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<th>Statistical and geographic analysis of out-of-hospital cardiac arrest using registry data</th>
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<td>Author(s)</td>
<td>Masterson, Siobhán</td>
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<tr>
<td>Publication Date</td>
<td>2018-10-08</td>
</tr>
<tr>
<td>Publisher</td>
<td>NUI Galway</td>
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<tr>
<td>Item record</td>
<td><a href="http://hdl.handle.net/10379/14589">http://hdl.handle.net/10379/14589</a></td>
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Statistical and Geographical Analysis of Out-of-Hospital Cardiac Arrest using Registry Data

A thesis submitted to the School of Medicine, National University of Ireland Galway in fulfilment of the requirements for the degree of Doctor of Philosophy

By
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Discipline of General Practice
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2018
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List of Abbreviations

AED  Automated External Defibrillator
AHA  American Heart Association
ALS  Amyotrophic Lateral Sclerosis
AMPDS® Advanced Medical Priority Dispatch System
AusROC Australian Resuscitation Outcomes Consortium
B-CPR  Bystander Cardiopulmonary Resuscitation
CAD  Coronary Artery Disease
CAR  Conditional Autoregression
CARES Cardiac Arrest Registry to Enhance Survival
CFR  Community First Responder
CI  Confidence Interval
CoSTR Consensus on CPR and ECC Science with Treatment Recommendations
CPR  Cardiopulmonary Resuscitation
CPRN Civil Personal Registration Number
Crl  Credible Interval
CRI  Call-Response Interval
CSO  Central Statistics Office
CVD  Cardiovascular Disease
DFB  Dublin Fire Brigade
DIC  Deviance Information Criteria/Criterion
ED  Electoral Division
EMS  Emergency Medical Services
ERC  European Resuscitation Council
GDPR  General Data Protection Regulation
GP  General Practitioner
GRC  Graduate Research Committee
HPF  Health Professionals Fellowship
HRB  Health Research Board
HSE  Health Service Executive
ICD  Implantable Cardioverter Defibrillator
ILCOR International Liaison Committee on Resuscitation
IQR  Inter-Quartile Range
IR  Incidence Ratio
KDE  Kernel Density Estimation
MAUP  Modifiable Areal Unit Problem
McMC  Markov chain Monte Carlo
MERIT Medical Emergency Responders: Integration and Training
mOR  Median Odds Ratio
OR  Odds Ratio
NAS  National Ambulance Service
NASA  National Aeronautics and Space Administration
NS  Not Significant
NUIG  National University of Ireland Galway
OHCA  Out-of-Hospital Cardiac Arrest
OHCAR National Out-of-Hospital Cardiac Arrest Registry
PAR  Population Attributable Risk
PAROS Pan-Asian Resuscitation Outcomes Consortium
<table>
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<tr>
<td>PCR</td>
<td>Ambulance Patient Care Report</td>
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<tr>
<td>PEA</td>
<td>Pulseless Electrical Activity</td>
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<tr>
<td>PHECC</td>
<td>Pre-Hospital Emergency Care Council</td>
</tr>
<tr>
<td>PPSN</td>
<td>Personal Public Service Number</td>
</tr>
<tr>
<td>pVT/VF</td>
<td>Pulseless Ventricular Tachycardia/Ventricular Fibrillation</td>
</tr>
<tr>
<td>RCT</td>
<td>Randomised Controlled Trial</td>
</tr>
<tr>
<td>ROC</td>
<td>Resuscitation Outcomes Consortium</td>
</tr>
<tr>
<td>ROSC</td>
<td>Return of Spontaneous Circulation</td>
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<tr>
<td>RR</td>
<td>Relative Rate</td>
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<tr>
<td>SAHRU</td>
<td>Small Area Health Research Unit</td>
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<td>SD</td>
<td>Standard Deviation</td>
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<tr>
<td>SEDAC</td>
<td>Socioeconomic Data and Applications Centre</td>
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<tr>
<td>SIR</td>
<td>Standardised Incidence Ratio</td>
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<tr>
<td>STEMI</td>
<td>ST-Elevation Myocardial Infarction</td>
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<tr>
<td>UA</td>
<td>Unavailable Data</td>
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<td>VACAR</td>
<td>Victoria Ambulance Cardiac Arrest Registry</td>
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Declaration

This work is submitted to fulfil the requirements of the degree of Doctor of Philosophy at the National University of Ireland, Galway. No part of this thesis has been previously submitted at this or any other university. Apart from the due acknowledgements, it is entirely my own work.

Signed: ___________________________  Date: ______________

Siobhán Masterson
Acknowledgments

I have been very lucky to have had the opportunity to take this PhD journey, and wish to thank the people whose personal and professional calibre has inspired me throughout.

Thank you to the people in NUIG and the HRB who have helped me with grant and research administration. Especial thanks are due to Breda Kelleher and Una St. John of the Discipline of General Practice for their ‘can do’ response to any query, and to Claire Keane of the Research Accounts Office for ensuring I navigated the budgetary and reporting requirements successfully.

My sincere thanks to Professor Andrew Murphy for acting as chairperson of my Graduate Research Committee (GRC), and more particularly for the encouragement to follow my research interests which ultimately led to this PhD. I would also like to thank all the members of my GRC, Professor Conor Deasy, Dr Rónán O’Sullivan and Dr Benjamin Thébaudeau for engaging so fully in my research and for giving me the chance to reflect on my progress at important stages throughout the process.

Especial thanks are due to Dr Conor Teljeur for his practical assistance with analysis in this thesis, but more importantly for his inspiring generosity with his expertise, and readiness to keep explaining until I understood. Sincere thanks also to Dr Claire Armstrong for reviewing the final draft of this thesis, and for providing a fresh perspective, just when it was needed.

In the course of this research, I have had the privilege of meeting OHCA survivors and I am grateful to them all for sharing their stories with me. I have also had many conversations with volunteer responders and my ambulance service colleagues, whose care and compassion for their patients was a daily inspiration to me. Thank you also to the OHCAR Steering Committee, the National Ambulance Service, and the Dublin Fire Brigade for facilitating and granting permission for this research.

I could not have been more fortunate in having Dr Akke Vellinga, Dr John Cullinan and Professor Bryan McNally fulfil the supervision roles for this PhD. It would be difficult the count the ways in which they helped me throughout this journey, but I am particularly grateful to John and Akke for when they mentored me in those inevitable times when I struggled, and their ability to make me believe I could reach the end. Thank you especially to Bryan for adding me to the list of international researchers that he has helped, and for providing the patient-centred, clinician’s perspective that is so critical in epidemiological research.

Thank you to my friends and family and especially to Gareth, Eoin and Aoife for your patience throughout this process. I promise I will always try and show you as much respect for your endeavours as you have always done for mine.
**Thesis Outputs and Impact**

**Peer-Reviewed Publications**

**Masterson, S., Cullinan, J., McNally, B., Deasy, C., Murphy, A.W., Wright, P.W., O'Reilly, M., & Vellinga, A.**
Out-of-Hospital Cardiac Arrest attended by Ambulance Services in Ireland: First 2 Years' Results from a Nationwide Registry.  

**Masterson, S., Cullinan, J., Teljeur, C., & Vellinga, A.**
The Spatial Distribution of Out-of-Hospital Cardiac Arrest and the Chain of Survival in Ireland: An Analysis across the Urban-Rural Spectrum.  
*Irish Geography* 2016, 49, 1-27

**Masterson, S., Teljeur, C., Cullinan, J., Murphy, A.W., Deasy, C., & Vellinga, A.**
The Effect of Rurality on Out-of-Hospital Cardiac Arrest Resuscitation Incidence: An Exploratory Study of a National Registry Utilising a Categorical Approach.  

**Masterson, S., Teljeur, C., Cullinan, J., Murphy, A.W., Deasy, C., & Vellinga, A.**
Out-of-Hospital Cardiac Arrest in the Home: Can Area Characteristics identify At-Risk Communities in the Republic of Ireland?  
*International Journal of Health Geographics* 2018, 17, 6

**Masterson, S., Strömsöe, A., Cullinan, J., Deasy, C., Vellinga, A.**
Apples to Apples: Can Differences in Out-of-Hospital Cardiac Arrest Incidence and Outcomes between Sweden and Ireland be explained by Core Utstein Variables?  

Out-of-Hospital Cardiac Arrest Survival in International Airports  

* Listed in F1000 Prime at time of publication ([https://f1000.com/prime/about/whatis](https://f1000.com/prime/about/whatis))
Student and Co-Author Contributions

For all peer-reviewed publications, Ms Masterson was the principal author and responsible for: study concept and design; literature review; data collection; data analysis and interpretation; drafting of the manuscripts for co-author consideration; and, for all final editing. Dr Vellinga and Dr Cullinan provided supervisory oversight for all publications and all co-authors reviewed drafts of all manuscripts, and contributed to text where appropriate.

Co-authors made the following additional contributions to articles:

- Out-of-Hospital Cardiac Arrest in the Home: Can Area Characteristics Identify At-Risk Communities in the Republic of Ireland?
  - Dr Teljeur performed Bayesian CAR analysis and results interpretation

- Apples to Apples: Can Differences in Out-of-Hospital Cardiac Arrest Incidence and Outcomes between Sweden and Ireland be explained by Core Utstein Variables?
  - Dr Strömsöe obtained ethical approval from Sweden and provided Swedish data used in analysis

- Out-of-Hospital Cardiac Arrest Survival in International Airports
  - Ms Vellano, Dr Escutnaire, Dr Fitzpatrick, Professor Perkins, Dr Koster, Dr Nakajima, Ms Pemberton, Mr Quinn, Professor Smith, Dr Jónsson and Dr Strömsöe obtained ethical approval/permission and provided data from their respective countries for use in analysis
  - Ms Tandan performed analysis to obtain 95% credible intervals for median odds ratios reported as part of study results.
Awards and Presentations

Awards
A Geographic Model for Improving Out-of-Hospital Cardiac Arrest Survival in Ireland (June 2015) Oral presentation at the Ryan Institute GIS Centre Research Day (GIS & Spatial Modelling in Research Seminar 2015), NUI Galway – Best Presentation

Comparing Apples to Apples: Differences in Out-of-Hospital Cardiac Arrest Outcomes between Sweden and Ireland (November, 2017) Oral presentation at the Multidisciplinary Research Symposium Donegal Medical Academy 2017, Letterkenny University Hospital – Best presentation

Presentations
National Out-of-Hospital Cardiac Arrest Register OHCAR (January 2015) NUI Galway Population Health Research and Health Service Research (PHR and HSR) Alliance, Galway

A Geographical Model for Improving Cardiac Arrest Survival in Ireland (May 2015) NUI Galway Population Health Research and Health Service Research (PHR and HSR) Alliance, Galway

Comparison of Swedish and Irish OHCA Incidence and Outcome – What are the Key Differences? PreHospen Conference (March 2016), Borås, Sweden

The Geographic Distribution of Out-of-Hospital Cardiac Arrest and the Chain of Survival in Ireland (August 2016) Joint International Conference on Environment, Health, GIS and Agriculture, Galway

The Value of Data in Saving Lives (October 2016) Irish Association of Emergency Medicine, Dublin

Comparing Apples to Apples - Differences in Out-of-Hospital Cardiac Arrest Incidence and Outcomes between Sweden and Ireland (September 2017) European Resuscitation Council Conference, Freiburg im Breisgau, Germany

Cardiac Arrest Registry and Data Quality (November 2017) European Resuscitation Academy, Palmerstown House, Kildare

Poster
Out-of-Hospital Cardiac Arrest in Ireland – Results of a Nationwide Study (October 2015) European Resuscitation Council Conference, Prague, Czech Republic
Abstract

Background: Out-of-hospital cardiac arrest (OHCA) is the most critical health event that occurs in the community. When the heart stops pumping blood, if resuscitation is not started, biological death will occur within minutes. It is known that patient-level factors significantly affect OHCA incidence and outcome however, area-level variation is often observed. The aim of this thesis was to investigate if area-level grouping or area-level characteristics could be identified that influence OHCA incidence and outcome, and their impact quantified.

Methods: Using data from the Irish OHCA registry, descriptive and geographical analysis of OHCA incidence was performed. Cases were geocoded to Electoral Division (ED) level and combined with national census data, and area-level deprivation data, and classified by urban-rural category. The impact of urban-rural grouping was quantified using multilevel linear regression. To adjust for the impact of a small number of cases at ED-level, and the spatial properties of EDs, Bayesian conditional autoregression (CAR) was used to estimate the relative risk of OHCA. Swedish and Irish registry data was compared using logistic regression to identify the predictors of outcome, and to quantify variation measured. Finally, multilevel logistic regression analyses of outcomes in international airports was performed to allow for a differing effect of predictor variables between countries.

Results: The incidence of OHCA where resuscitation was performed was higher in City and Town EDs (51/100,000 population per year; 95% confidence interval [CI], 46 to 55) than in Rural EDs (35/100,000 population per year; 95% CI, 28 to 42). However, urban-rural grouping accounted for only 2% of variation. Bayesian CAR modelling showed that a one-point increase in relative deprivation was associated with an 11% increased risk of OHCA that occurred at home. Logistic regression analysis of the Utstein comparator group (adults, bystander-witnessed, initial shockable rhythm, presumed medical cause) explained only 17% of outcome variation between Sweden and Ireland, with a 4-fold ‘country effect’ in favour of Sweden. Country-level differences in survival in international airports were also evident, particularly when adjusted for age, gender, and attempted bystander defibrillation (median odds ratio 3.0; 95% credible interval, 1.6 to 14.3]).

Conclusions: Findings did not support changes in provision of resuscitation services based on area-level differences, and only a small proportion of between-country variation was explained by routinely collected variables. As patient-level factors are likely to explain the greater proportion of variation in OHCA outcome, it is recommended that there is international collaboration to ensure comparability of data collection and data interpretation, and to promote comprehensive case capture and maximise data quality. It is also recommended that more explanatory variables are incorporated into OHCA registry data collection. Finally, improvements in survival cannot be achieved without cooperation from local communities, but community preparedness should include: discussion on the inevitability of cardiac arrest as part of life; the prospect of patient survival; and, the need for innovative thinking to make sure that pre-hospital resuscitation is initiated efficiently and effectively.
Chapter 1: Introduction

“No medical emergency is more dramatic than a sudden cardiac arrest”
Global Resuscitation Alliance, 2016

This thesis by publication presents a statistical and geographical analysis of out-of-hospital cardiac arrest (OHCA) using registry data. Differences in OHCA incidence and outcomes are observed within countries and between countries, and the aim of this thesis is to add to the knowledge of the factors that contribute to these differences. Through six article-based chapters, the roles of data validity, geography, data comparability and best achievable outcomes following OHCA are explored.

This introductory chapter sets the context for the six article-based chapters by describing OHCA and the strategies used to manage this emergency event. OHCA registries are the primary data sources used in this thesis and therefore, the rationale and rules for this form of data collection are discussed, together with a description of the Irish OHCA registry (OHCAR). The case for including a spatial perspective on OHCA epidemiology is outlined, as are the main geographical techniques used for analysis of the Irish data. Comparison of incidence and outcomes at between-country level are discussed, as is the concept of best achievable outcomes for OHCA survival.

1.1 Out-of-Hospital Cardiac Arrest and the Chain of Survival

This section provides an overview of the mechanism, aetiology and demography of OHCA, together with a description of the interventions needed to treat OHCA i.e. the chain of survival. Additional information on OHCA and the chain of survival is provided in Chapter 3.

