PARTICIPANT INFORMATION SHEET AND CONSENT FORM FOR RESEARCH SUBJECTS

1. Study Information

IRB Reference Number: IRB-2020-03-040

Protocol Title:
Low Energy Availability (LEA) Threshold in Male Athletes

Principal Investigator & Contact Details:

Principal Investigator	Stephen Burns, PhD Associate Professor, Physical Education and Sports Science (PESS) National Institute of Education (NIE) Nanyang Technological University (NTU) Telephone: (65) 6219 6214 Mobile phone: (65) 9725 6699 E-mail: stephen.burns@nie.edu.sg
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Co-Investigator	Bernhard Boehm, MD Nanyang Professor Lee Kong Chian School of Medicine, NTU Telephone: (65) 6592 3637 E-mail: bernhard.boehm@ntu.edu.sg
Co-Investigator	Alvin Tan Wai Kit, MBBS, MRCP (Edin), FAMS (Endocrinology) Consultant Department of Endocrinology Tan Tock Seng Hospital (TTSH) E-mail: alvin_tan@ttsh.com.sg
	Tan Hui Qing Undergraduate student PESS, NIE, NTU E-mail: HTAN112@e.ntu.edu.sg
Study Location	All testing will take place at: Human Bioenergetics Laboratory Physical Education and Sports Science Block 5, Level 3, Room 1 National Institute of Education Nanyang Technological University S637616

Study Sponsor:
The study is being funded by an internal grant from the National Institute of Education Academic Research Fund.

2. Purpose of the Research Study

You are invited to participate in a research study. It is important to us that you first take time to read through and understand the information provided in this sheet. Before you take part in this research study, the study will be explained to you and you will be given the chance to ask questions. After you are properly satisfied that you understand this study, and that you wish to take part in the study, you must sign the accompanying Consent Form. You will be given a copy of this Consent Form to take home with you.

You are invited because we are studying what happens to athletes who do not have enough energy in their diet for them to function properly. This is called low energy availability (LEA) and it is a condition that has been found to impact male athletes' physiological and performance functions. LEA can also result in a severe condition known as Relative Energy Deficiency in Sport which can compromise athletes' health. It has been found that endurance athletes may be at a higher risk of LEA, as compared to non-endurance athletes. For female athletes we know the LEA threshold level at which physiological functions become impaired but for male athletes no definite level has been established. It is therefore necessary to have an established LEA threshold for clearer diagnosis of the condition and development of preventive guidelines in the future. We are asking you to take part in the present study as we want to know what happens when healthy well-trained adult endurance athletes experience LEA over a period of a few days. You are considered one of those athletes.

Thus, this investigational study is carried out to determine the LEA threshold in male endurance athlete that elicits change in bone turnover markers and resting metabolic rate (RMR) over a 4-day period. Your energy availability will be controlled in the study.

This study will recruit 12 participants from Nanyang Technological University over a period of 1 year.

3. Inclusion/Exclusion Criteria

This study will be undertaken in men. In order to participate in this study, you must be:

1) Male
2) Age: 21-35 years
3) Completing endurance training for at least 3 sessions/week during the past 12 months
4) Running at least 24km a week on a regular basis
5) An IPPT 2.4 km run time of 11:00 or less at their last test or maximal oxygen uptake ($\dot{V}O_{2max}$) of 47 ml/kg/min
6) Weight stable (±3 kg) in the past three months and not actively trying to lose weight by self-report
7) Body mass index: 19-25 $kg \cdot m^{-2}$
8) Normal blood pressure (less than 130/80 mmHg and greater than 90/60 mm Hg)
9) Normal blood glucose level (less than 7.0 mmol/ L and more than 3.9 mmol/L)

10) Healthy and injury-free (e.g. no cardiovascular disease, diabetes mellitus, orthopaedic impairment that interferes with moderate-to-vigorous exercise)
11) No previous or current diagnosis of eating disorder(s)
12) No known or deliberate disordered eating behaviours
13) No special diets (e.g. vegan, vegetarian, ketogenic diet)
    a. Halal dietary requirement is acceptable
14) Non-smoker

You will not be able to participate in the study if you have:

1) Any diagnosed form of cardiometabolic disease (heart disease, stroke, peripheral vascular disease, diabetes, metabolic syndrome, high blood pressure)
2) Any symptoms contraindicating exercise testing (e.g. chest pains)
3) Any balance or dizziness problems
4) Any chronic medical conditions (whether medicated or not)
5) Any bone joint problems
6) Any Physician diagnosed contraindications to exercise
7) If you are actively trying to lose weight when enrolling into the study
8) If you drink alcohol more than 3 times each week and more than 3 drinks each time
9) Any allergies to food items used in the prescribed meals
10) SCOFF score: 2 or more
11) Exercise Addition Inventory score: 24 or more

Any other health problems that may be a cause for concern or contraindication to exercise. Upon questioning the researchers reserve the right to deny study entry if there are health problems of concern until Physician approval is provided.

