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## Protocol paper

# European Registry of Cardiac Arrest – Study-THREE (EuReCa THREE) – An international, prospective, multi-centre, three-month survey of epidemiology, treatment and outcome of patients with out-of-hospital cardiac arrest in Europe – The study protocol



Jan Wnent<sup>a,b,c,\*</sup>, Siobhan Masterson<sup>d</sup>, Holger Maurer<sup>e</sup>, Ingvild Tjelmeland<sup>a,f,g</sup>, Johan Herlitz<sup>h</sup>, Fernando Rosell Ortiz<sup>i</sup>, Esther Kurbach<sup>a,j</sup>, Leo Bossaert<sup>k,l</sup>, Gavin Perkins<sup>l,m,n</sup>, Jan-Thorsten Gräsner<sup>a,b,l</sup>

### Abstract

**Background:** The aim of the European Registry of Cardiac Arrest (EuReCa) network is to provide high quality evidence on epidemiology of out-of-hospital cardiac arrest (OHCA) in Europe by supporting and developing cardiac arrest registries and performing European-wide studies. To date, the EuReCa ONE and EuReCa TWO studies have involved around 28 countries, with population covered increasing from the first to the second study. The aim of the EuReCa THREE study is to build on previous work and to support the promotion of quality data collection on OHCA throughout Europe.

**Methods/design:** EuReCa THREE will be the third prospective cohort study on epidemiology of OHCA and will involve around 30 European countries. The study will be conducted between 1st September and 30th November 2022. Data will be collected on cardiac arrest cases attended, resuscitation attempted, patient and cardiac arrest event characteristics and outcomes (including return of spontaneous circulation, status on hospital arrival and discharge). A particular focus for EuReCa THREE will be to describe key time intervals in OHCA management; time from call to EMS arrival on scene, time from cardiac arrest to start CPR, time from EMS arrival to delivery of patient to hospital. EuReCa THREE was registered with the German Registry of Clinical Trials Registration Number: DRKS00028591 searchable via WHO meta-registry (<https://apps.who.int/trialsearch/>).

**Discussion:** The EuReCa THREE study will increase our knowledge on longitudinal OHCA epidemiology and provide new knowledge on crucial time intervals in OHCA management in Europe. However, the primary aim of building a network to support quality data on OHCA, remains the central tenant of the EuReCa project.

**Keywords:** Out-of-hospital cardiac arrest, Epidemiology, EuReCa, Survival

## Introduction

The importance of establishing out-of-hospital cardiac arrest (OHCA) registries as a critical step in improving OHCA outcomes is

recognised from clinical, academic and political perspectives.<sup>1–5</sup> The aim of the European Registry of Cardiac Arrest (EuReCa) project is to provide quality benchmarking for OHCA measurement in Europe by building and improving registries. Registries must be based on a standardised data collection following international

\* Corresponding author at: Institute for Emergency Medicine, University Hospital Schleswig-Holstein, Arnold-Heller-Str. 3, Building 808, 24105 Kiel, Germany.

E-mail address: [wnent@reanimationsregister.de](mailto:wnent@reanimationsregister.de) (J. Wnent).

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recommendations, so that variations in OHCA incidence, management and outcomes can be identified.<sup>6,7</sup>

Good quality data are needed to enhance knowledge on OHCA incidence, management and outcomes. To support Emergency Medical Services (EMS) in achieving quality OHCA data collection, the EuReCa project established a collaboration between 27 European countries already in 2014. In the EuReCa ONE study in October 2014, data on OHCA patients were collected, resulting in the most comprehensive estimate of European OHCA incidence and outcomes at the time.<sup>8</sup> To understand variations in OHCA incidence and outcomes, data collected on each link of the Chain of Survival, had to be comparable across participating countries. Ensuring this comparability is one of the main aims of EuReCa. Therefore, after EuReCa ONE, a survey on how the definition of a bystander was interpreted was conducted, and the results were used to further define the concept of a bystander.<sup>9</sup> The extended definition, covering all aspects of resuscitation before EMS arrival, was used in the EuReCa TWO study in addition to the Utstein variables. For EuReCa TWO, the data collection period was increased to three months and 28 countries participated, with many countries also increasing the population covered and improving the overall data quality.<sup>10,11</sup>