1.1.1 Out-of-Hospital Cardiac Arrest – An Unexpected and Devastating Event

Cardiac arrest occurs when the heart either stops beating, or beats in a manner that prevents blood from circulating around the body. Blood carries life-giving oxygen to every body cell and in the absence of circulation, cell death will occur. In the event of cardiac arrest, the most critical scenario to be avoided is cerebral hypoxia or oxygen starvation of the brain. In less than 5 minutes, cerebral hypoxia will begin to cause severe brain damage. Without intervention to restart circulation, biological death will quickly occur.

The term OHCA is used to describe an unexpected cardiac arrest event that occurs in a location other than an acute hospital, and OHCA is the primary cause of unexpected death in Ireland. In 2016 in Ireland 2,204 people died from an OHCA where
interventions to restore consciousness or other signs of life were attempted by the 
emergency medical services (EMS) i.e. resuscitation attempted 3, followed by 399 
deaths as a result of suicide, and 187 fatalities as a result of road traffic incidents 4,5. 
The sudden and acute nature of bereavement that results from unexpected death will 
have traumatic effects for families and communities, regardless of the cause.

1.1.2 Mechanism
The overarching mechanism for OHCA is the cessation of blood circulation due to an 
electrical rhythm disturbance (cardiac arrhythmia) within the heart. The most 
common cardiac arrest arrhythmias are:

- Pulseless ventricular tachycardia and ventricular fibrillation (pVT/VF)
- Asystole
- Pulseless electrical activity (PEA).

Pulseless ventricular tachycardia and ventricular fibrillation are the most common 
cardiac arrhythmias 6. A pVT/VF rhythm causes the heart to fibrillate or ‘flutter’, 
preventing normal blood flow. On an electrocardiogram (ECG), pVT/VF appears as an 
erratic and disorganised tracing. It is difficult to accurately estimate the proportion of 
OHCA which is caused by pVT/VF because without intervention, pVT/VF descends into 
asystole in a matter of minutes. Asystole is when the heart ceases to beat entirely and the 
rhythm appears as a flat line on an ECG trace. PEA or electromechanical 
dissociation is a common cardiac arrhythmia where electrical activity continues in the 
heart and will appear as an organised, regular trace on an ECG. However, a PEA 
rhythm does not allow the heart to beat mechanically, causing effective circulation to 
cease 7.

1.1.3 Aetiology and Population Profile
Approximately 80% of all OHCAs have a cardiac cause and coronary artery disease 
(CAD) is the primary cause of OHCA 8. Transient ischaemia (lack of blood supply) or 
scar tissue due to CAD can interfere with the electrical activity of the heart. This in 
turn may lead to the sudden cardiac arrhythmias that cause cardiac arrest 9. Structural 
abnormalities such as congenital heart and artery diseases, myocarditis, 
cardiomyopathies and channelopathies may interfere with the heart’s electrical 
system, leading to arrhythmias that cause cardiac arrest. Inherited syndromes such as 
long QT syndrome, Brugada syndrome, and Wolff-Parkinson-White syndrome can 
cause chaotic and often unpredictable disruptions to heartbeats that may also result 
in cardiac arrest. OHCA may be the first sign of heart disease, unless other clinical 
symptoms of CAD have manifest, or if family screening has been carried out as a 
result of a known risk of structural abnormalities or cardiac arrhythmias 10,11.

There are differences in the occurrence of OHCA between populations due to differing 
risk profiles, depending on age, gender, ethnic, genetic, chronic disease, and lifestyle 
factors. However it is generally accepted that the majority of OHCA is caused by CAD, 
particularly in the Western population (approximately 80%) 9. Structural heart disease
accounts for approximately 10-15% of cardiac OHCAs in Western countries, with a higher proportion of cases among women. Inherited arrhythmias account for 1-2% of cardiac OHCAs in Western countries but may account for 10-15% of OHCAs in Asia. Non-cardiac OHCA may be due to an internal cause such as intracranial haemorrhage, pulmonary embolism or abdominal aortic aneurysm. External causes include trauma, drug overdose, electrocution, drowning and, asphyxiation due to hanging, strangulation or foreign body airway obstruction. Since CAD is the primary cause of OHCA, and occurs later in life, OHCA in children is less common and usually has a different cause than in adults. Similarly, traumatic and other external causes of OHCA constitute a small proportion of overall OHCA cases. Childhood and traumatic OHCAs are also likely to require different interventions, or a different sequence of interventions than an adult or non-traumatic event.

1.1.4 The Chain of Survival
Death from OHCA is frequent but not inevitable if treatment is initiated immediately or within minutes of the patient’s collapse. The concept of a chain of survival was approved by the American Heart Association (AHA) in 1990 (Figure 1.1a). Since then, the chain of survival has been used as the way to describe the series of resuscitation interventions required to restore consciousness or other signs of life in an OHCA patient. The chain of survival includes:

(1) Early recognition of OHCA and immediate call for help to the EMS
(2) High quality cardiopulmonary resuscitation (CPR)
(3) Defibrillation within minutes of collapse
(4) Effective advanced EMS and post-resuscitation care.

In 2000, the AHA hosted the first International Liaison Committee on Resuscitation (ILCOR) conference to develop common resuscitation guidelines. On a 5-yearly basis, ILCOR provides updates through the International Consensus on CPR and ECC Science with Treatment Recommendations (CoSTR). Over the years, there has been a deviation in the graphical representation of the chain of survival between the AHA and the European Resuscitation Council (ERC) (Figures 1.1b&c). This deviation does not indicate disagreement on the interventions required, but rather reflects differences in resuscitation system organisation between continents. Modification of the graphical representation of the chain of survival to reflect system organisation is not unusual, as demonstrated in the ‘Enhanced Chain of Survival’ described in the Scottish OHCA Strategy (Figure 1.1d).
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Figure 1.1 Evolution and Modification of the Chain of Survival

Figure 1.1a The Original Chain of Survival from 1990

![Original Chain of Survival](image1)

(reproduced with permission from Cummins et al, 1991; 83: 1832-1847)

Figure 1.1b The 2015 American Heart Association Chain of Survival

![American Heart Association Chain of Survival](image2)

(reproduced with permission. Highlights of the 2015 American Heart Association Guidelines Update for CPR & ECC ©2015 American Heart Association, Inc.)

Figure 1.1c The 2015 European Resuscitation Council Chain of Survival

![European Resuscitation Council Chain of Survival](image3)

(reproduced with permission from Monsieurs et al, 2015; 1-80)

Figure 1.1d The Enhanced Chain of Survival

![Enhanced Chain of Survival](image4)

(reproduced under the Open Government Licence for Public Sector Information from: Out-of-Hospital Cardiac Arrest – a Strategy for Scotland (2015).)
(1) Early recognition of OHCA and immediate call for help
In order for OHCA to be treated, it must be recognised and the EMS must be activated (emergency call for help made) immediately or within minutes of the patient’s collapse \(^{24}\). Recognition of OHCA at the time of EMS dispatch is associated with increased likelihood that CPR will be commenced by a bystander (bystander CPR), shorter EMS response intervals and increased patient survival \(^{26-28}\). Absence of consciousness and absence of breathing are the primary indicators of OHCA, however ineffective ‘agonal’ breathing or gasping may be present in up to 60% of patients after collapse \(^{29,30}\). Recognising agonal breathing is an essential skill to ensure rapid recognition of OHCA \(^{31}\).

(2) High quality cardiopulmonary resuscitation
As described above, when the heart stops beating entirely or effectively, circulation and breathing also cease. Within four to five minutes, the body will become starved of oxygen, leading to cerebral hypoxia and imminent death. CPR compensates for the inability to breathe through the provision of manual or mechanical ventilations, and for the pumping action of the heart through the provision of manual or mechanical chest compressions. Interruptions to chest compressions reduce circulatory perfusion, with delays as short as four seconds reducing the likelihood of survival in animal models \(^{32}\). Evidence of similar effects in humans has led the recommended ratio of chest compressions to ventilation for trained rescuers to increase from 15:2 in the first ILCOR guidelines \(^{33}\) to 30:2 in the 2015 update \(^{23}\). As well as the need for minimum interruption, the depth and speed of compressions affect CPR quality \(^{34,35}\). However, the use of audio and visual feedback during training and practice can significantly improve these quality metrics \(^{36}\). In view of the rapid decline in circulation perfusion following collapse, it is critical that CPR is commenced as quickly as possible. In the majority of OHCA cases, this means that members of the public must be willing to attempt bystander CPR. Bystander CPR is independently associated with increased survival from OHCA, though assuring effective and efficient provision is difficult \(^{37}\). The 2015 resuscitation guidelines recognised that skills and confidence may vary and emphasised the value of telephone instruction from ambulance controllers in supporting the provision of bystander CPR (dispatch-assisted CPR) \(^{38}\). A recent Cochrane systematic review supported this advice by concluding that bystander administration of chest-compression CPR supported by telephone instruction is associated with increased OHCA survival \(^{39}\).

(3) Defibrillation within minutes of collapse
The most common rhythm disturbance in OHCA of a cardiac cause is pVT/VF and when the heart is in pVT/VF, a controlled electrical shock can be applied using a defibrillator. This controlled shock terminates the irregular rhythm, thereby allowing the heart to reset to a regular, productive rhythm \(^{40}\). The ‘electrical phase’ of cardiac arrest, when pVT/VF is present, lasts for approximately 4 minutes from the time of collapse \(^{41}\), and the likelihood of successful defibrillation decreases dramatically when the electrical phase ends, as shown in Figure 1.2. Ireland has been a world leader in the provision of pre-hospital defibrillation. Pre-hospital manual defibrillation was first practiced in Belfast in 1966, when a mobile coronary care unit staffed with a physician and nurse was dispatched to patients \(^{42}\). The first ever paramedic staffed ambulances
with defibrillators were used in Dublin in 1968\textsuperscript{43}. Since then, automated versions of defibrillators (AEDs) have been developed and refined for public use. The evolution of defibrillators has been so successful that if a defibrillation shock is delivered in the first four minutes after collapse, survival of up to 70% has been observed, regardless of the clinical training level of the bystander\textsuperscript{38,44}.

**Figure 1.2 Relation of Collapse to CPR and Defibrillation to Survival: Simplified Model**

Graphical representation of simplified (includes collapse to CPR and collapse to defibrillation only) predictive model of survival after witnessed, out-of-hospital cardiac arrest due to ventricular fibrillation. Each curve represents change in probability of survival (y-axis) as a function of the delay (minutes) to defibrillation (x-axis) increases for different collapse-to-CPR intervals (1, 5, 10 or 15 minutes). Reproduced with permission from “Estimating Effectiveness of Cardiac Arrest Interventions: A Logistic Regression Survival Model.” Circulation 96(10):3308-3313, November 18, 1997\textsuperscript{45}

(4) Effective advanced EMS and post-resuscitation care
EMS interventions that maximise CPR quality and ensure rapid defibrillation are associated with improved OHCA survival\textsuperscript{46}. ‘Pit crew’ resuscitation is modelled on the principles used by pit crew team members in Formula One racing, where team members perform tasks in an intricately planned and extensively practiced manner. Each EMS team member is assigned a predefined position and dedicated tasks during the resuscitation attempt, all of which are directed by the EMS team leader\textsuperscript{47}. An essential element for success is that regular drilling and practice is incorporated into the routine duties and responsibilities of the EMS,\textsuperscript{36} and that post-resuscitation debriefing is part of practice\textsuperscript{48,49}. Mechanical CPR (the use of a mechanised device to provide chest compressions) is another EMS intervention that is essentially designed to maximise quality and minimise interruptions. In theory, the advantages of mechanical CPR include elimination of the EMS fatigue, and high quality chest compressions with elimination of interruptions caused by EMS personnel changes or patient transfer. To date, however, there is no evidence that mechanical CPR improves OHCA survival over manual CPR\textsuperscript{50,51}.  

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In addition to routine EMS interventions there are advanced interventions, including epinephrine administration and pre-hospital endotracheal intubation. However, the results of a large-scale controlled trial carried out in Ontario showed that such additional advanced interventions did not improve survival in an optimized EMS system of rapid defibrillation\textsuperscript{52}. Finally, there is increasing evidence that the type of in-hospital treatment and even the type of hospital to which the patient is brought may also impact OHCA outcomes\textsuperscript{53-55}, though achievement of a sustained return of spontaneous circulation (ROSC) pre-hospital continues to be the main determinant of OHCA survival\textsuperscript{57}. 
1.2 Out-of-Hospital Cardiac Arrest Registries and Epidemiological Research

The Global Resuscitation Alliance recommend “establish[ing] an OHCA registry” as a first step in improving OHCA outcomes in any jurisdiction or country. Registry data collection in itself is not a guarantee for improved survival, but in the absence of regular data collection mechanisms, routine monitoring, and surveillance of OHCA outcomes may be difficult and onerous. This section outlines the reasons for collecting data on an OHCA registry, describing the data standards and quality required, and how OHCA registry data has contributed to the evidence base for OHCA management.

1.2.1 The Case for an Out-of-Hospital Cardiac Arrest Registry

The process of data collection to improve healthcare quality is based on the premise that quality improvement requires a continuous cycle of measuring and monitoring. A medical or clinical quality registry can be used to collect data for quality improvement and involves “systematic collection of a clearly defined set of health and demographic data for patients with specific health characteristics, held in a central database for a predefined purpose” (Arts et al. 2002).

The impact of clinical quality registries has been rigorously evaluated in a limited number of studies and has been shown to positively influence healthcare outcomes and processes. Use of registries to provide feedback has led to improvements in the care process and health outcomes, and registries are also associated with enhanced transparency and accountability in healthcare. Additionally, duration of participation in registry data collection is associated with improved adherence to quality improvement indicators.

Achieving optimal OHCA survival requires “coordination, expert judgement, effective communication and timeliness”, and an OHCA registry should be configured to collect, process and analyse data that measures such attributes. In Ireland, statutory EMS services respond to approximately 320,000 emergency calls annually but less than 0.7% of calls are for OHCA where resuscitation is attempted. The skills required to perform well in relation to OHCA are however equally applicable to the EMS management of other clinical emergencies. Therefore, even though OHCA registries include a small proportion of patients, they have the potential to reflect the overall quality of EMS emergency management.

1.2.2 Registry Quality and the Utstein Template

The primary purpose of a clinical patient registry is to measure the quality of a service or system, and the need for quality logically extends to the registry itself. Attributes that are required for data quality include: data that is aggregated from multiple sources; data collection based on a defined dataset; rules to govern data collection; and, inclusion of knowledge of patient outcomes. In OHCA registries, the availability
of the Utstein template for data collection greatly assists in meeting these quality requirements.

In the Utstein Abbey in 1990, an international, multidisciplinary working group devised a dataset containing terms and definitions for the OHCA population, associated interventions and, outcomes. The ‘Utstein template’ is internationally accepted as the basis for collecting OHCA data and was reviewed and updated in 2004 and in 2015. The template consists of 22 core and 30 supplemental data elements, spread over the five domains of: system; dispatch; patient; process; and, outcome. The ability to report standardised results on patient and event characteristics is therefore dependent on the consistent application of Utstein data definitions during registry data collection and processing.

Even when Utstein data definitions are applied however, the difficulty with achieving a common definition of the OHCA population remains. This is because the threshold for resuscitation and recognition of OHCA differs between and even within countries. In order to account for these differences in population definition, Chamberlain and Eisenberg proposed reporting the incidence and outcomes for the ‘Utstein subgroup’ which includes patients for whom pre-hospital resuscitation is most likely to affect survival (adults; OHCA of presumed cardiac/medical cause; witnessed collapse; initial heart rhythm shockable). Reporting of the incidence and outcomes associated with this subgroup is an internationally recommended standard.