<u>Screening procedures and tests (Questionnaires, maximum oxygen uptake ($\dot{V}O_2$) test)</u>

In order to determine your eligibility to participate in this study a number of pre-screening procedures and other tests will be performed, after an overnight fast. You will not be obliged to take part in these pre-screening procedures and tests if you are not comfortable with sharing any of the information we will collect. You may verbally indicate this at any time. Any information collected during the screening will be kept confidential.

The pre-trial screening and maximal oxygen uptake ($\dot{V}O_2$) test will include:

1) Researcher(s) to provide a detailed explanation of the study
2) Review medical history
3) Complete questionnaires:
    a. Standard health screening form (Physical Activity Readiness Questionnaire for Everyone, PAR-Q+)
    b. Measure eating behaviours (called the SCOFF questionnaire)
    c. Measure exercise behaviours (called Exercise Addiction Inventory)
4) Height
5) Weight
6) Resting blood pressure (Figure 1A)
7) Taking a blood sample from your fingertip to measure blood glucose

8) Measuring your body composition (amount of muscle and fat in body) using Dual Energy X-ray Absorptiometry (DXA) scan and a technique called Bioelectrical Impedance Analysis (BIA) (Figure 1B and 1C).
9) $\dot{V}O_2$ test: This test will be to measure your cardiorespiratory fitness (ability of your body to deliver and use oxygen). For this test you will run on a treadmill. The protocol will begin at a speed of 8 km/h and increase by 2 km/h every 3 minutes until a speed of 16 km/h at a 0% grade. Subsequently, the grade will increase by 1% at the start of every additional minute, until volitional exhaustion. Every minute the incline on the treadmill will increase until you cannot continue exercising. At the end of the test the exercise will be your maximal and so it will feel very strenuous. During the test you will wear a heart rate monitor and we will show you a 'perceived exertion' scale which is a continuous number scale rating how tired you feel (Figure 1D).
10) 3-day food diary and exercise log (2 weekdays and 1 Sunday). You will also photograph any food and drinks consumed and we ask that you do not consume any alcohol on these days.
11) Heart rate monitor to be worn during exercising periods.

You will be deemed suitable to proceed on with the study if your energy availability status is considered adequate, as determined by the food diary and exercise log.

Figure 1. Blood pressure measurement (A), DXA scan (B), Body Impedance Analysis (C), and maximal oxygen uptake test (D).

Waiver for HBRA Section 37(3) Requirement
This study **does not involve** the removal of tissues from (a) an adult who lacks mental capacity; (b) a minor who lacks mental capacity; or (c) a minor who lacks sufficient understanding and intelligence to give consent for research purposes.

4. What Procedures will be Followed in this Study?

If you take part in this study, you will undergo three trial conditions in a random order. Each trial condition involves 5 continuous days and there is a wash-out period of at least 7 days between each trial condition. Randomisation means assigning you to different orders of the three conditions by chance, like tossing a coin or rolling dice. The three conditions will be LEA1, LEA2, and adequate energy availability (AEA). This will be represented randomly by Condition A, B, and C.

If you take part in this study, you will be asked to make multiple visits to the laboratory, the total study commitment time is 35 hours. If you agree to take part in this study, you will be asked to follow the procedures as outlined below.

Your participation in the study will last 6 weeks. You will be prescribed diet and exercise for four days for about three times. The study will consist of 16 visits to the lab in the course of the study. If you are injured or feeling unwell, inform us 48 hours beforehand as we may re-schedule your visit.

If you agree to take part in this study, the following procedures will be carried out:

- **Day 1- Day 4: Pre-measures and intervention**

For all conditions, you will come to the laboratory on the 1st day of the week (i.e. Monday), between 7am to 9am, in a fasted state (no food or drinks should be consumed, except water for 8 hours beforehand). This will be considered as Day-1. We ask that you come to the laboratory by public transport or car (do not walk/ cycle). Once in the laboratory the following procedures will take place:

- Complete a questionnaire that measures mood (BRUMS questionnaire)
- You will lie on the bed for 30 minutes under a clear plastic helmet and sheet called a ventilated hood (Figure 2A). The helmet of the ventilated hood looks like an astronaut helmet. The measurement period will be 30 minutes long and we ask that you do not talk, fidget, or fall asleep or use electronic devices. The helmet is attached to a machine which measures samples of the air you breathe to determine how much energy you are using at rest (RMR).
- Upon completion of this resting measure, we will draw a blood sample (15mL, 3 teaspoons) from your forearm vein.
- Following this, we will provide you with a standardised meal (Meal 1) (Figure 2B) for breakfast at 9am.
- One hour after finishing the meal you will run on a treadmill at a moderate speed until you expend a certain amount of energy. The duration of the treadmill run will vary among individuals but is likely to take 1-1.5 hours.
- You will be provided an isotonic sports drink after completion of the run.
- Lunch and dinner on Day 1 will be provided to you and are to be consumed on your own, by 2pm and 8pm, respectively.
- On, Day-2 to Day-4 you will report to the laboratory each day and we will provide you breakfast. You will then repeat the same treadmill run as on Day 1 and consume your lunch and dinner that we provide in the same way.

