BRocccoli **I**n **O**steoarthritis (**BRIO**)

PARTICIPANT INFORMATION SHEET

Study Title: A dietary intervention trial to examine the protective effect of broccoli bioactives (specifically sulforaphane) on osteoarthritis.
IRAS ID: 250371

What is the purpose of this study?

The purpose of this study is to find out if eating broccoli will improve pain and physical function in osteoarthritis. A naturally occurring compound sulforaphane (SFN), found in broccoli, has been shown to protect articular cartilage in our laboratory studies of osteoarthritis. We also know that by eating broccoli, SFN gets into our joint tissues.

The study will compare broccoli soup (rich in SFN) with a soup that does not contain broccoli (control), but looks and tastes the same.

Participants will be randomly assigned to either the broccoli or the control soup and will eat this on 4 days per week for 3 months. We will measure pain and physical function at the start of the trial, at 6 weeks and at 12 weeks and assess changes. We will also collect blood and urine samples.

Who has funded this research?

Versus Arthritis (versusarthritis.org) formally known as Arthritis Research UK (arthritisresearchuk.org), and Action Arthritis (actionarthritis.org.) have funded the study. The study will be conducted by investigators at the University of East Anglia (UEA), working in collaboration with the University of Leeds. The Chief Investigator is Professor Alexander MacGregor, Professor of Chronic Disease & Genetic Epidemiology, UEA.

Who has reviewed this study?

An independent group of people, called a Research Ethics Committee, to protect your interests, looks at all research in the NHS. This study was reviewed and given a favourable opinion by the East of England – Cambridge East Research Ethics Committee.

Why am I invited to participate?

We have invited you to participate in the study because you have osteoarthritis (OA) in at least one knee and have met the key inclusion/exclusion criteria for the study.

Do I have to take part?

No, this is voluntary. It is up to you to decide whether to take part. This study will not be suitable for someone with a dislike of broccoli. People taking some long-term anticoagulants such as warfarin will be excluded from the study as the effects of warfarin are weakened by vitamin K, which is present in broccoli. If you do decide to take part, you will be asked to sign a consent form. You are free to withdraw from the

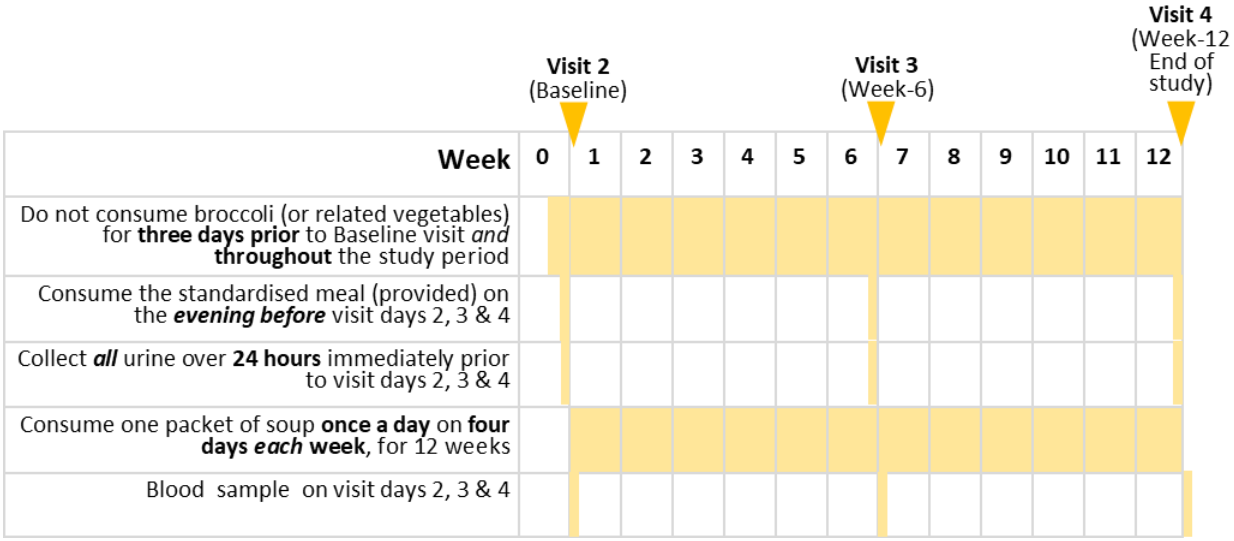
study at any time without giving a reason. A decision to withdraw or not to take part will not affect the standard of care you normally receive.

What will happen to me if I want to take part?

If, after reading this Participant Information Sheet, you would like to take part, your involvement would be for approximately **12 weeks**. You will need to visit the study team four times during the study period:

- Visit 1 Screening
- Visit 2 Baseline
- Visit 3 Week 6 Follow up
- Visit 4 Week 12 Follow up and end of study.