1.2.3 Using an Out-of-Hospital Cardiac Arrest Registry for Research

As well as being a quality improvement tool, OHCA registries may have a role as a source of data for epidemiological research, such as in this thesis. The “practice of capitalising on available data” dates back to John Graunt’s use of the weekly ‘London Bills of Mortality’ to produce population-based health reports, which is generally accepted to have heralded the birth of epidemiology. While the majority of OHCA registries mainly exist for quality improvement purposes, some have been established for the primary purpose of research, most notably the ARREST database in the Netherlands and the Resuscitation Outcomes Consortium (ROC) in North America.

The advantage of data from an OHCA registry is that they reflect care as it is provided in everyday practice, and provide information on patient outcomes, thereby providing a picture of the comparative effectiveness of interventions in a ‘real world’ setting. Examples of how OHCA registry data has been used to show the effectiveness of resuscitation interventions in improving OHCA outcomes include: the impact of increased percentage bystander CPR; effect of shorter EMS call-response interval; increased proportion of time spent on chest compression performance; effectiveness of lay rescuer use of AEDs; and, impact of dispatching fire and police services in tandem with ambulance services. OHCA registries can be used to show historical trends in survival as demonstrated by Chan et al. using the US
Cardiac Arrest Registry to Enhance Survival (CARES) registry in the US, and by Kajino et al. using the all-Japan OHCA registry. OHCA registries may also be used for sub-studies or as sampling frames for clinical trials, as is the case with ROC ‘epistry’ designed specifically for that purpose.

One of the greatest advantages of registries is that they do not exclude patients, and therefore should be generalisable to the population under study. It is however unsafe to assume registry research output is generalisable until potential sources of bias are identified and controlled for, or at least acknowledged. The primary risk to generalisability is selection bias, and routine monitoring for comprehensive case capture is critical. There is a constant risk of observer bias because case ascertainment is carried out by individual service providers who may apply differing criteria for case inclusion. Analysis of the Swedish Registry of Cardiopulmonary Resuscitation showed that between 2008 and 2010, of the 3,198 cases reported to the registry, 800 (25%) cases were identified as a result of a missing case search. Patients in the missing group tended to be older, less likely to have received bystander CPR, but more likely to survive to hospital discharge. In order to maximise case capture and to minimise the risk of observer bias, processes and systems are needed. For example, CARES registry staff monitor the volume of cases per month for substantial changes, and notify EMS agencies to determine the cause of changes where appropriate. Additionally, a standardised template is used to perform twice yearly assessment of population coverage and case ascertainment. If outlying areas are identified, registry staff work with EMS agencies to determine the cause of change and to help resolve any issues with data collection if they arise. Similarly, missing case identification for the Irish registry is carried out on a monthly and quarterly basis. All ambulance incidents that were not reported to the registry but were attended by ambulance services, where the dispatch code or chief complaint indicated possible OHCA are reviewed. Additional cases identified are then added to the registry. Put simply, managing the risk of selection bias is an important activity within OHCA registries to ensure valid and reproducible results.

Even if comprehensive case capture can be achieved, ensuring the collection of key data variables for each patient (i.e. case validity) will still be challenging. A survey conducted across 13 countries to determine whether OHCA registries were able to collate common data using the Utstein template found that only 62% of recommended core variables and 43% of time event variables were collected in all cases. Failure to address missing data for individual variables may incorrectly estimate associations between interventions and outcomes and lead to erroneous conclusions. In an OHCA registry, as for any other source of research data, it must be determined whether data are missing at random (at patient level) or not at random (due to a systematic data collection error in one or more area). When data are missing at random, one option is to compensate by using the multiple imputation technique which has been successfully applied in registry-based research. In order to apply this technique, the outcome variable must be included in the imputation procedure, and non-normality of variables must be addressed. The use of multiple imputation is limited by the extent of missing data, even when the other conditions for imputation are met. However, even if results are generated using original data,
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the multiple imputation technique is a useful way to check validity of results. Data ‘not missing at random’ are more problematic and introduce bias in the outcomes and conclusions of statistical analysis. Data that are not missing at random cannot be imputed or inferred from existing data. The potential impacts of this type of missing data on outcomes should be assessed using sensitivity analyses, and should be clearly acknowledged as part of study limitations.

Registry data has the advantage of reflecting real world outcomes from actual OHCA events. Using registry data to determine the impact of interventions where there is clinical equipoise is challenging, primarily due to the bias introduced by non-controlled selection of patients. This problem is well illustrated in the study of the effect of epinephrine administration in OHCA. Observational studies have shown conflicting results, ranging from: no difference to survival; no difference to survival but more severe brain damage; worse survival; worse survival and increased risk of severe brain damage; better survival with no improvement in neurological outcomes; and, better survival with better neurological outcomes. The range of findings can in part be explained by the inclusion of different patient subgroups, but even in studies which examined similar subgroups, differences in outcomes were not explained by the available variables, despite the use of controlled propensity matching. This may be partly due to the fact that while patient subgroup selection and propensity matching can help control for differences between patients, they cannot fully control for differences between EMS practitioners, including training, experience, expertise or ethical outlook. In the case of epinephrine, the value of adding more randomised controlled trials (RCTs) to the evidence base may seem obvious, but both RCTs published to date which examined the effect of epinephrine were unable to achieve statistical power in results, due to small patient numbers and difficulty in patient recruitment. The principal of allowing patients to maintain autonomy of choice makes conduct of trials difficult in a patient group who are unconscious at the time of treatment, however investigators in the PARAMEDIC2 RCT in the UK, designed to assess the relationship between epinephrine administration and OHCA survival, have succeeded in recruiting over 8,000 patients, and results are expected in 2018. While patient randomisation can manage patient differences, managing the EMS practitioner differences which impact on observational results may prove to be a difficult issue, even in a RCT.

In conclusion, when limitations are acknowledged and addressed, OHCA registries that represent or encompass the entire population, and that adhere to registry quality requirements can facilitate the production of estimates and results for a country and provide reproducible and robust data for use in epidemiological research. The Swedish Registry of Cardiopulmonary Resuscitation, the CARES in North America, and the Victoria Ambulance Cardiac Arrest Register (VACAR) in Victoria (Australia) are examples of large OHCA registries. All are routinely used to drive local quality improvement through analysis of data and academic publication of results.
1.2.4 National Out-of-Hospital Cardiac Arrest Registry for Ireland (OHCAR)

The Irish National Out-of-Hospital Cardiac Arrest Registry (OHCAR) is funded by the National Ambulance Service (NAS) and the Pre-Hospital Emergency Care Council (PHECC), administered by the Discipline of General Practice, NUI Galway and hosted by the Department of Public Health Medicine, Health Service Executive-West. OHCAR was implemented in 2007 as a result of the following recommendation from the Report of the Task Force on Sudden Cardiac Death:

“PHECC should build on work already under way to establish a register of witnessed cardiac arrest and attempted resuscitation. This should include collecting data, using the Utstein template, from the EMS, general practitioners, other health personnel and uniformed responders, and those participating in first responder programmes.”

Report of the Task Force on Sudden Cardiac Death R 6.5, pg.122

OHCAR data collection commenced in the North West region of Ireland and national data collection was achieved in 2012. Patients registered in OHCAR include all those attended by statutory EMS who suffered an OHCA where resuscitation was attempted. Patients who were declared dead before the arrival of the statutory EMS, or those who did not have resuscitation due to obvious signs of death, injuries incompatible with life, or a ‘do not resuscitate’ order are not included in OHCAR.

The primary sources of OHCAR data are ambulance Patient Care Records (PCRs) and ambulance control dispatch data from the NAS and DFB. For patients who are transported to hospital, OHCAR obtains data on patient survival from the receiving hospital i.e. was the patient discharged alive from hospital. The OHCAR dataset is based on the Utstein template and as shown in Figure 1.3 OHCAR currently captures 16 of the 22 core data items recommended in the Utstein guidelines.
Figure 1.3 Utstein Data Elements for OHCA (Elements included in OHCAR highlighted in BOLD CAPITALS)

- **POPULATION SERVED**
- **SYSTEM DESCRIPTION**
- Cardiac arrests attended
- **RESUSCITATION ATTEMPTED**
- Resuscitation not attempted

- **AGE**
- **SEX**
- **CAUSE**
- **LOCATION**
- **WITNESSED CARDIAC ARREST**
- **Bystander CPR or use of an AED**
- **FIRST MONITORED CARDIAC RHYTHM**

- **RESPONSE TIME**
- **DEFIBRILLATION TIME**
- **PHARMACOTHERAPY**
- Targeted temperature management
- Coronary perfusion attempted

- **A RETURN OF SPONTANEOUS CIRCULATION**
- **SURVIVAL TO DISCHARGE AND/OR SURVIVAL AT 30 DAYS**
- **CEREBRAL PERFORMANCE CATEGORY**

Figure format adapted from Perkins et al, 2018
1.3 Spatial Epidemiology and OHCA

Spatial epidemiology is one of the terms used to describe the theories and methods that are concerned with the distribution of disease across populations and places. This section outlines the benefits of adding a spatial component to OHCA epidemiology, and outlines the various processes and considerations required to prepare for a spatial analysis of OHCA. The analytical techniques used in this thesis to assess the impact of area-level variables on OHCA incidence are also introduced.

1.3.1 Does ‘Place’ Matter?

In the event of OHCA, the likelihood of survival is largely determined by pre-existing patient factors, the circumstances of the event, and the availability of pre-hospital resuscitation within minutes of collapse. However, an understanding of the distribution of OHCA incidence in relation to the general population, and an appreciation of how area-level factors might affect incidence, could facilitate the strategic provision of the pre-hospital resuscitation services that can predict OHCA survival.

From a health perspective, an appreciation that ‘place’ can affect health was first documented in the ‘Airs Water and Places’ text of the Hippocratic Corpus which dates from the first half of the 4th century BC:

“...when one comes into a city to which he is a stranger, he ought to consider its situation, how it lies as to the winds and the rising of the sun; for its influence is not the same whether it lies to the north or the south, to the rising or to the setting sun...and the mode in which the inhabitants live, and what are their pursuits, whether they are fond of drinking and eating to excess, and given to indolence, or are fond of exercise and labour, and not given to excess in eating and drinking...For if one knows all these things well, or at least the greater part of them, he cannot miss knowing, when he comes into a strange city, either the diseases peculiar to the place, or the particular nature of common diseases.”


From a geographical perspective, the need to consider the role of ‘place’ is based on the observation of positive spatial autocorrelation in disease and health-related event incidence – when pairs of observations taken nearby are more alike than those taken further apart. This phenomenon was famously demonstrated in John Snow’s study of London’s cholera epidemic in 1854. From an OHCA perspective, if there is area-related similarity, this may have policy implications for how resuscitation services are planned and provided.
An appreciation of the need to recognise and understand if there are spatial patterns in OHCA incidence has been part of OHCA epidemiology literature since 1981 when Mayer plotted OHCA events in Seattle to the census tract in which they occurred \(^\text{122}\). Plotting the locations of events adds a visual dimension which can powerfully highlight areas where event incidence is most prevalent. As for any epidemiological analysis however, the characteristics of the underlying population should be adjusted for to avoid incorrect interpretation of crude representations. In OHCA, defining the ‘underlying population’ can be complicated by the fact that when an OHCA occurs in a public location, this is independently associated with improved patient survival \(^\text{118}\). In such locations, the resident population does not reflect the number of people who may be present at these locations at different times of the day. The relative frequency of OHCA over a given time period in such public locations is likely to be a more useful indicator of higher than expected incidence, as demonstrated by Folke \textit{et al.} in their study of strategic AED placement in Copenhagen \(^\text{123}\).

Spatial epidemiology includes tools that acknowledge the difference between individual and group level data, and also allow accounting for the geographic characteristics of the area in which the events occur. Since the initial work of Mayer, studies have shown associations between OHCA incidence and population and area-level characteristics such as: race/ethnicity \(^\text{124}\); deprivation \(^\text{125}\); urbanisation \(^\text{126}\); and family structure \(^\text{127}\). While the descriptive and analytic techniques used in these studies are transferable, the localised nature of the characteristics used means that the results of these studies may not be globally relevant. This means that the first step in any spatial analysis of OHCA is to decide the area unit of measurement and the area-level factors that may affect incidence in that local area.

1.3.2 Settlement Patterns
The dispersal of the population may play a role in the incidence and outcomes from OHCA, and Figure 1.4 shows how the population dispersal pattern in Ireland differs from other European countries. The understanding of urban and rural also differs according to country and context. Therefore, in order to create a common scale which reflects settlement patterns, data from NASA’s Socioeconomics Data and Applications Centre (SEDAC) was used to plot population density in five European countries against the proportion of land area occupied by that density interval \(^\text{128}\). As shown, in Figure 1.4, in Finland, Sweden, and Norway, almost all of the population are concentrated in less than 20% of the land area, while in the Netherlands almost all of the land area is heavily populated. This is in contrast to Ireland, where population density varied across approximately 80% of the total land area. Such variation has implications for the provision of and the expectation from resuscitation services in the event of OHCA, in that the more dispersed the population, the more difficult it becomes to assure equitable service provision.
1.3.3 Choosing the Area and Attributes of Interest

In order to carry out area-level analysis, the area or geographical unit of measurement must be chosen. The unit chosen will influence both the way and the level to which data is aggregated, and is known as the modifiable areal unit problem (MAUP) 129. Geographical or area units of measurement can be defined by administrative (census) or territorial (natural) boundaries 130. It is generally accepted that there should be a theoretical basis to the choice of unit so that associations between potentially causative factors can be linked to the occurrence of a condition 131. While such an approach is intuitive, the area level at which data is available will also influence the decision 132.

The NAS is organised into three administrative areas. NAS Area West covers a land area of over 31,000km$^2$ along the Western seaboard, with a population of approximately 1.1 million*, and includes the two major urban centres of Galway and Limerick. NAS Area North Leinster includes Dublin City and its surrounding areas, has a population of approximately 2.4 million, and covers an area of over 18,500km$^2$ in the Eastern region. NAS Area South covers a land area of approximately 21,000km$^2$ in the southernmost region of Ireland with a population of approximately 1.1 million, and includes Cork City. Spatial analysis at NAS area level would not account for the disparate geography and varying settlement pattern in each NAS area. For this reason, the administrative unit of Irish electoral division (ED) was chosen as the geographical unit of measurement for this thesis. EDs are the smallest legally defined administrative areas in Ireland for which national census data are collected 133. There are 3,441 legally defined EDs; 32 have been amalgamated into neighbouring EDs for

* Population estimates in this section are based on 2011 census data 133
confidentiality reasons. This gives a total of 3,409 EDs for which census data are available. The NAS areas of responsibility encompass multiple EDs (NAS Area West – 1,203; Area North Leinster – 1,183; Area South – 1,023), but analysis at ED level provides a level of detail and disaggregation that would be lost if measurement were solely undertaken at NAS area level.

For this thesis, three types of area attributes that describe the demography and characteristics of the population, and account for the geography of the area were considered in relation to OHCA:

- Population-related attributes
  - Population density
  - Characteristics of the underlying population
- Geography-related attributes
  - Distance to nearest ambulance station
- Composite measures
  - Urban-rural classification
  - Deprivation index

**Population density**
Population density at ED level refers to the ratio between the number of people and the area in which they reside. Failure to adjust incidence and outcome estimates for the underlying population could lead to spurious associations between area-level characteristics and OHCA, whereas the reality may be that high incidence and a large number of survivors are simply associated with high population density.