- Please note that the amount of food provided for breakfast, lunch and dinner will vary depending on which Condition you are completing at the time.
- During the Condition period, we ask that you do not consume additional food or any sports or exercise training other than what has been prescribed by the study.

Figure 2. Measurement of RMR (A), and example of prescribed meal (B).

- **Day-5: Post measures**

For each condition, at least 18 hours after the completion of the exercise protocol on Day-4, you will undergo a series of post-intervention measures. This will include:

1) Body weight
2) Body composition (including FFM)
3) BRUMS questionnaire
4) RMR
5) Blood sample (15mL, 5 teaspoons)

After Day 5 of Condition A, a break, also known as a washout period, of at least 7 days will commence. During this time, you may return to your usual living habits.

After the washout period, Condition B and C will proceed, which follow the same procedures as Main Condition A. There will be a washout period of at least 7 days in between each Condition.

Condition A, B, and C will be randomised. The study design is shown in Figure 3.

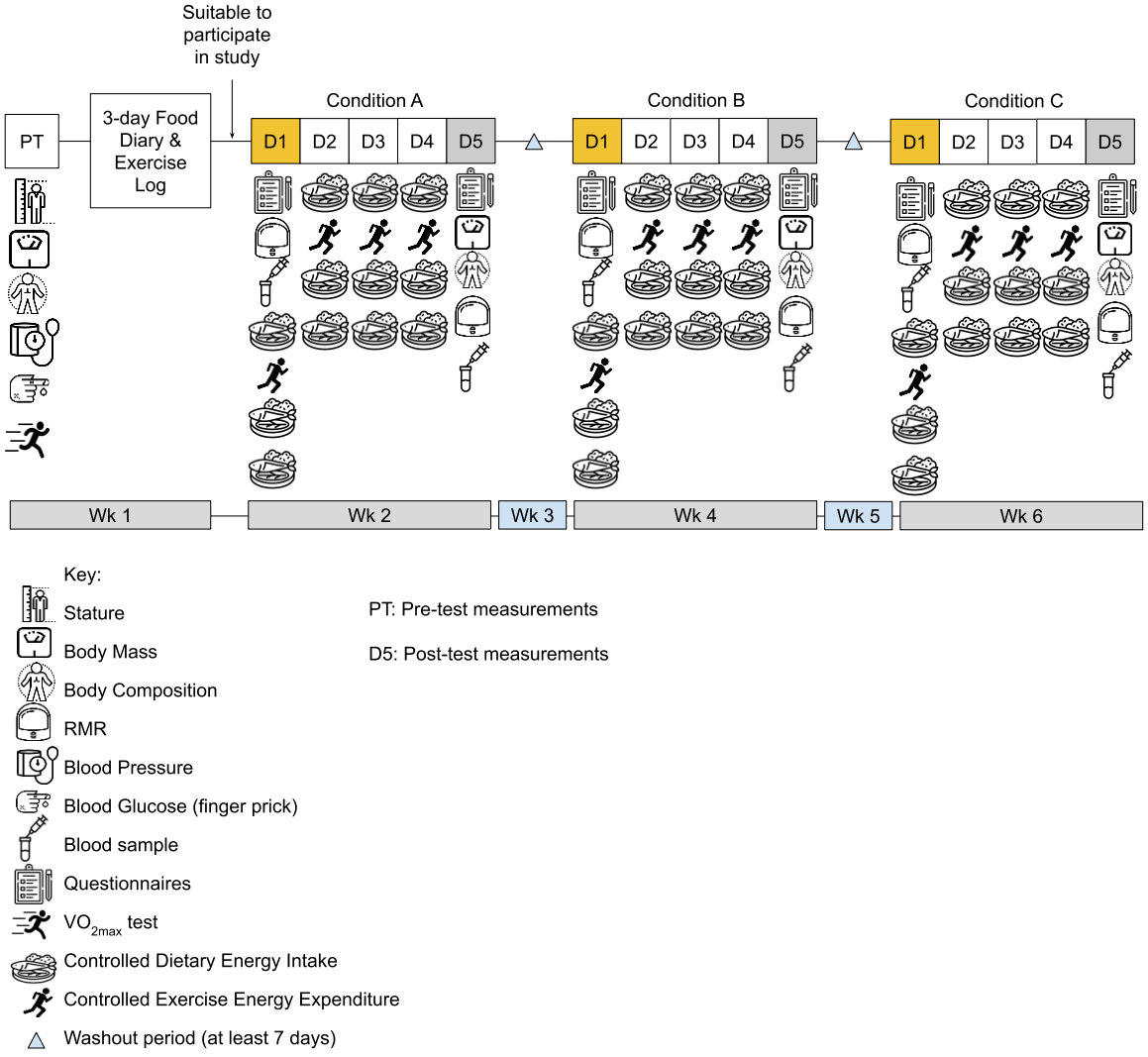

Figure 3. Study Design

Schedule of Visits and Procedures:

