The effect of an anti-inflammatory diet on clinical and biochemical features of knee osteoarthritis: a pilot RCT. The research is being carried out by the following researchers: **Mr Indiana Cooper, Dr Adam Culvenor, Dr Brooke Devlin,** **Ms Anjana Reddy, Dr Joanne Kemp, Prof. Peter Brukner** The research is being carried out in partial fulfilment of Honours (Doctor of Medicine) under the supervision of Professor Peter Brukner. The following researchers will be conducting the study:		
Role	**Name**	**Organisation**
Principle Investigator	Dr Brooke Devlin	La Trobe University, Dietetics and Human Nutrition
Associate Investigator	Prof. Peter Brukner	La Trobe University , La Trobe Sport and Exercise Medicine
Associate Investigator	Dr Adam Culvenor	La Trobe University, La Trobe Sport and Exercise Medicine
Associate Investigator	Ms Anjana Reddy	La Trobe University, Dietetics and Human Nutrition
Associate Investigator	Dr Joanne Kemp	La Trobe University, La Trobe Sport and Exercise Medicine
Medical Student	Indiana Cooper	University of Melbourne, School of Medicine
Research funder	This research is supported by a La Trobe Sport, Exercise and Rehabilitation Research Focus Area grant.	

1. **What is the study about?**

   You are invited to participate in a study focussing on the treatment of knee pain through dietary modifications. We hope to learn whether a 12-week diet low in processed foods and high in "good" fats can improve your knee symptoms, function and maximise your quality of life. We will assess whether changes in how your knee feels are due to changes in your body composition (using a DEXA scan) or changes to the amount of inflammation in your blood. A diet low in processed foods and high in "good" fats has been shown to be effective at reducing body weight and inflammation – now we are evaluating if it is effective as a treatment option for people with knee pain and osteoarthritis. If this research is successful it will provide additional treatment options for many people experiencing knee osteoarthritis. There will be 60 people who will be part of this study.

   Your contact details were obtained from your participation in the GLA:D program, which one of our researchers, Dr Joanne Kemp, manages. Alternatively, you may have contacted us after seeing a flyer online or in the community.

2. **Do I have to participate?**

   Being part of this study is voluntary. If you want to be part of the study we ask that you read the information below carefully and ask us any questions.

   If you decide you do not want to participate, this won't affect the treatment you are currently receiving, or your relationship with La Trobe University or any other listed organisation. You can read the information below and decide at the end if you want to participate.

3. **Who is being asked to participate?**

   You have been asked to participate because:
   - You have experienced moderate knee pain in the last week
   - You are between 40 and 85 years of age and speak fluent English
   - You are willing to complete a 12-week diet and attend all scheduled appointments (detailed below)

   You are not eligible and cannot participate in this study if you meet any of the following:
   - Your knee pain is not primarily due to osteoarthritis (e.g. tumour, fibromyalgia, referred pain)
   - You are already participating in a specific diet (e.g. low carbohydrate, high-fat, paleo, Mediterranean)
   - You have experienced ≥5kg weight loss in the past three months
   - You have a body weight of above 200kg
   - You are either pregnant or breastfeeding

4. What will I be asked to do?

Eligibility process and consent

The study will be explained to you by a trained researcher who will also ask you some questions to make sure you are eligible to participate. Once you have understood and agree that you would like to take part in the study, you will be invited to La Trobe University for assessment and asked to sign the participant consent form before any study assessments are performed.

This project is a randomised controlled research project and you will be asked to either follow a specific anti-inflammatory diet over a 12-week period or be allocated to a control group and continue with your normal diet.

First appointment

This appointment will be arranged at a convenient time for you at La Trobe University, Bundoora and will take approximately 2 hours. You will be asked to not eat/drink anything of the morning of your appointment (i.e. fasting for 12-hours) for the purpose of a blood test. At the appointment, you will have your height, weight, and waist/hip circumference measured. You will then have your body composition measured via a Dual-energy X-ray Absorptiometry Scan (DXA). This involves you laying on your back on the scanning bed for the duration of the ~7-minute scan. The machine uses small doses (<1% of the yearly radiation dose) of radiation to estimate tissue density (to assess how much muscle and adipose tissue you have). The total effective dose of radiation has been calculated by a Medical Physicist (see risks below). For the DXA scan, you need to be fasted with no food, fluid or exercise/activity prior to the test (from the time you wake up that day). Light clothing with no metal items (i.e. zips, clips, underwire etc.) should be worn (gowns available if required) and all jewellery must be removed. All measures will be taken by trained researchers who hold radiation licenses with Victorian Government and comply to the Code of Practice set out by the Australian Radiation Protection and Nuclear Safety Agency.

