ADVANCE Study
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PARTICIPANT INFORMATION SHEET
(Version 7.0, 20220617)

The ADVANCE Study

ArmeD SerVices TrAuma RehabilitatioN OutComE Study
MoDREC Reference No:357/PPE/12

We would like to invite you to continue to participate in this research project being undertaken by a collaboration of the Defence Medical Rehabilitation Centre at Stanford Hall, King's College London and Imperial College London. You should only participate if you want to; choosing not to take part will not disadvantage you in any way. Before you decide whether you want to take part, it is important for you to understand why the research is being done and what your participation will involve. Please take time to read the following information carefully and discuss it with others if you wish. Ask us if there is anything that is not clear or if you would like more information.

Commonly Asked Questions:

What is the purpose of the study?

The purpose of the study is to investigate the long-term outcomes of battlefield physical trauma casualties and to compare these outcomes to those of a similar group of individuals who were not physically injured.
The outcomes we are investigating include medical (in particular cardiovascular disease and osteoarthritis) and psychosocial outcomes. There is some evidence to suggest that battlefield trauma casualties may have some unfavourable outcomes but this evidence is limited and often only covers shorter periods of time. Also, the types of injuries sustained in previous conflicts are different from those sustained in recent conflicts and therefore it is still unclear whether or how the type of injuries we are seeing from Afghanistan and Iraq will affect the long-term outcome of injured servicemen.
We think it is important to investigate these different medical and psychosocial outcomes so we can, where possible, support the injured individuals but also to learn from these outcomes and try and prevent any adverse outcomes in future injured serving personnel.

Why have I been chosen?

You have been asked to continue participation in the study as you are already enrolled on to the ADVANCE Study for your baseline visit. You either sustained significant physical battlefield trauma while on deployment with the British Armed Forces or you had been deployed but not physically injured and were therefore suitable for the comparison group. We are inviting all the cohort for follow-up visits over the next 20 years.

Do I have to take part?

You do not have to continue to take part. If you do decide to continue, you can keep this sheet and you will be asked to sign a consent form. We ask you to complete a consent form at each follow-up visit as there may be updates to the study investigations and how we handle your data between each of your visits. You are still free to withdraw at any time without giving a reason. Your participation will not interfere with the standard of care you receive, nor will it impact on your career.

What will happen to me if I take part?
Your participation will involve the following:

1. A follow-up visit to DMRC Stanford Hall. A research nurse will explain all the tests we plan to do during this visit and any new investigations introduced since your last visit to us and explain what happens to your data. They will ask you to review and sign a consent form and we will provide you with a copy of this form. They will also ask you to provide your contact details.

2. Follow up visits to DMRC Stanford Hall will occur at approximately 3yrs (Follow-up 1), 6yrs (follow-up 2), 10yrs (follow-up 3), 15yrs (follow-up 4) and 20yrs (follow-up 5) after the baseline visit.

3. Each visit will include the assessments below: Each visit will be approximately 4-5 hours.
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a. History:

Basic details including:

- Current regiment/unit/work & social circumstances
- Past medical history, including all traumatic injuries
- Medication/drug history
- Smoking history
- Method of discharge from the armed services (if appropriate)

b. Physical Examination:

- Blood pressure
- Resting heart rate and heart rate variability testing
- Height and weight
- Abdominal and hip circumference

c. Participant filled questionnaires covering outcomes such as:

- Mobility
- Pain
- Prosthetic use/satisfaction/comfort (if applicable)
- Knee, hip and shoulder pain and function
- Quality of life
- Educational and social outcomes
- Symptoms of post traumatic stress

- Alcohol intake
- Sexual function
- Mood
- Physical activity and competitive sport
- Sleep

d. Blood tests (which will be after a 8hr fast):
- Cholesterol
- Kidney and liver function
- Blood count measuring for anaemia
- Blood sugar measuring for diabetes
- Markers of inflammation
- Male sex hormones
- Genetic test for: 1. predisposition to inflammatory back pain (which characteristically occurs in young men), 2. factors that may influence brain health in the long term.
- Long term storage of serum, plasma and blood (which include genetic material) to test for markers of and associations with disease that may be developed in the future

e. Urine test:
- Storage of urine to test for new markers of disease that may be developed in the future

f. Imaging:
- X-rays of hips and knees assessing for evidence of osteoarthritis
- DEXA scan (non invasive painless scan) assessing for total body fat and bone mineral density (bone strength)

g. Ultrasound
- Ultrasound assessment of pulse wave velocity. This is a non-invasive, pain free assessment of the stiffness of your arteries and is used to establish cardiovascular risk.