Week1:

Pre-test measurements (screening) 3-day Food diary and exercise log

Week 2: Main Trial: Condition A

Day 1 to Day 4: Primary outcomes measurement, Diet and exercise prescription

Day 5: Post-test measurements

Week 3:

Washout period (at least 7 days) Week 4:

Main Trial: Condition B

Day 1 to Day 4: Primary outcomes measurement, Diet and exercise prescription

Day 5: Post-test measurements

Week 5:

Washout period (at least 7 days) Week 6:

Main Trial: Condition C

Day 1 to Day 4: Primary outcomes measurement, Diet and exercise prescription

Day 5: Post-test measurements

When your participation in the study ends, you will no longer have access to the prescribed food, treadmill for exercise unless special additional arrangements are made by the Principal Investigator.

Incidental Findings:

During the course of the current study (and future studies), there is a possibility that we might unintentionally come to know of new information about your health condition from the questionnaires and blood samples that are taken as part of the study. These are called "incidental findings" derived from experimental tests/scans that are not of clinical grade. These findings might be expected or unexpected, and might cause you to feel anxious and could potentially have serious implications for your well-being and/or health insurance coverage.

"Incidental findings" are findings that have potential health or reproductive importance to research participants like you and are discovered in the course of conducting the study, but are unrelated to the purposes, objectives or variables of the study.

You will be asked to indicate whether you wish to be re-identified and notified in the event of incidental finding that is related to you. Examples of potential incidental findings that may be discovered during the course of this study may include but are not limited to potential eating disorders, diabetes, low bone density, low hormonal levels.

If you agree to be re-identified and notified, the Principal Investigator (or a qualified healthcare professional or trained personnel) will explain the incidental finding to you and discuss and advise you on the next steps to follow, including referral to registered medical professionals for further consultations. For this purpose, please inform the study team members listed in this document whenever there are changes in your/your next of kin contact details. You may wish to do more tests and seek advice to confirm this incidental finding.

The costs for any care that will be needed to diagnose or treat an incidental finding **would not be paid** for by this research study. These costs would be your responsibility.

5. Your Responsibilities in this Study

If you agree to participate in this study, you should follow the advice given to you by the study team and be prepared to undergo all the procedures that are outlined above. You should also inform the Principal Investigator as soon as possible about any side effects that you may have encountered.

6. What is Experimental in this Study?

Although blood sampling may be part of standard medical care, in this study this procedure is only being performed for the purposes of the research and is not part of your routine care.

7. Possible Risks and Side Effects

There are several possible risks and discomforts associated with undertaking this study:

Body composition: The body composition machine uses a technique called bioelectrical impedance (BIA). There are no risks from BIA as it is a non-invasive, safe and quick procedure to measure body composition. The current from the BIA runs at low frequency and is unlikely to stimulate any electrically stimulated tissues, such as nerves or cardiac muscle. Even in the course of thousands of individuals undergoing measurement using BIA, there is an absence of any reports of untoward events occurring. However, it you have an Implantable Cardioverter-Defibrillators (CDs) you are not allowed to participate in the present study.

DXA scan: The DXA scan will be used to measure bone health and body composition. During the DEXA procedure you will be exposed to a low dose of radiation from a whole body x-ray. This low exposure is less than 2% of the radiation received from a chest x-ray, less than 1% of the radiation received from a dental x-ray, and less than half the radiation exposure from six hours outdoors. There is no minimum level of radiation exposure that is considered totally free of the potential risk of causing genetic changes (cellular abnormalities). However, the risk associated with the total amount of radiation exposure you will receive from taking part in this study is considered low and comparable to other everyday risks.

Exercise: The exercise tests may leave you slightly breathless, although this should only last for a few seconds at the termination of the test. If you have a history of asthma or are taking medication for asthma you will be excluded from the study. There is a small risk of injury (falling over) on the treadmill, However, you will be given safety instructions and the harness will support you during testing. There is also a risk of getting dizzy or fainting from blood pooling at the end of the exercise tests. You will be provided with a standardised cool-down procedure to reduce this risk. As with any exercise tests there is also an increased risk of mortality. However, the risk of death or a myocardial infarction (heart attack) during or immediately after an exercise test is very small. If you have a heart defect of any kind you will not be able to take part in this study. To protect against risks, we will use the PAR-Q+ before you exercise and whilst exercising you will be monitored continuously for exercise work rate and adverse signs and symptoms for termination of an exercise test. You will not be left alone during any exercise testing. The Principal Investigator is a qualified Exercise Physiologists and will supervise all exercise testing. Staff within the laboratory are qualified in the use of automated external defibrillators (AED, there is one located in the laboratory), cardiopulmonary resuscitation (CPR) and basic first aid. We have standard laboratory evacuation and safety procedures.

