Incidence and Outcomes of in-Hospital Cardiac Arrest and Cardiopulmonary Resuscitation in The Kidney Replacement Therapy Population: A linked national disease registry study protocol

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Abstract

Background: Background
Every patient receiving kidney replacement therapy (KRT) i.e. haemodialysis, peritoneal dialysis or a kidney transplant, should have an advanced treatment escalation plan. This should include a decision on cardiopulmonary resuscitation (CPR) status.

The existing literature suggests KRT recipients who undergo in-hospital CPR have outcomes similar to the general population. However, these data originate exclusively from North America and Taiwan, do not include transplant recipients, and neurological outcomes are poorly reported. This paucity of evidence is preventing KRT recipients, their families and care providers from having informed discussions on their CPR status. It also leaves KRT recipients vulnerable to false assumptions of poor suitability for CPR.

Objective: Our primary objective is to calculate the incidence and survival rates of in-hospital CPR in the KRT population in England over a 10-year period (2012-2022). Further, we aim to compare the characteristics of survivors vs non-survivors and describe neurological outcomes.

Methods: We will conduct a retrospective cohort study of patients receiving KRT aged ?28 days in England that underwent in-hospital CPR between 2012 and 2022. Individuals receiving KRT will be identified as reported to the UK Renal Registry (UKRR). Case matching will occur between The UKRR and The Intensive Care National Audit & Research Centre (ICNARC) which holds the UK National Cardiac Arrest Audit (NCAA) database.

The annual cumulative incidence of in-hospital CPR events will be ascertained by KRT modality. Survival and neurological outcomes will be reported aligned with international data reporting standards. The characteristics of survivors versus non-survivors and subjects with favourable, versus subjects with non-favourable neurological outcomes, will be compared respectively to identify individual or situational factors that associate with outcomes.

Results: As of July 2025, ethical approval has been granted by The University of Bristol (UoB) Research Ethics Committee. Section 251 support has been granted to allow the processing of confidential information (limited to date of birth, NHS number and date of KRT start) without consent between the UKRR and ICNARC, and date of death only between ICNARC and the UoB researchers. This excludes individuals who have opted out of their data being used for research purposes by the UKRR

Conclusions: By linking registry data this study will provide a whole-of-population approach to describing the incidence and outcomes of in-hospital CPR in the English KRT population. This will better inform patients, their loved ones and care providers

of the likelihood of CPR success.

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Incidence and Outcomes of in-Hospital Cardiac Arrest and Cardiopulmonary Resuscitation in The Kidney Replacement Therapy Population: A linked national disease registry study protocol

Version 1.0

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Robert McLaren: literature review, methodology, manuscript production
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Conflicts of Interest
Nil to declare

Structured Abstract (423/450 words)

Background
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Objectives

Our primary objective is to calculate the incidence and survival rates of in-hospital CPR in the KRT population in England over a 10-year period (2012-2022). Further, we aim to compare the characteristics of survivors vs non-survivors and describe neurological outcomes.

Methods

We will conduct a retrospective cohort study of patients receiving KRT aged ≥28 days in England that underwent in-hospital CPR between 2012 and 2022. Individuals receiving KRT will be identified as reported to the UK Renal Registry (UKRR). Case matching will occur between The UKRR and The Intensive Care National Audit & Research Centre (ICNARC) which holds the UK National Cardiac Arrest Audit (NCAA) database.

The annual cumulative incidence of in-hospital CPR events will be ascertained by KRT modality. Survival and neurological outcomes will be reported aligned with international data reporting standards. The characteristics of survivors versus non-survivors and subjects with favourable, versus subjects with non-favourable neurological outcomes, will be compared respectively to identify individual or situational factors that associate with outcomes.

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Conclusions
By linking registry data this study will provide a whole-of-population approach to describing the

incidence and outcomes of in-hospital CPR in the English KRT population. This will better inform patients, their loved ones and care providers of the likelihood of CPR success.