h. Other assessments:
- Distance you are able to walk in 6 minutes
- Basic lung function test, a short maximum blowing test as would be used to assess for asthma
- Audiometry – discharged personnel only
- Physiotherapy assessment – participants with amputated limbs only
- Activity monitor – (from 2nd follow-up visit onwards). This is a monitor or 'watch' which records all your movements throughout the day as well as your sleep patterns; we would like you to wear it for 24 hours a day, for 9 consecutive days. The monitor cannot be used to locate you and does not transmit any live data while you are wearing it. We will ask you to complete a short diary of when you go to bed and get up in the morning. It will supplement the information you complete in your health questionnaire in relation to activity and sleep. You will be provided a more detailed instruction leaflet before you decide whether you want to wear the watch (ADVANCE Study sleep record Appendix Z24, ADVANCE Study activity monitor instructions_v1 Appendix Z25)

What do I have to do if I am interested in participating?

If you wish to participate in this study you can contact the research team on the numbers/email address provided at the bottom of this booklet. A member of the research team will contact you and

explain the study and offer you the opportunity to ask any questions you may have. They will find a date to suit you to come in for your follow-up visit to Stanford Hall.

If you are still in the military then military transport will be provided to get you to and from your research appointments. If you have left the military reasonable travel expenses will be covered if receipts are provided. If you are driving we provide a 'per mile' reimbursement. We have a travel agent who helps us with train/flight bookings and with your permission we will forward them your contact details so they can contact you directly to make arrangements to suit you.

If accommodation is required then this will be provided by the DMRC free of charge. Accommodation will either be provided on site within DMRC Stanford Hall, at Norton House or a B&B which is a short journey away from Stanford Hall. Again, with your permission we can organise this and will need to provide them with your personal contact details to secure the booking. When your visit is arranged we will send you detailed joining instructions.
As an appreciation for your significant time and effort in participating in the study you will be given £200 for each follow-up visit as a 'thank you'. There is also a cash prize draw for each follow up point, which with your consent you will be entered into, to encourage participants to return for follow up appointments. The total cash prize available is £25,000 and this will be divided up at each of the 5 follow up points with cash prizes ranging from £100 to £3000. We expect up to 1145 participants to be included in each draw.

What are the possible benefits of taking part?

The results of the study are primarily designed for benefitting battlefield trauma casualties of the future. However, the extra medical assessments that you would receive during the study are in some cases above and beyond what you would receive as standard clinical care in the military or NHS, whether you be a battlefield physical trauma casualty or the comparison group. Any clinically significant medical issues/ abnormalities detected will be reported back to your regular doctors whether they be GPs or hospital specialists. At the end of your visit to us we will ask you whether you would like to receive a results booklet which explains the results of your tests in more detail. This will be sent out to you in the post when all the results have been returned.
The study may hopefully also give you an opportunity to catch up with old friends and colleagues and we would do our best to co-ordinate visits if requested.

Will my taking part in the study be kept confidential?

All information which is collected about you during the course of the research will be treated with the utmost care and attention to confidentiality. We will inform your GP or MO that you are taking part in the study and we will send any clinically significant findings to your GP or MO.

Will the research influence the treatment I receive?

The study is not designed to provide you with specific treatments, however, as mentioned above if any significant medical issues are uncovered the study team will be able to advise you and, will pass on the information to your GP or MO.

What happens to the data/samples you collect from me, how is it stored and who can see it?

Your data is stored in one of 3 ways:

1. *Identifiable data*

We need to store your identifiable data such as your name, address & post code, email address, telephone number, date of birth, NHS number and alternative contact details. We use these details so we can contact you to invite you to your follow-up visits or other ADVANCE related sub-studies, and to contact you and your GP/MO regarding any medical issues identified during your visits. We also use this information to trace any changes of address. We would also like to send you updates on the progress of the study including when we have significant news and this will be through newsletters and emails. This data is stored securely in a password protected database within the MoD IT systems and the MoD act as the 'Data Controllers' meaning that they have the responsibility and control as to what happens with your data and ensures it is protected. These data will also be stored within our collaborating organisations such as Imperial College London and King's College London secure IT systems who jointly with the MoD act as 'Data Controllers' meaning they will store and review the data in line with our study objectives. Only the research team have access to these databases. Your identifiable data is also used when booking in your tests such as xrays, and blood sampling, and any clinical reports received will contain this identifiable data. Paper copies are stored within locked cupboards, within securely locked rooms at Stanford Hall. Only the research team have access to these physical areas.