Energy deficit and hunger: In the two LEA conditions your body will be in a cumulative energy deficit over the 4 days. This state of lowered energy intake is not harmful but may be associated with other risks/symptoms such as hypoglycaemia (below). You are likely to feel hungry at times over the 4 days. The total amount of energy deficit over the 4 days is equivalent to approximately 0.5 to 1.0 kg of body fat (although please note that this does not account for any additional loss/gain in body water experienced over the time).

Hypoglycaemia: There is a low possibility that the trial conditions may leave you in a state of hypoglycaemia (low blood sugar), which includes symptoms such as shakiness, confusion, irritation, tachycardia. To protect against this risk, you will be provided one sports drink for consumption throughout the exercise session, and another sports drink after the session. If you were to display any symptoms of hypoglycaemia, we will have you to lie on a bed and will provide a sugary drink. We will monitor your blood glucose level till it returns to normal (>3.9 mmol/L) and your symptoms, and blood pressure too, before you can leave the laboratory. If you display any signs of hypoglycaemia after leaving the laboratory, please seek medical assistance and/or to phone the PI. We will provide you with a sugary sports drink to carry throughout the duration of each condition in case you are feeling unwell or show any symptoms related to hypoglycaemia. However, should you record any symptoms of hypoglycaemia or a blood glucose of <3.9 mmol/L then you will be excluded from the study. Moreover, as symptoms of hypoglycaemia may manifest in different ways, we will stop the study if you are unable to maintain a constant running speed on the treadmill for 1 minute or if you show signs of an irregular running gait. We will feed you any necessary caloric intake and provide monitoring until you are recovered in this instance. Should you require any medical attention at any time then we will accompany you to seek this as needed. However, you will be excluded from any further participation in the study.

RMR measurement (ventilated hood): There are no risks from the ventilated hood but if you are claustrophobic (have a fear of enclosed or small places) you may not find it pleasant. Please alert us at any time if you wish to come out from under the hood. You will not be left alone when the measurement is taken.

Fingertip blood sample: We only take a very small amount of blood during fingertip blood sampling. Fingertip blood sampling may cause slight pain or occasionally bruising and, in some instances, people may feel dizzy or faint. To reduce this possibility, you will always be seated during blood sampling. Infection is an extremely unlikely issue with fingertip blood samples. However, appropriate procedures will always be used by trained researchers: gloves, laboratory coats, alcohol swabs, one-time use needles, cotton wool compressors.

Blood sampling: There are several risks associated with blood sampling, this includes pain, bleeding, bruising, infection, dizziness, and fainting. One or more of these occur commonly (in 10 to 25 out of 100 people). All blood sampling will be performed with you lying on a bed to minimise the risk of fainting and any injury that might happen from a fall, including concussion (head injury) which occurs in less than 1 out of 100 people. Haematoma (a collection of blood under the skin that forms a lump) is a rare complication (occurs in less than 1 out of 100 people). You will be monitored for any sign of haematoma. If one occurs the line will be removed, and pressure will be maintained over the affected area for 5 minutes. The Principal Investigator is trained in blood sampling and all equipment used in blood sampling is one time use only.

Meals: The meals provided will be made from everyday food stuff. It will contain milk products, poultry, protein powder, nuts, dried fruits, etc. Individuals with known intolerance or allergies to these products will be excluded.

8. Possible Benefits from Participating in the Study

There is no known benefit from participation in this study. However, your participation in this study may add to the medical knowledge about the effects of low energy availability in male athletes.

9. Alternatives to Participation

Not applicable - as this study is only being completed for research purposes and is not part of any standard medical treatment there is no alternative to the participation outlined.

10. Costs & Payments if Participating in the Study

If you take part in this study, all procedures outlined in Sections 3 and 4 of this document will be performed at no charge to you: as stated in Section 3 and 4. These costs will be borne by the researchers.

You will be reimbursed $150 for your time, inconvenience, and transportation costs, upon completion of the entire study.

11. Voluntary Participation and Participant's Rights

Your participation in this study is entirely voluntary. You are free to withdraw from the study at any time without any obligation or need to explain to your decision. Your decision not to take part in this study or withdrawal will not affect your relationship with the University to which you are entitled. If you decide to stop taking part in this study, you should tell the Principal Investigator that you like to withdraw from the study. However, the data / research information that have been collected until the time of your withdrawal will be kept and analysed. The reason is to enable a complete and comprehensive evaluation of the study.

If you withdraw from the study, you will be required to simply notify the Principal Investigator, or another member of the study team listed on Page 1 in person or in writing. There are no consequences of withdrawal.

