Health Research Authority

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22 July 2021

Professor Gavin Perkins,
University of Warwick
Gibbet Hill Road
Coventry
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Dear Professor Perkins,

Application title:	**PARAMEDIC 3 - Pre-hospitAl RAndomised trial of MEDICation route in out-of-hospital cardiac arrest**
CAG reference:	**20/CAG/0092**
IRAS project ID:	**298182**
REC reference:	**21/SC/0178**

Thank you for submitting a **research** application under Regulation 5 of the Health Service (Control of Patient Information) Regulations 2002 ('section 251 support') to process confidential patient information without consent.

Supported applications allow the controller(s) of the relevant data sources, if they wish, to provide specified information to the applicant for the purposes of the relevant activity without being in breach of the common law duty of confidence. Support provides a lawful basis to allow the information to be processed by the relevant parties for the specified purposes without incurring a breach of the common law duty of confidence only. Applicants must ensure the activity remains fully compliant with all other relevant legislation.

The role of the Confidentiality Advisory Group (CAG) is to review applications submitted under these Regulations and to provide advice to the Health Research Authority on whether application activity should be supported, and if so, any relevant conditions. This application was considered at the CAG meeting held on 08 July 2021.

Health Research Authority decision

The Health Research Authority, having considered the advice from the Confidentiality Advisory Group as set out below, has determined the following:

1. The application, to allow the research paramedics from Warwick CTU to process confidential patient information for patients who are enrolled into PARAMEDIC-3 by treating paramedics, and who do not survive until either consent or a consultee opinion can be sought, or who survive but for whom a consultee

opinion cannot be sought, and support for the disclosure of confidential patient information from Warwick CTU to NHS Digital, the Out-of-hospital cardiac arrest outcome registry, the Intensive Care National Audit and Research Centre (ICNARC), the Patient Episode Database for Wales (PEDW), the National Institute for Cardiovascular Outcomes Research (NICOR), ONS mortality data, GP records, the UK Transplant Registry (UKTR) and Health Data Research UK (HDR UK), and the return of linked datasets to the Warwick CTU, is conditionally supported, subject to compliance with the standard and specific conditions of support.

Context

Purpose of application

This application from the University of Warwick sets out the purpose of medical research that seeks to determine whether giving drugs through a vein or into the bone improves survival at 30-days in adults that have an out-of-hospital cardiac arrest.

Cardiac arrest is an important health condition. Each year NHS ambulance services treat 30,000 patients who have experienced an out-of-hospital cardiac arrest (OHCA). Survival is poor, with less than 10% of patients surviving to hospital discharge. The main treatments for cardiac arrest are chest compressions, defibrillation, artificial ventilations and drug treatments. The results of the previous PARAMEDIC-2 trial, conducted by the same applicants, had shown that drug treatments are effective at restarting the heart. However, in the PARAMEDIC-2 trial, the drug treatments were given 21 minutes after the cardiac arrest, on average. This delay likely influenced the effectiveness of the treatment. The statistical analysis from that study showed that, for every one-minute reduction in the time taken to give treatment, survival increased by 0.7%. Currently, guidelines advise that paramedics administer drugs into a vein, referred to as intravenous (IV) route. It can take several minutes to insert a drip into a vein. If paramedics are unable to insert the drip after two attempts, then an alternative form of vascular access, intraosseous route (IO) may be used. IO is a faster way of giving drugs, which involves the insertion of a small needed into an arm or leg bone, and allows drugs to be injected directly into the rich blood supply found in the bone marrow. It is currently unknown whether use of IO access, rather than IV access, as a first attempt would allow vascular access to be obtained more quickly and, consequently, improve survival. Data from research audits has found that use of the IO route has doubled between 2014 and 2018 and the London Ambulance Service reported that the amount of money spend on IO equipment has doubled over a two-year period, which provides evidence of a change in clinical practice in the absence of evidence. The International Liaison Committee on Resuscitation (ILCOR) have conducted a systematic route in which they evaluated the current studies on IO and IV routes for administering drugs, and concluded that there is insufficient evidence to support the routine use of IO access and highlighted the need for a randomised controlled trial to determine the most effective approach.

