# Pain management using ibuprofen after major gut surgery (PROTECT-AEGIS)

| Submission date   | Recruitment status Recruiting                   | [X] Prospectively registered    |  |  |
|-------------------|---|---------------------------------|--|--|
| 20/11/2024        |   | [X] Protocol                    |  |  |
| Registration date | Overall study status Ongoing Condition category | Statistical analysis plan       |  |  |
| 27/05/2025        |   | Results                         |  |  |
| Last Edited       |   | ☐ Individual participant data   |  |  |
| 17/09/2025        | Surgery   | [X] Record updated in last year |  |  |

### Plain English summary of protocol

Background and study aims

Each year, 50,000 patients undergo major gut surgery in the NHS. Pain after major surgery is to be expected, but it can be managed through careful use of analgesia. This often leads to longer stays in hospital. Ibuprofen is a very safe and effective pain medicine which you can buy in high street shops. Ibuprofen may help prevent pain after gut surgery, but currently only one in five patients are offered this because some research studies suggest complications of gut surgery (gastric ulcers, poor gut healing and kidney damage) may be more frequent when patients take drugs similar to ibuprofen. Newer research did not have the same results, but doctors remain uncertain about what to do. As a result, patients miss out on the extra pain relief that ibuprofen can provide. We are performing a small feasibility trial, designed to see if patients would be prepared to take part if the surgeon and anaesthetist agree. If we can show that patients and doctors are comfortable taking part in this trial, we will then perform a much larger clinical trial to prove the value of ibuprofen pain relief one way or the other.

#### Who can participate?

Patients aged 18 years and over undergoing major elective gut surgery with bowel anastomosis

#### What does the study involve?

After the participant's operation, they will receive one of two study treatments, either ibuprofen and standard pain control or only standard pain control. Standard pain control usually involves morphine-like medicines and local anaesthetic which can be placed straight into the surgical wound, or given through an epidural. Paracetamol is also widely used. This decision will be made at random and neither the participant nor their doctor will be able to decide which study treatment they receive. If participants are in the ibuprofen group, they will be given ibuprofen along with standard pain control and all their usual medications for five days after surgery. In the standard care group, participants will receive the standard pain management for their hospital without ibuprofen. If participants are in the ibuprofen arm, they will also receive medication to prevent stomach ulcers. All of their other treatments will be the same regardless of which study treatment they get. Their doctors at the hospital will be aware that they are in this study and will be closely monitored throughout their hospital stay. If necessary, adjustments to their treatment will be made to ensure they are safe. The GP will also be informed of their participation in the study so they are aware the patient might have received ibuprofen during

their hospital stay. Participants will also be asked some questions about their health before and after their operation, which will be online or by telephone if at home, and face to face if they are still in hospital. We will record information about any pain they experience on the first five days after surgery, which will take about two minutes each day. If participants have a carer or proxy, they would be welcome to help answer these questions. The last time we contact participants will be 30 days after their operation.

What are the possible benefits and risks of participating? Ibuprofen will be used within its license and only patients known to be at low risk of the potential side effects of NSAIDs will be enrolled.

Where is the study run from? Queen Mary University of London (UK)

When is the study starting and how long is it expected to run for? November 2024 to June 2027

Who is funding the study? National Institute for Health and Care Research (NIHR) (UK)

Who is the main contact?
Dr Caroline Thomas, caroline.thomas27@nhs.net

# Contact information

## Type(s)

Scientific

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# Additional identifiers

#### Clinical Trials Information System (CTIS)

Nil known

### **Integrated Research Application System (IRAS)**

1011239

#### ClinicalTrials.gov (NCT)

Nil known

#### Protocol serial number

**CPMS 67094** 

# Study information

#### Scientific Title

Analgesia with ibuprofen for patients undergoing elective major gastro-intestinal surgery

#### Acronym

**PROTECT-AEGIS** 

## Study objectives

Is it feasible to deliver a randomised controlled trial of oral ibuprofen added to standard analgesic care in patients undergoing elective major gut surgery, compared to standard analgesia without a Non-Steroidal Anti-Inflammatory Drug? The findings in this feasibility trial will not be used in managing the patient's care.

There are four main patient and hospital level objectives with the overarching aim to provide a comprehensive portfolio of evidence to evaluate support for a definitive randomised trial:

- 1. To demonstrate wthe illingness of patients to participate in the trial
- 2. To demonstrate whether relevant healthcare staff within participating hospitals are willing to randomise patients into the trial
- 3. To provide pilot data on the clinical effects of oral ibuprofen in reducing pain after major elective gut surgery, compared to usual analgesia alone without a Non-Steroidal Anti-Inflammatory Drug
- 4. To provide safety data on the use of oral ibuprofen as an analgesic in patients undergoing major elective gut surgery

# Ethics approval required

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# Ethics approval(s)

approved 03/02/2025, London - South East Research Ethics Committee (Health Research Authority, 2 Redman Place, London, E20 1JQ, United Kingdom; -; londonsoutheast.rec@hra.nhs.uk), ref: 24/LO/0885

#### Study design

Open randomized controlled trial

#### Primary study design

Interventional

#### Study type(s)

Treatment

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

Pain management for patients undergoing major gastro-intestinal surgery

#### **Interventions**

Oral ibuprofen 400 mg three times daily for 5 days, started on postoperative day one, plus usual analgesic measures (epidural, patient-controlled analgesia, etc) and proton pump inhibitor (e.g. lansoprazole).