The Principal Investigator may stop your participation in the study at any time if they decide that it is in your best interests. They may also do this if you do not follow instructions required to complete the study adequately. If you have other medical problems or side effects, the Principal Investigator will decide if you may continue in the research study.

In the event of any new information becoming available (including but not limited to occurrences of serious adverse events, and changes in proposed research) that may be relevant to your willingness to continue in this study, you (or your legally acceptable representative, if relevant) will be informed in a timely manner by the Principal Investigator (or his/her representative) and will be contacted for further consent if required.

12. Compensation for Injury

If you follow the directions of the investigators in charge of this study and you are physically injured due to the procedures carried out for this study, without prejudice or any admission of liability, will compensate you for the injuries arising from your participation in the study without you having to prove Nanyang Technological University is at fault. There are however, conditions and limitations to the extent of compensation provided. You may wish to discuss this with your Principal Investigator.

By signing the accompanying Consent Form, you will not waive any of your legal rights or release the parties involved in this study from any liability for negligence.

13. Confidentiality of Data

Your participation in this study will involve the collection, use and disclosure of data / human tissues / human biological materials in an individually-identifiable form (or "**Personal Data**"). "Personal Data" means data about you, which makes you identifiable from (i) such data, and/or from (ii) other information which we have or likely have access to. This includes medical conditions, medications, investigations and treatment history.

Information and Personal Data collected for this study will be kept confidential and stored for a minimum of 10 years in a secure environment within NIE at NTU with restricted access given only to the Principal Investigator, study team members and School Administrators. Your records, to the extent of the applicable laws and regulations, will not be made publicly available, in accordance with NTU Personal Data Protection Statement.

However, government ministries or regulatory agencies, NTU Institutional Review Board will be granted direct access to your Personal Data to check study procedures and data, without making any of your information public. Your Personal Data may be shared with government bodies when acquisitioned by law or when ordered to do so by a court or legislations.

By signing the Informed Consent Form attached, you (or your legally acceptable representative, if relevant) are authorizing (i) collection, access to, use and storage of your Personal Data, and (ii) disclosure to, and use and storage by, authorised service providers and relevant third parties, whether located in Singapore or overseas, for the purposes of this study or future research studies.

Data collected are the property of NIE of NTU. In the event of any publication regarding this study, only aggregated research data without identifiable personal details will be used, and your identity will remain confidential.

Any heath information / data / blood and/or information containing your Personal Data that is collected for the purposes described in this Participant Information Sheet and Consent Form will be stored in Singapore. Only de-identified blood samples may be transferred out of Singapore for some analyses.

Any individually-identifiable data / blood samples obtained during the course of this study will be stored for 10 years. All blood samples stored will be coded (de-identified) with the code held by the Principal Investigator in secure form (locked cabinets and password protected electronic form). The data and samples will be stored in this form and used for future research studies examining the effects of low energy availability on athlete health. All blood samples will be destroyed and discarded after 10 years of storage and will not be used for any other purposes than that described. None of the samples or your health information will be transferred out of Singapore beyond those purposes already described. Your samples will **not** be used in any restricted human biomedical research involving human-animal combinations.

Your Personal Data will **not** be used for future research, unless otherwise consented by you in the accompanying Consent Form.

Your health information / personal data / blood collected in this study will be used in an individually-identifiable form for future research **only** if **explicit consent** has been provided by

you in the accompanying Consent Form and approval has been obtained from the Institutional Review Board or local ethics committee.

14. Whom To Contact if You Have Questions?

If you have any questions, complaints or feedback about this research study and in case of any injuries during the course of the study, you may contact the Principal Investigator,

Stephen Burns, PhD
Associate Professor
Physical Education and Sports Science (PESS)
National Institute of Education
Nanyang Technological University (NTU)
Telephone: (65) 6219 6214
Mobile phone: (65) 9725 6699
E-mail: stephen.burns@nie.edu.sg

The study has been reviewed by NTU Institutional Review Board (the central ethics committee) for ethics approval. If you want an independent opinion to discuss problems and questions (complaints / feedback), obtain information and offer inputs on your rights as a research participant, please contact:

NTU-Institutional Review Board
Research Integrity and Ethics Office
Blk N1.2, B1-02A
62 Nanyang Drive
Singapore 637459
Tel: 6592 2495, Email: irb@ntu.edu.sg

INFORMED CONSENT FORM FOR HUMAN BIOMEDICAL RESAERCH

Protocol Title:
Low Energy Availability (LEA) Threshold in Male Athletes.

Principal Investigator & Contact Details:
Stephen Burns, PhD
Associate Professor
Physical Education and Sports Science (PESS)
National Institute of Education
Nanyang Technological University (NTU)
Telephone: (65) 6219 6214
Mobile phone: (65) 9725 6699
E-mail: stephen.burns@nie.edu.sg

Consent to Take Part in the Study

I voluntarily consent to take part in this research study. I have fully read, discussed and understood the purpose and procedures of this study as noted in the Participant Information Sheet attached to this consent form. This study, including its nature, risks and benefits, has been explained to me directly by the investigator or through a translator, in a language that I understand. I have been given enough time to ask any questions that I have about the study, and all my questions have been answered to my satisfaction.