Patients that sustain an out-of-hospital cardiac arrest will be enrolled into the trial by the treating ambulance clinician. On arrival at the scene, the treating ambulance clinician will assess patient eligibility and, where appropriate, randomise the patient to receive either IO (the intervention arm) or IV (the control arm) as a first strategy. For patients randomised to the intervention group, initial vascular access attempts will be via the IO route and two attempts at vascular access will be made. Once IO vascular access has been successfully achieved, cardiac arrest drugs (including fluid) will be administered through the IO cannula. 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. In

patients randomised to the control group, initial vascular access attempts will be via the intravenous route and the usual NHS guidelines will be followed. The treating paramedics will inform the treating hospital that the patient has been recruited into PARAMEDIC-3 on the patient report form, routinely used by ambulance services to record the treatment received from the ambulance service. The ambulance service NHS trust research team will also be informed via the patient report form or other secure communication method, such as telephone call or secure email. Once the research paramedic is aware of the recruitment, they will enter the patient's information on to the secure Warwick CTU database.

Information about patients' cardiac arrest and hospital stay will be collected from patients' records by research paramedics and from other data linkage sources. Long-term follow up will be conducted at 3 and 6 months following randomisation, to investigate how patients recover from their cardiac arrest. Survival status will be obtained from NHS Digital or other electronic data sources. Quality of life questionnaires will be posted by the research paramedics to the patient for completion at 3 and 6 months, and patients will be asked to return these to the Warwick CTU. Alternatively, if the research paramedic completed the follow up questionnaire with the patient over the telephone or in person, the research paramedic will enter the participant's responses directly on to the CTU database. These questionnaires may be completed on the participant's behalf by someone that has a good awareness of their health state.

All patients will be unconscious at the time of treatment, therefore patients will be recruited under a deferred consent model, in accordance with the Mental Capacity Act 2005. The applicants are seeking support to process confidential patient information for all patients from the end of the emergency event until patient death or until either patient consent or a consultee opinion is obtained. For non-survivors, support is needed for the collection of confidential patient information from the treating hospital and linkage to other data sources. For surviving patients, confidential patient information will be collected until either the patient or a consultee explicitly refuses agreement to the processing of their confidential patient information. If the patient survives but the researchers are unable to contact the patient or a consultee to seek consent, support will also be needed to continue to collect confidential patient information and link to other data sources.

Confidential patient information will also be disclosed from the Warwick CTU to NHS Digital, the Out-of-hospital cardiac arrest outcome registry, the Intensive Care National Audit and Research Centre (ICNARC), the Patient Episode Database for Wales (PEDW), the National Institute for Cardiovascular Outcomes Research (NICOR), ONS mortality data, GP records, the UK Transplant Registry (UKTR) and Health Data Research UK (HDR UK).

A recommendation for class 1, 2, 4 and 6 support was requested to cover access to the relevant unconsented activities as described in the application.

Confidential patient information requested

The following sets out a summary of the specified cohort, listed data sources and key identifiers. Where applicable, full datasets and data flows are provided in the application form and relevant supporting documentation as this letter represents only a summary of the full detail.

Cohort	Male and female patients aged 18 years and over who have experienced an out of hospital cardiac arrest.

	15,000 patients will be included, recruited on a 1:1 ratio between control and intervention.
Data sources	1. Participating NHS hospital trusts – to be confirmed 2. Participating NHS ambulance trusts: a. North East Ambulance Service NHS Foundation Trust b. North West Ambulance Service NHS Trust c. West Midlands Ambulance Service University NHS Foundation Trust d. East Midlands Ambulance Service NHS Trust e. South Western Ambulance Service NHS Foundation Trust f. South Central Ambulance Service NHS Foundation Trust g. South East Coast Ambulance Service NHS Foundation Trust h. London Ambulance Service NHS Trust i. East of England Ambulance Service NHS Trust j. Welsh Ambulance Services NHS Trust k. Potentially the Yorkshire Ambulance Service NHS Trust (participation to be confirmed). 3. HES and Mortality datasets at NHS Digital 4. Out-of-hospital cardiac arrest outcome registry, held by the University of Warwick 5. Intensive Care National Audit and Research Centre (ICNARC) 6. Patient Episode Database for Wales (PEDW) 7. National Institute for Cardiovascular Outcomes Research (NICOR) 8. ONS mortality data 9. GP records 10. UK Transplant Registry (UKTR) 11. Health Data Research UK (HDR UK)
Identifiers required for linkage purposes	1. Name 2. NHS Number 3. Date of birth 4. Date of death 5. Postcode – unit level 6. Ethnicity
Identifiers required for analysis purposes	1. Date of birth 2. Date of death 3. Postcode – unit level 4. Gender 5. Ethnicity

Confidentiality Advisory Group advice

The following sets out the Confidentiality Advisory Group advice which formed the basis of the decision by the Health Research Authority.