The EuReCa studies have shown that collecting high quality data on OHCA across a whole continent is possible. It has also shown that studies of this magnitude can be used to collect information on additional data points, such as data on resuscitation before EMS arrival.<sup>10</sup>

EuReCa THREE is expected to be the largest ever collection of OHCA data in Europe, providing the opportunity to generate more robust estimates of overall OHCA incidence and outcome, including information on specific subgroups. To enhance the key quality requirements of comprehensiveness and reliability, the aims of the EuReCa THREE project will be as follows:

- Expand and consolidate the EuReCa network
- Improve the understanding of how response time and transport time influence return of spontaneous circulation (ROSC) and survival
- Provide an overview of the longitudinal changes from EuReCa ONE and EuReCa TWO
- Continue collecting data on established data-points/items to strengthen the robustness of European data collection.

To achieve these aims, the following objectives will be fulfilled:

- Encourage participating countries to aim for national data collection and encourage additional countries to participate
- To provide robust estimates of incidence, management and outcome, the data collection period will be three months (1st September to 30th November 2022)
- Identify consistency and variation in the measurement of time points and time intervals in connection with response times
- Describe the time intervals of response time and transport time.

## Material and methods

### Study design

*EuReCa THREE is a multi-centre, prospective cohort study*  
**Inclusion criteria.** All patients who have an out of hospital cardiac arrest and are attended by the EMS at any stage during the event are eligible for inclusion. This includes patients who receive resuscitation (chest compression, and/or defibrillation of any type).

- By the EMS
- Before the arrival of the EMS with continued resuscitation by the EMS
- Before the arrival of the EMS, that is immediately stopped (for any reason) when the EMS arrives
- Patients defibrillated before the arrival of the EMS, who achieve ROSC before the arrival of the EMS

Patients will be included irrespective of their age, sex or personal factors. Patients found or declared dead (for any reason) by EMS, even if no CPR was attempted will also be included. Some countries or registries may not be able to provide all necessary data to answer every research question. These registries will not be included in the analysis of the related research questions.

**Timeframe.** This study will include all events that occur between 00:00 on 1st September 2022 and 23:59 on 30th November 2022.

**Participating registries/centres.** All registries throughout Europe, able to provide at least the core data required (see [supplement 1](#)), are invited to participate in this study. For every country there will be one national coordinator who is responsible for all requirements. They may be supported by others within that country at the request of the national coordinator. In order to participate, the national coordinator must provide a written letter of intent to participate in this study, written consent to follow this study protocol and a valid ethical approval (see below) if needed. Should there be more than one registry serving the same region and population, or if there is more than one registry within a country, the national coordinator will be responsible for avoiding multiple submissions of patients' data and is responsible for combining data from different registries within the country. The national coordinator will be required to submit all the data for the whole country.

All participating registries must guarantee the existence of written approval from the EMS organisations they serve, to use and submit data for the EuReCa THREE study. These approvals may follow local policy and do not need to have a specific format but must include terms clearly describing the permission to use and transmit defined data for research purposes on an international basis. The national coordinator is responsible for obtaining this approval.

## Ethical approval

EuReCa THREE was approved by the University of Kiel ethics committee with reference number D422/22 on 14.03.2022, and the study

is registered with the German Registry of Clinical Trials, Registration Number: DRKS00028591 searchable via WHO meta-registry (<https://apps.who.int/trialsearch/>).

If there is a national requirement for ethical approval, this must be sought and obtained by the national coordinators. While ethical approval may not be required data will only be accepted if ethical approval or a documented waiver (stating there is no requirement for ethical approval) is provided by the national coordinator. As only anonymised data will be reported, and the data is recorded as part of routine care, a requirement for patient consent is not expected. It is however the role of the national coordinator to ensure that patient consent is not required in his/her jurisdiction.

