European Registry of Cardiac Arrest – Study Two (EuReCa TWO)

An international, prospective, multi-centre, three-month survey of epidemiology, treatment and outcome of patients suffering an out-of-hospital cardiac arrest in Europe

Study protocol

Version 1.2.1[*]

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Principal Investigator

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Jan-Thorsten Gräsner, MD

[*] V 1.2.1 consists changes about an additional participating country and amended National coordinators.

Steering committee (last name in alphabetical order)

Bernd W. Böttiger

Leo Bossaert

Jan-Thorsten Gräsner (Principal Investigator)

Johan Herlitz

Ruud W. Koster

Fernando Rossell Ortiz

Gavin Perkins

National coordinators (in alphabetical order by country)

Austria	Michael Baubin
Belgium	Pierre Mols
Bosnia-Herzegowina	Hajriz Alihodžić
Croatia	Irzal Hadžidbegović
Cyprus	Marios Ioannides
Czech Republic	Anatolij Truhlář
Denmark	Mads Wissenberg
Finland	Ari Salo
France	Josephine Escutnaire
Germany	Jan Wnent
Greece	Nikolaos Nikolaou
Hungary	Gerda Lóczi
Iceland	Hildigunnur Svavarsdóttir
Italy	Federico Semeraro
Ireland	Peter Wright
Luxemburg	Carlo Clarens
Malta	Christopher Giordimaina
Netherlands	Steffie Beesems
Norway	Ingvild B. M. Tjelmeland
Poland	Grzegorz Cebula
Portugal	Vitor Hugo Gouveia Correia
Romania	Diana Cimpoiesu
Serbia	Violetta Raffay
Slovakia	Stefan Trenkler
Slovenia	Andrej Markota
Spain	Fernando Rossell Ortiz
Sweden	Anneli Strömsöe
Switzerland	Roman Burkart
United Kingdom	Scott Booth

Study Management Team (SMT)

Holger Maurer	Germany
Siobhán Masterson	Ireland
Ingvild B. M. Tjelmeland	Norway
Jan Wnent	Germany

Student assistant

Johanna Eggeling	Germany

Statistician

Rolf Lefering	Germany

Contact – Principal Investigator

Jan-Thorsten Gräsner, MD, F.E.R.C.
Institute for Emergency Medicine
University Hospital Schleswig-Holstein
Arnold-Heller-Str. 3, Building 808
24105 Kiel
Germany
Tel: +49 431 500-31501 E-Mail: graesner@eureca-two.eu

Deutsches Reanimationsregister - German Resuscitation Registry (GRR)®
Roritzerstraße 27
90419 Nürnberg
Tel: +49 911 933780
Fax: +49 911 3938195
E-Mail: info@eureca-two.eu Internet: www.eureca-two.eu

Funder[†]

ERC – European Resuscitation Council
Emile Vanderveldelaan 35
BE-2845 Niel
Belgium
Tel: +32 3 246 46 66
Internet: www.erc.edu

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CONTENTS

1. Introduction

The importance of the establishment of out-of-hospital cardiac arrest (OHCA) registries as a critical step in improving OHCA outcomes is recognised from clinical, academic and political perspectives [1-4]. The aim of the EuReCa project is to establish a European Registry of Cardiac Arrest to provide quality benchmarking for OHCA measurement in Europe based on Utstein style data collection, so that variations in OHCA incidence, management and outcomes can be identified [5,6].

The EuReCa ONE project secured the collaboration of 27 European countries. During October 2014, data was collected from each of these countries, resulting in the most comprehensive estimate of OHCA incidence and outcomes to date [7]. As expected, the proportion of variation between data collection from individual countries was considerable. While much of this variation is likely to be attributable to patient and system level differences, some variation was a consequence of the difference in proportions of countries covered by data collection, and may also have been caused by differences in how key variables were interpreted.

Improving data quality is an incremental process therefore in EuReCa TWO, we aim to build on the work of EuReCa ONE and further improve understanding of OHCA incidence, management and outcome across the continent. Key to the overall aim of achieving quality benchmarking is to ensure that EuReCa data collection is comprehensive and reliable. Additionally, EuReCa TWO is expected to result in the creation of the largest ever database of OHCA European data, which has been collected over a single time period, using consistent data definitions.