Strengths:

- Whole-of-population approach: all patients reported to the UKRR as receiving kidney replacement therapy that experienced in-hospital CPR across a national healthcare system (England) over a 10-year period.
- Reliable and specific cardiac arrest outcome data due to linkage with the National Cardiac Arrest Audit
- Patient focussed: study objectives align with patient priorities and address a paucity of information in a crucial aspect of care.

Weaknesses:

- Sample size and extent of missing data unknown due to novel use of respective registries' data.
- Unable to confidently capture cases with kidney failure who are unreported to the UKRR, meaning limited acquisition of outcomes for those with acute kidney injury and others whose kidney failure is treated with conservative kidney management.
- Patients who have opted out of their data being used for research purposes will not be included and they may not be missing at random.

Introduction

Cardiopulmonary resuscitation (CPR) is an emergency intervention to restore cardiac function following a cardiac arrest. It involves manual chest compressions, intravenous medications and, where indicated, defibrillation (1). In the absence of a 'do not attempt resuscitation order (DNACPR)', CPR is usually initiated in the event of witnessed cardiac arrest (2). Some patients may decide upon a DNACPR due to the burden of multiple medical conditions and the potential for diminished quality of life and limited functional ability after successful resuscitation (3). For patients and their care providers to make informed decisions regarding DNACPR status, data relating to the likely outcomes following resuscitation are needed.

In the United Kingdom (UK) the survival to discharge rate following in-hospital cardiac arrest is 24% (4) meaning 76% of those who receive CPR either do not experience a return of spontaneous circulation, or do, but die before leaving hospital. Approximately 80% of survivors have a 'favourable' neurological function, defined by the cerebral performance category (CPC) grade one or two. This encompasses normal to moderate cerebral dysfunction, compatible with at least part-time work in a sheltered environment and independent activities of daily life (Figure 2)(4). The 20% with 'unfavourable' outcomes are dependent upon others for daily support. Survival following CPR is associated with significant psychological trauma and can be associated with memory loss and severe musculoskeletal injury (5).

Historically, individuals receiving kidney replacement therapy (KRT) i.e. haemodialysis, peritoneal dialysis or a kidney transplant, have been depicted as poor candidates for CPR (5). This group are known to be at high risk of cardiac arrest (6) and may experience unique risk factors. Examples include end-organ damage secondary to diabetes mellitus, hyperkalaemia and hypervolaemia due to end stage kidney disease, and intradialytic fluid shifts and changes in serum electrolyte levels that occur during dialysis (7,8). However, some of these aetiologies are reversible causes of cardiac arrest, which may mean that those with kidney failure are simultaneously at high risk for cardiac arrest, and – in some circumstances – favourable CPR outcomes (7,8)

Our systematic literature review found that survival to discharge from hospital after in-hospital or in-dialysis unit CPR amongst patients receiving KRT was 18-30% (9). These outcomes are broadly comparable with those of the general inpatient population. A recent systematic review of CPR amongst haemodialysis recipients confirmed the association between dialysis sessions and cardiac arrest, and found favourable outcomes, with 30% surviving to hospital discharge – likely due to early CPR and the presence of shockable dysrhythmias (6). In our systematic review, standardised neurological outcomes were only reported in two studies and kidney transplant recipients were not represented (10) . None of the included studies differentiated between individuals receiving acute and chronic KRT, nor time since KRT initiation, despite the higher rates of death early after KRT initiation (11). The eleven identified studies were conducted in the United States of America, Canada and Taiwan. Regarding CPR outcomes, these data must be understood in the light of the population at risk and the practices surrounding CPR decision-making, both likely to vary between countries.

