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Pain relief after instrumented spinal surgery trial

Submission date 02/09/2023	**Recruitment status** Recruiting	[X] Prospectively registered [X] Protocol
Registration date 03/11/2023	**Overall study status** Ongoing	[ ] Statistical analysis plan [ ] Results
Last Edited 26/02/2025	**Condition category** Surgery	[ ] Individual participant data [X] Record updated in last year

Plain English summary of protocol
Background and study aims
Spinal surgery is common in the NHS and can result in severe postoperative pain limiting recovery and rehabilitation. Pain after instrumented lumbar spinal surgery is severe and can persist for many weeks, with a mean length of hospital stay of 4.7 days. Severe postoperative pain can delay early mobilisation, with potential complications such as venous thromboembolism and infection, all of which carry costs for the NHS. The treatments under evaluation each carry a different harm:benefit profile. Multimodal analgesia with strong opioids (Usual Care) is standard treatment but there is some evidence from systematic reviews that the alternatives offer superior pain relief. Both intrathecal opioids and ESB are currently used in some centres, but without a rational basis for treatment selection in scientific evidence.

The PRAISE trial aims to investigate the clinical and cost effectiveness of three approaches to postoperative pain relief following lumbar spine surgery: Control (Usual care), Intervention 1 (Intrathecal Opioid injection) or Intervention 2 (Erector Spinae plane Block).

Who can participate?
Participants aged over 16 years scheduled for elective posterior lumbar-instrumented spinal surgery who are able to give informed consent

What does the study involve?
Patients will be randomised 1:1:1 to one of the three approaches above.

The primary outcome is back pain on moving around bed (sitting up and/or turning) on a 0-100 VAS at 24 hours post-surgery. Secondary outcomes include EQ-5D-5L, back pain at rest, leg pain, QoR-15, cumulative postoperative opioid consumption, quality of life, time to mobilisation, length of stay, adverse events and healthcare resource use. Parallel economic evaluation with the trial will estimate incremental cost-effectiveness ratios. Outcomes will be collected at baseline, on admission to theatre recovery, at 6, 24 and 72 hours after surgery, and at routine 6-8 week follow up.

What are the possible benefits and risks of participating?
Benefits:

Not provided at time of registration
Risks:
In addition to surgical complications attendant with spinal procedures, potential harms differ somewhat for each group allocation:

ESP Block complications - ESPB has very rare but potentially serious complications of delivery of local anaesthetic including intravenous injection, local anaesthetic toxicity, intraneural injection, infection at needle insertion site and pneumothorax. SAEs will be continually monitored throughout the trial accordingly and patients will undergo a detailed risk-benefit conversation with a consultant anaesthetist prior to consent and randomisation.

Usual Care UC also carries some risk of inadequate analgesia (severe, acute postoperative pain) postoperative nausea and vomiting (PONV), sedation. Intrathecal Opioid (ITO) also carries risk of Respiratory depression, pruritus (itching)and urinary retention - but both these procedures are standard of care treatments.

Where is the study run from?
Sheffield Teaching Hospitals NHS Foundation Trust (UK)

When is the study starting and how long is it expected to run for?
August 2023 to August 2026

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

Who is the main contact?
Sienna A Hamer-Kiwacz, s.a.hamer-kiwacz@sheffield.ac.uk

Study website
https://www.sheffield.ac.uk/ctru/current-trials/praise

Contact information

Type(s)
Scientific

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Additional identifiers

EudraCT/CTIS number
Nil known

IRAS number
1008666

ClinicalTrials.gov number
Nil known

Secondary identifying numbers
STH22261, IRAS 1008666

Study information

Scientific Title
Pain Relief After Instrumented Spinal surgEry trial

Acronym
PRAISE

Study objectives
Primary objective:
A randomised controlled trial powered to test the hypothesis that enhanced anaesthetic techniques, intrathecal opioids or Erector Spinae plane Block, improve postoperative back pain on moving around the bed (sitting up and/or turning) at 24 hours by at least 10 points (0-100 Visual Analogue Scale) compared to usual care in patients undergoing spinal surgery +/- decompression.

Secondary objectives:
To determine:
1. if there is a difference in cumulative opioid consumption after surgery, at 24 hours and 72 hours (or discharge) between UC, ITO and ESB;
2. if there is a difference in quality of recovery between the three intervention groups using the

Quality of Recovery Scale;
3. if there is a difference in the need for further clinical intervention between UC, ITO and ESB;
4. if there is a difference in time to mobilisation after surgery and length of hospital stay (readiness for discharge) between UC, ITO and ESB;
5. if there is a difference in readmissions between discharge and routine 6-8 week postoperative follow up, between UC, ITO and ESB;
6. if there is a difference in quality of life between the three intervention groups;
7. if there is a difference in healthcare resource use between three groups and to compare the adverse events between UC, ITO and ESB. Also feasibility and Health Economic objectives.

