Participant Information Sheet

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Project title: **Determining optimal sampling times for concussion blood biomarkers for prediction of recovery in females**

Research Team

Co-ordinating Investigator: Professor Patria Hume

Co-Principle Investigators: Dr Ed Maunder, Professor Alice Theadom, Dr Beth McQuiston, Dr Chris Puliu'vea, Dr Doug King, Dr Stephen Kara, Assoc Prof Mangor Pedersen

Co-Associate Investigators: Dr Ryu Yoshida, Dr Helen Danesh-Myer, Scott Crawford, Dr Mark Fulcher, Dr Anja Zoellner, Dr Swati Pradhan-Bhatt, Christi Essex, Katherine Forch, Dr Trevor Clark, Prof Andrew Kilding, Dr Sharon Olsen, Dr Stacy Sims, Dr Brian Russell, Dr Ken Quarrie, Nikki Reynolds, Charlotte Bray, Sapi Mukerji, Christina Emmerson, Marguerite Sandleback, Dr Naaz Shaikh, Dr Qi Zhang.

Sponsor: Auckland University of Technology

Study Sites: AUTM: AUT Millennium in Rosedale, **AUT-city:** AUT City Campus in Auckland CBD, **ASM:** Axis Sports Medicine in Auckland, **HVED:** Hutt Valley emergency department in Lower Hutt **WgtnED:** Wellington emergency department in Wellington.

Contact phone numbers:

AUCKLAND: Dr Ed Maunder 09 921 9999 ext 6227

WELLINGTON: Dr Doug King 022 034 1580 and Sapi Mukerji 022 312 8766

Ethics committee ref.: HDEC 2024 EXP 21888

Trial Registry ref: ANZCTR ACTRN12625000260426

AN INVITATION

Tēnā koe (greetings to you). My name is Professor Patria Hume and on behalf of the research team, you are invited to participate in this research study that aims to assess the levels of blood biomarkers and clinical measurements that may be useful for determining if someone has suffered an injury to their brain after concussion and how serious the injury might be. You are invited to participate in the study because you have sustained a recent head injury (mTBI group = mild traumatic brain injury/concussion) or you have not had a recent head injury (healthy control group).

Participation is voluntary and your decision to participate or not will not affect any healthcare you or your whānau will receive. If you agree to participate you will be given the option of being assessed at one of our participating clinics in Auckland, Palmerston North, Lower Hutt or Wellington.

We will collect some basic information about you, such as your age, height, weight, lifestyle information, any medical conditions you have, what medications you currently take, your ethnicity and we will ask you to fill some surveys about head injury and do some eye tests. During the lab/clinic visits (only one visit if you are in the healthy control group), we will collect a blood sample. For the mTBI group, we will collect several samples, with your permission, across your recovery period. This is to determine when (how many days/weeks after the injury) we can diagnose someone with mTBI using these blood-based protein markers and if they might be a good marker of recovery.

The data collected within this research will be analysed only by the research team and will be presented as de-identified group data before being published.

Please ensure you read the information below and understand this prior to partaking in the study. If you have further questions or concerns, you can contact the research team using the details at the bottom of this document.

This Participant Information Sheet will help you decide if you'd like to take part. It sets out why we are doing the study, what your participation would involve, what the benefits and risks to you might be, and what would happen after the study ends. We will go through this information with you and answer any questions you may have. You do not have to decide today whether or not you will participate in this study. Before you decide you may want to talk about the study with other people, such as family, whānau, friends, or healthcare providers. Feel free to do this.

If you agree to take part in this study, you will be asked to sign the Consent Form. You will be given a copy of both the Participant Information Sheet and the Consent Form to keep.

This document is 9 pages long. Please make sure you have read and understood all the pages.

WHAT IS THE PURPOSE OF THE STUDY?

There are two key reasons why we are conducting this study.

The first reason is to find out if two protein markers in blood can be used to determine how injured someone's brain might be. Traumatic brain injury is a concerning injury that often occurs in sports or during activities where there is a likelihood that someone's head will connect, with force, to something or someone else. So far, the only way to diagnose if someone has a mild or moderate traumatic brain injury (often called a concussion) is by scanning their brain with a CT or MRI scanner and performing several medical exams. There can be quite a delay between someone being injured and when they can be seen by medical specialist and given a CT scan. Scientists have been trying to develop blood tests that would diagnose a person faster and easier than how we currently do it. This research is trying to test if two protein markers in particular (GFAP and UCH-L1) are useful for measuring how well someone recovers after their injury.