**Characteristics of the underlying population**
Characteristics of the Irish population were derived exclusively from Irish census of population data. As part of the data collection requirements mandated under the Central Statistics Act 1993, the Central Statistics Office (CSO) collects census data on a 5-yearly basis on all people in the country on census night. For the 2011 census, data collected included information on the age and sex of the population, and included questions relating to: households and family; occupation; health and disability; travel; education; and, housing. Census data for 2011 at ED level is available from the CSO website using the StatBank dissemination service.

**Distance to nearest ambulance station**
As described previously, early access to EMS care is a link in the chain of survival. Therefore an estimate of the availability of ambulance resources was a relevant area-level measure. Location coordinates for each ambulance station were obtained. The location of the OHCA was identified for each incident and linked to the centroid coordinates of EDs. Using ArcGIS’s Network Analyst Extension, the central ED coordinates were ‘snapped’ to Irish road network data and the distance between each ED centroid and the closest ambulance station was calculated.
Urban-rural classification
In a spatial analysis of OHCA, the area where people live is of interest for its cultural and societal impact. The importance of geographical factors such as air and water quality in the incidence of OHCA are likely to be of less consequence than in the incidence of a communicable disease and for this reason, while inclusion of geographical factors is desirable, a measure that does not overestimate the role of geography was required for this thesis. In 2008 using 2006 census data, Teljeur and Kelly devised an urban-rural classification for Irish health service planning which acknowledged that service accessibility may be affected by settlement size, population density, proximity to urban centres, and land use. Most importantly, the use of multiple categories acknowledges the presence of an ‘urban-rural spectrum’ rather than a simple dichotomous divide. For this thesis, an updated version of this validated classification was created by Dr Teljeur using data from the 2011 census.

Deprivation index
A deprivation index reflects the level of disadvantage in one area relative to another. In order to reflect internal values and absolute deprivation, the measures included and weighting applied to those measures vary from country to country. A particular benefit of using an index rather than multiple indicators of deprivation is that the problem of correlation between census values can be managed using techniques such as principal components analysis, as part of the construction of the index. In order to construct the 2011 deprivation index used in this thesis, Kelly and Teljeur used principal components analysis to combine the following four indicators from the 2011 census: unemployment; low social class; no car; and, type of housing tenure.

1.3.4 Converting OHCA Registry Data to Spatial Data
Identification and preparation of area-level variables is an obvious requirement for OHCA spatial analysis, but without accurate and precise geocoding, the value of spatial analysis is questionable. Geocoding in health-related research is the process of transforming text-based addresses into explicitly geo-referenced data that can be used for spatial analysis. Errors introduced at the initial point of geocoding will cascade from one level of analysis to the next, suggesting effects and impacts that may not be real. For his 1981 study of OHCA events in Seattle, Mayer relied on event address data collected by the fire paramedics who attended the patients. Despite the advances in geolocation tools and the availability of technology to track location coordinates on EMS vehicles, the patient record remains by far the most common source of location data in studies using OHCA registry data internationally. However, address-match coding has been found to be prone to inaccuracy particularly where a large proportion of addresses are rural or where the population density is less than 44 people per km². This is an issue in a country such as Ireland, where address-specific postcodes were not in widespread use at the time of this study. Additionally, geocoding positional errors tend to be spatially autocorrelated, potentially creating another source of bias in results.
jurisdictions with a large number of addresses that do not use postcodes, as was the case in Ireland, a high degree of manual matching is required in order to optimise the positional accuracy of geocoding. In the case of rural or incomplete addresses, there is the option of geocoding to the centroid of the area unit of measurement. However, care is required to ensure that cases are geocoded to the correct geographic unit.

1.3.5 Spatial Analysis I – Correcting for Area-Level Effects

Once cases have been correctly matched or geocoded to the appropriate area unit, assessment of the impact of group level factors on case incidence and outcome can be undertaken. In spatial epidemiology, due to the presence of spatial autocorrelation, the assumption of independent observations is weakened. When trying to correct for area-level grouping in multivariate models, area can be included as a categorical variable. Each category in such a model will have a measure of strength, for example, a coefficient or odds ratio. When underlying factors rather than the actual grouping effect is of interest, multilevel modelling is a more appropriate technique. Multilevel modelling controls for the influence of a group effect. First used in educational research, multilevel regression techniques account for the hierarchy or grouping of cases within classifications, such as students in classes. Students in a ‘good’ class may do better compared to students in a ‘bad’ class, which may be due to the other students (inter-individual effects) or a good teacher (class effect). Multilevel modelling adjusts the regression coefficients of individual-level variables for the grouping effect. While multilevel modelling allows for the ‘assumption of independent observations’ to be managed, it is effectively an extension of linear, Poisson and logistic regression, meaning that all other rules pertaining to the structure of data should be observed, such as normality and homogeneity of variance.

Multilevel linear regression is used to analyse continuous outcomes. However, in OHCA epidemiological research, the multilevel logistic technique is more common and has been used to analyse dichotomous outcomes particularly survival and the provision of bystander CPR. Sasson et al. used multilevel logistic regression to control for ‘nesting’ of OHCA cases within US census tracts while Cudnik et al. used a three-level logistic model to account for interaction between patient-level, hospital characteristics, and data site characteristics. In a direct application to geographical boundaries, Girotra et al. used multilevel logistic regression to adjust for patient nesting within counties in their study of OHCA survival across the United States.

Multilevel regression analysis techniques can be used to quantify the proportion of variation in incidence and outcomes that is due to group or area-level effects. In multilevel linear modelling, the importance of the different levels in a model is estimated using the variance partition coefficient (VPC). The VPC allocates a proportion of the variance to each level, which helps to interpret the relative importance of the individual versus higher level factors.
In multilevel logistic regression, individual variance is expressed on the probability scale and group level variance is expressed on the logistic scale, and therefore the two are not directly comparable as in multilevel linear regression. In order to ease interpretation of area-level variance in the logistic model, the calculation of the median odds ratio (mOR) was proposed by Larsen and colleagues:\textsuperscript{160}

\[
MOR = \exp(\sqrt{2 \times \sigma^2 \times \Phi^{-1}(0.75)})
\]

where \(\Phi(\cdot)\) is the cumulative distribution function of the normal distribution with mean 0 and variance 1, \(\Phi^{-1}(0.75)\) is the 75th percentile, and \(\exp(\cdot)\) is the exponential function\textsuperscript{161}. The mOR is always greater than or equal to 1, and quantifies the level of difference between groups and allows direct comparison between predictor variable effects and the level of difference between groups using the familiar concept of odds ratios. A result close to 1 indicates little difference between the groups whereas a large mOR suggests considerable between-group difference. It can be conceptualised as the median value of the odds ratio between the area at highest risk and the area at lowest risk\textsuperscript{162}.

\subsection*{1.3.6 Spatial Analysis II – Spatial Smoothing}

Using multilevel modelling allows the contribution of grouping to be both controlled for and contextualised in relation to OHCA incidence and outcome. In geographic analysis, the technique accounts for the fact that cases in a defined geographical area may be similar, but it does not account for the fact that geographical areas that are close together are more alike than those that are further apart. Additionally, when incidence is relatively low compared to the overall population and there is a large number of geographical units, there is more potential for small differences at area or unit level to disproportionately influence local incidence. Bayesian conditional autoregression (CAR) modelling ‘smooths’ incidence estimates by adjusting for small numbers, and allowing areas to ‘borrow strength’ from neighbouring areas\textsuperscript{163}. By adding a spatial component to the error term of the regression equation, Bayesian CAR modelling adjusts for the spatial properties of areas and predictor variables\textsuperscript{164}. In Bayesian CAR modelling, the effect of area-level variables is estimated using coefficients which can be converted into relative rates, that can then be interpreted in a similar way to odds ratios. For example, a relative rate of 1.3 for a predictor variable would suggest that for every unit change in the predictor variable, a 30% increase in the continuous outcome variable (e.g. disease incidence rate) might be expected.

To date, the use of Bayesian CAR modelling in OHCA epidemiology has been limited. Using Bayesian CAR modelling to smooth incidence estimates, Ong et al. found no association between the incidence of OHCA that occurred at home and area-level factors in Singapore, while Straney et al. observed a 3-fold difference in area-level
OHCA incidence rates in the Australian state of Victoria \(^{115,165}\). Rooney \textit{et al.} demonstrated that the technique could be applied to Irish data for a relatively rare condition in their study of Amyotrophic Lateral Sclerosis incidence \(^{166}\), while Villani \textit{et al.} have applied the methodology to ambulance data on diabetic emergencies in Victoria \(^{167}\). Unlike the other analytical techniques used in this thesis, Bayesian CAR modelling uses a combination of a likelihood model with suitable prior distributions for the parameters to form a posterior distribution which contains the true value \(^{168}\).

The added value of Bayesian CAR modelling is that it also provides a method of cluster analysis through the identification of specific areas where incidence of a condition or an event was higher than expected. Other methods of cluster analysis have been applied to OHCA data including kernel density estimation \(^{169}\), Local Moran’s I analysis, Global Empirical Bayes Smoothed Rates, and the Spatial Scan Statistic \(^{170,171}\). However, Sasson \textit{et al.} demonstrated incomplete overlap of clusters when applying three different methods of detection to the same OHCA population suggesting that there is no ‘best’ method \(^{124}\).
1.4 Beyond National Borders – Comparison of Out-of-Hospital Cardiac Arrest Incidence and Outcomes

“The Utstein elements collectively do not fully predict outcome, indicating that additional measures influence prognosis”
Rea, 2010 172

In the previous section, the bulk of discussion concentrated on the impact of factors at small area level within Ireland. The Republic of Ireland is also a unit of measurement, and comparison of OHCA incidence and outcomes between countries is a routine part of OHCA epidemiology. There is variation in OHCA incidence and outcomes internationally, and this section considers some of the reasons for this variation. Despite the potential for variation at small area level within countries, the impact of within-country variation is not a routine part of interpreting differences between countries. Additionally, whether countries are defined by natural or administrative boundaries, they are affected by the shared values, shared behaviours, and shared risks for the national population. In an event such as OHCA where incidence and outcome is so strongly associated with individual-level factors and circumstances, an appreciation of what makes countries ‘different’ is just as important as that which makes countries similar, so that the significance of between-country differences are properly interpreted. The concept of ‘best achievable outcomes’ for OHCA is also considered, particularly in the context of ethical concerns that can affect survival.

1.4.1 Comparing National Incidence and Outcomes – What do We Know?

Multiple studies of OHCA incidence and outcome have been published and a selection of the larger and/or nationally representative studies is described below. The Institute of Medicine published the results from the CARES registry for 2013, which covered a population of 62.8 million, approximately 20% of the US population 86. In the patients who suffered a non-traumatic arrest and were treated by EMS, a crude incidence of 57/100,000 population/year was reported, with survival of 11%. In a study of regional variation across CARES sites between 2005 and 2014, Girotra et al. reported percentage survival of 9.6% in the subgroup of adult patients with presumed cardiac aetiology where the event was not witnessed by the EMS 159. Incidence was not reported due to varying levels of data collection comprehensiveness during the study period. In the Pan-Asian Resuscitation Outcomes Study (PAROS) across 7 countries, using data collected between 2009 and 2012, Ong et al. reported that percentage survival ranged from 3% to 6% in the EMS-treated, non-traumatic arrest subgroup 173. Again, incidence was not estimated due to varying levels of data comprehensiveness during the study period. The EuReCaONE study – a one-month prospective data collection of OHCA across 27 European countries – reported annual crude incidence of all-cause EMS-treated OHCA that varied from 19 to 104 per 100,000 population per year, with percentage survival of 10% 68. Most recently, the Australian Resuscitation Outcomes Consortium (AusROC), which covers a population of 19.8 million in
Australia and New Zealand, reported a crude incidence of 48/100,000 population for EMS-treated OHCA in 2015, with average survival of 12% \(^{174}\). While some of the international variation observed between studies is due to patient, area and, country-level differences, there are calculation and categorisation differences which add to the degree of variation. Like most diseases, OHCA incidence and outcome is age and gender dependent and the use of crude rates only may mask actual changes in disease rates \(^{175}\). Direct standardisation can be used to account for the age and gender profile of the underlying population \(^{176}\), but this is not routinely done in OHCA epidemiological studies.

With so much potential for variation, an obvious question is why the Utstein comparator group is not more routinely used for between-country comparison. As previously described, the Utstein comparator group includes those patients who are considered to have some of the best prospects of survival when the chain of survival is efficiently and effectively applied \(^{69}\). This is a select group of patients who are not representative of the ‘true’ OHCA population in a country. The difficulty is, however, that the understanding and definition of the ‘true’ population is affected by myriad issues including data availability, data coverage, subgroup exclusion and local interpretation. For example, Ireland, Sweden and Norway all have established OHCA registries but as the primary source of data for these registries is the EMS, they all include only cases that are attended by the EMS \(^{3,177,178}\). When there are differences in the denominator population across studies, it is possible to standardise estimates. In 2010, Berdowski et al. performed a systematic review of international OHCA incidence and outcome, \(^{179}\). They calculated estimates of individual studies by correcting for the adult census population at the time of each study, and weighted and averaged estimates according to the size of the study population. Incidence of OHCA attended by EMS where resuscitation was attempted per 100,000 population per year was significantly higher in North America (55) compared to Europe (35), Asia (28), and Australia (44) \((p<0.001)\). Berdowski et al.’s review also described a wide range of survival in the same subgroup across the continents (Asia 2%; North America 9%; Europe 6%; Australia 11%). While standardisation of subgroups and denominators was carried out in this systematic review, even these results should be interpreted with caution as studies included were not required to be nationally representative and therefore may not be reflective of the true OHCA incidence and outcome across the continents.

Due to the heterogeneity of causes and poorer prospect of survival, OHCAs of less common aetiologies may be routinely excluded from OHCA registries, as in the case of the CARES registry where only non-traumatic OHCAs are included \(^{86}\). The subgroup of the OHCA population included may also vary depending on the research question to be answered. For example, in a study examining the impact of pre-EMS interventions on OHCA outcome, Wissenberg and colleagues excluded patients who had an EMS-witnessed arrest \(^{180}\). Daya et al. studied changes in OHCA outcome over time, using the ROC ‘epistry’ \(^{181}\), but excluded children due to the risk of a disproportionate effect of small changes in the childhood subgroup on overall estimates. Exclusion of OHCA patient subgroups may be pragmatic for research related reasons, but with every exclusion, estimates of OHCA incidence and outcome becomes less representative of
the overall OHCA population. Finally, while nationally representative data can be adjusted to some extent to account for differences in incidence, and population denominators can be aligned, a further potential confounder in international comparison is how variables are interpreted in different languages and dialects, and the extent to which key variables are available for collection across different countries.

