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# Methoxyflurane versus usual Analgesia for Prehospital Injury & Trauma

**Submission date**
10/11/2017

**Recruitment status**
Stopped

**Registration date**
08/01/2018

**Overall study status**
Stopped

**Last Edited**
04/11/2019

**Condition category**
Signs and Symptoms

[ ] Prospectively registered
[ ] Protocol
[ ] Statistical analysis plan
[ ] Results
[ ] Individual participant data
[ ] Record updated in last year

## Plain English summary of protocol

Background and study aims
Inhaled methoxyflurane has been used safely by ambulance staff in Australia over the past 40 years for the treatment of patients with moderate to severe acute pain due to injury or trauma. This drug is now being promoted for use in UK ambulance services but evidence is lacking of the effectiveness of methoxyflurane compared with current treatments, which include intravenous or oral morphine (or other opiates), intravenous paracetamol or nitrous oxide – oxygen (1:1) mixture. Of these analgesics (painkillers) only Entonox can be given by Emergency Medical Technicians as usual analgesia. The UK licence for methoxyflurane is for emergency relief of moderate to severe pain in conscious adult patients (aged 18 and over) with trauma and associated pain. There are a number of contraindications and cautions to its use although the drug has a good safety profile when used in pre-hospital urgent care. Methoxyflurane can be given by both paramedics and emergency medical technicians. In the UK emergency medical technicians are limited to giving only Entonox as an analgesic for moderate to severe acute pain. The aim of this study is to investigate the clinical and cost effectiveness of methoxyflurane in adults presenting for treatment to ambulance services with moderate to severe acute pain due to trauma or injury.

Who can participate?
Paramedics and Emergency Medical Technicians (EMTs) attending adult patients with moderate to severe pain due to injury or trauma

What does the study involve?
Paramedics and EMTs are randomly allocated into the intervention group or the control group. Paramedics and EMTs in the intervention group then receive training on how to use methoxyflurane, its side effects and adverse reaction reporting process. Methoxyflurane is given to patients in an inhaler self-administered under supervision. On finishing the 3 ml dose another 3 ml may be used. The dose should not exceed 6 ml in a single administration. Paramedics and EMTs in the control group administer the standard or usual analgesia, which is morphine (intravenous or oral), paracetamol (intravenous) nitrous oxide and oxygen (1:1) mixture (Entonox), or non-steroidal anti-inflammatory. Of these analgesics only Entonox can be

administered by Emergency Medical Technicians as usual analgesia. Patients' pain scores are measured before and 5 minutes after use of analgesic, and then after 30 minutes or arrival at the hospital, whichever is soonest, or upon use of an additional analgesic.

What are the possible benefits and risks of participating?
This study will provide valuable evidence for ambulance services in determining whether methoxyflurane is as effective or more effective at reducing patients' pain compared with the existing analgesic options used by paramedics and Emergency Medical Technicians. If the intervention is shown to be cost effective it is likely to be introduced across other UK ambulance services. Benefits would be felt by patients as they would be given access to a drug that can be self-administered and which could be very effective at managing their pain following a traumatic incident. It would also increase the scope of practice for Emergency Medical Technicians in managing this group of patients more effectively. As the study involves measuring the effectiveness of a new analgesic not routinely used in the UK ambulance service, there is a risk that it may not be effective in reducing patients' pain. However, paramedics and Emergency Medical Technicians are still able to use other analgesics that are within their scope of practice.

Where is the study run from?
The study takes place in one or more counties served by East Midlands Ambulance Service NHS Trust (EMAS) (UK)

When is the study starting and how long is it expected to run for?
February 2017 to June 2018

Who is funding the study?
Galen Limited (UK)

Who is the main contact?
1. Tanya Payne (public)
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2. Prof. Niro Siriwardena (scientific)
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## Additional identifiers

### EudraCT/CTIS number
2017-004156-38

### IRAS number

### ClinicalTrials.gov number

### Secondary identifying numbers
236062

## Study information

### Scientific Title
Pragmatic cluster randomised controlled trial to evaluate the effectiveness and cost effectiveness of inhaled methoxyflurane (Penthrox) versus usual analgesia for prehospital injury and trauma

### Acronym
MAPIT

### Study objectives
Pain will be managed more effectively with the use of methoxyflurane in terms of reduction in pain severity and cost compared to currently used analgesia.

### Ethics approval required
Old ethics approval format

### Ethics approval(s)
Nottingham Research Ethics Committee 2 - submission pending

## Study design
Cluster randomised controlled trial

## Primary study design
Interventional

## Secondary study design
Randomised controlled trial

## Study setting(s)
Other

## Study type(s)
Treatment

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

## Health condition(s) or problem(s) studied
Pre-hospital pain management for patients in moderate to sever pain from injury or trauma

## Interventions
Ambulance clinicians will be randomised following initial training on trial procedures. Paramedics and EMTs will be allocated into two equal blocks, and individuals in each block randomised into intervention or control arms by the trial statistician using computer generated simple randomisation method.