### **Funding**

EuReCa THREE is funded by the European Resuscitation Council (ERC) (Emile Vanderveldelaan 35, BE-2845 Niel, Belgium, <https://www.erc.edu>) together with the German Resuscitation Registry (Deutsches Reanimationsregister - German Resuscitation Registry (GRR)<sup>®</sup>, Deutsche Gesellschaft für Anästhesiologie und Intensivmedizin, Roritzerstraße 27, 90419 Nürnberg). The ERC provides the network and hosted a national coordinator meeting in Kiel and covered travel expenses. The German Resuscitation Council provides administrative support, organised the NC meeting, and covered part of the NC meeting expenses. Members of the study management team and National Coordinators are supported in their work by their National Registries and National Resuscitation Committees/Councils.

### **Research questions**

To build on previous work and improve the robustness of estimates, the research questions in EuReCa THREE will closely mirror those of the previous EuReCa studies. Since EuReCa THREE focuses on response time and time intervals, the EuReCa THREE specific research questions are highlighted (see [Table 1](#)):

### **Governance and oversight**

The “European Registry of Cardiac Arrest – Study-three (EuReCa THREE)” will be conducted by the EuReCa THREE study group on behalf of the European Resuscitation Council (ERC). The members of the steering committee are appointed by the ERC. The steering committee will be chaired by the Principal Investigator. The steering committee is responsible for the scientific conduct. A study management team has been appointed by the steering committee. This team is responsible for the administration of all project tasks.

The study protocol V1.6 (March 2022) – please see [supplement 2](#).

## **Dataset**

The Utstein dataset has been developed and refined over decades, therefore, core Utstein variables will provide the basis for the mandatory data variables to be transmitted to the study centre. Registries must ensure that their collected data variables are in exact concordance with the nomenclature and descriptions of the items (see appendix 1). Participating registries will be requested to extend their regular data collection to at least the items of this dataset for at least the length of the study period of EuReCa THREE. Participating EMS systems should be informed about the extension of the registry’s dataset and support the data collection.

For this study, the items are divided into core and optional. It is hoped that by using a simple and user-friendly dataset, that the study group will encourage participation in the study while ensuring the data quality required is attained.

Quality control of data is the responsibility of the national coordinator. All variables collected for the project will be uniformly checked also by the study group prior to analysis. These checks will include range checks, cross checks, and plausibility checks. Time stamps will be checked for logical sequence. In cases where the integrity of data is questionable, queries will be sent to the national coordinator. If there is sufficient concern about the quality of data, a national coordinator may be asked to submit a new data set where this issue is resolved.

## **Statistical analyses**

The statistical analysis will be performed in cooperation with the head statistician of the German TraumaRegister DGU, as in the previous EuReCa studies.

The calculation of incidence rates (for out-of-hospital cardiac arrests and CPR) will be done per 100,000 inhabitants per year, based on the region covered by the registry.

Statistical analysis will be based on the research questions listed above. For each research question, the appropriate population will first be defined (for example, patients with confirmed arrest for whom CPR was started). Results will be presented for the whole group as well as for each participating country separately, if possible. Descriptive analysis will be performed with adequate measures of statistical precision: for both, categorical and continuous variables, 95% confidence intervals (CI95) will be calculated.

For certain endpoints like ROSC, hospital admission and survival, multivariate logistic regression analysis will be performed on the whole dataset. Independent predictor variables were selected from the Utstein Core Dataset for this study if their relevance was proven by published data. The source of data (participating country, or registry) will be included in these analyses in order to adjust for local variations. Country-specific effects (like bystander CPR) may be evaluated for interactions. Countries could be excluded from those models in case of serious deviation from completeness (for example, insufficient data about final hospital outcome), or if selected items of interest were missing or incomplete (like mode of bystander CPR, or time variables).

## **Data processing and ownership**

The University Hospital Schleswig-Holstein, Institute for Emergency Medicine/The University of Kiel, faculty of medicine, will act as custodian of the data. Data will be handled according to national laws concerning data security.