I understand that I may withdraw my consent and stop participating in the study at any time without giving any reasons and without my benefits being affected.

By participating in this research study, I confirm that I consent to the collection, use and disclosure of my Personal Data for the purposes set out in the Participant Information Sheet.

I agree that I will be contacted for **further consent**, including but not limited to changes in the proposed research, serious adverse events that would lead to a change in the proposed research, and any other circumstances which is specific to this research study or future research study.

Consent for the Use of Data or Health Information for Future Research
☐ Yes, I agree to have my health information and data stored for future research in an individually-identifiable form with the understanding that this would only be done upon approval from the Institutional Review Board or local ethics committee.

Please also check one of these boxes:
☐ The Investigator may use my health information and data for future research as long as the research is related to low energy availability in athletes.
☐ No, I do not agree to donate my health information and data for future research.

Consent to be Re-Identified and Notified in the Case of an Incidental Finding
☐ Yes, I want to be contacted for any incidental findings that may uncovered by this study and/or future studies.

[Optional] In the event that I cannot be reached, please contact my next of kin.
Name of next of kin: _____
Contact: _____

☐ No, I do not want to be contacted for any incidental findings that may be uncovered by this study and/or future studies.

Notwithstanding the above, I agree that I may be contacted should incidental findings that are of serious (e.g. life-threatening) clinical significance be uncovered during the course of this study.

Consent to be Contacted for Future Research Opportunities
Occasionally, investigators may have additional follow-on studies that may be of interest to you. Please indicate if you wish to be contacted for such studies.

☐ Yes, I agree to be contacted for future research that I may be eligible for.
I agree to be contacted via:
- ☐ Phone:
- ☐ Mail :
- ☐ Email :
- ☐ Others :

☐ No, I do not agree to be contacted for future research.

Name of Participant	Signature	Date

Witness Statement
I, the undersigned, certify that
- I am 21 years of age or older and has mental capacity.
- To the best of my knowledge that the participant / the participant's legally acceptable representative signing this informed consent form had the study fully explained in a language understood by him / her and clearly understands the nature, risks and benefits of his / her participation in the study.
- I have taken reasonable steps to ascertain the identity of the participant / the participant's legally acceptable representative giving the consent.
- I have taken steps to ascertain that the consent has been given voluntarily without any coercion or intimidation.

Name of Witness	Signature	Date

Investigator Statement

I, the undersigned, certify that I explained the study to the participant and to the best of my knowledge the participant signing this informed consent form clearly understands the nature, risks and benefits of his / her participation in the study.

_____	_____	_____
Name of Investigator / Person administering consent	Signature	Date

ADDITIONAL CONSENT FOR THE REMOVAL, DONATION OR USE OF HUMAN TISSUE

Protocol Title:
Low Energy Availability (LEA) Threshold in Male Athletes.

Principal Investigator & Contact Details:
Stephen Burns, PhD
Associate Professor
Physical Education and Sports Science (PESS)
National Institute of Education
Nanyang Technological University (NTU)
Telephone: (65) 6219 6214
Mobile phone: (65) 9725 6699
E-mail: stephen.burns@nie.edu.sg

Consent for the Removal, Donation or Use of Human Tissue

The tissue samples / human biological materials collected from this study will not be used for any purposes other than research.

Consent for the Use of Human Tissues for Future Research
☐ Yes, I agree to have my blood samples stored for future research in a de-identified form with the understanding that this would only be done upon approval from the Institutional Review Board or Tissue Banking Board.

Please also check one of these boxes:

☐ The Investigator may use my blood for future research as long as the research is related to as long as the research is related to low energy availability in athletes.

☐ No, I do not agree to donate my blood for future research.

Consent to Transfer Human Tissues out of Singapore
☐ Yes, I agree for my de-identified human tissues to be transferred outside of Singapore for this study or future research.

☐ No, I do not agree for my de-identified human tissues to be transferred outside of Singapore for this study or future.

The human biological material collected will **NOT** be used in restricted human biomedical research involving human-animal combinations.

Restricted Biomedical Research
The human biological material collected will **NOT** be used in restricted human biomedical research involving human-animal combinations.

Renunciation of Donor's Rights to the Human Tissue
The donation of the human tissues / blood / biological materials is voluntary and there may be no direct benefit to you personally. These will be deemed to be gifted to National Institute of Education of Nanyang Technological University and will not be returned to you. You will also

not have any intellectual property right or claim to any share in the commercial gain that may be derived from the research (if any).