#### Intervention Type

Drug

#### Phase

Phase IV

## Drug/device/biological/vaccine name(s)

Ibuprofen

## Primary outcome(s)

Patient outcome measures:

- 1. Number of doses of ibuprofen or other NSAID administered to each patient within 5 days after surgery, measured by reviewing the patient's medical records
- 2. Clinical effects of oral ibuprofen in reducing pain after major elective gut surgery measured using the Overall Benefit of Analgesia Scores (OBAS) recorded daily for 5 days after surgery
- 3. Total opioid dose (Oral Morphine Equivalents) within 5 days after surgery, measured by reviewing the patient's medical records
- 4. Clinical effects of oral ibuprofen in reducing pain after major elective gut surgery measured using the Numeric Rating Scale (NRS) pain scale on postoperative days 1 to 5
- 5. All complications within 30 days of surgery, measured by reviewing the patient's medical records
- 6. Mortality within 30 days of surgery, measured by reviewing the patient's medical records
- 7. Duration of hospital stay within 30 days of surgery, measured by reviewing the patient's medical records
- 8. Anastomotic leak graded within 30 days of surgery, measured by reviewing the patient's medical records
- 9. Acute kidney injury (KDIGO creatinine definition only) within 30 days of surgery, measured by reviewing the patient's medical records
- 10. Gastro-intestinal bleed within 30 days of surgery, measured by reviewing the patient's medical records

#### Hospital-level feasibility outcomes:

1. Number of eligible patients per year in each hospital, measured using screening log data

- 2. Number of eligible patients randomised per year in each hospital, measured using screening log data
- 3. Participating hospitals randomising at least one patient within the 12-month recruitment period, measured using enrolment data
- 4. Number of consultant surgeons and anaesthetists in each hospital who support the recruitment of patients in their care in principle and the total number delivering care for elective colorectal surgery, measured using the feasibility site questionnaire

#### Key secondary outcome(s))

There are no secondary outcome measures

#### Completion date

30/06/2027

# **Eligibility**

#### Key inclusion criteria

Patients aged 18 years and over undergoing major elective gut surgery with bowel anastomosis

#### Participant type(s)

Patient

#### Healthy volunteers allowed

No

#### Age group

Adult

#### Lower age limit

18 years

#### Sex

All

#### Key exclusion criteria

- 1. Inability or refusal to provide informed consent
- 2. Previous enrolment in the PROTECT-AEGIS trial
- 3. Concomitant administration of any of the below:
- 3.1. Another Non-Steroidal Anti-Inflammatory Drug
- 3.2. Mifepristone within 2 weeks before surgery
- 4. History of specific risk factors:
- 4.1. Severe organ dysfunction defined as American Society of Anaesthesiologists (ASA) Physical Status Classification System 4 and/or eGFR <45
- 4.2. Known hypersensitivity or allergic reactions to ibuprofen (or its excipients), or other Non-Steroidal Anti-Inflammatory Drugs
- 4.3. Peptic ulcer disease: two or more episodes of proven ulceration or bleeding, or upper gastrointestinal perforation
- 4.4. Third trimester of pregnancy
- 4.5. Solid organ or bone marrow transplant

# Date of first enrolment

01/07/2025

#### Date of final enrolment

01/12/2026

# Locations

#### Countries of recruitment

**United Kingdom** 

# Study participating centre

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**United Kingdom** 

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# Sponsor information

#### Organisation

Queen Mary University of London

#### ROR

https://ror.org/026zzn846

# Funder(s)

## Funder type

Government

#### **Funder Name**

National Institute for Health and Care Research

#### Alternative Name(s)

National Institute for Health Research, NIHR Research, NIHRresearch, NIHR - National Institute for Health Research, NIHR (The National Institute for Health and Care Research), NIHR

# Funding Body Type

Government organisation

# **Funding Body Subtype**

National government

# Location

**United Kingdom** 

# **Results and Publications**

# Individual participant data (IPD) sharing plan

The data-sharing plans for the current study are unknown and will be made available at a later date

# IPD sharing plan summary

Data sharing statement to be made available at a later date

# **Study outputs**

| Output type                   | Details                       | Date created | Date added | Peer reviewed? | Patient-facing? |
|-------------------------------|-------------------------------|--------------|------------|----------------|-----------------|
| Participant information sheet | version 2.0                   | 20/01/2025   | 17/09/2025 | No             | Yes             |
| Participant information sheet | Participant information sheet | 11/11/2025   | 11/11/2025 | No             | Yes             |
| Protocol file                 | version 2.0                   | 30/01/2025   | 17/09/2025 | No             | No              |
| Protocol file                 | version 2.0                   | 30/01/2025   | 17/09/2025 | No             | No              |