1.4.2 Why Compare National Incidence and Outcomes?
Despite the limitations described above, the work of developing comprehensive, robust, and standardised national data collection systems that allow like-for-like comparison across countries and jurisdictions is important. The aim of international comparison is to motivate change by providing comparisons of system effectiveness (i.e. OHCA survival) between individual countries. However, as has been argued by Rea et al., even if standardised international comparison is achieved, it is likely that the Utstein variables that are currently used to represent ‘systems of care’ within countries will not fully explain all the differences. The power of the Utstein elements as “a platform for scientific discovery” has been emphasised, and Buick et al. have estimated that up to 89% of variance in survival at an individual level can be accounted for by Utstein variables. As described by Rose, the determinants of individual cases and the determinants of disease rates are distinct issues, therefore in comparing countries, it is important to acknowledge what is unmeasured or unmeasurable, and indeed, what can and cannot be changed. Additionally, the more pragmatic role of OHCA registry data in monitoring changes in incidence and outcomes within countries should always be emphasised.

1.4.3 From Comparison to Improved Outcomes – Is there a Meaningful Goal?
The ultimate purpose of comparing OHCA registry data, whether within a country or between countries, is to improve OHCA survival. In 1989, Camp defined ‘benchmarking’ as “a search for industry best practice that lead[s] to superior performance”. A similar approach of focusing on improving practice in order to improve OHCA outcomes has been promoted, first by the Resuscitation Academy and latterly through the Global Resuscitation Alliance through their ‘ten step’ programme, outlined in Figure 1.6. Examples of the successful use of this approach to improving OHCA survival have been demonstrated in: Norway; Sweden; Denmark; the United States; and Korea.
While improving the ‘system of care’ may improve outcomes, even the assumption that all OHCA patients in a country can avail of the ‘system of care’ is open to challenge. For example, in some Asian countries where EMS systems are newly developed, it is suspected that a significant proportion of patients are either attended to by primary care providers and pronounced dead at home, or brought directly to hospital by private means rather than by the EMS ¹⁷³. Moreover, the setting of survival targets has an ethical dimension in that the proportion of attempted resuscitation that is desirable or even acceptable in those who suffer an OHCA needs to be considered. As the percentages of OHCA survival described in the last section shows, resuscitation has been shown to be ineffective in the majority of patients for whom it is attempted. Even in the best performing systems, the majority of patients will not survive, meaning that in most cases, an individual’s death is accompanied by the application of an aggressive and invasive therapy ¹⁹². If resuscitation is to be effective, it must be performed immediately after collapse, so the rescuer does not have the opportunity to reflect on whether it is appropriate or acceptable. Additionally, the patient is unconscious and incapable of expressing their wishes when the cardiac arrest occurs. In a non-EMS witnessed OHCA, successful resuscitation requires the intervention of lay members of the public, often a friend or a family member, who must live with the consequences of their immediate actions at the time of the patient’s collapse. This is further complicated by the fact that cardiac arrest is the ultimate cause of all deaths, and within the cohort of people who have resuscitation attempted are those who have reached the inevitable end of their life but have had their passing accompanied by an intervention which is effectively designed to ‘cheat death’. Additionally, while most survivors are described as having ‘good neurological function’, the study of what constitutes good quality of life in OHCA survival is an emerging field ¹⁹³.

Identifying those who can benefit from resuscitation is an essential part of survival goal setting. Eisenberg and colleagues have suggested that a ‘mantra’ of “everyone in VF survives” should be used, yet in the same paragraph state that “of course not everyone in VF will survive out of hospital cardiac arrest” ¹⁸⁶. In order to be achievable, goals for OHCA survival must also be realistic. The distinction between efficacy (the extent to which a treatment has the ability to bring about its intended effect under ideal circumstances) and effectiveness (the extent to which a treatment

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**Figure 1.5 Ten Steps for Improving Survival from Sudden Cardiac Arrest**

| Step 1. | Establish a Cardiac Arrest Registry |
| Step 2. | Implement Dispatcher-Assisted CPR |
| Step 3. | Implement High Performance CPR |
| Step 4. | Implement Rapid Dispatch |
| Step 5. | Voice Record all Attempted Resuscitations |
| Step 6. | Begin a Program in Police Defibrillation |
| Step 7. | Establish a Public Access Defibrillation Program |
| Step 8. | Supplemental Funding & Support for Training & Quality Improvement |
| Step 9. | Institute Hypothermia in all Receiving Hospitals |
| Step 10. | Work towards a Culture of Excellence. |

Eisenberg, 2013 ¹⁸⁶
can achieve its intended effect in the usual clinical setting) is critical when setting OHCA survival goals and ensuring realistic expectations for both the public and health professionals. Identifying those who wish to have resuscitation attempted is even more difficult. Advanced care planning is one way in which individuals can make decisions about whether they want to have resuscitation attempted, but the adoption of such approaches are affected by the wider issues of societal attitudes to death and dying.

All these factors mean that achievable survival is likely to vary from country to country, and that defining meaningful improvements for survival will be predicated on the ‘starting point’ in individual countries, i.e. current national survival rate. In the examples cited in the first paragraph in this section, increases in survival were as follows: Stavanger, Norway – from 18% to 25%\(^ {187}\), Sweden – from 5% to 11%\(^ {188}\), Denmark – from 7% to 10%\(^ {180}\), North Carolina, US – from 7% to 11%\(^ {190}\), South Korea, from 3% to 6%\(^ {191}\). Despite the wide variation in overall survival achieved, the improvements in each individual country are significant and meaningful. While OHCA registries do not collect data on the cultural, societal and emotional factors that affect the outcome following OHCA, these studies show the role of population-representative OHCA registries in monitoring survival and highlighting opportunities for improvement and goal setting.

In summary, the goal for OHCA registries should be to optimise both internal and external quality so that the data they contain can be used to add to the national and international OHCA evidence base, helping the achievable goals for OHCA survival to become clearer.
1.5 Research Aim and Objectives

As outlined in the previous sections, there is a wide body of literature that describes and investigates the causes of variation in OHCA incidence and outcome. The potential role of area-level grouping and area-level characteristics in determining OHCA incidence and outcome has not been widely considered, particularly in Ireland. The purpose of this thesis is therefore to add to the knowledge of the role of area in OHCA incidence and variation.

OHCA epidemiological analysis in Ireland has been limited to date, as national data collection was achieved only in recent years. Previous work has however suggested differences in urban-rural incidence and outcomes, but the extent of difference or explanation for these differences have not been explored. Similarly, differences in OHCA incidence and outcomes between countries are acknowledged, but the proportion of difference that is explained by commonly used predictor variables has not been defined. Finally, the purpose of OHCA epidemiology is to improve OHCA outcomes. However, patient-level analysis of best achievable survival in a ‘real world’ location that is common to all or most countries has not been previously carried out.

The primary aim of this thesis is therefore to investigate if area-level grouping or area-level characteristics that influence OHCA incidence and outcome can be identified and their impact quantified, through the following objectives:

Objective 1. Provide an up-to-date overview of OHCA where resuscitation is attempted in Ireland (Chapter 2)
Objective 2. Describe the pattern of OHCA incidence and pre-hospital resuscitation interventions across the Irish urban-rural spectrum (Chapter 3)
Objective 3. Quantify the effect of urban-rural grouping on OHCA incidence in Ireland using multilevel linear regression (Chapter 4)
Objective 4. Use Bayesian CAR modelling to adjust for the effect of few cases when estimating OHCA incidence at small area level (Chapter 5)
Objective 5. Identify differences in adjusted OHCA incidence and outcome between Sweden and Ireland, and quantify the extent of variation explained by common Utstein predictor variables using logistic regression analysis (Chapter 6)
Objective 6. Estimate best achievable OHCA outcomes following OHCA in international airports and quantify the impact of area-level grouping using multilevel logistic regression analysis (Chapter 7).

These objectives will be addressed in the following six article-based chapters using existing registry data.
Chapter 2  Out-of-Hospital Cardiac Arrest Attended by Ambulance Services in Ireland: First 2 Years’ Results from a Nationwide Registry

Key Points

- Understanding the pattern of OHCA incidence and survival in Ireland is best served by analysis that is based on nationally representative data
- From a local or national perspective, this chapter gives impetus to the need to examine the pattern of OHCA in Ireland more closely
- From an international or global perspective, this chapter provides robust estimates of Irish OHCA incidence, management and outcomes in a standardised format that facilitates comparison of findings with other population-based OHCA registries.

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Published in the Emergency Medicine Journal 2016; 33:776-781
(See Chapter 2 Appendix)
Chapter 2: Out-of-Hospital Cardiac Arrest Attended by Ambulance Services in Ireland: First 2 Years’ Results from a Nationwide Registry

2.1 Abstract

Background: National data collection provides information on out-of-hospital cardiac arrest (OHCA) incidence, management and outcomes that may not be generalisable from smaller studies. This retrospective cohort study describes the first 2 years’ results from the Irish National Out-of-Hospital Cardiac Arrest Register (OHCAR).

Methods: Data on OHCAs attended by emergency medical services (EMS) where resuscitation was attempted (EMS-treated) were collected from ambulance services and entered onto OHCAR. Descriptive analysis of the study population was performed, and regression analysis was performed on the subgroup of adult patients with a bystander-witnessed event of presumed cardiac aetiology and an initial shockable rhythm (Utstein group).

Results: 3,701 EMS-treated OHCAs were recorded for the study period (1 January 2012–31 December 2013). Incidence was 39/100 000 population/year. In the Utstein group (n=577), compared with the overall group, there was a higher proportion of male patients, public event location, bystander cardiopulmonary resuscitation (CPR) and early defibrillation. Median EMS call–response interval was similar in both groups. A higher proportion of patients in the Utstein group achieved return of spontaneous circulation (35% vs. 17%) and survival to hospital discharge (22% vs. 6%). After multivariate adjustment for the Utstein group, the following variables were found to be independent predictors of the outcome survival to hospital discharge: public event location (OR 3.1 (95% CI 1.9 to 5.0)); bystander CPR (2.4 (95% CI 1.2 to 4.9)); EMS response of 8 minutes or less (2.2 (95% CI 1.3 to 3.6)).

Conclusions: This study highlights the role of nationwide registries in quantifying, monitoring and benchmarking OHCA incidence and outcome, and providing baseline data upon which service improvement effects can be measured.

Key Messages
What is already known on this subject?
- Data from out-of-hospital cardiac arrest (OHCA) studies that are carried out in small populations or single communities may not be generalisable to entire countries
- Comprehensive national data collection is required for monitoring of nationwide OHCA incidence, management and outcomes.

What might this study add?
- Our study describes Irish OHCA incidence and outcomes and shows that nationwide OHCA data collection in a population of 4.6 million is feasible and sustainable.
2.2 Introduction

While studies of single communities provide data on out-of-hospital cardiac arrest (OHCA) outcome, nationally representative data are essential in monitoring national trends in OHCA survival. In Europe and North America, over 575,000 cases of OHCA occur annually, and the clinical and societal impact of OHCA is such that the American Heart Association has recommended that it be classified as a reportable disease. In the absence of rapid recognition, good-quality cardiopulmonary resuscitation (CPR) and early defibrillation, there is a negligible prospect of survival from OHCA.

Reported incidence of and outcomes from OHCA vary widely internationally. The reasons for this variation include: variation in age and gender distribution; levels of urbanisation; bystander CPR; availability of community defibrillators; and configuration of emergency medical services (EMS). Inter-country differences are affected by these factors and are also complicated by variation in study sample definition and denominator. This is despite the widespread acceptance and use of the Utstein criteria for OHCA data collection.

The Irish National Out-of-Hospital Cardiac Arrest Register (OHCAR) was established in 2007 to provide data to estimate the incidence and survival of OHCA in Ireland, with the aspiration of improving it. OHCAR is funded by the NAS and Pre-hospital Emergency Care Council. It is administered and academically supported by the National University of Ireland, Galway and hosted by the Department of Public Health Medicine in the Irish Health Service Executive. In 2012, OHCAR achieved comprehensive national data collection.

Within this context, the aim of this paper is to provide an overview of the first 2 years of comprehensive national data collection and describe the incidence, key interventions and survival outcomes for OHCA attended by ambulance services where resuscitation was attempted (EMS-treated OHCA) in Ireland. In line with the Utstein guidelines and as recommended by Chamberlain and Eisenberg, we focus our analysis on the subgroup of adult patients, with presumed cardiac aetiology, with a bystander-witnessed event and an initial shockable rhythm (Utstein group).
2.3 Methods

In Ireland, 62% of the total population of 4.6 million lives on 2.4% of the total land area \(^{201}\). The remaining population is dispersed in low-density settlements across the country. In Dublin city and county, the National Ambulance Service (NAS) and the Dublin Fire Brigade (DFB) provide the statutory EMS response, while throughout the rest of the country, statutory ambulance services are solely provided by the NAS. All pre-hospital emergency practitioners who work for statutory ambulance services must be registered with the Pre-Hospital Emergency Care Council. Practitioners use clinical practice guidelines to inform decisions not to resuscitate or cease resuscitation \(^{202}\). Emergency medical technicians and emergency first responders are trained in basic life support, including automated external defibrillator (AED) use. Paramedics can perform supraglottic airway placement and advanced paramedics are additionally trained to intubate in cardiac arrest situations, attempt manual defibrillation and administer cardiac resuscitation drugs. All ambulance vehicles are staffed with paramedics and/or advanced paramedics. For cardiac arrest calls, the DFB also deploy practitioners on fire engines. Community response to OHCA in Ireland varies. In some areas, the community response depends on the training and willingness of people to perform basic life support and the opportunistic availability of AEDs in the vicinity of the event. In other areas, the level of response is highly organised and coordinated by voluntary Community First Responder programmes. Irish general practitioners, primarily in some rural areas and some county fire services, also respond to OHCA at the request of the NAS \(^{203}\).

Statutory ambulance services in Ireland use a standardised Patient Care Report (PCR) which includes an ‘OHCA’ section for Utstein required data. For incidents attended by the DFB, all PCRs are received at a central location where PCRs for OHCAR incidents are manually identified. Data from each OHCAR incident are entered onto a Microsoft Access database. Each incident is electronically linked to corresponding dispatch data, and completed records are sent to OHCAR on a quarterly basis. Data are then checked to ensure compliance with OHCAR definitions as well as to avoid double entries.

In the rest of the country, immediately after attending an OHCA incident, NAS practitioners put completed PCRs for OHCAR incidents in specially provided envelopes. These PCRs are digitally processed at a central location and then electronically forwarded to OHCAR for case-by-case validation. Dispatch data are then added to all cases. In order to identify cases that may not have been placed in envelopes, missing case searches are performed in the NAS digital PCR archive. Outcome data are also obtained for patients brought to hospital. Data for this study were anonymised and extracted from the OHCAR database for the study period.

2.3.1 Ethical Approval

Ethical approval for research using non-identifiable OHCAR data was obtained from the Research Ethics Committee, National University of Ireland, Galway.
2.4 Statistical Analysis

This is a retrospective cohort study of incidence, interventions and outcomes of EMS-treated OHCA in Ireland during 2012 and 2013. The reported population for 2012 and 2013 is described. To allow international comparisons and be in line with Utstein recommendations, a subgroup of patients was extracted, which includes only adult patients with a bystander-witnessed OHCA, of presumed cardiac aetiology and an initial shockable rhythm (Utstein group) \(^69\). To ensure our data can be compared with data from other national registries, incidences per 100,000 population per year for the total group and the Utstein subgroup were standardised for age and sex using the 2013 EUROSTAT population projections. In order to describe the difference in OHCA incidence according to age, age-adjusted incidence for the total group and Utstein subgroup is graphically presented. The key outcomes from our analysis are to calculate survival to discharge for the overall group and for the Utstein group, and to determine predictors of survival in the Utstein group.