With your consent we will use your identifiable data to request information from an organisation known as NHS Digital (and/or its equivalent in Scotland, Wales and NI) at intervals during and beyond the study duration so we can keep informed of your health. The information we will obtain relates to hospital attendances/episodes for any reason and includes the number of visits or admissions, reason for visits/admissions, length of stays and treatments received. NHS Digital (and its equivalent organisations in Scotland, Wales and NI), will also provide us with information about study participants who develop cancer or who may have passed away since the start of our study – such information includes dates, types of cancer or cause of death. The data we obtain will be stored securely within our IT systems. By participating in this study you will be consenting to the research team requesting this data from NHS Digital and equivalent organisations. We provide updates on our study website regarding obtaining information from organisations such as NHS Digital and their equivalent organisations. www.advancestudydmrc.org.uk.

2. *Pseudonymised data*

The term 'pseudonymised data' means that we strip away any identifiers, such as name, date of birth, and replace it with a unique study code. For example, we ask you to complete questionnaires and we complete forms with the data obtained from the tests we perform on you such as xrays. These data are then added to a database and only the unique study code is attached to that data, not your name or date of birth. It means you cannot be identified by anyone looking at it.
These data are stored on electronic databases and/or in paper form. Paper copies are stored within locked cupboards, within securely locked rooms at Stanford Hall. Only the research team have access to these areas. Electronic records are stored on secure IT systems between MoD, Imperial College London and King's College London. Only members of the research team have access to these IT systems. Your pseudonymised data will only be shared with ADVANCE researchers and approved

collaborators in line with the study objectives. The ADVANCE data controllers have full oversight and control as to who has access to these data.

3. *Storage of samples*

Blood samples obtained from you in clinic are sent to a local laboratory for routine tests (as described above) with full identifiers attached. We receive the results and these are then transferred into our databases using only your unique study code. 20mls of the blood collected is stored within secure freezers within Stanford Hall for batch testing for levels of inflammation and for testing any future markers of disease that are not currently available but may be discovered during the course of the study. 10mls of whole blood/plasma will be stored for genetic analysis at a later date. 50mls of urine will also be stored for testing of future markers of disease. All stored samples have only your unique study code attached, no personal identifiers. Stored samples will only be analysed by the ADVANCE study researchers or approved collaborators. Some samples may be sent to commercial laboratories for specialised analysis and these samples will not contain identifiable details. Only analyses approved by the ADVANCE study project board will be performed on your samples.

For regulatory reasons we are required to hold all data collected in the study until 15 years after the study has finished. If any participants pass away during study period their previously collected data will still be used in the study.

What are your rights and who can you contact if you have a concern about data?

To find out your rights under GDPR, please see the relevant section of the Information Commissioner's wesbite: https://ico.org.uk/for-organisations/guide-to-data-protection/guide-to-the-general-data-protection-regulation-gdpr/individual-rights/
If you have concerns about privacy and data protection related to the ADVANCE Study, you can contact the MoD Data Protection Team (cio-dpa@mod.gov.uk)
We regularly update information and therefore you can find the most up to date information on our website in the 'Data confidentiality and Privacy Notice' section: https://www.advancestudydmrc.org.uk/?page_id=522

Who is organising and co-ordinating the study?

The study is being co-ordinated by Gp Capt Alex Bennett, DMRC Stanford Hall. He is the Principal Investigator and has overall responsibility for the conduct of this study. We have co-investigators within Imperial College London and King's College London and these co-investigators along with Gp Capt Alex Bennett form the ADVANCE Steering Committee. The wider ADVANCE research team is made up of project managers, research nurses, research assistants, PhD students and other support staff. Collectively they share the organising and coordination of the study.

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

You are free to withdraw from the study at any time without having to give a specific reason, and this will not affect your future treatment or career in any way. We would just ask that if you do decide to withdraw from the study that you inform the research team on the contact numbers provided below. If you withdraw from the study your data which has already been processed and used in our analyses will be retained in the study unless you specifically ask for it to be erased.

Will I be exposed to large amounts of radiation from the x-rays or DEXA scans?

No you will not. The total doses of radiation that you will receive over the period of the study is very small (2.5mSv) and is equivalent to a maximum of 13 months background radiation based on the UK average.

The lifetime risk of fatal cancer for an effective dose of 2.5 mSv is approximately 1 in 8000 based upon the nominal risk coefficient for an adult published in the 2007 recommendations of the International Commission on Radiological Protection. This can be compared against the natural lifetime risk of fatal cancer of 1 in 3 to 1 in 4.

What will happen to the results of the research study?