Essential to the aims of the EuReCa project is that the data collected on each link of the Chain of Survival is comparable across participating countries. During EuReCa ONE, it was noted that the term 'bystander CPR' was interpreted differently across countries. A subsequent European survey of interpretation of the term 'bystander' and 'bystander CPR' confirmed this observation.

In order to enhance the key quality requirements of comprehensiveness and reliability, and to take advantage of the opportunity of European-wide data collection, the aims of the EuReCa TWO project will be as follows:

- Expand the EuReCa network
- Improve the understanding of the role, age, and gender profile of bystanders in OHCA in Europe
- Generate estimates of European OHCA incidence and outcome for patient subgroups that make up a small proportion of overall cases at national level e.g. traumatic aetiology, patients transferred to hospital with CPR ongoing.

In order 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
- In order to provide more robust estimates of incidence, management and outcome, increase the data collection period, increase the period of data collection to three months (1st October to 31st December 2017)
- Identify consistency and variation in the use of the term 'bystander CPR'
- Describe the incidence of 'bystander CPR' and its influence on OHCA outcome

2. Research Questions

In order to build on previous work and improve the robustness of estimates, the Research Questions in EuReCa TWO will closely mirror those of EuReCa ONE:

- What proportion of each country's national population is covered by data collection?
- What is the incidence of confirmed OHCA attended by the EMS in different European regions?
- What is the incidence of any CPR (cardiopulmonary resuscitation) attempted in OHCA throughout Europe?
- What proportion of CPR is started by:
    - Bystander – on scene by chance
    - Person alerted to scene by ambulance dispatch
    - EMS?
- What is the age and gender profile of those who provide CPR before EMS arrival?
- In OHCA, what is the initial cardiac arrest rhythm of the patients where bystanders or EMS starts CPR or any other resuscitation intervention - shockable or non-shockable?
- In patients where CPR was started by bystanders or EMS, what is the incidence and rate of any return of spontaneous circulation (ROSC) after out-of-hospital cardiac arrest?
- What is the incidence of patients never transported due to being declared dead on scene?
- What is the patient status at handover from EMS to 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 still alive 30 days (whether in-hospital or discharged) after their cardiac arrest event and/or what is the incidence of patients who are discharged alive from hospital?
- In patients with a witnessed collapse (witnessed by bystanders and/or EMS), found in a shockable rhythm and with an event of medical aetiology (i.e. Utstein comparator group):
    - What is the incidence of ROSC at hospital admission (at time of being handed over from EMS to emergency department or hospital system with ongoing additional treatment e.g. PCI) for the Utstein group
    - What is the incidence of patients who are still alive at 30 days (whether in-hospital or discharged) after their cardiac arrest event and/or what is the incidence of patients who are discharged alive from hospital in the Utstein group?
- What factors determine ROSC, admission and survival (as defined in questions above)?

Secondary Research Questions

- What is the European incidence of and percentage survival from OHCA with a traumatic aetiology?
- What is the European incidence of and percentage survival from OHCA in cases brought to hospital with unsustained ROSC and/or ongoing CPR?

3. Methods

Inclusion criteria

All patients who suffer a presumed out of hospital cardiac arrest[‡]* and are attended by the EMS at any stage during the event. This includes all events where dispatch assisted CPR is provided, even if cardiac arrest is NOT confirmed by attending EMS. This study will include all events that occur between 00:00 on 1st October 2017 and 23:59 on 31st December 2017. Patients will be included irrespective of their age, gender or personal factors.

These inclusion criteria include all 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 who achieve ROSC before the arrival of the EMS

It also includes patients found or declared dead (for any reason).

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.

Participating registries/centres:

All Registries throughout Europe, able to provide at least the core data demanded (see appendix 1), are invited to participate in this study. Requirements are a written letter of intent to participate in this study, a 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, the national coordinator is responsible for avoiding multiple submissions of patients' data. The national coordinator will be required to submit all the data for the whole country to the study management team.

