

# Medication route in out-of-hospital cardiac arrest

<b>Submission date</b> 19/07/2021	<b>Recruitment status</b> No longer recruiting	<input checked="" type="checkbox"/> Prospectively registered <input checked="" type="checkbox"/> Protocol
<b>Registration date</b> 16/08/2021	<b>Overall study status</b> Completed	<input type="checkbox"/> Statistical analysis plan <input checked="" type="checkbox"/> Results
<b>Last Edited</b> 01/11/2024	<b>Condition category</b> Circulatory System	<input type="checkbox"/> Individual participant data

## Plain English summary of protocol

### Background and study aims

Each year over 30,000 people's hearts suddenly stop beating in communities around the UK (a condition known as cardiac arrest). Within seconds of this happening the person becomes unconscious. Unless the heart is restarted quickly, the brain will become permanently damaged and the person will die. Injecting drugs such as adrenaline through a vein is very effective at restarting the heart. However, for many people drugs are given too late to save them. This partly explains why less than one in ten people survive an out of hospital cardiac arrest.

Each year over 30,000 people's hearts suddenly stop beating in communities around the UK (a condition known as out-of-hospital cardiac arrest). Giving drugs, such as adrenaline, is very effective at restarting the heart. However, for many people drugs are given too late to save them. This partly explains why less than one in ten people survive an out of hospital cardiac arrest.

Current guidelines advise paramedics to inject drugs into a vein. It can take several critical minutes to put a drip in to a vein, ready to give drugs. A faster way to give drugs is to put a small needle into an arm or leg bone. This allows drugs to be given directly into the rich blood supply found in the bone marrow. Currently, none of the existing research is good enough to help paramedics decide how best to treat people with cardiac arrest.

Current guidelines advise paramedics to inject drugs in to a vein. The problem with this is it can take several critical minutes to put a drip in to a vein, ready to give drugs. A new, faster way of giving drugs is to put a small needle into an arm or leg bone. This allows drugs to be injected directly into the rich blood supply found in the bone marrow. Some research studies suggest this may be as good, if not better, than injecting drugs into the vein. Other studies suggest it may be less effective. None of the existing research is good enough to help paramedics decide how best to treat people with cardiac arrest. Both of these approaches are already currently used in NHS practice.

In this trial, we will test these two ways of giving drugs (into the vein or into the bone) to work out which is most effective at improving survival in people that have a cardiac arrest.

Who can participate?

Adults that have an out-of-hospital cardiac arrest.

What does the study involve?

Adults that have had an out-of-hospital cardiac arrest will be randomly allocated to one of two groups. In the first group, the paramedic will aim to place a needle into the bone. Once this has been successfully inserted, the paramedic will give cardiac arrest drugs, such as adrenaline, through that needle. If the paramedic cannot insert a needle in the bone after two attempts, they may decide whether to have further attempts at placing a needle in the bone or to try and place a drip in a vein. In the second group, the paramedic will aim to place a drip in a vein. Once this has been successfully inserted, the paramedic will give cardiac arrest drugs, such as adrenaline, through that drip. If the paramedic cannot insert a drip in the vein after two attempts, they may decide whether to have further attempts at placing a drip in a vein or try and place a needle in the bone. Both these treatments are already used routinely in the NHS.

Treatment in a cardiac arrest is urgent. Even very small delays may affect how likely it is that someone survives. As the patient that has had a cardiac arrest will be unconscious and there won't be enough time to talk to a family member or friend about study involvement, we will immediately enrol individuals and defer the consent process until after the emergency situation has passed. We will speak to individuals that survive the cardiac arrest to inform them as to what has happened and seek their agreement to complete study follow-up questionnaires.

We will follow-up study participants for six-months. We will record how many patients have survived and how well they have recovered using some brief questionnaires. We will also see how long people spend on intensive care units and in hospital.

What are the possible benefits and risks of participating?

The planned treatments are already in routine use across NHS ambulance services. Placing a needle in a bone, rather than a drip in a vein, may increase how many patients survive following cardiac arrest. However, there may be some minor side-effects, such as infection, extravasation (misplacement of the needle and giving drug outside of the vein or bone), and dislodgement.

Where is the study run from?

The trial is led by the University of Warwick Clinical Trials Unit (UK)

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

May 2021 to September 2025

Who is funding the study?

The National Institute for Health Research (UK) Health Technology Assessment programme.

Who is the main contact?

Dr Keith Couper,

**Study website**

<https://warwick.ac.uk/fac/sci/med/research/ctu/trials/paramedic3/>

## Contact information

**Type(s)**

Scientific

**Contact name**

Dr Keith Couper

**Contact details**

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Warwick Medical School  
University of Warwick  
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United Kingdom  
CV4 7AL  
+44 (0)2476151179  
Paramedic3@warwick.ac.uk

**Additional identifiers****EudraCT/CTIS number**

Nil known

**IRAS number**

298182

**ClinicalTrials.gov number**

Nil known

**Secondary identifying numbers**

CPMS 49465, NIHR131105, IRAS 298182

**Study information****Scientific Title**

Pre-hospital RANdomised trial of MEDICATION route in out-of-hospital cardiac arrest (PARAMEDIC3)

**Acronym**

PARAMEDIC-3

**Study objectives**

The primary objective of this trial is to evaluate the effectiveness of using the intraosseous route (small needle into an arm or leg bone) to give drugs to out of hospital cardiac arrest patients measured by survival status at 30 days.