At this appointment, you will also have your blood pressure measured and undergo a blood test by a trained researcher qualified to take blood. A small amount of blood (~24 mL, equivalent to 3-4 teaspoons) will be collected from a forearm vein. Following this, you will be provided a snack/drink before being asked to complete several questionnaires. These include a 3-day food diary (2 week days and 1 weekend) and questionnaires about your knee pain, activity level and quality of life. The final assessment involves two short mobility tests: i) how many times you can stand from a chair in 30secs, and how fast you can walk 40meters.

Random assignment to one of two different diets

At the end of the first appointment at La Trobe University, you will be randomly assigned (50:50 chance, like a coin toss) by a computer system to receive either i) an anti-inflammatory diet low in processed foods and high in “good” fats or ii) control diet (your normal diet). This means neither you or the researchers will be able to choose which group you are assigned to. We do not know which treatment is best. To find out we need to compare the anti-inflammatory diet to a control ‘normal’ diet. There is equal chance that you will be allocated to either the intervention or the control arm. If you are allocated to continue with your usual diet, you will be offered the anti-inflammatory diet information at the final assessment at the completion of the study period (12-weeks after first appointment).

If you are randomised to receive the **anti-inflammatory diet**, you will receive specific anti-inflammatory dietary education and advice in person and via written materials by an Accredited Practicing Dietitian (APD) about the types of foods to consume and avoid. You will be encouraged to avoid processed foods and instead focus on natural foods and those containing “good” fats. You will be asked to follow this diet for 12-weeks with ongoing support from the study dietician throughout the study. No food will be provided to you and you will continue to purchase and prepare your meals as usual.

If you are randomly assigned to the control diet you will speak to the study dietician about your food diary and will be encouraged to continue with **your normal diet** for the 12-week study period, after which you will have the option to complete the anti-inflammatory diet.

During the 12-week study period, we will ask you to record your food intake for 3 days (3-day food diary) after 2 weeks, half-way through (6 weeks), after 9 weeks and at the end of the 12-week period. This will be done using a smart phone application or food diary (personal preference) and detailed instructions will be provided to you on how to complete this. It will take approximately 10 minutes per day to complete the food record.

Follow-up Phone Call
To see how you are going with the diet that you have been allocated to, we will contact you at 2-weeks (and 9-weeks) after the initial appointment, answer any questions and follow your progress by checking your 3-day food record. This phone call will take approximately 15 minutes. At these times, we will also ask you to complete the same questionnaires via a secure link provided by e-mail.

Second Appointment
Six weeks after the initial appointment you will be asked to return for the second of three face-to-face appointments. This appointment will be similar to the first appointment where we will do all the same tests, questionnaires and food diary, except there will be no DEXA scan at this appointment. You will need to fast (not eat/drink anything the morning of your appointment) for the blood test. You will have another consultation with the study dietitian who will provide support for you to continue with the diet you have been allocated. You should allow at least 1.0 hours for this appointment.

Third Appointment
After 12-weeks, you will be asked to attend the final face-to-face appointment and study assessment. The week 12 appointment will be exactly the same as your first (initial) appointment including all the tests, DEXA scan, physical measures and the consultation, with the requirement to fast prior (not eating/drinking anything the morning of your appointment). You should allow up to 2 hours for this appointment.

You may also be asked if you are willing to have a separate interview with one of the study researchers. The purpose of this interview is to seek feedback on the study diets, satisfaction with the process received and whether there are any suggestions for improvement. The interview will take approximately 30 minutes. To ensure responses are correctly interpreted, responses to questions will be audio recorded and transcribed. Audio recording transcriptions will be completed by 'Transcription Australia' on their secure, encrypted Australian-based software. Although voice in your audio recording could lead to your identification, this file will not be used during analysis. Instead a re-identifiable transcription, which you will have the opportunity to check for accuracy, will be used for analysis. Re-identifiable means that we will use a code number and not your name on data collected to ensure your anonymity. Following the completion of analysis of this transcription, the audio file associated with your interview will be deleted. After analysis, overall findings and conclusions from all interviews will also be sent to you, to allow an opportunity to make any further comments. We will seek around 20 participants to be interviewed. It is your decision or not whether you wish to be interviewed.

Study Procedure Table

	Assessment/task	**Visit 1 Time: 2 hours**	**Phone call 1 Time: 15 mins**	**Visit 2 Time: 1 hours**	**Phone call 2 Time: 15 mins**	**Visit 3 Time: 2 hours**
		Baseline	*2-weeks later*	*6-weeks later*	*9-weeks later*	*12-weeks later*
Study procedures	**Informed consent**	**x**				
	Demographic information	**x**				
	Clinical measurements	**x**		**x**		**x**
	DEXA	**x**		**x**		**x**
	Questionnaires	**x**	**x**	**x**	**x**	**x**
	Blood Collection	**x**		**x**		**x**
	Post-study interviews					**x (optional)**

5. What are the benefits?
The benefit of you taking part in this study is that you may experience improvement of symptoms, function, quality of life, physical activity, and confidence in your knee. You may gain valuable insight into how to manage your diet and specific anti-inflammatory foods, nutrients and eating habits. The expected benefit to society is the development of a drug-free treatment option to help manage the pain and disability associated with osteoarthritis. This will give doctors

and patients alternative ways to manage symptoms of osteoarthritis, which in turn may lead to improvements in the quality of life for patients.