Public interest

The CAG noted that this activity fell within the definition of medical research and was therefore assured that the application described an appropriate medical purpose within the remit of the section 251 of the NHS Act 2006. The CAG was satisfied that the project was in the public interest.

Practicable alternatives

Members considered whether a practicable alternative to the disclosure of confidential patient information without consent existed in accordance with Section 251 (4) of the NHS Act 2006, taking into account the cost and technology available.

- Feasibility of consent

The applicants noted the difficulty in consenting patients prior to enrolment or at enrolment, due to the nature of OHCA. Patients are likely to be unconscious or otherwise unable to consent and it is likely that, should a potential consultee be in attendance, they will be too distressed to be approached for consent. Also, patients must receive treatment as soon as possible. Consent, or a consultee opinion, will be sought as soon as practical. The CAG noted that an emergency research model under the Mental Capacity Act 2005 will be used. Under this process, treatment under this study may be started prior to either consent from the participant or a consultee declaration under the Mental Capacity Act given the emergency nature. REC have a specific remit to approve studies using this design and, at the time of the CAG review, the REC had issued a Provisional Opinion.

- Use of anonymised/pseudonymised data

Confidential patient information is needed to conduct patient-level data linkage of data collected from participating ambulance services to NHS Digital, the Out-of-hospital cardiac arrest outcome registry, the Intensive Care National Audit and Research Centre (ICNARC), the Patient Episode Database for Wales (PEDW), the National Institute for Cardiovascular Outcomes Research (NICOR), ONS mortality data, GP records, the UK Transplant Registry (UKTR) and Health Data Research UK (HDR UK), and the return of linked datasets to the Warwick CTU. The CAG accepted that the research could not be undertaken in any other way.

'Patient Notification' and mechanism for managing dissent

It is part of the CAG responsibility to support public confidence and transparency in the appropriate sharing and use of confidential patient information. Access to patient information without consent is a privilege and it is a general principle of support for reasonable measures to be taken to inform the relevant population of the activity and to provide a right to objection and mechanism to respect that objection, where appropriate. This is known as 'patient notification'. This is separate to the local obligation to comply with the principles of the General Data Protection Regulation and Data Protection Act 2018.

The applicants refer to "passive methods" of making relatives aware of this trial, but the materials were not provided with the initial application. Following queries from the CAT, the applicant explained that a patient notification strategy had been devised in collaboration with the study's Patient and Public Involvement panel. Information about the study would be made available in the public domain. This would include posters,

NHS communications, and a trial website, which was in development. The poster was provided for review.

For survivors, ambulance service researchers will, wherever possible, approach the participant and invite them to participate in the follow-up part of the trial. The participant information sheet details the activities being undertaken, the purpose of these activities, and how the individual might opt-out.

In the case of cardiac arrest non-survivors, the passive information strategy relies on placing information in the public domain, as outlined above. This strategy will provide relatives with the opportunity to seek further information at a time when they are ready if this is desired. The applicants will place information in locations where individuals may visit following the death of a relative, including, where possible, emergency department waiting rooms and register offices.

The applicants advised that the National Data Opt-Out will be applied.

Patient and Public Involvement and Engagement

Meaningful engagement with patients, service users and the public is considered to be an important factor for the CAG in terms of contributing to public interest considerations as to whether the unconsented activity should go ahead.

The applicant explained that they had worked closely with patients and members of the public when designing the trial, including discussions with their PPI co-applicant and presentation. The trial has also been presented to the Clinical Research Ambassador Group at University Hospitals Birmingham NHS Foundation Trust. The applicants will follow the INVOLVE best practice guidance to embed meaningful patient and public involvement throughout the project. A PPI group, with membership chosen to reflect the diversity of people at risk of cardiac arrest, will be convened at the start of the trial. This group will meet regularly throughout the trial. Two PPI members will also be included as independent members of the Trial Steering Committee, who will be responsible for oversight of the trial and advising the Sponsor and Funder in accordance with the NIHR terms of reference.