Participants randomised to the intervention arm will then receive training on how to use methoxyflurane (Penthrox), its side effects and adverse reaction reporting process. Methoxyflurane will be administered according to its current licence, one bottle of 3 mL PENTHROX vapourised in a PENTHROX inhaler self-administered under supervision of a person trained in its administration. On finishing the 3 mL dose another 3 mL may be used. Dose should not exceed 6 mL in a single administration.

The control arm is standard or usual analgesia administered in the East Midlands Ambulance Service NHS Trust, which is morphine (intravenous or oral), paracetamol (intravenous) nitrous oxide and oxygen (1:1) mixture (Entonox), or non-steroidal anti-inflammatory. Of these analgesics only Entonox can be administered by Emergency Medical Technicians as usual analgesia.

## Intervention Type
Drug

## Phase
Phase III/IV

## Drug/device/biological/vaccine name(s)
Methoxyflurane, morphine (or other opiates), paracetamol, nitrous oxide – oxygen (1:1) mixture

### Primary outcome measure
Pain measured using the verbal numerical pain score (VNPS), which is used as standard method of assessment for all patients attended by East Midlands Ambulance Service NHS Trust. Baseline pain scores will be taken as standard prior to the administration of any analgesia, 5 minutes after initial analgesia and again at 30 minutes or arrival at the emergency department whichever is sooner.

### Secondary outcome measures
1. Incremental cost effectiveness ratio (including the drug costs, costs of associated consumables, cylinder rental, number cylinders used, refilling and maintenance costs (regarding Entonox) in addition to requirements for duplication of resources at scene (i.e. EMT crew having to call paramedic back-up for purposes of stronger analgesic requirements) and also the necessity to take the patient to ED if given an opioid)
2. Tolerability of methoxyflurane
3. Proportion of patients in whom pain between baseline, pain 5 minutes after administration and at final (i.e. after 30 minutes or at arrival at ED) is reduced
4. Time to addition of second analgesic versus current standard of care (Entonox)
5. Percentage of patients with a ≥ 30% reduction in baseline pain at first and subsequent timepoints/measurements

### Overall study start date
17/02/2017

### Completion date
30/06/2018

### Reason abandoned (if study stopped)
Lack of staff/facilities/resources

## Eligibility

### Key inclusion criteria
Ambulance staff:
1. Qualified Paramedic or Emergency Medical Technician contracted by East Midlands Ambulance Service NHS Trust

Patients:
1. Adult aged 18 years and above
2. Emergency attendance by ambulance paramedic or EMT
3. In moderate to severe pain (VNPS 4-10) due to trauma (injury) and associated pain

### Participant type(s)
Mixed

### Age group
Adult

### Lower age limit
18 Years

### Sex
Both

### Target number of participants
40 ambulance staff and 1040 patient records

### Key exclusion criteria
Ambulance staff:
1 East Midlands Ambulance Service NHS Trust staff who are pregnant or breastfeeding

Patients:
1. Child or young person aged under 18 years
2. Altered level of consciousness (Glasgow Coma Scale [GCS] <15) due to any cause including head injury, drugs, or alcohol
3. Suspected cardiac chest pain, sickle cell crisis
4. Hypersensitivity to methoxyflurane or any fluorinated anaesthetic
5. Malignant hyperthermia: patients with known or genetically susceptible to malignant hyperthermia or a history of severe adverse reactions in either patient or relatives
6. History of showing signs of liver damage after previous methoxyflurane use or halogenated hydrocarbon anaesthesia
7. Clinically significant renal impairment
8. Clinically evident cardiovascular instability
9. Clinically evident respiratory depression
10. Pregnancy and females who are breastfeeding

### Date of first enrolment
01/12/2017

### Date of final enrolment
31/03/2018

## Locations

### Countries of recruitment
England

United Kingdom

### Study participating centre
**East Midlands Ambulance Service NHS Trust**
Trust Headquarters
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# Sponsor information

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### Sponsor type
Other

### ROR
https://ror.org/055pdxb86

# Funder(s)

### Funder type
Industry

### Funder Name
Galen Limited

# Results and Publications

### Publication and dissemination plan
The study protocol will be available on request by contacting the chief investigator or EMAS research team. The trialists will prepare reports for the funder and interested stakeholders (e.g. Galen, Association of Ambulance Chief Executives [AACE], National Ambulance Service Medical Directors [NASMed]), presentations for national (or international) conferences and publications for peer-reviewed journals.

### Intention to publish date
31/12/2018

### Individual participant data (IPD) sharing plan

Anonymised data will be published at the time of publication of the study and will be available from the author via the Community and Health Research Unit website (www.cahru.org.uk).

## IPD sharing plan summary

Available on request