No personal identifiable data will be processed as part of the EuReCa-3 project. The participating registries will transfer anonymised data. After validation and anonymisation of data by the participating registries, all data will be transferred by the national coordinator (computer-based in one single document meeting the requirements specified) to the data custodian via a secure online webpage.

The registries will maintain the ownership of their data. They will provide the data (by submission) to the data custodian for the eval-

**Table 1 – EuReCa THREE research questions. Items in bold are key priorities for the EuReCa THREE study.**

- What proportion of each country's national population is covered by data collection?
  - What is the incidence of confirmed OHCA attended by emergency medical services (EMS) in different European countries/regions?
  - What is the EMS response interval for OHCA?
  - How long is the EMS treatment interval for OHCA?
  - How long is the transport interval from scene to hospital for OHCA?
  - What is the influence of response interval and transport interval on survival?
  - What is the incidence of any CPR (cardiopulmonary resuscitation) attempted in OHCA throughout Europe?
  - What is the incidence and the proportion of CPR by:
    - o Bystander – on scene by chance
    - o Person alerted to scene by ambulance dispatch
    - o EMS
  - What is the response interval for persons alerted by dispatch and time from their arrival to EMS arrival on scene?
  - What is the initial cardiac arrest rhythm for OHCA patients?
  - In patients where resuscitation was started or continued by EMS, what is the incidence and rate of any return of spontaneous circulation (ROSC) after OHCA?
  - What is the incidence of patients never transported due to being declared dead on scene?
  - What is the incidence of patients transported with ongoing CPR?
  - What is the patient status at handover from EMS to an emergency department or hospital system with ongoing additional treatment in the next step of care (ROSC, ongoing CPR, dead)?
  - What is the incidence of patients who are discharged alive from hospital?
  - What is the incidence of patients who are still alive at 30 days (whether in-hospital or discharged) after their cardiac arrest event?
  - In the Utstein comparator group (Collapse bystander-witnessed where the first rhythm is shockable):
    - o What is the incidence of OHCA
    - o What is the incidence of ROSC at hospital admission (at time of being handed over from EMS to an emergency department or hospital system with ongoing additional treatment, e.g. PCI)
    - o What is the incidence of patients who are discharged alive from hospital?
    - o What is the incidence of patients who are still alive at 30 days (whether in-hospital or discharged) after their cardiac arrest event?
  - What factors determine ROSC, admission and survival in patients with confirmed arrest and CPR started (as defined in questions above)?
- Secondary Research Questions*
- What is the European incidence of and incidence of survival from OHCA with a traumatic aetiology?
  - What is the European incidence of survival from OHCA in cases brought to a hospital with unsustained ROSC or ongoing CPR?
  - What is the incidence of OHCA in children less than 16 years of age

uation of the research questions listed. Submitted data cannot be revoked. Submitted data may not be published elsewhere before acceptance of the EuReCa THREE results for publication. Inclusion of the data in national yearly reports is permitted. Members of the EuReCa THREE study group will have the right to access the data for scientific and other purposes. The use of the data for additional analysis can be applied for by the national coordinators. A written application must be sent to the steering committee, who will decide if the objective falls within the aim of this study. Breach of confidentiality will result in exclusion of the country from all analyses and publications, including authorship.

## Publication and authorship

The study team aims to publish the study results in a peer-reviewed scientific journal in early 2024. Authorship will follow the recommendations of the International Committee of Medical Journal Editors. In brief, a core writing group will coordinate preparing papers for review and approval by co-authors. The writing group comprising the Principal Investigator, study statistician, the steering committee and the study management team will prepare the first draft of the paper before circulating to the national co-ordinators for review. The Principal Investigator will be the first author. The EuReCa team and the national coordinators will contribute to the manuscript and will be named as co-authors. All other contributors, including individuals

identified as making a substantial contribution to the collection of data by a national co-ordinator will appear as named collaborators in the appendix, which will allow journals to index individuals as collaborators in “medline”.