Written approval of participation: All participating registries must guarantee the existence of written approvals from the EMS organisations they serve to use and submit data for the EuReCa TWO study. These approvals may follow local policy and do not need to have a specific format but must include

[‡] A cardiac arrest that occurs in any location other than an acute hospital.

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: Ethical approval must be applied for by national coordinators (see above) if necessary. Ethical approval may not be required in every nation of the participating registries. Participants are not allowed to report data unless ethical approval or a documented waiver (stating there is no requirement for ethical approval) exists for their country. The ethical approval or the documented waiver must be sent to the Study Management Team. 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.

There are no interventions in this study other than the effort required by EMS personnel or systems to report the required information 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. The benefit to the patient is that countries get to benchmark their results and compare with best practice.

4. Data collection

The core dataset for EuReCa TWO (see section 5) will be collected and submitted in electronical format to the study team.

In some countries there exist already registries for out-of-hospital cardiac arrest, or at least for resuscitation. Those countries will submit an extraction of their already collected data. Some variables might require a recoding process in order to fit to the data definition for EuReCa TWO. In case that not all required data items were covered, an additional data collection for the three months study period may be considered. If an existing recuscitation registry does not cover out-of-hospital cardiac arrests without any intervention (i.e. no CPR), then these registries may provide just cases with CPR. Calculation of incidence rates of CA will not be possible in these countries.

In countries where no such registries exist the required data will be collected prospectively, for example, with paper-based documentation forms. Data collection may be limited to a representative subset of regions, or EMS areas, or even a single (large enough) region.

The participating countries / registries will transfer unprocessed pseudonymised data. National coordinators have to expect that there were queries regarding incompleteness or inconsistencies in the data which they would have to resolve. Therefore, a pseudonym will be required during the submission process.

Participating countries will have to provide details of the local EMS organization, and the inhabitants of the region served. This country-specific information must only be transmitted once during the study period by the national coordinator.

All data will be handled according to national laws concerning data security; the national coordinator is responsible for maintaining the necessary standards.

5. Dataset

A consistent and uniform dataset is fundamental for valid study results. The Utstein dataset has been developed and refined over decades. Therefore, the core Utstein variables will provide the basis for the mandatory data to be collected for EuReCa TWO.

Registries must ensure that their collected data variables are in exact concordance with the definition and descriptions of the study data points (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 TWO. Participating EMS systems should be informed about the extension of the study´s dataset and support the data collection.

For this study, the items are divided into core and optional. There were only a few core data items for which nearly complete information is required. There core data points refer to the boxes A – D in the flow chart in the next section, which were: CA confirmed (A); CPR started (B); status on hospital admission (C), and outcome (D). It is hoped that by using a simple and user-friendly dataset the study group will encourage participation in the study while ensuring the data quality required is attained.

National coordinators and the study management team will ensure local monitoring of EMS data return and local manual check of all recorded cases. If any missing information is uncovered later, this will be reported retrospectively.

6. Statistical Analysis

The statistical analysis of the data collected will be provided centrally by Rolf Lefering (Cologne, Germany) who did already the analysis for EuReCa ONE. His background is statistics, with long-lasting experience in medical registries (TraumaRegister DGU®, consultant for the German Resuscitation Registry, Intensive Care Registries, German Severe Burns Registry, etc.). All results will be discussed internally in the Study Management Group, the Steering Group, and with all National coordinators who submitted data, before any publication.

Each submitted national dataset will be checked for completeness and plausibility before being merged into a central database for analysis. In case of inconsistencies or relevant missing data, the National coordinator will be contacted to resolve the problem.

Annual incidence rates for of out-of-hospital cardiac arrests and CPR for each country will be calculated per 100,000 inhabitants based on the reported population covered. In case of relevant deviation from the average rate, the covered population will be verified together with the National coordinator.