The limited geographical range of data, paucity of neurological outcome reporting, and heterogeneity of survival outcome measures leaves a substantial knowledge gap. More comprehensive and international data describing the survival and functional outcomes for people with kidney failure who receive CPR will inform patients and their care providers making treatment escalation plans. We present a protocol for a retrospective observational cohort study which aims to describe the incidence and outcomes following in-hospital CPR in the English KRT population. Our

objectives are to:

1. Determine the annual incidence of in hospital cardiac arrest treated with CPR in the prevalent English KRT population.
2. Determine the cumulative incidence of in hospital cardiac arrest treated with CPR in the incident English KRT population.
3. Calculate the probability of survival following in hospital cardiac arrest treated with CPR at pre-determined time points: return of spontaneous circulation (ROSC), survival to 30 days, discharge from hospital, or survival to 1 year. adjusted for confounders determined a priori using multivariable logistic regression, at each of these time points. The characteristics of survivors and non-survivors of in-hospital CPR at the aforementioned time points will also be described.
4. Determine the CPC at discharge of KRT recipients who survived in hospital CPR, comparing the characteristics of those who had 'favourable' neurological outcome (CPC 1 or 2) versus those who did not (CPC 3-5).

Methods

Overview

This protocol outlines a retrospective observational cohort study of in-hospital cardiac arrest in the English KRT population from 2012-2022. This will be facilitated by a one-off data linkage between two UK-based registries, the UK Renal Registry (UKRR) and the Intensive Care National Audit & Research Centre (ICNARC), which holds the National Cardiac Arrest Audit (NCAA) database.

Datasets for linkage

UKRR is the UK Kidney Association's (UKKA) registry of people receiving nephrology specialist care (12). It receives data from NHS kidney services in England, Wales and Northern Ireland, which are mandated to provide information regarding all individuals receiving acute or chronic KRT, under their care. Since nearly all KRT is provided by NHS centres in England, the UKRR is believed to have almost complete coverage of individuals receiving long-term KRT for kidney failure.

NCAA is the national clinical audit of in-hospital cardiac arrests in the UK. It holds data on cardiac arrests attended to by in-hospital resuscitation teams for all individuals aged ≥28 days (13). Criteria for inclusion is "any resuscitation event, commencing in-hospital, where an individual (excluding neonates) receives chest compression(s) and/or defibrillation and is attended by the hospital-based resuscitation team (or equivalent) in response to a 2222 call"(14). Current coverage is approximately 93% of acute hospitals in England (15).

Data linkage process

Case-matching between the two registries will be conducted through exchange of encrypted NHS numbers, dates of birth and date of commencing KRT. Step 1: The UKRR will provide ICNARC with a list of encrypted NHS numbers, dates of birth, date of commencing KRT, plus a randomly generated study-ID for the population receiving KRT between 2012-2022. Step 2: Using a corresponding encryption/decryption key, ICNARC will identify individuals also present in their NCAA database. The encrypting will be irreversible (one-way) hashing as this will allow for the linkage to happen and

leave the output data securely pseudonymised. Step 3: For individuals who are matched, a secure platform will be used to send the requested data fields, uniquely identified by the encrypted NHS numbers, with the study-ID number to the University of Bristol researchers. Step 4: The UKRR will also send the corresponding requested data fields of the prevalent kidney replacement therapy population to the University of Bristol researchers with the study-ID number but not the encrypted NHS number or full date of birth to allow linkage to the NCAA dataset. This method will ensure that at no point does the encrypted NHS number or full date of birth flow with clinical data and that the University of Bristol Researchers do not have access to the encrypted NHS number or full date of birth (month/year only).

The data will be securely stored within the University of Bristol, with access to the physical server will be restricted to IT services and Security staff employed by the University. University of Bristol researchers will not have access to identifiable information of included or excluded individuals, except for the date of death. The data flow is summarised in Figure 1. The total number of patients in the English KRT cohort who receive in-hospital CPR is unknown and will be an output of this work.

Study Population

Eligible cases will be individuals ≥28 days old i) reported to the UKRR by an English kidney centre, ii) as having received KRT in the form of acute or chronic dialysis (haemodialysis or peritoneal), or a kidney transplant, iii) who underwent in-hospital CPR for cardiac arrest between Jan 1st 2012 and Dec 31st 2022. Acute and chronic dialysis will be defined as per the UKRR (16).