The second reason is to determine if other measurements, questionnaires specific to mTBI/concussion and a new device that can track eye movements, can enable us to better track your recovery. Using the blood-based markers and these other measurements will enable us to determine which of our tests can detect and reliably track recovery from mTBI/concussion.

The third reason is that females seem to suffer from longer and worse symptoms after mTBI/concussion. To identify if the menstrual cycle (period) plays a role in the severity of mTBI symptoms, blood tests will be performed to look at the levels of female sex hormones. The levels of these hormones after injury may help to determine why females have worse symptoms compared with males.

HOW WAS I IDENTIFIED TO PARTICIPATE IN THIS SURVEY?

You would be identified for this study by a healthcare professional who strongly suspects you have a mTBI/concussion or has diagnosed you with one. This professional may inform you about this study themselves, or they may ask your permission for a member of the study team to contact you about this study.

HOW DO I AGREE TO PARTICIPATE IN THIS STUDY?

You can contact a member of the study team to participate in this study. If you would like to get involved, a member of the study team will walk you through this document and answer any questions you or your whānau might have. You have the option of either doing an online consent form or completing the consent form when you attend the first session.

WHAT WILL MY PARTICIPATION IN THE STUDY INVOLVE?

You will need to be willing to fill in some forms that ask you about concussions, your ethnic background and your sex. You will also need tofill out a general health questionnaire. This is to make sure we know there are no conditions or medications that might affect the testing. You must also be willing to provide several blood

samples. This will only be taken by someone trained to do so. There are also some non-invasive tests of your eye movement that will also happen.

If you are in the healthy control group, you will only need to come to clinic once.

If you are in the mTBI group you will need to come to one of our clinics (ideally at 24 and 72 hours, then at two and three weeks and finally at months three, five and seven post mTBI injury). This is a total of up to 7 visits and these dates will be provided for you.

None of the research tests are diagnostic, they will not be recorded in your medical files. They are for research only. Here is a list of the test we would like to perform:

- Height and weight (5 min)
- Surveys (20 min): Brain Injury Screening Tool-10, Perceived Recovery Scale, Glasgow Outcome Scale Extended.
- Eye tracking (15 min)
- Blood sample collection (10 min).

This research includes basic information such as your ethnic group, age range, and sex. It is possible that this research could one day help people in the same groups as you. However, it is also possible that research findings could be used inappropriately to support negative stereotypes, stigmatize, or discriminate against members of the same groups as you. The study team will take utmost care with regards to this but are unable to control how other people choose to use the information we may publish.

There is also a small risk the study team may make an incidental finding that might affect your health. In this case, we would immediately report the result to your General Practitioner (GP). GP notification of clinically significant abnormal results is a mandatory component of study participation. Therefore, GP contact details are requested on the consent form.

Some of the questionnaires may make you feel upset or stressed. If you feel you need counselling or support due to taking part in this research study AUT Health Counselling and Wellbeing is able to offer three free sessions of confidential counselling support for adult participants in an AUT research project. These sessions are only available for issues that have arisen directly as a result of participation in the research and are not for other general counselling needs. To access these services, you will need to:

- drop into our centres at WB219 or AS104 or phone 921 9992 City Campus or 921 9998 North Shore campus to make an appointment. Appointments for South Campus can be made by calling 921 9992.
- let the receptionist know that you are a research participant and provide the title of our research and the name and contact details as given in this Information Sheet.

You can find out more information about AUT counsellors and counselling on http://www.aut.ac.nz/being-a-student/current-postgraduates/your-health-and-wellbeing/counselling.

VOLUNTARY PARTICIPATION AND WITHDRAWAL FROM THIS STUDY

Your participation is voluntary, and you can withdraw from the study at any time. You do not have to give us a reason why and it will not affect any care you receive in the future. If you choose to withdraw from the study, you will be offered the choice between having any data that is identifiable as belonging to you removed or allowing it to continue to be used. You may also request that any blood samples be removed and disposed of. You may also have any blood samples that have not yet been analysed returned to you by written arrangement with the study team.

HOW IS THE STUDY DESIGNED?

This is an observational study; no drugs or therapeutics are offered.