The secondary objectives of the trial are to evaluate the effect of the intraosseous route as paramedics first method of treatment (referred to as first strategy) on the brain function, quality of life and survival of patients at other time points. It will also determine the cost-effectiveness of paramedics using the intraosseous route as their first strategy.

**Ethics approval required**

Old ethics approval format

## **Ethics approval(s)**

Approved 12/07/2021, South Central – Oxford C Research Ethics Committee (Level 3, Block B, Whitefriars, Lewins Mead, Bristol, BS1 2NT, UK; +44 (0)207 104 8241; oxfordc.rec@hra.nhs.uk), ref: 21/SC/0178

## **Study design**

Interventional randomized 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 the contact details to request a patient information sheet

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

Cardiac arrest

## **Interventions**

### **INTERVENTIONS**

Patients will be randomly allocated to receive either IO first strategy (intervention) or IV first strategy (control) through use of opaque, sequentially numbered sealed envelopes (or an equivalent system, such as peelable stickers or scratch cards). In patients randomised to the intervention group, initial vascular access attempts will be via the intraosseous (IO) route. At least two attempts at vascular access via the intraosseous route will be made. The anatomical site of IO attempts will be at the discretion of the treating ambulance clinician. In making a decision as to site selection, the ambulance clinician will be mindful of contraindications to specific sites (e.g. fracture in target bone, prosthetic limb/ joint).

Once IO vascular access has been successfully achieved, cardiac arrest drugs (including fluid) will be administered through the IO cannula. Where clinically required, more than one IO cannula may be sited.

If the treating clinician has made two attempts at vascular access via the IO route and been unsuccessful at both attempts, then further attempts at vascular access may be made via the IO or IV route at the clinician's discretion.

Where IO access fails at any point following successful insertion, further attempts at vascular access may be made via the IO or IV route at the clinician's discretion.

Following return of spontaneous circulation, the treating clinician may choose to continue to use any established IO access or to insert an intravenous cannula.

In patients randomised to the control group, initial vascular access attempts will be via the intravenous route. At least two attempts at vascular access via the intravenous route will be made. The anatomical site of IV attempts will be at the discretion of the treating paramedic. This reflects current NHS practice.

Once IV vascular access has been successfully achieved, cardiac arrest drugs (including fluid) will be administered through the IV cannula. Where clinically required, more than one IV cannula may be sited.

If the treating clinician has made two attempts at vascular access via the IV route and been unsuccessful at both attempts, then further attempts at vascular access may be made via the IO or IV route at the clinician's discretion.

Where IV access fails at any point following successful insertion, further attempts at vascular access may be made via the IO or IV route at the clinician's discretion.

#### CONSENT

The trial will recruit individuals that will be unconscious (having sustained a cardiac arrest) and who require time-critical treatment. On this basis, we plan to recruit individuals to the trial under a deferred consent model, in accordance with the Mental Capacity Act 2005. When patients regain capacity after being discharged from ICU, they will be approached to obtain consent. If the patient does not survive the cardiac arrest, relatives will be informed about their participants through passive methods to reduce the emotional burden during this distressing time.

#### DATA COLLECTION AND FOLLOW-UP

During this time information about their cardiac arrest and hospital stay will be collected from the patients hospital record by research paramedics. Information will also be obtained through data linkage sources. Long-term follow up will be conducted at 3 and 6 months following randomisation. Survival status will be obtained from NHS Digital or other electronic data sources. Quality of life questionnaires will be posted to the patient for completion at 3 and 6 months. They may be completed on the participant's behalf by someone that has a good awareness of their health state.

Follow-up for post discharge neurological outcomes and health related quality of life will be co-ordinated by ambulance services and follow an established system for contacting patients or their legal representatives ensuring effective follow up.

#### TIMETABLE FOR RESEARCH

The trial duration is schedule for 48 months with trial recruitment to take place over a 25 month period.

#### PLAN FOR INTERIM ANALYSIS/REPORT

The role of the Data Monitoring Committee and the Trial Steering committee will be to assess recruitment, the interim analyses in terms of the statistical monitoring.

#### SAMPLE SIZE

We will aim to recruit 15,000 patients to the trial.

#### PPI INVOLVEMENT

We have worked closely with patients and members of the public in designing the trial, including

detailed discussions with our PPI co-applicant and presentation of the proposed trial to the Clinical Research Ambassador Group at University Hospitals Birmingham NHS Foundation Trial.

We will continue to embed meaningful patient and public involvement throughout the project, based on INVOLVE best practice guidance. We have convened a PPI group with a membership that reflects the diversity of people who are at risk of cardiac arrest. The PPI group will meet regularly throughout the trial. The group will support the development of patient and public facing information, advise on the strategy for approaching / informing patients about their participation in the trial, and advise on how we use information collected about people. The group will support development of a communication strategy (including social media), and support the dissemination of information to the public both during and at the end of the trial.