Objective 1 – Annual incidence of in-hospital CPR in the prevalent KRT population

The annual incidence of in-hospital CPR will be calculated as the number of recorded in-hospital CPR events within the annual cohort of prevalent dialysis and kidney transplant recipients, expressed as CPR events per 1,000 KRT recipients per annum between 2012 to 2023. The size of the prevalent population will be calculated on 31st December of every year. Incidence will be expressed within clinicodemographic strata, including age, sex, and KRT modality.

Objective 2 – Cumulative incidence of in-hospital CPR in incident KRT population

Cumulative incidence of in-hospital CPR events per 1,000 incident KRT recipients will be calculated as the number of recorded in hospital CPR events for either incident dialysis or incident kidney transplant recipients. The day of commencing KRT (either dialysis or transplantation) will be the starting point, and individuals will be followed up to the point of either the outcome of interest (first CPR) or censored for a change of modality i.e., to kidney transplantation or dialysis respectively, death or end of the follow-up period set at 31-12-2023 or loss to follow-up. The cumulative incidence will be adjusted for confounders which have been determined a priori i.e., age, sex, primary kidney disease, diabetes status.

Objective 3 – Survival following in-hospital CPR in the prevalent KRT population

For all survival analysis, the date of first CPR event will be the start date. Individuals will be followed until the event of interest i.e., ROSC, survival to 30 days, survival to discharge, survival to 1 year or censored for death or loss to follow up. If more than one CPR event occurs within a single hospital admission only the first CPR event will be considered. Further CPR events occurring in subsequent admissions for the same individuals will be treated as separate events. We will include a random intercept in the generalised linear mixed model, using a binomial distribution, to account for the

dependency of these subsequent admissions and CPR events.

The characteristics of individuals who survived to discharge from hospital will be compared with those of individuals who did not. Continuous variables and categorical variables of survivors and non-survivors will be compared using the Mann-Whitney U test and Chi-squared test, respectively. Crude survival outcomes for those who survived CPR will be determined by drawing Kaplan-Meier curves and calculating the median survival time post CPR. Long-rank test for survival by treatment modality, sex, and age group will be performed.

Multivariable logistic regression will be used to determine the odds of survival to ROSC, 30 days, discharge and 1 year. The output of this model will also be presented by treatment modality, age group, primary renal disease and diabetes. The model will be adjusted by KRT duration, age (when not stratified by age), sex (when not stratified by sex), primary renal disease (when not stratified by primary renal disease), diabetes status (when not stratified by diabetes status) and presenting cardiac rhythm as these are established predictors of CPR survival(17).

Objective 4 – Neurological outcome following in-hospital CPR

Characteristics of those who survived with favourable neurological outcome and those with unfavourable neurological outcomes (defined by a cerebral performance category of 3 or greater i.e., having at least severe disability dependent in activities of daily living) will be presented. Continuous variables and categorical variables will be compared using the Mann-Whitney U test and Chi-squared test respectively.

Multivariable logistic regression will be used to determine the odds of favourable versus non-favourable CPC. Favourable CPC will be defined as a CPC of 1 or 2. CPC 1 is described as good cerebral performance with none/mild neurological or psychiatric deficit, while CPC 2 represents moderate cerebral disability with sufficient cerebral function to allow for independent activities of daily living. The output of this model will also be presented by treatment modality, age group, primary renal disease and diabetes. The model will be adjusted by KRT duration, age (when not stratified by age), sex (when not stratified by sex), primary renal disease (when not stratified by primary renal disease), diabetes status (when not stratified by diabetes status) and presenting cardiac rhythm as these are established predictors of CPR survival.(17)

Outcomes will be presented by unit if sample size allows. Units will only be presented anonymously in any subsequent research output (most likely as funnel plots) which will help to identify centres that outlie expected variation.