As a healthy control we will use your information and to compare your data to people with mTBI.

As a mTBI patient you may receive advice from healthcare professional during the course of the study. We want to compare your data to those of healthy controls to help us determine which of these measures might be able to diagnose mTBI/concussion and whether they can be used to track your recovery over time.

WHO CAN TAKE PART IN THE STUDY?

You have been invited to take part in this study because you are aged 16 years and older and are either healthy or have recently suffered a mild traumatic brain injury (mTBI). You will be able to start the study if you meet the inclusion criteria outlined below.

To take part in the study you need to be aged 16 or older, reside in New Zealand, be able to provide informed consent, able to provide a blood sample and (for the mTBI group) have sustained a recent mTBI/concussion.

You can NOT take part in the study is you have a suspected or confirmed neurodegenerative conditions or dementia, including, but not limited to, dementia (Alzheimer's disease, and vascular, Lewy body, or frontotemporal dementia), Parkinson's, Huntington's, motor neurone disease and mild cognitive impairment, and no history of acute neurological events or structural brain abnormalities including TBI, stroke, seizure, epilepsy, chronic headache, and brain tumour and no unstable severe medical conditions for example; cancer, severe coagulopathy, terminal illness, end-stage organ failure, acute kidney dysfunction, chronic kidney dysfunction or renal failure.

If you are a control, you can NOT take part in this study if you have experienced a mTBI within the last 12 months or are experiencing lingering symptoms from a previous mTBI.

WHAT WILL HAPPEN TO MY DATA?

Your data will be de-identified in all analysis, reports and publications. Once the data have been analysed and findings have been produced, removal of your data may not be possible.

We would also like to use the data we collect here for future studies. At this stage we cannot tell you exactly what that research might be other than it would be related to mTBI. Your data will be de-identified before it is used. We will ask you to sign an additional consent form if this is the case.

WHAT WILL HAPPEN TO MY BLOOD?

When your blood is drawn, it will be tested for GFAP, UCH-L1 and other protein markers we think might be useful to understand mTBI. We will also do a hormonal panel that included estradiol, progesterone, luteinising hormone, follicle stimulating hormone, DHEA-S, prolactin, and testosterone. We will take no more than 40 mL of blood. For reference, a donation to NZ Blood is 457 mL, ten times as much as we will take.

You must alert the study team before we take any blood if you wish your samples to be disposed of with Karakia or if you wish them returned to you. We cannot post these samples by mail so you will need to return to the site where you donated the blood to collect them or to AUTM if they have been sent for storage.

Here is a list of all the tests we will perform on your blood:

- Glial Fibrillary Acidic Protein (GFAP)
- Ubiquitin C-terminal Hydroxylase 1 (UCH-L1)
- Neurofilament Light chain (NfL)
- Phosphorylated tau -217 (pTau-217)
- Follicle Stimulating Hormone (FSH)
- Estradiol
- Progesterone
- Luteinising Hormone
- Cortisol
- C-reactive protein (CRP)
- Ferritin

- Vitamin D
- Creatinine
- Cystatin C
- Procalcitonin (PCT)
- Active B12
- Prolactin
- Thyroid stimulating hormone (TSH)
- Free thyroxine (FT4)
- Thyroxine (T4)
- Magnesium
- Testosterone
- Dehydroepiandrosterone sulfate (DHEA-S)

If you consent to the use of your blood for future research related to mTBI and brain health, we will keep some of your blood secure in a freezer. We will ask you to sign an additional consent form if this is the case.

WHAT ARE THE POSSIBLE RISKS OF THIS STUDY?

Although routine blood collection is generally safe you may experience some pain or discomfort when having your blood taken. Your arm may be sore for a few hours afterwards. There is a minor risk of bruising or haematoma, which is when blood pools under the skin causing a dark bump to form. These are not likely to seriously affect you but they may be distressing. If you have concerns about anything involving the collection of blood you are welcome to contact the study team and have them respond to any concerns you might have.

In rare cases the eye movement tests may cause a temporary headache or make you dizzy.

WHAT ARE THE BENEFITS?

There is unlikely to be any direct individual benefits to participation. However, the benefit of participating in this study is you are helping the researchers find out more about how to diagnose and manage mTBI/concussion as well as the difference between males and female and how they experience mTBI/concussion.

HOW WILL MY PRIVACY BE PROTECTED?