Ethics approval required
Ethics approval required

Ethics approval(s)
Approved 02/11/2023, London - Dulwich Research Ethics Committee (2 Redman Place, Stratford, London, E20 1JQ, United Kingdom; +44 (0)2071048236; westminster.rec@hra.nhs.uk), ref: 23/LO/0811

Study design
Multicentre parallel-group superiority patient-blind individual participant-randomized controlled trial

Primary study design
Interventional

Secondary study design
Randomised parallel trial

Study setting(s)
Hospital

Study type(s)
Safety, Efficacy

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
Patients scheduled for elective, posterior lumbar-instrumented spinal surgery +/- decompression.

Interventions
Patients will be identified and screened for eligibility by their surgical clinical team when the decision for lumbar spinal surgery has been taken. Patients will be provided with written information materials and referred to an anaesthetist for an in-depth trial discussion. There will be a clear explanation of study procedures including the interventions and associated risks, and the opportunity for patients to have any questions. Consent will only be sought after the discussion with the anaesthetist has taken place. Recruitment will be aligned around the

standard care pre-operative assessment appointment, which will take place sometime after the patient has been listed for surgery, allowing sufficient time for patients to consider the information and decide whether they would like to take part.

Once eligibility has been confirmed and consent acquired, the participant will be randomly allocated to one of the following groups: (1) Usual Care; (2) Intrathecal Opioids (ITO); (3) Erector Spinae plane Block (ESB) using the Sheffield CTRU online randomisation system (SCRAM). Participants will be allocated to their intervention using minimisation with a random element and the following factors ensuring baseline balance: site; levels of fusion (1 level vs. >1 level (2-3)), receiving Step 3 opioid therapy at randomisation (yes vs no). Trial participants can only be randomised if staff trained in delivery of all interventions are available.

The trial interventions are as follows:

1. Usual Care (with local wound infiltration):
Involves analgesia administered at the time of surgery whilst under General Anaesthesia and in the immediate post-operative period. Intravenous opioid, Paracetamol, NSAID (if not contraindicated). This will be administered by the anaesthetist providing clinical care. Trial participants will also receive local infiltration of surgical incision with Local Anaesthetic (Levo-Bupivacaine) administered by the Operating Surgeon
How: Intravenous injection during surgery in Operating Theatre. Local anaesthesia administered at surgical closure.
Timing: Intravenous drugs administered intra-operatively. Local anaesthetic infiltration at completion of surgery.
Dose: Intravenous analgesia administered at the discretion of the Consultant anaesthetist: Local Anaesthetic Infiltration: up to maximum dose Levo-Bupivacaine 100mg
Tailoring: Opioid Analgesia Drug Type and Dose administered according to Anaesthetist's clinical opinion and local practice. Paracetamol as per local standard of care, NSAID if not contraindicated.
Modifications: Local anaesthetic infiltration volume adjusted to maximum dose of Levo-Bupivacaine 2 mg/kg to avoid toxicity.
Accountability: All drugs administered during surgery are routinely recorded in anaesthetic record.

2. Usual Care plus Intrathecal Opioid (with local wound infiltration)
Involves pain relief with central (neuraxial) opioid pain relief, reducing onward transmission of nociceptive stimulus to reduce patient pain sensation for sustained period post operatively. Intrathecal Opioid Analgesia administered by operating surgeon at the time of surgery whilst under General Anaesthesia. Morphine (Preservative Free); diamorphine according to local clinical practice guidelines. ITO plus Usual Care as above.
How: Intrathecal Opioid administered by Operating Surgeon in Operating Theatre. Intrathecal injection under direct vision, via narrow gauge "pencil point" spinal needle via Ligamentum Flavum. ITO is permitted to be administered by an appropriately trained surgeon who does this procedure as part of their clinical care. The usual care and intrathecal opioid interventions are routinely used in the NHS and require no specific training.
Timing: At the time of surgery. Local wound infiltration at completion of surgery.
Dose: Preservative Free Morphine: 0.1 mg (minimum dose); or Diamorphine (dose range 0.2mg to 0.4mg).
Modifications: Choice of drug (morphine vs diamorphine) dictated by local practice and requirements for post-operative care. Paracetamol as per local standard of care. Omit NSAID if contraindication.
Accountability: Morphine or Diamorphine must be dispensed from research pharmacy.

Confirmation of intrathecal administration by cerebrospinal fluid aspiration prior to injection. All drugs administered during surgery are routinely recorded in anaesthetic records, which will inform the per protocol analysis.
Intrathecal Opioid Group will receive Usual Care, as described above plus the Intervention described above.