Minimising re-Identification risk

Where any strata or cell in the report of these analyses includes fewer than five individuals, the cell will be expressed as 0-5 to reduce the risk of re-identification.

Missing data

If data are found to be missing at random and <30% missing, multiple imputation will be used to impute missing data. If the data are missing not at random, we will only use observed data, and report on the extent of the missing data and the associated limitations.

Ethical approval

Approval was granted on 26th June 2024 by the Health Research Authority South West - Cornwall & Plymouth Research Ethics Committee(18). 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 was made to the Health Research Authority and with support granted on 19th September 2024 (CAG reference: 24/CAG/0087). This support covers the flow of patient identifiable information (i.e., NHS number, date of KRT start and date of birth) from the UKRR to ICNARC and the flow of date of death from ICNARC to the University of Bristol. The UKRR has screened research cohorts against NHS England National Data Opt-Out portal prior to use or transfer of data intended for research purposes and removes any opted-out patients from the cohort. Information regarding this study is available on the UKRR website (https://ukkidney.org/project/incidence-and-outcomes-hospital-cardiac-arrests-united-kingdom-kidney-replacement-therapy)

Patient and public involvement (PPI)

Our study proposal was reviewed and approved by three patient groups; the UKRR's patient group whist reviewing this study proposal, a public panel reviewed our application as part of the local funding process and agreed on the positive impact the project will have on the NHS, and the patient group in the Bristol Kidney Health Integration Team who also agreed on the positive impact this project would have on patient care.

Results

As of July 2025, ethical approval and Section 252 support has been granted. The UKRR have shared with ICNARC the variables required to link to the NCAA database. We now await the data sharing agreement to be approved by out institution to allow data release. A timeline of study progress is presented in Figure 3.

Discussion

This study will describe in-hospital CPR incidence, survival and neurological outcomes for the English KRT population for the first time. This information will directly benefit patients by allowing them, their loved ones and care providers to make evidence-based decisions on CPR status. The findings will provide objective evidence of the suitability of KRT recipients for CPR.

This will be the first study investigating CPR outcomes in this population out with North America and Taiwan. It will also be the first such study to incorporate kidney transplant recipients. The use of a novel setting is key as culture influences DNACPR usage (19,20), and the case mix of individuals

receiving KRT differs across the world(21). This will substantially widen the applicability of the current literature base to European populations.

The strengths of this study include its whole-of-population approach with the use of dedicated data registries. This will allow for accurate identification of eligible patients, as well as thoroughly reported outcome data presented as per internationally accepted Utstein template (22). Further, the study explores an area of healthcare that we have demonstrated is important to patients and could directly impact how they are treated.

The limitations of this study are that sample size and extent of missing data cannot be predicted due to the novel use of linked registry data. The study will be unable to capture cases of kidney failure not reported to the UKRR, therefore excluding individuals who opt for conservative kidney management.

On completion this study, a manuscript will be prepared for submission to a peer reviewed journal. An abstract will also be submitted for presentation at an international conference. A lay article will be prepared for submission to the patient magazine 'Kidney Matters'.

