

# Knee injury and the biological basis for outcomes: How does local and systemic inflammation affect outcomes including pain and function following knee injury, a prospective observational study

<b>Submission date</b> 05/06/2024	<b>Recruitment status</b> Recruiting	<input checked="" type="checkbox"/> Prospectively registered
		<input type="checkbox"/> Protocol
<b>Registration date</b> 11/07/2024	<b>Overall study status</b> Ongoing	<input type="checkbox"/> Statistical analysis plan
		<input type="checkbox"/> Results
<b>Last Edited</b> 18/06/2024	<b>Condition category</b> Injury, Occupational Diseases, Poisoning	<input type="checkbox"/> Individual participant data
		<input type="checkbox"/> Record updated in last year

## Plain English summary of protocol

### Background and study aims

This study aims to find out if there is a link between knee injury and pain that is mainly from the brain and spinal cord and not from the knee. The researchers will perform tests on the knee and use patient questionnaires to assess this. It is possible that the pain is linked to inflammation so blood samples and fluid from the knee will be taken to test this.

### Who can participate?

Patients over 18 years old who have suffered a fracture that involves the knee joint

### What does the study involve?

The study involves taking samples of blood and knee fluid up to three times after the injury, as well as two stool samples. Then as an outpatient patients will be reviewed every 3 months where they will undergo specialist knee pain tests and complete questionnaires on their pain and function.

### What are the possible benefits and risks of participating?

There is a small risk of discomfort and infection from the sampling procedures. Occasionally aspiration of a swollen joint can have a pain-relieving effect.

### Where is the study run from?

University of Nottingham (UK)

### When is the study starting and how long is it expected to run for?

February 2023 to July 2028

Who is funding the study?  
NIHR Biomedical Research Center - Nottingham (UK)

Who is the main contact?  
Chris Busby, christopher.busby@nhs.net

## Contact information

### Type(s)

Public, Scientific, Principal investigator

### Contact name

Mr Chris Busby

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## Additional identifiers

### Clinical Trials Information System (CTIS)

Nil known

### Integrated Research Application System (IRAS)

340204

### ClinicalTrials.gov (NCT)

Nil known

### Protocol serial number

IRAS 340204

## Study information

### Scientific Title

Knee injury: evaluation of biological Factors and Clinical Trials Study

### Acronym

KneeFACTS

**Study objectives**

To evaluate if certain characteristics (such as injury severity and surgical insult), affect the inflammatory response in individuals with knee injury and if this has a relationship with psychology. This will improve our knowledge about the relationship between knee injury, surgery, psychological distress, pain and inflammation, which will help in advancing interventions to improve health outcomes.

**Ethics approval required**

Ethics approval required

**Ethics approval(s)**

notYetSubmitted

**Study design**

Single-center single-cohort descriptive study

**Primary study design**

Observational

**Study type(s)**

Other

**Health condition(s) or problem(s) studied**

Development of centrally mediated pain in knee trauma

**Interventions**

Recruitment will be of patients with an intraarticular knee injury, both conservatively treated and operatively treated. The study involves taking samples of blood and synovial fluid up to three times after the injury, as well as two faecal samples. Then as an outpatient patients will be reviewed every 3 months where they will undergo specialist knee pain tests and complete questionnaires on their pain and function. The analysis of collected samples (blood and synovial fluid) will take place either within the University of Nottingham or transported to commercial providers for specialist analyses where a material transfer agreement has been arranged.

**Intervention Type**

Other

**Primary outcome(s)**

Changes in cytokine levels and inflammatory marker levels in blood in response to injury at presentation, measured using ELISA at time of surgery (if occurring) at day 3 post-surgery (if still an inpatient), and day 7-8 post-surgery (if still an inpatient)

**Key secondary outcome(s))**

1. Changes in cytokine and inflammatory marker levels in knee synovial fluid measured using ELISA at presentation, at the time of surgery (if occurring) at day 3 post-surgery (if still an inpatient), and day 7-8 post-surgery (if still an inpatient)
2. Measured at 6 weeks, 3 months, 6 months, 9 months, 12 months post-injury/operation:
  - 2.1. Changes in post-trauma pain phenotype over time measured with quantitative sensory testing, patient-reported outcome measures (PROMs) (numerical rating scale, central sensitisation inventory, PainDETECT)
  - 2.2. The effect of knee injury on mental health measures measured with the Hospital Anxiety

and Depression Scale

2.3. Knee function post-injury measured with PROMS (Knee Injury and Osteoarthritis Outcome Score [KOOS] and Central Aspects of Pain in the Knee [CAP-Knee])

2.4. Health-related quality of life score changes measured using EQ-5D-5L

3.0 Gut microbiome expression measured using faecal samples on discharge from hospital and at 6 months

### **Completion date**

01/07/2028

## **Eligibility**

### **Key inclusion criteria**

1. Adult patients (>17 years old, no maximum age) who attend Nottingham University Hospitals under the care of orthopaedic trauma and are undergoing treatment for intraarticular knee injuries. Must include one or more of the injury groups outlined below and include an intraarticular component as defined in AO Classification (2018):

1.1. Patella fracture

1.2. Tibial plateau fracture

1.3. Distal femur fracture

2. Able to give informed consent

3. Able to complete required questionnaires

### **Participant type(s)**

Patient

### **Healthy volunteers allowed**

No

### **Age group**

Adult

### **Lower age limit**

18 years

### **Sex**

All

### **Key exclusion criteria**

1. Aged 17 years or under

2. Concomitant fracture involving another joint

3. Taking anticoagulants (direct oral anticoagulants [DOACs], warfarin) or coagulopathy

4. Intra articular knee fracture that involves preceding prosthesis or implant.

5. Significant soft tissue injury making aspiration not feasible or safe as determined by one of the investigative team

6. Presence of local (knee) or systemic infection

7. Immunomodulating medication or treatments with systemic impact

8. Systemic chronic inflammatory diseases

9. Active malignancy

10. Pregnancy or breastfeeding

- 11. People in the custody of the police or incarcerated persons
- 12. Inability to read or write English.
- 13. People with significant mental health disease under section

**Date of first enrolment**

01/08/2024

**Date of final enrolment**

01/08/2027

## **Locations**

**Countries of recruitment**

United Kingdom

England

**Study participating centre**

**Queen's Medical Centre**

Derby Road

Nottingham

United Kingdom

NG81FS

## **Sponsor information**

**Organisation**

University of Nottingham

**ROR**

<https://ror.org/01ee9ar58>

## **Funder(s)**

**Funder type**

Government

**Funder Name**

NIHR Nottingham Biomedical Research Centre

**Alternative Name(s)**

Nottingham Biomedical Research Centre, Nottingham Biomedical Research Centre - NIHR, NIHR  
Nottingham BRC, BRC, NIHR NBRC

### **Funding Body Type**

Government organisation

### **Funding Body Subtype**

Research institutes and centers

### **Location**

United Kingdom

## **Results and Publications**

### **Individual participant data (IPD) sharing plan**

The datasets generated during and/or analysed during the current study will be stored in a non-publicly available repository: University of Nottingham servers

### **IPD sharing plan summary**

Stored in non-publicly available repository

### **Study outputs**

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
<a href="#">Participant information sheet</a>	Participant information sheet	11/11/2025	11/11/2025	No	Yes