Study data will be recorded in an online database called REDCap. This database is securely hosted at AUT and is inaccessible to people other than the study team. Results will be provided as de-identified group data. All data collected during the study will be in storage at the AUT SPRINZ ethics storage room. All data will be stored under the AUTEC policy, which secures this data for ten years.

Individual information will not be shared or discussed. Although efforts will be made to protect your privacy, absolute confidentiality of your information cannot be guaranteed. Even with coded and anonymised information, there is no guarantee that you cannot be identified. The risk of people accessing and misusing your information (e.g. making it harder for you to get or keep a job or health insurance) is currently very small but may increase in the future as people find new ways of tracing information.

WHAT IF SOMETHING GOES WRONG?

If you were injured in this study, you would be eligible to apply for compensation from ACC just as you would be if you were injured in an accident at work or at home. This does not mean that your claim will automatically be accepted. Your healthcare provider will have to lodge a claim with ACC, which may take some time to assess. If your claim is accepted, you will receive funding to assist in your recovery. If you have private health or life insurance, you may wish to check with your insurer that taking part in this study won't affect your cover.

WHAT WILL HAPPEN TO MY INFORMATION?

When you consent to take part in this study, you will be assigned a unique identifier number (e.g. CH001) so that your information can be de-identified for analysis. This number will be noted on your consent form. During this study the study team will record information about you and your study participation. This includes your consent form.

We may collect survey information either online through our REDCap database or hardcopy when you attend your visit. The choice is yours. That information, along with the clinical measurements and the results of our blood tests will be stored on REDCap.

All of the research data collected in this study will be stored on a secure and password protected cloud service (OneDrive). Only Professor Patria Hume, Dr Ed Maunder and Dr Doug King and will have access to your identifiable research data.

For research purposes, a master spreadsheet will be created with all information that could identify you removed, your unique identifier number will be used to record data in this spreadsheet. Only this second de-identified spreadsheet will be shared with the rest of the research team and used for analysis and in publications/presentations.

IDENTIFIABLE INFORMATION

Identifiable information is any data that could identify you (e.g. your name, date of birth, or address). Only Professor Patria Hume and members of the study team will have access to your identifiable information.

DE-IDENTIFIED (CODED) INFORMATION

To make sure your personal information is kept confidential, information that identifies you will not be included in any report generated by Professor Patria Hume. Instead, you will be identified by a code. Dr Ed Maunder will keep a list linking your code with your name, so that you can be identified by your coded data if needed.

The following people may have access to your de-identified (coded) information:

- Biostatistician assisting in final data analysis.
- Other members of the Study Team
- Abbott Diagnostics (USA) if you consent to it

The results of the study may be published or presented, but not in a form that would reasonably be expected to identify you.

SECURITY AND STORAGE OF YOUR INFORMATION

All of your personal information will be stored on a secure password protected cloud service (OneDrive). Only named members of the research team will have access to this information.

Research data will be stored on REDCap, a cloud-based database hosted at AUT. This database shares all of AUT's cybersecurity protections. Only the study team will have access to this database.

For research purposes, you will be assigned a unique identifier code so that your data can be de-identified. A second master spreadsheet will be created with all information that could identify you removed. Only this second de-identified spreadsheet will be shared with the rest of the research team and used for analysis and used in publications/presentations. Analysis and reporting of data will be de-identified and at the group level. All reporting of data in reports and publications will be de-identified and at the group level.

RIGHTS TO ACCESS YOUR INFORMATION

You have the right to request access to your information held by the research team. You also have the right to request that any information you disagree with is corrected.

Please ask if you would like to access the results of your tests during the study.

If you have any questions about the collection and use of information about you, you should ask Dr Ed Maunder.

RIGHTS TO WITHDRAW YOUR INFORMATION

You may withdraw your consent for the collection and use of your information at any time, by informing Dr Ed Maunder, Dr Doug King or Professor Patria Hume. If you withdraw your consent, your study participation will end, and the study team will stop collecting information from you. If you agree, information collected up until your withdrawal from the study will continue to be used and included in the study. You may ask for it to be deleted when you withdraw, unless you withdraw after the study analyses have been undertaken.

ARE THERE ANY CULTURAL CONSIDERATIONS?