The applicants will adopt the same approach as used in the PARAMEDIC-2 study model. Significant input and agreement from patient, public and service user representatives had been included in the design of this model. For this new trial, the applicants have explored the acceptability of the approach at the first meeting of the Patient Public Involvement panel. This panel is comprised of six members, who have a range of back grounds and experiences, including those who have survived cardiac arrest, those with experience of critical illness and others with experience through family members. The panel were supportive of the approach. The panel cautioned against the use of leaflets as their recent experience was that few places allow leaflets to be left out due to COVID restrictions, and that the poster was adequate to provide the relevant information.

The CAG noted the patient and public involvement undertaken and recommended that the scope was broadened to include families of those who had suffered cardiac arrest and to explore their views on the issue.

Confidentiality Advisory Group advice conclusion

The CAG agreed that the minimum criteria under the Regulations appeared to have been met, and therefore advised recommending support to the Health Research

Authority, subject to compliance with the specific and standard conditions of support as set out below.

Specific conditions of support

1. Further patient and public involvement is to be undertaken while the study is ongoing. This further involvement is to include the families of those who had suffered cardiac arrest and to explore their views on the issue. Feedback is to be provided at the first annual review.

2. Favourable opinion from a Research Ethics Committee. **Confirmed 12 July 2021**

3. Confirmation provided from the IG Delivery Team at NHS Digital to the CAG that the relevant Data Security and Protection Toolkit (DSPT) submission(s) has achieved the 'Standards Met' threshold. See section below titled 'security assurance requirements' for further information.

    - **The NHS Digital DSPT review for University of Warwick Clinical Trials Unit for 2019/20 was confirmed as 'Standards Met' on the NHS DSPT Tracker (checked 12 July 2021).**

As the above conditions have been accepted or met, this letter provides confirmation of final support. I will arrange for the register of approved applications on the HRA website to be updated with this information.

Application maintenance

Annual review

Please note that this legal support is subject to submission of an annual review report, for the duration of support, to show that the minimal amount of patient information is being processed and support is still necessary, how you have met the conditions or report plans, any public benefits that have arisen and action towards meeting them. It is also your responsibility to submit this report every 12 months for the entire duration that confidential patient information is being processed without consent.

The next annual review should be provided no later than **22 July 2022** and preferably 4 weeks before this date. Reminders are not issued so please ensure this is provided annually to avoid jeopardising the status of the support. Submission of an annual review in line with this schedule remains necessary even where there has been a delay to the commencement of the supported activity, or a halt in data processing. Please ensure you review the HRA website to ensure you are completing the most up to date 'section 251' annual review form as these may change.

For an annual review to be valid, there must also be evidence that the relevant DSPT submission(s) for organisations processing confidential patient information without consent are in place and have been reviewed by NHS Digital. Please plan to contact NHS Digital in advance of the CAG annual review submission date to check they have reviewed the relevant DSPTs and have confirmed these are satisfactory.

Register of Approved Applications

All supported applications to process confidential patient information without consent are listed in the published 'Register of Approved Applications'. It is a statutory requirement for the Register to be published and it is available on the CAG section of the Health Research Authority website. It contains applicant contact details, a summary of the research and other pertinent points.

This Register is used by controllers to check whether support is in place.

Changes to the application

The application and relevant documents set out the scope of the support which is in place for the application activity and any relevant restrictions around this.

Any amendments which are made to the scope of this support, including but not limited to, purpose, data flows, data sources, items of confidential patient information and processors, require submission of a formal amendment to the application. Changes to processors will require evidence of satisfactory DSPT submission. The amendment form can be found in the Confidentiality Advisory Group pages on the Health Research Authority website.

Support for any submitted amendment would not come into effect until a positive outcome letter has been issued.

Changes to the controller

Amendments which involve a change to the named controller for the application activity require the submission of a new and signed CAG application form and supporting documentation to support the application amendment. This is necessary to ensure that the application held on file appropriately reflects the organisation taking responsibility for the manner and purpose of data processing within the application, and that the legal support in place is related to the correct legal entity.

Applicants are advised to make contact with the Confidentiality Advice Team to discuss a change in controllership for an existing application in sufficient time ahead of the transfer of project responsibility to discuss the submission process timings.