An overview of differences between the total group and the Utstein group is presented. A variable was derived to represent the availability of early defibrillation using the following rule: (defibrillation attempted=yes AND (EMS response interval of five minutes or less OR defibrillation attempted before EMS arrival)). Analysis of predictors of survival was limited to the Utstein group only.

Logistic regression analysis was performed to identify predictors of the main outcome of interest, that is, survival to hospital discharge. Variables were entered into the model based on: at least moderate univariate associations (p<0.15); validation of significance in previous literature; clinical relevance to support inclusion. Continuous variables, that is, age and ambulance response times, were categorised for regression analysis. Calibration of the model was assessed using the Hosmer and Lemeshow \(\chi^2\) statistic (p>0.05). In order to assess the potential effect of loss to follow-up, two potential scenarios were created: (i) assumed all missing cases had survived to hospital discharge; (ii) assumed all missing cases had died. Logistic regression analysis was repeated for both scenarios. Description and analysis of all cases of non-traumatic aetiology were also performed (see online supplementary tables S1 and S2).
2.5 Results

A total of 3,701 EMS-treated OHCAs were recorded for the study period (1,798 in 2012 and 1,903 in 2013). The overall incidence of EMS-treated OHCA was 39/100,000 population/year. The Utstein group had an incidence of 6/100,000 population/year. Age-adjusted incidence was highest for overall cases in the 85+ age group, but peaked in the 70–74 year age category for the Utstein group (Figure 2.1).

Figure 2.1 Age and Sex Adjusted Incidence per 100,000 Population per Year (EUROSTAT, 2013)

For the overall group, 855 cases were missing one or more descriptive variables (23%), including 30 patients who were lost to follow-up. In the Utstein group, nine patients were lost to follow-up. As shown in Table 2.1, 6% of all patients survived to hospital discharge, compared with 22% of patients in the Utstein group. Median age for all cases was 67 years (IQR 52–78 years), with the majority of patients aged over 65 years. Over half of patients (54%) had a bystander-witnessed arrest, and 70% of these patients received bystander CPR. Most cases were presumed to be of a cardiac aetiology (86%). Trauma (including self-harm and road traffic accidents) accounted for 7% of cases. Other causes included submersion and drug or alcohol overdose. The Utstein group comprised 15% of all cases (n=577). Patients in this subgroup were similar in age and gender to the overall group, but had higher percentage survival to discharge (22%) and better secondary outcomes, that is, return of spontaneous circulation, than the overall group. The Utstein group also had higher proportions of publicly located events, bystander CPR and defibrillation attempted. The Utstein group also had, as shown in figure 2.2, a higher percentage of EMS call response within eight minutes, and this marginal difference in proportions persisted for the majority of response intervals.
Chapter 2: Out-of-Hospital Cardiac Arrest Attended by Ambulance Services in Ireland: First 2 Years’
Results from a Nationwide Registry

Table 2.1 Overview of the Differences in Descriptive Variables and Outcomes between All Cases and the Utstein group

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>All Cases (n=3701)</th>
<th>Utstein Group (n=577)</th>
<th>Missing Variables</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>(Median (IQR))</td>
<td>(Median (IQR))</td>
<td>n (%)</td>
</tr>
<tr>
<td>Age in years</td>
<td>67 (52-78)</td>
<td>65 (55-75)</td>
<td>107 (2.9)</td>
</tr>
<tr>
<td>EMS CRI*</td>
<td>12 (8-20)</td>
<td>12 (8-18)</td>
<td>235 (7.0)</td>
</tr>
<tr>
<td></td>
<td>n (%)</td>
<td>n (%)</td>
<td></td>
</tr>
<tr>
<td>Under 65 years</td>
<td>1602 (45)</td>
<td>278 (48)</td>
<td>107 (2.7)</td>
</tr>
<tr>
<td>Male</td>
<td>2479 (67)</td>
<td>453 (79)</td>
<td>4 (0.1)</td>
</tr>
<tr>
<td>Presumed Cardiac Aetiology</td>
<td>3199 (86)</td>
<td>577 (100)</td>
<td>0 (0.0)</td>
</tr>
<tr>
<td>Urban Setting</td>
<td>2306 (64)</td>
<td>321 (57)</td>
<td>92 (2.5)</td>
</tr>
<tr>
<td>Public Location</td>
<td>812 (22)</td>
<td>239 (42)</td>
<td>28 (0.8)</td>
</tr>
<tr>
<td>Initial Shockable Rhythm</td>
<td>850 (24)</td>
<td>577 (100)</td>
<td>86 (2.3)</td>
</tr>
<tr>
<td>Bystander witnessed</td>
<td>1934 (54)</td>
<td>577 (100)</td>
<td>144 (3.9)</td>
</tr>
<tr>
<td>EMS witnessed</td>
<td>213 (6)</td>
<td>0 (0)</td>
<td>144 (3.9)</td>
</tr>
<tr>
<td>Bystander witnessed and Bystander CPR†</td>
<td>1316 (70)</td>
<td>453 (80)</td>
<td>41 (2.1)</td>
</tr>
<tr>
<td>Defibrillation attempted</td>
<td>1302 (36)</td>
<td>575 (98)</td>
<td>104 (2.8)</td>
</tr>
<tr>
<td>Early defibrillation attempted‡</td>
<td>297 (23)</td>
<td>180 (31)</td>
<td>0 (0.0)</td>
</tr>
<tr>
<td>EMS CRI eight minutes or less*</td>
<td>949 (27)</td>
<td>175 (32)</td>
<td>235 (7.0)</td>
</tr>
</tbody>
</table>

*Excludes EMS witnessed cases. All cases (n=3,488); Utstein Group (n=577).
†Includes only cases where the collapse was bystander-witnessed. All cases (n=1,934); Utstein Group (n=577)
‡Patients were defined as having received early defibrillation if defibrillation was attempted by a bystander or if the EMS call-response interval was five minutes or less. Includes only cases where defibrillation reported as attempted. All cases (n=1,302); Utstein Group (n=575)
CPR, cardiopulmonary resuscitation; CRI, call-response interval; EMS, emergency medical services; ROSC, return of spontaneous circulation.

Figure 2.2 Cumulative Percentage of Cases Responded to at each EMS Call-Response Interval*

---

*Time in minutes from call pick-up in ambulance control centre to first EMS vehicle arrival at scene. EMS witnessed cases excluded
As shown in Figure 2.3, complete data were available for 502 of the 577 patients in the Utstein group. As shown in Table 2.2, age under 65, collapse in an urban setting, collapse in a public location, bystander CPR, early defibrillation attempted and an EMS response of eight minutes or less were all associated with patients’ survival to discharge in the univariate analysis (model 1). In the logistic regression model (model 2), public location of the OHCA incident (OR 3.1 (1.9 to 5.0)), bystander CPR (OR 2.4 (95% CI 1.2 to 5.0)) and EMS response time of eight minutes or less (OR 2.2 (1.3 to 3.6)) remained significant predictors of survival to discharge. Interactions between variables were not significant and omitted from the model. Data on outcome were missing for nine patients in the Utstein group. The analysis was repeated using the assumption that (1) all missing cases had survived or (2) all missing cases had died. In both models, adjusted ORs for all variables remained similar.

Figure 2.3 Cases Included in Logistic Regression Analysis

*Some cases are missing data from more than one variable therefore the total number of missing variables is greater than the total number of missing cases
**The variables ‘Any ROSC’ and ‘ROSC on arrival at hospital’ were not used in logistic regression analysis which meant that 75 rather than 103 cases were omitted from this analysis
CPR, cardiopulmonary resuscitation; ROSC, return of spontaneous circulation
<table>
<thead>
<tr>
<th>Variable</th>
<th>Outcome</th>
<th>Model 1a (95% CI)</th>
<th>Model 2b (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Survived (n=106)</td>
<td>Died (n=396)</td>
<td></td>
</tr>
<tr>
<td>Under 65 years</td>
<td>63</td>
<td>175</td>
<td>1.8 (1.2-2.9)*</td>
</tr>
<tr>
<td>Male</td>
<td>88</td>
<td>305</td>
<td>1.5 (0.8-2.6)</td>
</tr>
<tr>
<td>Urban Setting</td>
<td>71</td>
<td>219</td>
<td>1.6 (1.0-2.6)*</td>
</tr>
<tr>
<td>Public Location</td>
<td>70</td>
<td>131</td>
<td>3.9 (2.5-6.2)*</td>
</tr>
<tr>
<td>Bystander CPR</td>
<td>95</td>
<td>310</td>
<td>2.4 (1.2-4.7)*</td>
</tr>
<tr>
<td>Was shock delivered</td>
<td>106</td>
<td>0</td>
<td>c</td>
</tr>
<tr>
<td>Early defibrillation attempted</td>
<td>48</td>
<td>112</td>
<td>2.1 (1.4-3.3)*</td>
</tr>
<tr>
<td>EMS CRI eight minutes or less</td>
<td>47</td>
<td>104</td>
<td>2.2 (1.4-3.5)*</td>
</tr>
</tbody>
</table>

*Univariate Analysis
†Multivariate Analysis. All variables listed in the rows, except 'Was shock delivered' were included in the multivariate analysis.
‡Statistically significant
§The variable "Was shock delivered" was omitted from analysis as it is a constant i.e. shock delivered to all cases included in the analysis
¶Patients were defined as having received early defibrillation if defibrillation was attempted by a bystander or if EMS defibrillation was attempted and the call-response interval was five minutes or less.

CPR, cardiopulmonary resuscitation; CRI, call-response interval; EMS, emergency medical services
Chapter 2: Out-of-Hospital Cardiac Arrest Attended by Ambulance Services in Ireland: First 2 Years’ Results from a Nationwide Registry

2.6 Discussion

Ireland is one of the few countries in Europe where nationwide reporting of OHCA is currently possible and a system has been developed that allows routinely collected data to be used to build a national register of OHCA capable of providing meaningful risk-adjusted quality indicators. This paper provides a description of EMS-treated patients with OHCA and their outcome in Ireland during 2012 and 2013. Our paper highlights the value of quality registries in describing, benchmarking and highlighting where challenges arise in care delivery and solutions hypothesised.

The incidence of OHCAR was 39/100 000 population/year. There is wide variation internationally in the reported incidence of OHCA, from 19 to 141 per 100,000 population per year, suggesting variation in the threshold to commence CPR. The total number of incidents was similar in 2012 and 2013, suggesting internal consistency in case identification and incidence. The proportion of incidents that occurred in urban areas reflects the proportion of the Irish population that resides in urban areas. The age and gender profile of patients was very similar to other large studies of OHCA, as was the difference in median male and female ages. The proportion of patients presumed to have suffered an arrest of cardiac aetiology is similar to North American data, but high compared with other population-based studies of EMS-treated OHCA. This may be explained by the fact that in Ireland cardiac aetiology is presumed in the absence of documented evidence of any other probable cause and may be considered analogous to ‘unknown cause’.

While the proportion of patients in our study with an initial shockable rhythm was 24%, there is significant variation in population-based studies, from 8.7% in Japan to 36% in North America.

Reported percentage survival to discharge globally varies from 0.8% to 25% in OHCA attended by ambulance services. At 6%, percentage survival in Ireland is low, but many other studies are region-specific and do not reflect national survival. While there is considerable heterogeneity in the overall group, the Utstein sub-group includes patients who have been proven to benefit most from a resuscitation attempt, that is, adults, cardiac cause, bystander-witnessed and initial shockable rhythm. Survival in the Utstein subgroup was 22%, which is substantially lower than in other population-based studies where percentage survival of up to 52% has been achieved. Opportunities to strengthen the chain of survival in Ireland are being vigorously pursued. In this study, we found that collapse in a public location, provision of bystander CPR and an EMS call–response interval (CRI) of eight minutes or less were independent predictors of survival to hospital discharge. Our finding that collapse in a public location accounted for a threefold increase in survival is not surprising and has been reported in other large-scale registry-based studies.

The proportion of bystander CPR provided in bystander-witnessed cases was high at 70% and even more impressive in the Utstein subgroup where bystander CPR was an independent predictor of survival. The proportion of bystander CPR provided is similar to the countries and regions where percentage survival is higher than that in Ireland.
Reliability of bystander CPR measurement is an issue for all OHCA registers, but we believe the nationwide introduction of dispatch-assisted CPR may help account for the high levels of bystander CPR observed in our study. Wissenberg et al.\textsuperscript{180} observed an association between improved OHCA survival in Denmark and increased bystander CPR rates following national initiatives to increase bystander interventions. Our results indicate willingness among the Irish population to attempt CPR and suggest that further extension of training initiatives may contribute to improve survival rates in Ireland.

An EMS CRI of eight minutes or less was also an independent predictor of survival. Identifying ways in which to minimise this interval is essential to improving Irish OHCA outcomes. In 2015, the NAS introduced ‘ONELIFE’, an extensive programme to improve OHCA outcomes within the NAS\textsuperscript{209}. As part of ONELIFE, dynamic deployment of EMS vehicles has been implemented, and strategies to improve dispatcher OHCA recognition and incident location are currently being introduced.

For this study, we derived a variable to represent early defibrillation and found that a minority of patients had access to early defibrillation. We had expected that early defibrillation would be a significant predictor of survival in multivariate analysis. The lack of significance may be because the derived variable overestimated the availability of early defibrillation, as we assumed that all defibrillation attempts before EMS arrival were made within minutes of collapse. This may not have been the case, particularly in more rural areas where travel times, even for first responders, may be prolonged. Blom \textit{et al.} described how AED use was an independent predictor of survival in the Netherlands\textsuperscript{210}. In their study area, AED use was tripled as a result of policy measures, including: introduction of AED programmes for police teams (together with existing fire service response); implementation of a ‘6-minute time zone’ and the introduction of a text alert system for registered volunteers. Structured AED programmes also have the advantage of efficiency as described by Ringh \textit{et al.}\textsuperscript{80}. They reported similar percentage survival as a result of 74 deployments from 5,016 public AEDs compared with 53 deployments out of a possible 135 first responder AEDs, suggesting that coordinated support of first responder programmes would be more cost-efficient than mass implementation of public AEDs. In Ireland, voluntary groups, general practitioners and county fire services already provide a community response to OHCA. Extension and support of such schemes is considered an important way in which to reduce time to defibrillation.

\textit{2.6.1 Limitations}

A substantial percentage of data was missing for the overall group, most notably resulting in 75 cases being omitted from the logistic regression analysis. In order to assess the impact of missing data, missing data imputation was performed for all cases, and logistic regression analysis was repeated for the Utstein group. The pooled results from regression analysis using imputed data did not differ significantly from the results found using original data (see online supplementary table S3).
Thirty patients were lost to follow-up. Most of these patients could not be traced due to unavailability of patient identification or poor legibility of PCRs. In our study, loss to follow-up did not significantly affect results, but it remains an issue for OHCAR.

We presumed a cardiac cause in over 86% of OHCAR cases. This presumption may have led to misclassification bias. Classification of cases as ‘presumed cardiac’ was originally proposed by the Utstein Committee to create ‘case equivalency’; however, such classification can be highly subjective. Reporting of EMS-treated cases of non-traumatic aetiology is a suggested way in which to decrease subjectivity and improve comparability of registries worldwide (please see online supplementary data).

### 2.6.2 Conclusions

This study provides a nationwide description of EMS-treated OHCA in Ireland. The incidence and demography of OHCA is similar to other population-based studies. Initiatives to increase public education in CPR, support further implementation of community first responder programmes and continued quality improvement in the EMS are keys to improving OHCA outcomes. This nationwide profile provides the dashboard by which improvements can be measured.

