgh managed computer in a password-locked Microsoft Excel / Access database.

Participant ID: **Centre ID (if applicable)**

To monitor and audit the study, we will ask your consent for responsible representatives from the study, sponsors to access your medical records and data collected during the study, where it is relevant to taking part in this research.

Besides the data got from the questionnaires, wrist-worn accelerometer, and cardiopulmonary exercise test, the following information about you will be thought from your electronic medical records:

- Name
- Age
- Gender
- CHI number (to contact your GP only)
- Contact details (to arrange a collection of the wrist accelerometer device only)
- Diagnosis (the main reason for the ICU admission)
- Comorbidities (additional disease or chronic health-related conditions that you might have such as diabetes, arterial hypertension, congestive heart failure)
- Haemoglobin concentration (laboratory test revealing your blood oxygen-carrying capacity)
- Severity of critical illness (disease severity scores used during your ICU stay)
- Duration of mechanical lung ventilation (how long you have been mechanically ventilated)
- Specific types of medication while at the critical care unit (Insulin and hormonal medication)
- Length of hospital stay

The affiliated members of the research team (doctors and research nurses) will use this information to do the research, check your records to make sure that the research is being done properly, and make sure that your personal information is stored securely.

Once we have finished the study, we will keep unidentifiable data so we can check the results. We will write our reports in a way that no one can work out that you took part in the study. We (Edinburgh Critical Care Research Group) will keep all information about you safe and secure on the NHS and the University of Edinburgh managed computers while paper-based information sources will be stored in the room with restricted access.

You can stop being part of the study at any time, without giving a reason, but we will seek your permission to keep information about you we already have. In case you do not want your information to be used further, we will totally withdraw it from the study.

We need to manage your records in specific ways for the research to be reliable. This means that we won't be able to let you see or change the data we hold about you.

Additional details on how we use your information, you can find on:

- at www.hra.nhs.uk/information-about-patients/
- by asking one of the research team

What will happen to the results of the study?

This study results will help understand recovery after ICU better and the feasibility of the cardiopulmonary exercise test in the early post-critical illness recovery period. The results may help us understand what treatments help recovery, along with what individual and hospital-related factors are interconnected with patients' functional capacity, daily activity,

Participant ID: **Centre ID (if applicable)**

quality of sleep, and fatigue. These may help in designing future research about supporting recovery.

In case you are interested in the study's results after the study ends, your inquiry regarding the results to the Edinburgh Critical Care Research Group available at https://www.ed.ac.uk/usher/anaesthesia will be welcomed.

Who is organising and funding the research?

This study has been sponsored by the University of Edinburgh and NHS Lothian. The funding came from the JSC Centre of International Programs (Kazakhstan).

Who has reviewed the study?

The study proposal has been reviewed by Deputy R&D Director Ms Fiona McArdle.

All research in the NHS is looked at by an independent group of people called a Research Ethics Committee. A favourable ethical opinion has been obtained from East of Scotland Research Ethics Service. NHS Management Approval has also been given.

Researcher Contact Details

If you have any further questions about the study, please contact:

Prof. Timothy Walsh
timothy.walsh@ed.ac.uk

or

Dawn Campbell
dawn.campbell@ed.ac.uk
Unit Administrator/PA to Prof Walsh
University of Edinburgh
Department of Anaesthesia, Critical Care & Pain Medicine
Room S8208, 2nd Floor
The Royal Infirmary of Edinburgh
NHS Lothian, 51 Little France Crescent
Edinburgh BioQuarter
Edinburgh EH16 4SA

Independent Contact Details

If you would like to discuss this study with someone independent of the study please contact:

Dr Elizabeth Wilson
Consultant in Anaesthesia and Critical Care
Royal Infirmary of Edinburgh
NHS Lothian, 51 Little France Crescent
Edinburgh BioQuarter
Edinburgh EH16 4SA
0131 242 1186

Participant ID: **Centre ID (if applicable)**

Complaints

If you wish to make a complaint about the study please contact:

Prof. Timothy Walsh
Chair of Critical Care
Professor of Anaesthesia, Critical Care and Pain Medicine, Consultant Critical Care The University of Edinburgh
Royal Infirmary of Edinburgh
51 Little France Crescent, Edinburgh
EH16 4SA
timothy.walsh@ed.ac.uk
01312426395

Or

Dawn Campbell
dawn.campbell@ed.ac.uk
Unit Administrator/PA to Prof Walsh
University of Edinburgh
Department of Anaesthesia, Critical Care & Pain Medicine
Room S8208, 2nd Floor
The Royal Infirmary of Edinburgh
NHS Lothian, 51 Little France Crescent
Edinburgh BioQuarter
Edinburgh EH16 4SA
0131 242 6395