Further information and relevant forms to amend the support is available on the HRA website.

Reviewed documents

The documents reviewed at the meeting are as follows.

Document	*Version*	*Date*
CAG application from (signed/authorised) [CAG_Form_ReadyForSubmission_Revised_24June21]		
Covering letter on headed paper [PARAMEDIC3_CAGCoverLetter_v1.0_27May21]	1.0	27 May 2021
Data Protection Registration [Information Commissioners - Data protection register - University of Warwick]		
Other [P3_DataFlowMap_v4.0_28June21]	4.0	28 June 2021
Other [P3_legal basis for processing data_v1_280621]	1	28 June 2021
Patient Information Materials [PARAMEDIC3_CoverLetterConsInHospital_v1.0_06May21]	1.0	06 May 2021

Patient Information Materials [PARAMEDIC3_CoverLetterPatPostDischarge_v1.0_06May21]	1.0	06 May 2021
Patient Information Materials [PARAMEDIC3_PIS_v1.0_10May21]	1.0	10 May 2021
Patient Information Materials [PARAMEDIC3_Protocol_v1.0_11May21]	1.0	11 May 2021
Patient Information Materials [P3_A4Poster_v1.0_22June21]	1.0	22 June 2021
Written recommendation from Caldicott Guardian (or equivalent) of applicant's organisation [00001561 - PARAMEDIC-3 CAG Support Letter 24.6.21]		24 June 2021

Membership of the Committee

The members of the Confidentiality Advisory Group who were present at the consideration of this item are listed below.

Professor Jenny Kurinczuk advised that she had a conflict of interest, as the application had been submitted from the institution she works in. Professor Kurinczuk left the room for the duration of the discussion.

Yours sincerely

Kathleen Cassidy
Confidentiality Advisor

On behalf of the Health Research Authority

Email: cag@hra.nhs.uk

Included: List of members who considered application
Standard conditions of support

Copy to: oxfordc.rec@hra.nhs.uk

Confidentiality Advisory Group meeting attendance
08 July 2021

Members present:

Name	
Dr Tony Calland MBE	CAG Chair
Dr Patrick Coyle	CAG Vice-Chair
Dr Sandra Duggan	CAG member
Professor Barry Evans	CAG member
Dr Rachel Knowles	CAG member
Dr Simon Kolstoe	CAG member
Mr Andrew Melville	CAG member
Professor Sara Randall	CAG member
Mr Marc Taylor	CAG member

Also in attendance:

Name	*Position (or reason for attending)*
Ms Katy Cassidy	HRA Confidentiality Advisor
Ms Caroline Watchurst	HRA Confidentiality Advisor
Ms Emma Marshall	HRA Confidentiality Specialist
Dr Paul Mills	HRA Confidentiality Advice Service Manager

Standard conditions of support

Support to process the specified confidential patient information without consent, given by the Health Research Authority, is subject to compliance with the following standard conditions of support.

The applicant and those processing the information under the terms of the support will ensure that:

1. The specified confidential patient information is only used for the purpose(s) set out in the application.

2. Confidentiality is preserved and there are no disclosures of information in aggregate or patient level form that may inferentially identify a person, nor will any attempt be made to identify individuals, households or organisations in the data.

3. Requirements of the Statistics and Registration Services Act 2007 are adhered to regarding publication when relevant, in addition to other national guidance.

4. All staff with access to confidential patient information have contractual obligations of confidentiality, enforceable through disciplinary procedures.

5. All staff with access to confidential patient information have received appropriate ongoing training to ensure they are aware of their responsibilities and are acting in compliance with the application detail.

6. Activities must be compliant with the General Data Protection Regulation and relevant Data Protection Act 2018.

7. Audit of data processing by a designated agent is facilitated and supported.

8. The wishes of patients who have withheld or withdrawn their consent are respected.

9. Any significant changes (for example, people, purpose, data flows, data items, security arrangements) must be approved via formal amendment prior to changes coming into effect.

10. An annual review report is submitted to the CAG every 12 months from the date of the final support letter, for the duration of the support.

11. Any breaches of confidentiality around the supported flows of information should be reported to CAG within 10 working days of the incident, along with remedial actions taken/to be taken. This does not remove the need to follow national/legal requirements for reporting relevant security breaches.