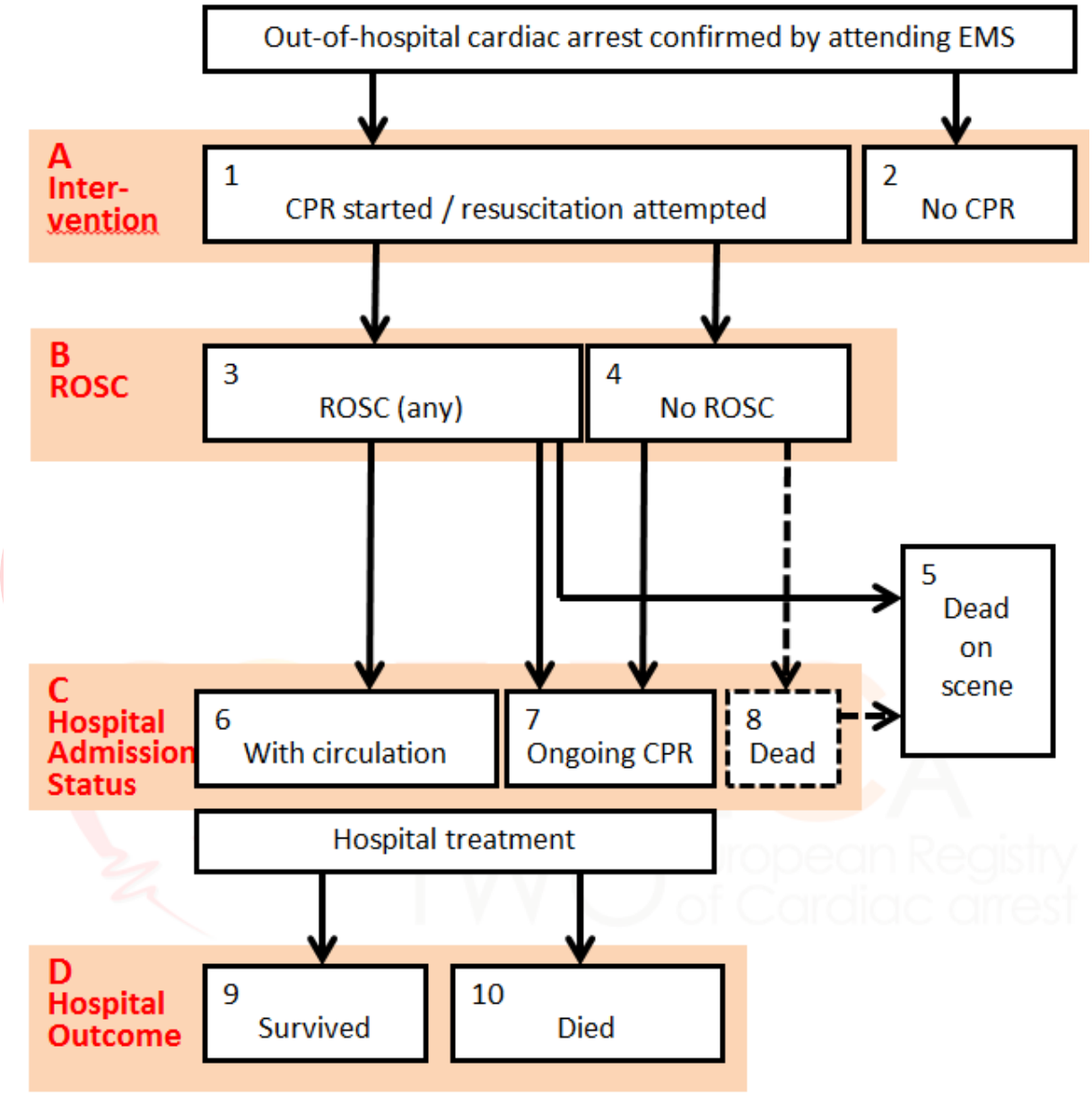
Statistical analysis will be based on the research questions listed in section two. The basic patient group is defined as all persons with confirmed cardiac arrest attended by EMS in whom CPR was attempted (group 1 in the flow sheet below). In case that CPR was not attempted (group 2), the reasons will be listed. Group 1 is the basis for determining the ROSC rate and for descriptive analysis (cause, location, witnessed, bystander, demographics, interventions, etc.).

All patients in group 1 will either be admitted to hospital or will be considered dead on scene (group 5). Patients brought to hospital but without therapeutic interventions in hospital (group 8) will also be considered as dead on scene. Hospital outcome will be calculated for admitted patients with sustained ROSC (group 6) or with ongoing CPR (group 7).