You may hold beliefs about sacred and shared values about your blood samples and/or data originating from this blood. The cultural issues associated with sending your data overseas and/or storing your blood and data should be discussed with your family/whānau as appropriate. If you wish to know more about the study, we can arrange for a member of the study team to come and talk to you and your whānau. Your samples can be disposed of with Karakia, you only need to ask the study team when you come to clinic.

Personal and health information is a tāonga and will be treated accordingly. The following data sovereignty principles are in place to ensure that the data generated from this research are protected and may benefit Māori now and into the future. The principles included are whakapapa, whanaungatanga, kotahitanga, manaakitanga and kaitiakitanga. This research programme is also establishing a Māori consultation committee to assist with the design and presentation of this and future research.

Whakapapa: We understand that all data have genealogy and special relationships to the community. We collect demographic and ancestry data to ensure these data still hold relevance to the communities they come from.

Whanaugatanga: The data kept in Aotearoa will be stored securely and accessed only by research staff members who maintain confidentiality, it is collected only from those participants who have consented to the collection – and participants are encouraged to consult with whānau if that is culturally appropriate for them. The distribution of any results will be done in a way that recognises the reciprocity of the participant-researcher relationship.

Kotahitanga: This research, whilst it may not offer personal benefit, will hopefully contribute to collective benefit. You information will be used in a way that benefits more than just the researchers, but people affected by mTBI.

Manaakitanga: Free and informed consent and clear communication between yourself and study team is a hallmark of respect and Manaakitanga. We acknowledge the personal investment you make by participating and the importance of reciprocity of the research process.

Kaitakitanga: this research is designed to empower and discover. Māori data will be accessible where required and any analysis specific to gender or ethnicity will contribute to overcoming historic data inequality.

WHAT HAPPENS AFTER THE STUDY OR IF I CHANGE MY MIND?

If you wish to withdraw from the study at any point you can contact either Dr Ed Maunder, Dr Doug King, Professor Patria Hume or another member of the Study Team if that is easier. If you do withdraw from the study, you can choose to either, allow the information collected up until your withdrawal to continue to be used or you may ask for it to be deleted when you withdraw. If you withdraw after the study analyses have been undertaken it may not be possible to remove your data/information.

WILL I RECEIVE FEEDBACK ON THE RESULTS OF THIS RESEARCH?

The overall study results will be published on the AUT SPRINZ SKIPP website Sports Kinesiology Injury Prevention and Performance - SPRINZ - AUT (https://sprinz.aut.ac.nz/areas-of-expertise/sports-kinesiology-injury-prevention-and-performance).

Within 120 days of the study finishing a 1–2-page summary of the research findings will be available. If you would like to receive a copy, please indicate on the consent form, and provide a contact email address.

WHO IS FUNDING THE STUDY?

There are no direct financial costs to you as a participant in this study. This research is part funded by Abbott Laboratories (USA), a medical device and research company.

Each participant will receive $20 voucher for each of the clinic visits. In addition, there is a prize draw for a pair of Asics shoes for those that complete the recovery testing sessions.

WHAT DO I DO IF I HAVE CONCERNS OR FURTHER QUESTIONS ABOUT THIS RESEARCH?

If you have any concerns regarding this project, please contact the lead investigator – Professor Patria Hume, patria.hume@aut.ac.nz mobile 021 805 591.

For Māori cultural support contact please contact Dr Doug King, doug.king@aut.ac.nz; and for Pacific cultural support please contact Dr Dion Enari, dion.enari@aut.ac.nz.

Concerns regarding the conduct of this study should be notified to the Executive Secretary of AUTEC, ethics@aut.co.nz (+649)9219999 ext 6083.

If you want to talk to someone who isn't involved with the study, you can contact an independent health and disability advocate on:

Phone:	0800 555 050
Fax:	0800 2 SUPPORT (0800 2787 7678)
Email:	advocacy@advocacy.org.nz
Website:	https://www.advocacy.org.nz/

You can contact the health and disability ethics committee (HDEC) that approved this study on:

Phone:	0800 4 ETHIC
Email:	hdecs@health.govt.nz

WHO HAS APPROVED THE STUDY?

This study has been approved by an independent group of people called a Health and Disability Ethics Committee (HDEC), who check that studies meet established ethical standards. The HDEC Northern Committee has approved this study.

Approved by

Health and Disability Ethics Committee on 14th March 2025

Reference number HDEC 2024 EXP 21888

Note: The Participant should retain a copy of this form.