6. **What are the risks?**

With any medical treatment there are (1) risks we know about, (2) risks we don't know about and (3) risks we don't expect. If you experience something that you aren't sure about, please contact us immediately so we can discuss the best way to manage your concerns.

We have listed the risks we know about below. This will help you decide if you want to be part of the study.

Side Effect	How often is it likely to occur?	How severe might it be?	How long might it last?
Distress due to diet assessment	Not often; although can occur while recording dietary intake (food diaries) prior to, or during, appointments	Minimal	While completing food diary or assessment
Discomfort due to body measurements	Can occur while measurements are being taken by your dietitian or researcher	Minimal Mild	During appointment only
Discomfort due to blood test	Rarely; while blood is being collected	Mild	Bruising or swelling may last 1-3 days
Exposure to ionising radiation	1x 7-minute scan at initial and final appointment	Minimal	Effect too small to measure

If you become upset or distressed during the study

If you become upset or distressed as a result of your participation in the research, the study coordinator together with the qualified dietician will assist you with appropriate support.

Risks associated with blood test

Having a blood sample taken may cause some discomfort or bruising. On rare occasions, the blood vessel may swell, or blood may clot in the blood vessel, or the spot from which tissue is taken could become inflamed. Some people may feel faint when having blood taken and may occasionally faint. Very rarely, there could be a minor infection or bleeding. A qualified person will take your blood using infection control procedures. If you notice increased redness, swelling or other signs of infection in the days following your blood sample, you should contact the researchers.

Risks associated with following anti-inflammatory diet

As you adjust to the anti-inflammatory diet, you may experience feelings of tiredness. The researchers will assess your diet and ensure you are meeting your energy and nutrient needs throughout the study intervention. The anti-inflammatory diet may be different than your normal diet and therefore influence your usually weekly shopping bill and expenses. As part of the consultations, you will be provided with some advice on how to follow the diet on a budget if required to ensure there is minimal financial risk.

Exposure to ionising radiation

If you choose to take part in this research, you will undergo two 7-minute DEXA scans (first and final assessment). DEXA scans are a non-invasive, fast and simple procedure. This research study involves exposure to a very small amount of radiation. As part of everyday living, everyone is exposed to naturally occurring background radiation and receives a dose of about 2 millisieverts (mSv) each year. The effective dose from this study is approximately 0.02 mSv. At this dose level, no harmful effects of radiation have been demonstrated as any effect is too small to measure. The risk is believed to be minimal.

The whole body DXA scan may identify participants with a low bone mineral density. However, a whole body DXA scan is not the established method for detecting low bone mineral density. Therefore, as a precaution if you are identified as having a low bone mineral density you will be encouraged to make an appointment with your General Practitioner to discuss the results.

Have you been involved in any other research studies that involve radiation? If so, please tell us. Please keep information contained within the Patient Information and Consent Form about your exposure to radiation in this study, including the radiation dose, for at least five years. You will be required to provide this information to researchers of any future research projects involving exposure to radiation.

7. **Will I be paid to be part of this study?**
   It will not cost you to be part of this study. We will not pay you for your time.

8. **What will happen to information about me?**
   We will **collect** information about you in ways that will reveal who you are.

   We will **store** information about you in ways that will not reveal who you are.

   We will **publish** information about you in ways that will not be identified in any type of publication from this study.

   We will **keep** your information for 15 years after the project is completed. After this time we will destroy all of your data.

   The storage, transfer and destruction of your data will be undertaken in accordance with the Research Data Management Policy https://policies.latrobe.edu.au/document/view.php?id=106/.

   The personal information you provide will be handled in accordance with applicable privacy laws, any health information collected will be handled in accordance with the Health Records Act 2001 (Vic). Subject to any exceptions in relevant laws, you have the right to access and correct your personal information by contacting the research team.

9. **Will I hear about the results of the study?**
   We will let you know about the results of the study by the end of 2021. You will be informed of any publications arising from the study via email. You can also review the dietary information booklet and the results of your body composition assessment.

10. **What if I change my mind?**
    You can choose to no longer be part of the study at any time. Once you have been allocated to either diet intervention, we can only withdraw information such as your name and contact details to ensure accurate and unbiased reporting of the study. You can let us know by:
    1. Completing the 'Withdrawal of Consent Form' (provided at the end of this document);
    2. Calling us; or
    3. Emailing us

    Your decision to withdraw at any point will **not** affect your relationship with La Trobe University or any other organisation listed.