At the end of your visit you will receive feedback on some of the tests performed during your visit. Results of the whole study will be published at various stages in scientific journals and presented at national and international medical meetings in an aim to improve international medical understanding and knowledge of the outcomes and potential treatment of battlefield trauma casualties. These will also be posted on our study website as they become available (www.advancestudydmrc.org.uk). You may also ask the Principal Investigator for copies of all papers, reports, transcripts, summaries and other published or presented material. All information will be subject to the current conditions of the Data Protection Act 2018. In no circumstances will any identifiable data be published.

What if I am unhappy with the conduct of the study or study staff?

If you have any concerns or complaints you are encouraged to contact the Principal Investigator or the research team on the contact numbers provided so we can try and address any issues as soon as possible. Alternatively, you can contact the independent medical officer (contact details available below) who will be available throughout the study. Their sole function is to act independently of the study team to ensure your safety and wellbeing. They may terminate your participation in the trial on medical grounds at any time, and you may consult with them at any time.

What happens if I suffer any side effects as a result of the study?

Given the type and design of this study, this is extremely unlikely, however, in the event of you suffering any adverse effects as a consequence of your participation in this study, you will be eligible to apply for compensation under the MoD's 'No-Fault Compensation Scheme'. A copy of this scheme is available on the study website (www.advancestudydmrc.org.uk).

Does this study have full ethical approval?

A full scientific protocol for this research has been approved by the Ministry of Defence Research Ethics Committee (Ref: 357/PPE/12) . This study complies and at all times will comply with the Declaration of Helsinki as adopted at the 52nd WMA General Assembly, Edinburgh, October 2000 and with the Additional Protocol to the Convention on Human Rights and Biomedicine, concerning Biomedical Research, (Strasbourg 25.1.2005). Please ask the Principal Investigator if you would like further details of the approval or to see a copy of the full protocol.

Name and contact details of Independent Medical Officer:

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For more information please call the study team on: 01509 251 500 ext 3408
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Thank you for taking the time to read the information sheet, which you should keep for future reference.

ARRANGEMENTS FOR THE PAYMENT OF NO-FAULT COMPENSATION TO HUMAN VOLUNTEERS

1. This section sets out the arrangements for the payment of no-fault compensation to volunteers who suffer illness and/or personal injury as a direct result of participating as a non-patient (healthy) human volunteer in research conducted on behalf of the Ministry of Defence. The no-fault compensation arrangements only apply to volunteers (Military, Civilian, or non-Ministry of Defence) who participate in a Trial that has been approved by the MoD Research Ethics Committee.

2. A volunteer wishing to seek no-fault compensation under these arrangements should contact the Directorate of Safety & Claims (DS&C) St. George's Court, 2 -12 Bloomsbury Way, London, WC1A 2SH who may need to ask the Claimant to be seen by a MoD medical adviser.

3. DS&C will consider reasonable requests for reimbursement of legal or other expenses incurred by volunteers in relation to pursuing their claim (e.g. private medical advice, clinical tests, legal advice on the level of compensation offered) provided that they have been notified of the Claimant's intention to make such a Claim.

4. If an injury is sufficiently serious to warrant an internal MoD inquiry, any settlement may be delayed at the request of the volunteer until the outcome is known and made available to the

volunteer in order to inform his or her decision about whether to accept no-fault compensation or proceed with a common law claim. An interim payment pending any inquiry outcome may be made in cases of special need. It is the Claimant's responsibility to do all that he or she can to mitigate his or her loss.

5. In order to claim compensation under these no-fault arrangements, a volunteer must have sustained an illness and/or personal injury as a direct result of participation in a Trial. A claim must be submitted within three years of when the incident giving rise to the claim occurred, or, if symptoms develop at a later stage, within three years of such symptoms being medically documented.

6. The fact that a volunteer has been formally warned of possible injurious effects of the trial upon which a claim is subsequently based does not remove MoD's responsibility for payment of no-fault compensation. The level of compensation offered shall be determined by taking account of the level of compensation that a court would have awarded for the same injury, illness or death had it resulted from the Department's negligence.

7. In assessing the level of compensation, DS&C, in line with common law principles, will take into account the degree to which the Claimant may have been responsible for his or her injury or illness and a deduction may be made for contributory negligence accordingly.

8. In the event of DS&C and the injured party being unable to reach a mutually acceptable decision about compensation, the claim will be presented for arbitration to a nominated Queen's Counsel. DS&C will undertake to accept the outcome of any such arbitration. This does not affect in any way the rights of the injured party to withdraw from the negotiation and pursue his or her case as a common law claim through the Courts.

World Medical Association (2000) Declaration of Helsinki. Ethical principles for medical research involving human subjects. 52nd World Medical Association General Assembly, Edinburgh, Scotland October 2000.