You will consume a portion of soup provided by the study team **once a day, on four days per week**. You will be asked to agree to not eat broccoli (or related vegetables) for **three days prior to the Baseline visit and throughout** the study period. We will provide you a list of vegetables to avoid. At each visit we will also collect **blood (20ml or 4 teaspoons) and a urine sample**. You will be reimbursed for your travel expenses for all study visits. We have provided an additional summary of participant activities at the end of this information document.



Consent to be in study

We will contact you to arrange a screening appointment at either the **Norfolk and Norwich University Hospital (NNUH) if you are local to Norwich (UK), or Chapel Allerton Hospital (CAH) if you are local to Leeds (UK)**. This Participant Information Sheet will be discussed in detail with you. It will be made clear that you are free to withdraw from the study at any time for any reason without it affecting your current or future care, and with no obligation to give the reason for withdrawal. You will be allowed as much time as you wish to consider the information and ask questions.

If you do decide to participate, we will ask you to sign and date a written informed consent form. A member of the research team will also sign and date the consent. We will give you a copy of this signed consent form for your records.

On-going verbal consent will be sought from you at every study visit. If you decide to withdraw, you will continue to receive standard care. Data collected up until the point of withdrawal will be retained in the study in line with General Data Protection Regulation (GDPR) 2018 Article 9 (2) (j). Due to the special category of research data you will have limited ability to make changes to the data collected up until the point of withdrawal.

Contact during the study

You can choose your preferred means of contact (phone call, text or email). Before each study visit, you will receive your reminder from the researchers to help you to follow the restricted vegetable diet and to give you an opportunity to ask any questions. We will also prompt you to eat a standardised meal (supplied by us) the night before your appointments, check that you are consuming the soup during the study and remind you of the 24-hour urine collection before your study appointments.

Screening Visit

At your screening visit, we will collect information from you about your medical history and any medications you may be taking. You will also have a physical examination of your knees and vital signs taken. To confirm the presence of osteoarthritis we will review an x-ray of your knee. If you have not had a knee x-ray within the last 24 months, with your permission, we will schedule one for the day of your screening visit.

If you pass all the screening assessments, we will invite you to take part in the study and return for a Baseline visit within 30 days of the screening visit and two additional visits at 6 and 12 weeks after the Baseline visit. We will also provide you with supplies and instructions for the urine collection.

Study Participation

For three days prior to the Baseline visit *and throughout the study period* participants will be asked to abstain from eating cruciferous (e.g., broccoli) vegetables. Below is a list of vegetables to avoid.

Types of vegetables to avoid:

broccoli	brussel sprouts	Cress (all varieties)
cabbage	radish	pak choi / bok choy
cauliflower	horseradish	collard greens
arugula (rocket)	kale	swede / rutabaga
canola/rapeseed	turnip root; greens	mustard
broccoli sprouts	mustard greens	kohlrabi

For the evenings before the Baseline, 6 and 12-week study visits participants will be provided with a standardised meal (e.g. vegetable lasagne and garden peas) to ensure all participants consume a similar background diet prior to the assessments on the

study days. This will be the last meal before your study visit the following day. **Please do not eat anything on the morning of your visits before your blood sample** is taken. Water, black tea and black coffee are allowed.

We will also ask you to complete a 24-hour urine collection before the Baseline, 6 and 12-week study visits. We will provide you with urine sampling materials and directions. During the study, we will ask you to report any medical events or side effects that you have experienced. The doctor or research nurse will also ask you about any medication or supplements that you are taking.

Baseline Study Visit

During the Baseline visit, you will undergo a physical examination of your knees, complete some questionnaires giving details on your quality of life and your usual diet and provide a blood sample and the 24-hour urine collection.

A computer will randomly select you to be in either the broccoli or the control soup group. You will consume one portion on 4 days per week for 12 weeks. Once the computer has randomly selected your treatment group, we will provide you with enough soups for the first 6 weeks of the study.

6 and 12 Week Study Visits

You will be asked to return for study appointments 6 and 12 weeks after your Baseline visit. During these visits, you will complete some further questionnaires about your diet, pain and physical function. You are free to decline to answer any of the questions at any time without giving a reason. On the Week-6 visit we will provide you with the remaining soups for weeks 7-12.

We will ask if you have been consuming the soup on 4 days per week. We will also check your vital signs, collect a blood sample and ask you to provide us with all your urine collected over a 24-hour period before each of your study visits.

Which group will I be in?

The computer will randomly allocate half of the participants to consume the soup containing broccoli (as well as base vegetables) and the other half will be in the Control Group that contains the base vegetables but does not contain broccoli in the soup. The soups are both based on peas and spinach and are identical in taste, colour and texture. Both soups will have identical packaging.

Neither you nor the researchers will know which soup you are consuming. If however a problem arises then the doctor in charge of this research at the hospital you attend, will be able to find out which soup you have been eating very quickly.