However, you can withdraw your consent at any time and retain your right to ask the Principal Investigator to discard or destroy any remaining blood samples if they are individually-identifiable and has not been used for the research, or if they have been used for the research but it is practicable to discontinue further use of the blood samples for the research. However, the withdrawal of consent does not affect the research information obtained before the consent is withdrawn and such information may be retained and used for the research.

Name of Participant	Signature	Date

Witness Statement (Compulsory section)

I, the undersigned, certify that

- I am 21 years of age or older and has mental capacity.
- To the best of my knowledge that the participant / the participant's legally acceptable representative signing this informed consent form had the study fully explained in a language understood by him / her and clearly understands the nature, risks and benefits of his / her participation in the study.
- I have taken reasonable steps to ascertain the identity of the participant / the participant's legally acceptable representative giving the consent.
- I have taken steps to ascertain that the consent has been given voluntarily without any coercion or intimidation.

Name of Witness	Signature	Date

Investigator Statement

I, the undersigned, certify that I explained the study to the participant and to the best of my knowledge the participant signing this informed consent form clearly understands the nature, risks and benefits of his / her participation in the study.

Name of Investigator / Person administering consent	Signature	Date

NANYANG TECHNOLOGICAL UNIVERSITY SINGAPORE

Annex

Checklist A: For HBR studies without the removal, donation or use of human tissue

If you are conducting **human biomedical research**, you must ensure that appropriate consent is obtained. Kindly ensure your ICF must include **all** of the following elements by ticking Yes/No/NA in the process of reviewing.

Section in ICF v6.0	HBRA Section 12 (1) requirements	Yes	No	NA
2. Purpose of the Research Study	Purpose and investigational nature of the study. [Elements A & B]	√		
4. What procedures will be followed in the study	Treatment of **Incidental Findings**. [Element M]	√		
7. Possible Risks and Side Effects	The reasonable foreseeable **risks, discomforts or inconveniences** to participant. [Element C]	√		
8. Possible Benefits from Participating in the Study	The reasonable expected **benefits** to participant. [Element D]	√		
9. Alternatives to Participation	[Where applicable] If there are any **alternative** procedures or treatments available, and the potential benefits and risks of such alternatives. [Element E]			√
10. Costs and Payments if participating in the study	Anticipated **expenses** likely to be incurred as a consequence of participating in the study [Element G]			√
11. Voluntary Participation and Participant's Rights	Participant's **right to withdraw** consent. [Element N]	√		
	The circumstances when participants will be **contacted for further consent**. [Element L]	√		
12. Compensation for Injury	Any **compensation** and treatment available in the event of injury arising from participation in the study. [Element F]	√		
13. Confidentiality of Study	Whether **individually-identifiable** information is being used. [Element K]	√		
	Maintenance of **confidentiality**. [Element H]	√		
	Whether individually identifiable information obtained will be used for **future research**. [Element I]	√		
	[Where applicable] Whether **biological material** taken from the research subject will be destroyed, discarded or stored for future biomedical research [Element J]	√		
14. Who To contact if you have questions	Investigator and IRB **contact details**. [Element O]	√		
Consent Form	The circumstances when participants will be **contacted for further consent**. [Element L]	√		
	Consent for tissues/ biological materials/ individually- identifiable data to be used for **future research**. [Element I]	√		
	Consent to be contacted in cases of **incidental findings**. [Element M]	√		
	Consent to be contacted for **future research**.	√		
	Signature Column: Participant, Parent, Translator, Witness, Investigator.	√		

Note: Kindly keep this checklist in your investigator/study file

Checklist B: For HBR studies <u>with</u> the removal, donation or use of human tissue

If you are conducting **human biomedical research that involves the collection, use or donation of Human Tissue**, you need to include the following additional elements to fulfil HBRA Section 12(2) requirements. Kindly ensure your ICF must include **all** of the following elements by ticking Yes/No/NA in the process of reviewing.

Section in ICF v6.0	HBRA Section 12 (2) requirements	Yes	No	NA
3. Inclusion/Exclusion Criteria	Waiver for HBRA Section 37(3) requirement [Element C]	√		
13. Confidentiality of Study	Purpose for which human biological materials will be used. [Element A]	√		
Additional Consent				
Removal, Donation or Use of Human Tissue	Use of tissue for any purpose other than research. [Element B]	√		
Use of Human Tissues for Future Research	Whether biological material and individually-identifiable information obtained from tissue donor will be stored and used for future research. [Element J & K]	√		
Transfer Human Tissues out of Singapore	Whether the tissue will be **exported or removed** to a place outside Singapore. [Element Q]	√		
Use of Biological Samples for Restricted Research	Usage of tissue in **restricted HBR** involving human-animal combination. [Element N]			√
Renunciation of Donor's Rights to the Human Tissue	**Voluntary participation, renunciation of rights** to tissue and any **intellectual property rights** that may be derived from its use. [Element E]	√		
	Participant's **right to withdraw** consent. [Element F]			

<u>Note:</u> Kindly keep this checklist in your investigator/study file