ROSC rate and hospital outcome will also be calculated within the Utstein comparator group. This group is defined as patients with a cardiac arrest due to a cardiac cause, with shockable rhythm, whose collapse has been witnessed by a bystander.

Most analyses will be performed for the whole patient group as well as for each participating country. 95% confidence intervals (CI95) will be calculated for country-specific values, both rates and mean values, in order to reflect the statistical uncertainty in varying sample sizes.

Specific subgroups with very low incidence rates will be analysed in the whole database but not at a national level due to the limited sample size. These analyses will include, but are not limited to, the outcome of trauma-associated CA, the outcome in cases with non-sustained ROSC and in those who never have had any ROSC in the pre-clinical phase (subgroups of group 7).



Multivariate logistic regression analysis will be performed in the whole dataset for the endpoints (dependent variables) survival and sustained ROSC. Sustained ROSC (group 4) will be considered in group 1 with prehospital and demographic variables as independent predictors. Survival will be considered in group 1 as well as in group 6+7 (i.e. survival after hospital admission). The country will be included as independent predictor in the prediction models.

7. Organisation

Established by the European Resuscitation Council (ERC) in 2007, the European Registry of Cardiac arrest, EuReCa, pursues the goal of recording and analysing Europe-wide cases of cardiac arrest. This establishment is intended to allow Europe-wide analysis of resuscitation treatments in different medical emergency service (EMS) systems. EuReCa is intended both to offer existing registries an option to collaborate internationally, providing a platform for joint scientific activities and also to offer additional countries and regions access to the scientific opportunities available.

The Steering Committee is responsible for the scientific conduct and is chaired by the Principal Investigator. The Steering Committee was appointed by the ERC Board.

The SC along with the SMT form the EuReCa Core group and do work together in the study. The Core group is responsible for planning and reviewing the research activities and the budget.

Countries participating in the EuReCa TWO study have only one National coordinator (NC) approved by the Steering committee. National coordinators are responsible for ensuring that mandatory approvals (e.g. ethical approval) exist, communication with the participating registry or registries, measures to generate good data quality, supervision of data collection and complete transmission of the data of their country.

The EuReCa network consists of all National coordinators and the EuReCa Core group.

In studies such as EuReCa ONE (2014) and EuReCa TWO (2017) the participating countries represented by their national coordinator provide the collected data. The ERC has full access to all results of the study on request. To gain access to original data to make separate calculations, there needs to be a separate agreement of every country.

8. Data Management 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; the national coordinator is responsible for maintaining the necessary standards.

The local, regional or national registries will keep the ownership of their data. They will provide the data (by submission) to the study management group for the evaluation of the research questions listed previously. Submitted data cannot be revoked. When submitting data the local, regional or national registries must undertake not to publish submitted data before acceptance of the EuReCa TWO paper. Members of the EuReCa TWO study group will have the right to access the data for scientific and other purposes after the study proposal has been reviewed. The steering committee has provided written approval for this measure.

All participants (registries, national coordinators, steering group, SMT, writing group) have committed to dealing in a confidential manner with data and unpublished results.

9. Publication plan

Publications will be organised by the writing group. The writing group comprises the Primary Investigator, a statistician, the Steering committee and the study management team. The Primary investigator is the first author followed by the steering committee, the statistician, the study management group and the national coordinators. All other contributors and all other representatives of all other countries will appear in the appendix and “medline”.
All publications should be in accordance to the STROBE-Statement [8].

The major results may be re-published in the different countries. Publication of regional or local data in participating countries may only be undertaken after the publication of the EuReCa TWO study results; exceptions to this requirement would need the approval of the steering committee.

10. Timeline

October 1, 2017	Begin study period, first patient in
December 31, 2017	Last patient, end of study period
January 31, 2018	Last patient in for 30-day-survival
April 2018	Last data submitted (incl. for 30-day-survival) by national coordinator
August 2018	Analysis and first draft
October 2018	ERC meeting present preliminary results to participants
Early 2019	Publication of EuReCa TWO

11. References

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Appendix 1 – Dataset