11. **What happens if the study needs to be stopped?**
    The study may be stopped if we find out:
    - The risks from side effects outweigh any benefits to you;
    - The treatment you are receiving doesn't give you any benefits

12. **What happens if I suffer an injury or complications because of being part of this study?**
    If you suffer an injury or have any concerns, please contact us immediately so we can help you. You will be assisted with arranging appropriate medical treatment. If you are eligible for Medicare, you can receive medical treatment required to treat the injury or complication, free of charge, as a public patient in any Australian public hospital. In the event of loss or injury, any question about compensation must initially be directed to the research team who will advise the university insurer of the matter.

13. **What happens when the study ends?**
When the study ends you may continue to follow the diet that has been recommended to you if you choose to. The results of this study will be provided to those who are interested. We will monitor your ongoing well-being by asking you to complete the same questionnaires at 6 months and 12 months after first appointment (mailed or online as preferred).

14. **What happens if you find out new information about the study?**
To ensure your safety we will make sure we look at the information we collect about this study. This may mean that we find out new information that you should know about. If this happens we will contact you and discuss what it means for you. New information may mean that we recommend you withdraw from the study, or that you may choose to withdraw.

15. **Who can I contact for questions or want more information?**
If you would like to speak to us, please use the contact details below:

Name/Organisation	Position	Telephone	Email
Dr Brooke Devlin	Lecturer, Dietetics and Human Nutrition, Accredited Practising Dietitian	+61 3 9479 5062	b.devlin@latrobe.edu.au

16. **What if I have a complaint?**
If you have a complaint about any part of this study, please contact:

Ethics Reference Number	Position	Telephone	Email
HEC19525	Senior Research Ethics Officer	+61 3 9479 1443	humanethics@latrobe.edu.au

Title: The effect of an anti-inflammatory diet on clinical and biochemical features of knee osteoarthritis: a pilot RCT.

Principal/Associate Investigators: Prof. Peter Brukner
Dr Adam Culvenor
Dr Brooke Devlin
Ms Anjana Reddy
Dr Joanne Kemp
Mr Indiana Cooper

Location: La Trobe University

Consent Form – Declaration by Participant

I (the participant) have read (or, where appropriate, have had read to me) and understood the participant information statement, and any questions have been answered to my satisfaction. I agree to participate in the study, I know I can withdraw at any time until [four weeks] following the collection of my data. I agree information provided by me or with my permission during the project may be included in a thesis, presentation and published in journals on the condition that I cannot be identified.

☐ I give permission for my doctors, health professionals, hospitals and/or laboratories to release information concerning my health and treatment for the purposes of this study. I understand this information will remain confidential.

I would like my information collected for this research study to be:
☐ Only used for this specific study;
☐ Used for future related studies;

Participant Signature

☐ I have received a signed copy of the Participant Information Statement to keep

Participant's printed name	
Participant's signature	
Date	

Declaration by Researcher

☐ I have given a verbal explanation of the study, what it involves, and the risks and I believe the participant has understood;
☐ I am a person qualified to explain the study, the risks and answer questions

Researcher's printed name	
Researcher's signature	
Date	

* All parties must sign and date their own signature

Title: The effect of an anti-inflammatory diet on clinical and biochemical features of knee osteoarthritis: a pilot RCT.

Principal/Associate Investigators: Prof. Peter Brukner
Dr Adam Culvenor
Dr Brooke Devlin
Ms Anjana Reddy
Dr Joanne Kemp
Indiana Cooper

Location: La Trobe University

Withdrawal of Consent

I wish to withdraw my consent to participate in this study. I understand withdrawal will not affect my relationship with La Trobe University of any other organisation or professionals listed in the Participant Information Statement. I understand the researchers cannot withdraw my information once it has been analysed.

I understand my information will be withdrawn as outlined below:

- ✓ Any identifiable information about me will be withdrawn from the study
- ✓ The researchers will withdraw my contact details so I cannot be contacted by them in the future.
- ✓ If new safety information about the drug/device is available after I have withdrawn, I understand the research team will keep my contact details so they can provide me with new safety information.

***if you have consented for your contact details to be included in a participant registry you will need to contact the registry staff directly to withdraw your details.*

I would like my already collected and unanalysed data
☐ Destroyed and not used for any analysis
☐ Used for analysis

Participant Signature

Participant's printed name	
Participant's signature	
Date	

Please forward this form to:

CI Name	Dr Brooke Devlin
Email	b.devlin@latrobe.edu.au
Phone	03 9479 5062
Postal Address	Rm 435, Health Sciences 3, LaTrobe University, Kingsbury Drive, Bundoora, 3086