Diet Questionnaires

We will ask you to complete a Food Frequency Questionnaire (FFQ) on the Baseline visit. The FFQ asks you about your usual/average dietary habits in the last year.

You will also be asked to fill in a 24-hour recall questionnaire at Baseline, week-6 and week-12 visit days. The 24-hour recall questionnaire will ask about all the food and drinks you have consumed in the last 24 hours:

- Include everything you eat and drink
- Remember to include snacks and items eaten outside the home
- Remember condiments, e.g., sauces, spreads, dips, salt, or sugar added to food
- Remember drinks, including alcohol

Blood and Urine Collection

All the blood and urine tests that you will have are summarised in the following table:

Procedure & Visit

Procedure	**Visit**
Fasting blood tests (20ml)	Baseline, 6 week & 12 week
24 hour urine collection (24 hours prior to each visit day)	Baseline, 6 week & 12 week

What are the possible benefits of taking part?

We need to increase our understanding of the influence that diet has on osteoarthritis. The information we get from this study may help us to provide better treatment in future for patients with osteoarthritis.

What are the possible disadvantages and risks of taking part?

You may experience discomfort when providing blood samples (please note that these are standard blood tests). You will be given the choice to lie on a hospital bed or sit upright, to minimise discomfort. You may also find the dietary restrictions a burden. If you have not received a knee x-ray in the last 2 years and require one in order to assess your suitability for the study, there is a risk associated with the exposure to radiation from the x-ray. The radiation risk of receiving one x-ray is the equivalent to that received, on average in the UK, from natural sources of background radiation in less than 4 hours. For adults in the general population, this dose is estimated to correspond to a cancer risk of around 1 in 25 million. You will have the opportunity to discuss your concerns with a research team member and decide if you wish to continue with the study.

What will happen to the results of the research study?

Final research outcomes will be published in peer-reviewed scientific journals with the view of carrying out a national intervention trial. A lay summary of the results of the study will also be published on the study website. You can also opt to receive a summary of the results after the trial has finished.

Will my involvement in the study be confidential?

All data will be handled in accordance with the General Data Protection Regulation 2018. The BRIO research team will hold personal details collected during the study for the purposes of carrying out the research project as detailed in the PIS only. Any personal information will be kept on a secure database, separate from the study data, which will **be anonymised to ensure participant confidentiality**. Authorised trial staff

will access these data only where absolutely necessary. The BRIO team will never share any personal details with anyone outside the BRIO study with the exception of a reasonable request from a regulatory authority.

Data Collection, Management and Analysis

All Investigators and staff involved with this study will comply with the requirements of the General Data Protection Regulation 2018 with regard to the collection, storage, processing and disclosure of personal information and will uphold the core principles.

The University of East Anglia (UEA) is the sponsor for this study based in the United Kingdom. We will be using information from you and your medical records in order to undertake this study and will act as the data controller for this study. This means that we are responsible for looking after your information and using it properly. UEA will keep identifiable information about you for 6-12 months after the study has finished.
Your rights to access, change or move your information are limited, as we need to manage your information in specific ways in order for the research to be reliable and accurate. If you withdraw from the study, we will keep the information about you that we have already obtained. To safeguard your rights, we will use the minimum personally-identifiable information possible.

You can find out more about how we use your information here: https://digital.nhs.uk/about-nhs-digital/our-work/keeping-patient-data-safe/gdpr and/or by contacting us using the contact details at the end of this information document.

What will happen if I do not want to carry on with the study?

You may withdraw from the study at any time and do not have to give a reason for doing so. We may ask you for your reason to withdraw, to help inform the design of our future studies, but you should not feel obliged to give a reason.

Any data and samples collected while you were taking part in the study will be retained in the study in line with GDPR.

What happens if there is a problem?

If you have a concern about any aspect of this study, you should ask to speak to the researchers who will do their best to answer your questions.

Norwich	Rose	01603 591471	**brio.study@uea.ac.uk**
Leeds	Angela	0113 392 4965	**oatrials@leeds.ac.uk**

If you remain unhappy and wish to complain formally, you can do this with the NHS Complaints Procedure through the Patient Advice & Liaison Service (PALS).

NNUH PALS (Norwich)	**CAH** PALS (Leeds)
Tel: (01603) 289036 24 hour answerphone service.	**Tel:** (0113) 2066261 (9:00am to 4:30pm Monday to Friday).
Email: pals@nnuh.nhs.uk	**E mail:** patientexperience.leedsth@nhs.net

UEA has relevant insurance for the research study. In the event that something does go wrong and you are harmed during the study, there are no special compensation arrangements. If you are harmed and this is due to someone's negligence then you may have grounds for a legal action for compensation but you may have to pay your legal costs. The normal National Health Service complaints mechanisms will still be available to you.

For further information about this research:

BRIO Study Team
University of East Anglia
Tel: 01603 591471
Email: brio.study@uea.ac.uk
Website: https://brio.uea.ac.uk/

Study Visit Summary