### 2.6.3 Acknowledgements

The authors wish to thank National Ambulance Service and Dublin Fire Brigade personnel who provided the clinical and dispatch data that have made this study possible.

### 2.6.4 Contributors

SM: performed data analysis and drafted the text of the manuscript. JC: co-supervised. SM: wrote, read and reviewed manuscript drafts. CD: contributed to the introduction and discussion text. MO: contributed to the methods section. PW: contributed to the discussion section. AM: contributed to the discussion and conclusion sections. BM: reviewed text and advised on data analysis. AV: co-supervised. SM: drafted the text, contributed to manuscript text, instructed on data analysis plan and checked results.

### 2.6.5 Funding

SM is funded by the Health Professionals Fellowship Award from the Health Research Board, Ireland (HPF-2014-609).

### 2.6.6 Competing interests

BM reports grants from American Red Cross, the American Heart Association, Medtronic Philanthropy and Zoll Corporation, outside the submitted work.

### 2.6.7 Ethics approval

Research Ethics Committee, NUI Galway.

### 2.6.8 Provenance and peer review

Not commissioned; externally peer reviewed.
2.7 Supplementary Data

Table 2.2 Descriptive Overview for Cases of Non-Traumatic Aetiology

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Cases of non-traumatic aetiology (n=3436)</th>
<th>Missing Data</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>(Median (IQR))</td>
<td>n (%)</td>
</tr>
<tr>
<td>Age in years</td>
<td>68 (55-79)</td>
<td>89 (2.6)</td>
</tr>
<tr>
<td>EMS call-response interval*</td>
<td>12 (8-19)</td>
<td>231 (7.1)</td>
</tr>
<tr>
<td>Under 65 years</td>
<td>1387 (40)</td>
<td>89 (2.6)</td>
</tr>
<tr>
<td>Male</td>
<td>2277 (66)</td>
<td>4 (0.1)</td>
</tr>
<tr>
<td>Presumed Cardiac Aetiology</td>
<td>3199 (93)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Urban Setting</td>
<td>2151 (64)</td>
<td>81 (2.4)</td>
</tr>
<tr>
<td>Public Location</td>
<td>687 (20)</td>
<td>28 (0.8)</td>
</tr>
<tr>
<td>Initial Shockable Rhythm</td>
<td>839 (25)</td>
<td>78 (2.3)</td>
</tr>
<tr>
<td>Bystander witnessed</td>
<td>1867 (57)</td>
<td>132 (3.8)</td>
</tr>
<tr>
<td>EMS witnessed</td>
<td>201 (6)</td>
<td>133 (3.8)</td>
</tr>
<tr>
<td>Bystander witnessed and Bystander CPR**</td>
<td>1280 (70)</td>
<td>40 (2.1)</td>
</tr>
<tr>
<td>Defibrillation attempted</td>
<td>1251 (38)</td>
<td>112 (3.3)</td>
</tr>
<tr>
<td>Early defibrillation attempted***</td>
<td>290 (24)</td>
<td>16 (1.3)</td>
</tr>
<tr>
<td>EMS CRI eight minutes or less*</td>
<td>897 (30)</td>
<td>231 (7.1)</td>
</tr>
<tr>
<td>Outcome</td>
<td></td>
<td></td>
</tr>
<tr>
<td>ROSC at any stage (n (%))</td>
<td>784 (24)</td>
<td>28 (0.8)</td>
</tr>
<tr>
<td>ROSC on arrival at hospital (n (%))</td>
<td>554 (17)</td>
<td>211 (6.1)</td>
</tr>
<tr>
<td>Survival to Hospital Discharge</td>
<td>214 (6)</td>
<td>28 (0.8)</td>
</tr>
</tbody>
</table>

*Excludes EMS witnessed cases. Non-trauma cases (n=3235)
**Includes only cases where the collapse was bystander-witnessed. Non-traumatic cases (n=1867)
***Patients were defined as having received early defibrillation if defibrillation was attempted by a bystander or if the EMS call-response interval was five minutes or less. Includes only cases where defibrillation reported as attempted. Non-trauma cases (n=1251)
Abbreviations: EMS, emergency medical services; CPR, cardiopulmonary resuscitation; CRI, call-response interval; ROSC, return of spontaneous circulation.

Table 2.3 Regression Analysis for Subgroup of Cases of Non-Traumatic Aetiology* for the Outcome Survival to Discharge

<table>
<thead>
<tr>
<th>Variable</th>
<th>Survived (n=107)</th>
<th>Died (n=402)</th>
<th>Model 1a (95% CI)</th>
<th>Model 2b (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Under 65 years</td>
<td>64</td>
<td>178</td>
<td>1.9 (1.2-2.9)**</td>
<td>1.6 (1.0-2.6)</td>
</tr>
<tr>
<td>Male</td>
<td>89</td>
<td>311</td>
<td>1.4 (0.8-2.5)</td>
<td>1.1 (0.6-2.1)</td>
</tr>
<tr>
<td>Urban Setting</td>
<td>72</td>
<td>223</td>
<td>1.7 (1.1-2.6)**</td>
<td>1.4 (0.8-2.3)</td>
</tr>
<tr>
<td>Public Location</td>
<td>71</td>
<td>134</td>
<td>3.9 (2.5-6.2)**</td>
<td>3.1 (1.2-5.0)**</td>
</tr>
<tr>
<td>Bystander CPR</td>
<td>96</td>
<td>315</td>
<td>2.4 (1.2-4.7)**</td>
<td>2.4 (1.2-4.9)**</td>
</tr>
<tr>
<td>Early defibrillation attempted</td>
<td>49</td>
<td>113</td>
<td>2.1 (1.4-3.3)**</td>
<td>1.5 (0.9-2.4)</td>
</tr>
<tr>
<td>EMS CRI eight minutes or less</td>
<td>48</td>
<td>105</td>
<td>2.3 (1.5-3.6)**</td>
<td>2.3 (1.4-3.7)**</td>
</tr>
</tbody>
</table>

*aUnivariate Analysis; bMultivariate Analysis
*Non-traumatic aetiology, aged over 18 years, witnessed arrest, shockable at time of first rhythm analysis
**Statistically significant
### Table 2.4 Regression Analysis for Utstein Group for the Outcome Survival to Discharge including Results of Pooled Logistic Regression Analysis following Multiple Data Imputation

<table>
<thead>
<tr>
<th>Variable</th>
<th>Outcome</th>
<th>Model 1a (95% CI)</th>
<th>Model 2b (95% CI)</th>
<th>Model 3c (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Survived (n=106)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Under 65 years</td>
<td>63</td>
<td>1.8 (1.2-2.9)*</td>
<td>1.6 (1.0-2.6)</td>
<td>1.5 (1.0-2.3)</td>
</tr>
<tr>
<td>Male</td>
<td>88</td>
<td>1.5 (0.8-2.6)</td>
<td>1.2 (0.6-2.2)</td>
<td>1.1 (0.7-1.9)</td>
</tr>
<tr>
<td>Urban Setting</td>
<td>71</td>
<td>1.6 (1.0-2.6)*</td>
<td>1.4 (0.9-2.3)</td>
<td>1.5 (0.9-2.3)</td>
</tr>
<tr>
<td>Public Location</td>
<td>70</td>
<td>3.9 (2.5-6.2)*</td>
<td>3.1 (1.9-5.0)*</td>
<td>3.3 (2.1-5.1)*</td>
</tr>
<tr>
<td>Bystander CPR</td>
<td>95</td>
<td>2.4 (1.2-4.7)*</td>
<td>2.4 (1.2-4.9)*</td>
<td>2.3 (1.2-4.5)*</td>
</tr>
<tr>
<td><strong>Died (n=396)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Was shock delivered</strong></td>
<td>106</td>
<td>C</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Early defibrillation attempted</td>
<td>48</td>
<td>2.1 (1.4-3.3)*</td>
<td>1.4 (0.9-2.3)</td>
<td>1.3 (0.8-2.0)</td>
</tr>
<tr>
<td>EMS CRI eight minutes or less</td>
<td>47</td>
<td>2.2 (1.4-3.5)*</td>
<td>2.2 (1.3-3.6)*</td>
<td>2.1 (1.3-3.4)*</td>
</tr>
</tbody>
</table>

*aUnivariate Analysis  
*bMultivariate Analysis  
*cThe variable "Was shock delivered" was omitted from analysis as it is a constant i.e. shock delivered to all cases included in the analysis  
*dPatients were defined as having received early defibrillation if defibrillation was attempted by a bystander or if EMS defibrillation was attempted and the call-response interval was five minutes or less.  
*Results from pooled analysis following multiple data imputation.  
*Statistically significant  

Abbreviations: CPR, cardiopulmonary resuscitation; CRI, call-response interval; EMS, emergency medical services.

In order to assess the impact of missing data on the results of logistic regression, for the whole dataset, data was imputed for the following variables: age; EMS call-response interval; gender; urban/rural location; public/private location; initial shockable rhythm; witness status, bystander CPR; Return of Spontaneous Circulation (ROSC) at any stage; ROSC on arrival at hospital and survival to discharge. Thirty imputations were performed, using predictive mean matching, with a specified maximum of twenty iterations. Following imputation, age and call-response interval were re-categorised into dichotomous variables and the variable ‘early defibrillation attempted’ was derived again, using imputed data. Using only cases that matched the Utstein criteria, logistic regression analysis for the outcome ‘survival to discharge’ was performed using imputed data. As can be seen from the table below, while odd ratios changed slightly, variables that were significant in the pooled analysis (Model 3) were identical to those found to be significant in the original logistic regression analysis (Model 2).
Chapter 3  The Spatial Distribution of Out-of-Hospital Cardiac Arrest and the Chain of Survival in Ireland: A Multi-Class Urban-Rural Analysis

**Key Points**

- This chapter introduces the concept of geographical analysis of Irish OHCA registry data
- The role of spatial distribution in the epidemiology of OHCA will be considered, together with the methods that were employed to create spatial data from OHCA registry data.
- In this chapter, urban-rural classification is considered as a spectrum rather than a simple dichotomous divide
- Building on Chapter 2, this chapter will provide a description of OHCA incidence and provision of pre-hospital resuscitation services (the chain of survival) across the Irish urban-rural spectrum
- The relevance of focussing on urban-rural categorisation as part of geographical analysis of OHCA will also be discussed
- The implications of findings will be discussed, and the rationale for further geographical analysis will be outlined.

**Authors**

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**Published in Irish Geography 2016; 49(2):1-27**

(see Chapter 3 Appendix)
3.1 Abstract

Cardiac arrest occurs when the heart suddenly ceases to pump blood around the body. To optimise survival from out-of-hospital cardiac arrest (OHCA), knowledge of the spatial distribution of OHCA and the availability of resuscitation, or ‘Chain of Survival’, is required. Thus, this study aims to describe OHCA incidence and chain of survival availability in a manner that can help inform pre-hospital planning in the Republic of Ireland. In view of Ireland’s heterogeneous settlement pattern, we analyse the association between varying degrees of rurality, OHCA incidence and the availability of the chain of survival. In addition to population density, settlement size, proximity to urban centres and land use is taken into account which results in six classes: city; town; accessible village; remote village; accessible rural; remote rural. Results show that, when adjusted for age and sex, the incidence of adult OHCA decreases with increasing rurality. Furthermore, while distance to the nearest ambulance station and call-response interval is greater with increasing rurality, the lowest levels of bystander cardiopulmonary resuscitation occur in the most urban class. To the best of our knowledge, this is one of the very first whole-country geographic descriptions of OHCA to be performed internationally. It is also the first OHCA study to use a multi-class urban-rural classification that considers rurality as more than a function of population density.

**Keywords:** cardiac arrest; resuscitation; spatial distribution; rurality
3.2 Introduction

The ultimate cause of all deaths is cardiac arrest, which occurs when the heart stops beating in a manner that interrupts blood circulation around the body. The term ‘Out-of-Hospital Cardiac Arrest’ (OHCA) is used to describe incidents where cardiac arrest occurs unexpectedly and is responded to by statutory emergency medical services (EMS). The tragedy of OHCA has caught the public’s attention in recent years with the sudden deaths of a number of young athletes during participation in sport. In many of such cases, there tends to be a pre-existing heart abnormality. However, the vast majority of OHCAs occur from middle-age onwards and are most commonly caused by coronary heart disease. OHCA presumed to be caused by heart disease results in approximately 1,500 unexpected deaths every year in the Republic of Ireland. This compares to 554 deaths from suicide and 186 deaths in road traffic accidents. OHCA accounts for 5% of the approximately 30,000 deaths per annum in Ireland. The societal and clinical impact of OHCA is such that the American Heart Association has recommended that it be classified as a reportable disease.

Death from OHCA is frequent, though not inevitable, with the chances of survival relying on resuscitation being initiated within minutes of the patient’s collapse. In the case of OHCA, the term ‘resuscitation’ is used to describe a series of interventions that are used in an attempt to restore consciousness or other signs of life. The vital resuscitation interventions that improve survival from OHCA are collectively known as ‘The Chain of Survival’ and include: early recognition of OHCA and immediate call for help to the EMS; high quality cardiopulmonary resuscitation (CPR); defibrillation within minutes of collapse; and effective advanced EMS and post-resuscitation care. Given the firm evidence that exists on how to improve survival, a Task Force to reduce deaths from OHCA was established in Ireland in 2006. This taskforce has established effective resuscitation services including: standardised resuscitation training; documentation and equipment for all ambulance personnel; implementation of dispatch-assisted CPR protocols in ambulance control centres; accreditation of resuscitation training for lay people and occupational first aiders; protocols for establishing community first responder (CFR) programmes. The need for data and surveillance was also highlighted in the 2006 report and, as a result, the National Out-of-Hospital Cardiac Arrest Register (OHCAR) was established.

Given the amount of resuscitation-related activity in recent years, an understanding of the spatial distribution of OHCA and the chain of survival is needed so that statutory services and community responses can be designed to optimise OHCA survival. OHCAR, with data on all OHCA incidents attended by the EMS where resuscitation was attempted, is available for the Republic of Ireland since January 2012. In an earlier study, Masterson et al., dichotomised OHCA events from the year 2012 into either an urban or rural setting, using a variable derived by the Central

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1 While resuscitation guidelines are derived by consensus by the International Liaison Committee on Resuscitation (ILCOR), the European Resuscitation Council lists four key interventions and the American Heart Association includes five.
Statistics Office. However, neither rural nor urban Ireland is homogenous. Indeed, for the former, there is a wide spectrum of settlement patterns, ranging from villages to one-off houses in isolated locations. Equally, urban settlements range from small towns to the city of Dublin, where almost one quarter of the national population resides. Considering the range of differences in urban-rural living, the need for a different structure of services and a different response to OHCA according to the degree of rurality deserves consideration. Teljeur and Kelly developed an index of urban-rural classification at electoral division (ED) level, based on 2002 census data. As well as population density, the index also accounted for settlement size, proximity to urban centres and land use. The resulting index included six classes: city; town; accessible village; remote village; accessible rural; remote rural. These six classes reflect the range of disparate settlement patterns in the Republic of Ireland, making the index a useful tool for examining disease incidence and health service availability.

Within this context, this paper uses an updated version of the index developed by Teljeur and Kelly to explore the spatial distribution of OHCA incidence and availability of the chain of survival. More specifically, it examines whether the incidence of OHCA cases and availability of the chain of survival differs across the range of urban-rural classes classified in the index. The Republic of Ireland is one of three European countries along with Sweden and Denmark with long-established national OHCA registers. This paper is the first to present a whole-nation geographic description of OHCA in Europe. This is also the first study on OHCA that considers rurality as more than a function of population density.