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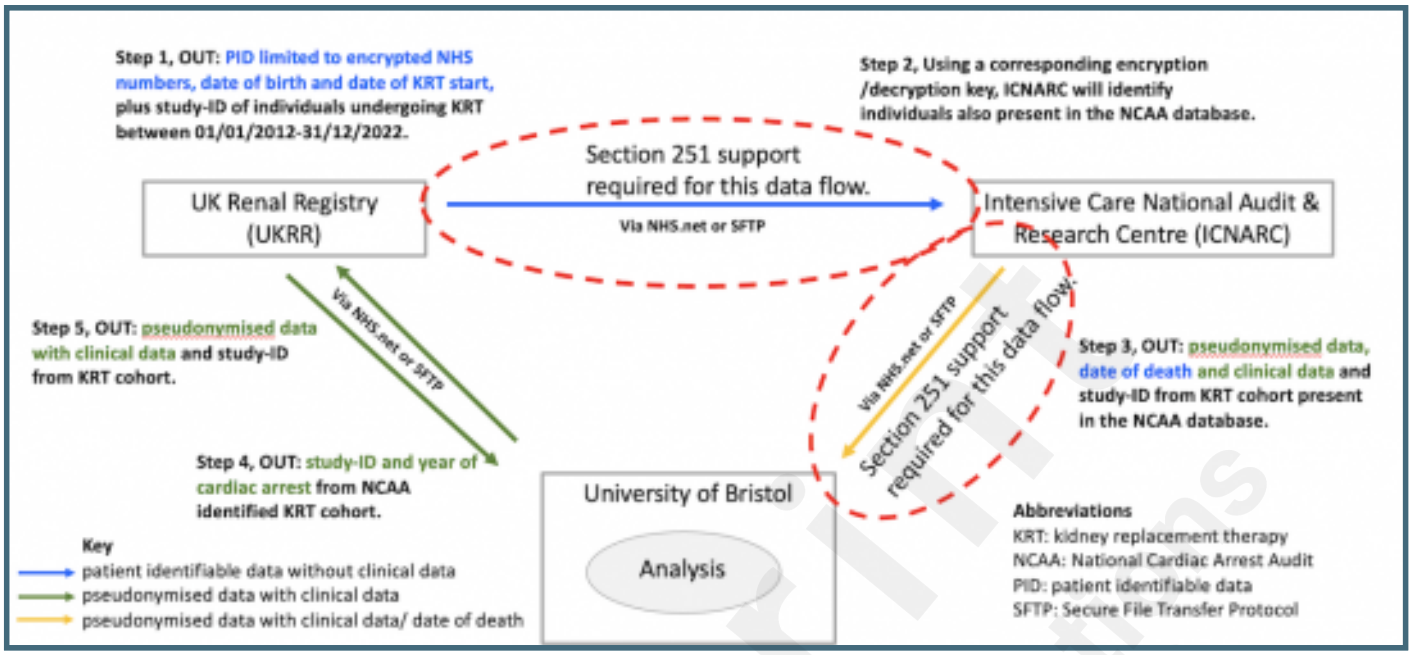
Supplementary Files

Figures

Proposed data flow for the study ‘Incidence and outcomes of in-hospital cardiac arrest in the United Kingdom kidney replacement therapy population.’.



Cerebral Performance category: table presenting the five categories of cerebral performance with attached description. Adapted from (23).

Score	Category	Description	Favourable/unfavourable
1	Normal	Conscious, alert, able to work and lead a normal life May have minor psychologic or neurologic deficits (eg, mild dysphasia, non-incapacitating hemiparesis, minor cranial nerve abnormalities)	Favourable
2	Moderate disability	Conscious, with sufficient cerebral function for part-time work in sheltered environment and independent activities of daily life (eg, dress, travel by public transportation, prepare food) May have hemiplegia, seizures, ataxia, dysarthria, dysphasia, or permanent memory or mental changes	Favourable
3	Severe disability	Conscious, but dependent on others for daily support; has at least limited cognition This category includes a wide range of neurologic dysfunction, from patients who are ambulatory but have severe memory disturbances or dementia that precludes independent existence to those who are paralyzed and can communicate only with their eyes (as in the locked-in syndrome).	Unfavourable
4	Unconscious	Unconscious, unaware of surroundings, no cognition; no verbal or psychologic interaction with environment	Unfavourable
5	Brain death	Meeting criteria for brain death or dead by traditional criteria	Unfavourable

Study Timeline: Table displaying key dates of project progress and expected dates of future progression.

Progress	Achieved or expected completion
Initial Application for registry data	02/2022
Funding acquired	03/2024
Ethical approval granted	06/2024
Section 251 support granted	09/2024
Data transfer to university server	expected 10/2025
Completion of Analysis	Expected 07/2026
Submission of manuscript for peer-reviewed publication	Expected 10/2026