All publications should be in accordance to the STROBE-Statement.<sup>12</sup>

## Discussion

EuReCa THREE will be the third European study on epidemiology of OHCA. Starting in 2014 with EuReCa ONE, to EuReCa TWO in the last quarter of 2017, proceeding now to EuReCa THREE from September till end of November 2022. This study aims to close the knowledge gap on the incidence of cardiac arrest and to provide more robust data on survival of OHCA in Europe. This will translate to better informed guidelines in the future.

A valuable contribution expected from EuReCa THREE will be to learn about the OHCA situation in Europe after the harshest waves of the Covid-19 pandemic. Its impact on time-dependent processes and especially on OHCA has been extensively documented.<sup>13–17</sup> The covid pandemic specifically impacted on the first links in the OHCA chain of survival<sup>18</sup>; the results of EuReCa THREE will help elucidate whether these links have recovered.

This study will provide a 3-month ‘snapshot’ of real-world OHCA incidence and outcomes in Europe, however it should be noted that

not every participating country has achieved national coverage of their country, and only one country in the world has cardiac arrest as a reportable condition.<sup>19</sup>

The goal of EuReCa THREE is to expand and consolidate the EuReCa network, and to increase the population covered by EMS systems reporting to cardiac arrest registries. There are no interventions in this study other than the effort required by EMS personnel or systems to report to the study. There is no reported or estimated risk related to participation in this study, and since the treatment is not changed, there is no increased risk involved for the patient. There are no direct benefits to the patients whose data will be used, however countries will be able to benchmark their results to other countries in Europe, and based on the results, initiate quality improvement projects to improve the treatment given to this specific patient population.

### Conflict of Interest

SM, JH, HM, FRO and EK have nothing to declare.

GP received grants from Resuscitation Council UK, British Heart Foundation and National Institute for Health Research (NIHR) Applied Research Collaboration (ARC) West Midlands. He is editor-in-chief of Resuscitation Plus and Director Science of the European Resuscitation Council.

JTG received grants from the German Resuscitation Registry. He is the chair of the German Resuscitation Registry, the EuReCa network and medical director of the Resuscitation Academy Germany.

JW is member of the German Resuscitation Registry steering committee.

IT received a grant from Laerdal Foundation to organize a resuscitation research masterclass.

LB is chair of the ERC governance committee.

### Appendix A. Supplementary material

Supplementary material to this article can be found online at <https://doi.org/10.1016/j.resplu.2022.100314>.

### Author details

<sup>a</sup>University Hospital Schleswig-Holstein, Institute for Emergency Medicine, Kiel, Germany <sup>b</sup>University Hospital Schleswig-Holstein, Department of Anaesthesiology and Intensive Care Medicine, Kiel, Germany <sup>c</sup>University of Namibia, School of Medicine, Windhoek, Namibia <sup>d</sup>National Ambulance Service and University of Galway (on behalf of the Out-of-Hospital Cardiac Arrest Register (OHCAR)), Ireland <sup>e</sup>University Hospital Schleswig-Holstein, Department of Anaesthesiology and Intensive Care Medicine, Lübeck, Germany <sup>f</sup>Division of Prehospital Services, Oslo University Hospital, Norway <sup>g</sup>Faculty of Medicine, Institute of Clinical Medicine, University of Oslo, Norway <sup>h</sup>Prehospiten-Centre for Prehospital Research, Faculty of Caring Science, Work-Life and Social Welfare, University of Borås, Borås, Sweden <sup>i</sup>Servicio de Urgencias y Emergencias, 061 de La Rioja, Spain <sup>j</sup>University Hospital Schleswig-Holstein, Department of Internal Medicine III, Cardiology, Angiology and Intensive Care Medicine, Kiel, Germany <sup>k</sup>University of Antwerp,

Antwerp, Belgium <sup>l</sup>European Resuscitation Council, Niel, Belgium <sup>m</sup>Warwick Clinical Trials Unit, Warwick Medical School, University of Warwick, Coventry, United Kingdom <sup>n</sup>University Hospitals Birmingham NHS Foundation Trust, Birmingham, United Kingdom

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