3. Usual Care plus bilateral Erector Spinae Plane Block (no local wound infiltration)
Interrupts pain signal transmission from the area of surgery to the Central Nervous System with local anaesthetic nerve blockade. Regional "Field" Block with local anaesthetic, given by Anaesthetist having completed ESPB training.
How: Ultrasound-guided injection of local anaesthetic, to produce a bilateral "Fascial Plane" block. Given in Operating Theatre at time of surgery, prior to emergence from anaesthesia.
Dose: 2 x 20 mls Levo-Bupivacaine 0.25% (2.5 mg/ml), 40 mls in total. 0.25% Levo-Bupivacaine is widely available "off the shelf" in all operating theatres. The volume and dose chosen will be effective in the majority of patients who will be substantially heavier than 50kg. Adjusting the volume down, rather than altering concentration, in the small number of patients below 50kg, likewise reduces the chance of drug error or local anaesthetic toxicity. The concentration and volume of Levo-Bupivacaine for local infiltration in Usual Care was chosen to emulate routine clinical practice and deliver the same dose of drug as local infiltration (20 ml 0.5% = 100 mg).
Modifications: If patient weight < 50kg: Reduced Volume of Levo-Bupivacaine to maximum dose 2 mg/kg (e.g. 45 kg patient would receive 90 mg Levo-Bupivacaine or 36 mls as 2 x 18 mls injections) to avoid the potential for local anaesthetic toxicity. Paracetamol as per local standard of care: Omit NSAID if contraindication.
Accountability: Drug delivered to correct "Plane" by direct, real time ultrasound visualisation. Confirmation of drug delivery by ultrasound "screen capture" after bilateral injection.

Erector Spinae Block group will receive Intervention described above plus Usual care, without Local Wound Infiltration.

Participants will be followed up for pain and other measures post-surgery whilst in hospital (in recovery, 6 hours post-surgery, 24 hours post-surgery and at discharge/72 hours post-surgery). Participants will also be followed up again 6-8 weeks post-surgery at their standard of care follow up visit.

Intervention Type
Drug

Pharmaceutical study type(s)
Bioequivalence, Pharmacoeconomic, Therapy

Phase
Phase III

Drug/device/biological/vaccine name(s)
Morphine, diamorphine, levobupivacaine

Primary outcome measure
Back pain on moving around the bed (sitting up and/or turning) from Visual Analog Scale (VAS) recorded at 24 hours after surgery, reported using a 10 cm line, 0-100 score. Patients unable to sit up and/or turn as a result of pain will be assigned the highest pain score (100).

Secondary outcome measures
Patient-reported outcomes
1. Pain scores (VAS) 13 back & leg pain, at rest and movement, on a 0-100 scale;
2. EQ-5D-5L14: Health status questionnaire used to derive quality adjusted life year (QALYs) and used in the cost-effectiveness analysis;
3. Quality of Recovery Questionnaire (QoR-15) 15 to measure the quality of recovery after surgery and analgesia;
4. Healthcare Resource Use: measured using a bespoke questionnaire.
5. Oswestry Disability Index16 to measure functional recovery after surgery

Clinical
1. Cumulative opioid consumption after surgery, at 24 hours and 72 hours (or discharge) (converted to oral morphine equivalent)
2. Adverse events
3.Intervention-related side-effects (including: Postoperative Nausea and Vomiting (PONV), pruritus, respiratory depression (respiratory rate <8 breaths/minute)
4. Further clinical intervention such as: antiemetic administration, urinary catheterisation, High Dependency Care/Intensive Care admission
5. Time to mobilisation after surgery
6. Length of hospital stay (readiness for discharge)
7. Readmissions between discharge and routine 6-8 week postoperative follow up.

Overall study start date
01/09/2023

Completion date
31/08/2026

Eligibility

Key inclusion criteria
Current inclusion criteria as of 26/02/2025:

1. People aged 16 or over.
2. Scheduled for elective, posterior lumbar-instrumented spinal surgery +/- decompression (including patients undergoing this surgery following a previous lumbar discectomy or decompression).
3. Able to give informed consent, with interpreters provided where necessary.

Previous inclusion criteria:

1. People aged 16 years or over
2. Scheduled for elective, posterior lumbar-instrumented spinal surgery +/- decompression
3. Able to give informed consent, with interpreters provided where necessary

Participant type(s)
Patient

Age group

Adult

Lower age limit
16 Years

Sex
Both

Target number of participants
456

Key exclusion criteria
Current exclusion criteria as of 26/02/2025:

1. Patients with drug sensitivity or allergy to any of the trial agents i.e. intrathecal opioid or local anaesthetic.
2. Patients undergoing fusion at more than three vertebral levels.
3. Patients with an infection or tumour at the block site or surgical site.
4. Patients meeting criteria for American Society of Anaesthesiologists Physical Status Classification Grade 4-5.
5. Patients undergoing surgery during an emergency admission (this would preclude a detailed risk-benefit conversation with a consultant anaesthetist, which our PPI group told us was vital pre-consent).
6. Patients scheduled for single-level microdiscectomy and decompression only.
7. Patients undergoing anterior surgery.
8. Patients who have previously had posterior lumbar instrumentation. Current pregnancy: a pregnancy test, in the female patients of childbearing age is routine immediately prior to surgery.

