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

Submission date
20/11/2024

Recruitment status
Recruiting

Registration date
27/05/2025

Overall study status
Ongoing

Last Edited
01/07/2025

Condition category
Surgery

[X] Prospectively registered
[_] Protocol
[_] Statistical analysis plan
[_] Results
[_] Individual participant data
[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

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Scientific

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Additional identifiers

EudraCT/CTIS number
Nil known

IRAS number
1011239

ClinicalTrials.gov number
Nil known

Secondary identifying numbers
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
Ethics approval required

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

Secondary study design
Randomised controlled trial

Study setting(s)
Hospital

Study type(s)
Treatment

Participant information sheet
Not available in web format, please use the contact details to request a participant information sheet

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

Pharmaceutical study type(s)
Others (Feasibility)

Phase
Phase IV

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

Primary outcome measure
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

Secondary outcome measures
There are no secondary outcome measures

Overall study start date
18/11/2024

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

Age group
Adult

Lower age limit
18 Years

Sex
Both

Target number of participants
200

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
30/06/2026

Locations

Countries of recruitment
United Kingdom

Study participating centre
-
United Kingdom
-

Sponsor information

Organisation
Queen Mary University of London

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Sponsor type
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ROR
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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

Publication and dissemination plan
1. Peer-reviewed scientific journals
2. Publication on website

Intention to publish date
30/06/2028

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