### **Intervention Type**

Procedure/Surgery

### **Primary outcome measure**

Survival at 30 days following randomisation measured using patient records

### **Secondary outcome measures**

Measured using patient records unless specified:

1. Return of spontaneous circulation and time to return of spontaneous circulation at any time following randomisation
2. Survived event (sustained return of spontaneous circulation) (yes/no) at hospital handover
3. Survival at hospital discharge, 3 and 6 months following randomisation
4. Neurological function (measured by modified Rankin Scale) at hospital discharge, 3 and 6 months following randomisation
5. Health related quality of life (measured by EQ-5D-5L) at 3 and 6 months following randomisation
6. Hospital length of stay
7. Critical care length of stay

### **Overall study start date**

01/05/2021

### **Completion date**

01/09/2025

## **Eligibility**

### **Key inclusion criteria**

1. Out-of-hospital cardiac arrest currently receiving cardiopulmonary resuscitation
2. Requirement for vascular access to administer cardiac arrest drugs

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

Patient

### **Age group**

Adult

### **Lower age limit**

18 Years

**Sex**

Both

**Target number of participants**

Planned Sample Size: 15,000; UK Sample Size: 15,000

**Key exclusion criteria**

1. Children (known or appear to be <18 years)
2. Known or apparent pregnancy
3. Already have vascular access

**Date of first enrolment**

12/11/2021

**Date of final enrolment**

01/07/2024

**Locations**

**Countries of recruitment**

England

United Kingdom

Wales

**Study participating centre**

**West Midlands Ambulance Service NHS Foundation Trust**

Trust Headquarters  
Millennium Point  
Waterfront Business Park  
Waterfront Way  
Brierley Hill  
West Midlands  
United Kingdom  
DY5 1LX

**Study participating centre**

**North East Ambulance Service NHS Foundation Trust**

Ambulance Headquarters  
Bernicia House  
Goldcrest Way  
Newburn Riverside

Newcastle upon Tyne  
United Kingdom  
NE15 8NY

**Study participating centre**  
**London Ambulance Service NHS Trust**  
Headquarters: Waterloo  
220 Waterloo Road  
London  
United Kingdom  
SE1 8SD

**Study participating centre**  
**Welsh Ambulance Services NHS Trust**  
Unit 7  
Ffordd Richard Davies  
St Asaph Business Park  
St. Asaph  
United Kingdom  
LL17 0LJ

**Study participating centre**  
**South Central Ambulance Service NHS Foundation Trust**  
7-8 Talisman Road  
Bicester  
United Kingdom  
OX26 6HR

**Study participating centre**  
**North West Ambulance Service NHS Foundation Trust**  
Ladybridge Hall HQ  
Chorley New Road  
Bolton  
United Kingdom  
BL1 5DD

**Study participating centre**  
**East Midlands Ambulance Service NHS Trust**  
Trust Headquarters  
Mellors Way  
Nottingham Business Park



Nottingham  
United Kingdom  
NG8 6PY

**Study participating centre**

**South Western Ambulance Service NHS Foundation Trust**

Westcountry House  
Abbey Court  
Eagle Way  
Sowton Industrial Estate  
Exeter  
United Kingdom  
EX2 7HY

**Study participating centre**

**South East Coast Ambulance Service NHS Foundation Trust**

Nexus House  
4 Gatwick Road  
Crawley  
United Kingdom  
RH10 9BG

**Study participating centre**

**East of England Ambulance Service NHS Trust Headquarters**

Whiting Way  
Melbourn  
United Kingdom  
SG8 6EN

**Study participating centre**

**Devon Air Ambulance - Sandpiper Court**

Unit 5  
Sandpiper Court  
Harrington Lane  
Exeter  
United Kingdom  
EX4 8NS

**Sponsor information**

**Organisation**

University of Warwick

**Sponsor details**

Research and impact services, University House  
Kirby Corner Road  
Coventry  
England  
United Kingdom  
CV4 8UW  
+44 (0)24 765 75733  
sponsorship@warwick.ac.uk

**Sponsor type**

University/education

**Website**

<http://www2.warwick.ac.uk/>

**ROR**

<https://ror.org/01a77tt86>

**Funder(s)****Funder type**

Government

**Funder Name**

NIHR Evaluation, Trials and Studies Co-ordinating Centre (NETSCC); Grant Codes: NIHR131105

**Funder Name**

National Institute for Health Research (NIHR) (UK)

**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

Planned publication in a high-impact peer-reviewed journal.

## Intention to publish date

01/09/2025

## Individual participant data (IPD) sharing plan

The datasets generated during and/or analysed during the current study are available from the corresponding author on reasonable request  
paramedic3@warwick.ac.uk

## IPD sharing plan summary

Available on request

## Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
<a href="#">HRA research summary</a>			28/06/2023	No	No
<a href="#">Protocol article</a>		30/12/2023	24/01/2024	Yes	No
<a href="#">Results article</a>		31/10/2024	01/11/2024	Yes	No