Previous exclusion criteria:

1. Patients with drug sensitivity or allergy to any of the trial agents i.e. intrathecal opioid or local anaesthetic
2. Patients undergoing fusion at more than three vertebral levels
3. Patients with an infection or tumour at the block site or surgical site
4. Patients meeting criteria for American Society of Anaesthesiologists Physical Status Classification Grade 4-5
5. Patients undergoing surgery during an emergency admission (this would preclude a detailed risk-benefit conversation with a consultant anaesthetist, which our PPI group told us was vital pre-consent).
6. Patients scheduled for single-level microdiscectomy and decompression.
7. Current pregnancy

Date of first enrolment
30/09/2024

Date of final enrolment
30/11/2025

Locations

Countries of recruitment
England

Scotland

United Kingdom

Wales

Study participating centre
Northern General Hospital
Northern General Hospital NHS Trust
Herries Road
Sheffield
United Kingdom
S5 7AU

Study participating centre
Queens Medical Centre
Nottingham University Hospital
Derby Road
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Study participating centre
Ninewells Hospital
Ninewells Avenue
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Study participating centre
Queen Elizabeth University Hospital
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Study participating centre
The Walton Centre NHS Foundation Trust
Lower Lane
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United Kingdom
L9 7LJ

Study participating centre
Royal Preston Hospital
Sharoe Green Lane North
Fulwood
Preston
United Kingdom
PR2 9HT

Study participating centre
Northumbria Healthcare NHS Foundation Trust
North Tyneside General Hospital
Rake Lane
North Shields
United Kingdom
NE29 8NH

Study participating centre
Hull University Teaching Hospitals NHS Trust
Hull Royal Infirmary
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HU3 2JZ

Study participating centre
South Tyneside and Sunderland NHS Foundation Trust
Sunderland Royal Hospital
Kayll Road
Sunderland
United Kingdom
SR4 7TP

Study participating centre

Royal National Orthopaedic Hospital
Brockley Hill
Stanmore
United Kingdom
HA7 4LP

Study participating centre
University Hospitals of Derby and Burton NHS Foundation Trust
Royal Derby Hospital
Uttoxeter Road
Derby
United Kingdom
DE22 3NE

Study participating centre
University Hospitals Coventry and Warwickshire NHS Trust
Walsgrave General Hospital
Clifford Bridge Road
Coventry
United Kingdom
CV2 2DX

Study participating centre
King's College Hospital
Denmark Hill
London
United Kingdom
SE5 9RS

Study participating centre
Leeds Teaching Hospitals NHS Trust
St. James's University Hospital
Beckett Street
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United Kingdom
LS9 7TF

Study participating centre
Whittington Health NHS Trust
The Whittington Hospital
Magdala Avenue

London
United Kingdom
N19 5NF

Study participating centre
The Robert Jones and Agnes Hunt Orthopaedic Hospital NHS Foundation Trust
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Sponsor information

Organisation
Sheffield Teaching Hospitals NHS Foundation Trust

Sponsor details
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Sponsor type
University/education

Website
http://www.sth.nhs.uk/research-innovation

ROR
https://ror.org/018hjpz25

Funder(s)

Funder type
Government

Funder Name
Health Technology Assessment Programme

Alternative Name(s)
NIHR Health Technology Assessment Programme, Health Technology Assessment (HTA), HTA

Funding Body Type
Government organisation

Funding Body Subtype
National government

Location
United Kingdom

Results and Publications

Publication and dissemination plan
Peer reviewed scientific journals
Internal report
Conference presentation
Publication on website
Submission to regulatory authorities
Anonymised datasets can be made available to other researchers upon request and appropriate ethical review. Participants are also asked to consent to future research (using their anonymised data) and that their anonymised datasets will be made publically available at the end of the study.

Intention to publish date
31/08/2027

Individual participant data (IPD) sharing plan
Anonymised datasets can be made available to other researchers upon request and appropriate ethical review. Participants are also asked to consent to future research (using their anonymised data) and that their anonymised datasets will be made publically available at the end of the study.

IPD sharing plan summary
Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Protocol file	version 3.1	12/02/2025	26/02/2025	No	No