The paper is structured as follows: in the next section, we describe the causes and demography of OHCA and provide an overview of the vital resuscitation interventions that make up the chain of survival with specific reference to the influence of potential spatial factors. We then review the literature that has considered the geography of OHCA in terms of incidence and resuscitation. The subsequent section describes data collection and processing, including a more detailed description of the national OHCAR, as well as the methods of analysis that are used. This is followed by a description of our results, a discussion of the relevance of our findings, and our conclusions.
3.3 Out-of-Hospital Cardiac Arrest and the Chain of Survival

3.3.1 Out-of-Hospital Cardiac Arrest
The primary cause of OHCA is coronary heart disease, with approximately 80% of OHCAs presumed to be of a cardiac aetiology. However, it has also been suggested that this may overestimate the proportion of cases due to cardiac cause, underestimating other causes. For example, Yoshida et al., 216 analysed laboratory and post mortem results for 165 patients who were presumed to have an OHCA of cardiac cause, and following investigation, 69 cases were re-classified as being of a non-cardiac cause. In fact, from a resuscitation perspective, there are six broad categories into which OHCA cause should be classified (see Figure 3.1).

Figure 3.1 Classification of Causes of Out-of-Hospital Cardiac Arrest

<table>
<thead>
<tr>
<th>Category</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Medical</td>
<td>Includes cases in which the cause of the cardiac arrest is presumed to be cardiac, other medical cause (e.g., anaphylaxis, asthma, gastrointestinal bleed), and in which there is no obvious cause of the cardiac arrest</td>
</tr>
<tr>
<td>Traumatic</td>
<td>Cardiac arrest directly caused by blunt, penetrating, or burn injury</td>
</tr>
<tr>
<td>Drug overdose</td>
<td>Evidence that the cardiac arrest was caused by deliberate or accidental overdose of prescribed medications, recreational drugs, or ethanol</td>
</tr>
<tr>
<td>Drowning</td>
<td>Victim is found submerged in water without an alternative causation</td>
</tr>
<tr>
<td>Electrocuton</td>
<td>Any case where electrocution is primary and obvious cause of arrest</td>
</tr>
<tr>
<td>Asphyxial</td>
<td>External causes of asphyxia, such as foreign-body airway obstruction, hanging, or strangulation</td>
</tr>
</tbody>
</table>

While medical causes are the most common, trauma accounts for approximately 7-9% of OHCA cases and is a more significant cause in children and younger adults, accounting for almost one-third of cases 217. The true proportion of OHCA caused by drug overdose is less well documented, but Katz et al., 218 found these patients to have comparable survival as other OHCA patients. Drowning is also a relatively minor cause of OHCA and is also associated with similar survival as other OHCA causes. Electrocuton is rarely documented as a cause of OHCA, while hanging is a significant cause of asphyxial OHCA, with poorer outcomes than for other major causes of OHCA 219.

While treatment of patients may vary within category subgroups, broadly speaking, the basic sequence and approach to resuscitation is largely determined by the type of rhythm cardiac arrest has caused in the heart. Cardiac arrest rhythms are classified as ‘shockable’ and ‘non-shockable’. Shockable rhythms include ventricular fibrillation (VF) or pulseless ventricular tachycardia (pVT). When the heart is in a shockable
rhythm it beats erratically, preventing blood from being pumped around the body. In the case of most cardiac or medical causes of OHCA, the heart is in a shockable rhythm for approximately five minutes, after which the rhythm stops entirely, becoming asystole. Another rhythm associated with OHCA is pulseless electrical activity (PEA), where the heart continues to pump but is unable to circulate blood due to an injury to the body. PEA is more commonly associated with non-cardiac causes of OHCA, including drowning, asphyxiation or severe blood loss.

In terms of demographics, OHCA occurs most commonly in adults aged over 65 years, a finding confirmed by Masterson et al., for Ireland. Significantly though, up to one third of cases occur in people aged 35-59 years old, highlighting that OHCA is not just a condition of older age. The incidence of OHCA in younger adults (aged less than 35 years) and children is lower, however, and the aetiology is also more heterogeneous than in older adults. This younger age group is the category most often affected by underlying heart abnormalities which can trigger heart rhythms that lead to OHCA. Females tend to comprise approximately one third of OHCA cases and this is a consistent finding across studies worldwide.

In Ireland, the overall incidence of OHCA where resuscitation was attempted is 39/100,000/year, though estimates of OHCA incidence vary widely internationally. In their systematic review of OHCA incidence and survival rates, Berdowski et al., reported that across four continents the incidence per 100,000 person-years of OHCA where resuscitation was attempted was as follows: America – 55; Europe – 35; Asia – 28; Australia – 44. Regional variability within countries has also been observed in North America, Japan, Finland and Victoria (Australia).

In summary, OHCA has a variety of causes, but in the majority of adults of middle and older age, the cause tends to be heart disease. Causes in the younger age groups are more varied, and the occurrence of OHCA is relatively rare. There is wide variation in OHCA incidence rates internationally, highlighting the importance of robust national data collection systems. Survival from OHCA also varies widely internationally. As reported by Berdowski et al., (2010), the proportion of survival in studies of OHCA where resuscitation was attempted ranged from 2% in Asia, to 11% in Australia (6% in America and 9% in Europe). The Irish proportion of survival for a similar population is approximately 6%. While some variation may be due to differences in the underlying population and variations in data collection methodologies, it is universally recognised that improved survival can only be achieved through rapid and effective provision of each link in the chain of survival.

3.3.2 The Chain of Survival
The first link in the chain of survival is early recognition of the emergency and activation of the EMS system. The inability to quickly recognise OHCA affects the chances of CPR being started, increases ambulance call-response interval and is associated with decreased survival. Some patients who have suffered OHCA may continue to gasp and have intermittent and/or noisy intakes of breaths (agal breathing). Agonal breathing is present in up to 40% of all OHCAs and reflects non-
effective air intake and is a sign of imminent death. Rapid recognition of OHCA and immediate contact with emergency services expedites the arrival of EMS in the event of OHCA, and also allows ambulance dispatch staff to provide the caller with ‘pre-EMS arrival instructions’, most notably dispatch-assisted CPR (described below). It should be noted, however, that the likelihood and benefits of rapid recognition are mediated by the location of the event. The vast majority of incidents occur in one of the following places: in the home; in a residential institution; on a street or road; at an industrial place/premises; in a public building; at a sports facility or airport; in a GP surgery; or, in an ambulance. The likelihood of OHCA being witnessed increases in more public areas, and the likelihood of rapid recognition further increases in locations where personnel trained in resuscitation are available.

The next step in the chain of survival is the provision of early, good quality CPR. In the event of OHCA, the heart becomes incapable of pumping and blood circulation ceases.

Additionally, the patient stops breathing. Within approximately four to five minutes without air intake and blood circulation, the body becomes starved of oxygen, and cell death begins. Good quality CPR compensates for the inability to breathe through manual ventilations, known as ‘rescue breaths’, and also compensates for the inability of the heart to pump blood by the use of ‘chest compressions’. Resuscitation guidelines advise that, for people trained in resuscitation, a cycle of thirty chest compressions to every two rescue breaths should be performed, with minimum interruptions between chest compressions. Guidelines also advise on the speed, depth and technique for good quality CPR. The introduction of CPR feedback technology has allowed the effect of CPR quality in EMS systems to be measured and Vadeboncoeur et al., have shown that compliance with guidelines for depth of chest compression improved OHCA survival. To maximise the chances of survival, CPR must be commenced immediately after a patient collapses. In most OHCA cases, this implies that members of the public must be willing to commence CPR, known as ‘bystander CPR’. Bystander CPR has long been recognised as a critical factor in OHCA survival and is proven to be an independent predictor of survival. In Irish ambulance dispatch centres, when OHCA is recognised and reported, the call taker follows an algorithm to provide instructions to the caller on how to perform CPR, even if the caller is untrained in resuscitation. This is known as dispatch-assisted CPR and has been shown to increase the performance of bystander CPR and improve survival. Spatial variation in the performance of bystander CPR has been found by Straney et al., (2015) in Australia, Ong et al., (2014) in Singapore, and Sasson et al., (2012b) in the United States (US).

In most cases of OHCA, the heart commonly goes through a five-minute interval where the rhythm of the heart is ‘shockable’. During this phase, a controlled electrical shock can be applied to ‘shock’ the heart back into a normal rhythm through a process known as defibrillation. Good quality CPR must be followed up with prompt access to defibrillation to maximise the chances of survival from OHCA. In fact, defibrillation within three to five minutes of patient collapse can result in percentage survival as high as 50-70% and each minute of delay to defibrillation reduces the
likelihood of survival by 10-12%. While defibrillation is a highly technical treatment, its application is simplified due to the availability of automated external defibrillators which can be used by trained and untrained people alike. In an Irish review of cost-effectiveness of a national public access defibrillation programme, Moran et al., \(^{225}\) estimated that there are between 8,000 and 10,000 functional AEDs available in Ireland, though few of these Irish AEDs had been used in the event of OHCA. Moon et al., \(^{226}\) found that the geographic location of AEDs in Phoenix, Arizona was weakly correlated with OHCA locations, mirroring the Irish finding that, despite proliferation of AED purchase, there is work to be done to ensure that these devices are located and deployed in the geographic locations where they are most needed.

The first three steps in the chain of survival are unequivocally linked to the likelihood of survival from OHCA. Evidence on the role of advanced care, however, is less concrete. For example, a variety of devices are used to ventilate unconscious patients, including advanced airway devices, but such methods are generally used with patients who are more seriously ill and, therefore, less likely to survive. \(^{227}\) While devices can be used to support ventilation of a patient, the provision of chest compressions can also be performed mechanically. Mechanical chest compression devices can deliver uninterrupted compressions at a consistent rate and depth but, to date, have not been shown to be superior to manual chest compressions. \(^{50}\)

Survival from OHCA is largely dependent on pre-hospital resuscitation but studies also suggest that the facilities at the hospital can influence OHCA outcome. The full-time availability of cardiac catheterisation is associated with improved survival. \(^{228}\) In summary, whatever the merits of advanced pre-hospital and post-resuscitation care, the main predictors of survival from OHCA are rapid recognition, good quality CPR and early defibrillation.
3.4 Spatial Analysis of Out-of-Hospital Cardiac Arrest

The response that occurs within the first few minutes of OHCA largely determines the likelihood of survival. In order to minimise response times and to target pre-hospital resources appropriately, the EMS need to know which communities are at highest risk of OHCA. Additionally, communities that are at higher risk of OHCA need to be targeted to ensure that the three first links in the chain of survival are optimised, i.e., OHCA recognition, good quality CPR and prompt defibrillation. In order to target services at more local levels, geographic information systems (GIS) can play a key role in the planning process. To this end, the American Heart Association has published a Science Advisory Statement recommending that GIS be used to ‘enable researchers to explore the links between neighbourhood environments and bystander CPR’ 229.

The utility of GIS methodologies in identifying spatial patterns in OHCA has been explored by many authors, starting with Mayer 122. He plotted 525 OHCA to the census tract of occurrence and found that underlying population was the only variable that was predictive of OHCA incidence. Similarly, Soo et al., 230 found variation in the spatial distribution of OHCA across the 191 electoral areas in Nottinghamshire, even when incidence was adjusted for age. They also investigated further and found that differences in OHCA incidence were in part explained by differences in deprivation across the electoral areas, thus highlighting that population density alone may be insufficient in explaining OHCA incidence. Instead of assigning cases to geographic areas, Lerner, Fairbanks and Shah 169 used kernel density estimation (KDE) to identify areas where cases of OHCA were clustered and then derived census-defined ‘blocks’ so that associations between underlying population, demography and OHCA occurrence could be investigated. Despite the difference in approach, higher OHCA occurrence was also mainly linked to the population structure. This finding was confirmed by Ong et al., 231 for Singapore. While these results suggest OHCA services should be planned around areas of high population density, this may not necessarily always be the case. For example, in a recent Australian paper, Straney et al., 115 found that some of the most sparsely populated ‘local government areas’ in Victoria had the highest incidence of OHCA. In Japan, Yasunaga et al., 232 found that planning services around areas of high population density augmented health inequalities due to prolonged ambulance response times and poorer survival. All these studies highlight that local geography plays an often-unseen role in OHCA incidence and outcomes.

Several methodologies for identifying areas of high OHCA incidence have been used. Sasson et al., 124 employed three different GIS methods, including Global Empirical Bayes rates (a form of smoothed adjusted rates), Local Moran’s I (hot spot identification), and the Spatial Scan statistic (identifies hot spots by comparing observed versus expected outcomes for an area). The three methods did not identify identical clusters, but five areas that were identified by all three were classified as ‘high risk’. The findings of Sasson et al. highlight that, even with precise data geocoding, the type of methodology used to identify clusters may affect results.

While precise geocoding of events is desirable, from a practical perspective it may in fact be more appropriate to consider the ‘area of action’, i.e., the geographical level at
which changes that can influence OHCA incidence and outcomes can be made. Correctly estimating the OHCA population in the geographical area of interest is challenging given the fact that OHCA does not necessarily occur in the area of residence. For example, approximately 25% of OHCAs occur in a location other than the patients’ home. One possibility is to geocode cases to patients’ home addresses. However, while home address data will be reliable for patients who collapsed at home, such data is not necessarily available or wholly accurate for patients who collapse in other locations. Whether or not event location data or patient address data is used is also influenced by the research question. For example, Soo et al., used patient address data in their analysis of the influence of deprivation and cardiovascular disease incidence on OHCA occurrence. From a resuscitation perspective, it can be argued that the incidence rate for the area where the event occurs is of most interest, as it is desirable to strengthen the chain of survival where events are most likely to occur. For example, Sasson et al., coded cases by incident location and used census tract data for those locations (similar to ED) to examine the relationship between likelihood of bystander CPR performance and neighbourhood characteristics, and found that income and race were predictors of bystander CPR performance across a population of 22 million people in the US.

In summary, the studies described in this section show that while methodologies are transferable, local analysis of local data will often reveal unique results and also highlight the importance of correct geocoding in area-based studies. In this context, it is worth stressing that to date no study has undertaken a detailed spatial analysis of OHCA in Ireland, a gap that is addressed in this paper using a unique dataset and innovative methods.
3.5 Data and Methods

This paper uses data from the OHCAR database for the period 1\textsuperscript{st} January 2012 to 31\textsuperscript{st} December 2014. In 2007, the OHCAR database project was implemented in response to a specific recommendation in the National Task Force on Sudden Cardiac Death Report \textsuperscript{116}. OHCAR collects data on all OHCA cases where resuscitation is attempted and where the scene is attended by statutory EMS in Ireland. Cases are reported to OHCAR by the EMS and, since 2014, systematic missing case identification is also performed by the OHCAR office \textsuperscript{87}. Variables for each OHCAR case are extracted from individual ambulance Patient Care Reports (PCRs) which are completed by EMS practitioners who attend the patient. Information extracted includes patient and location details, description of the resuscitation attempt and treatment provided and the outcome at scene. Each case is then matched to the corresponding dispatch data including: time emergency call was received; time first emergency vehicle arrival at scene; time of arrival at hospital (if patient transported). As missing case identification was not systematically performed before 2014, a search of the National Ambulance Service (NAS) PCR archive was performed for 2012 to 2013 to ensure complete case capture.

Before analysis could be conducted, geocoding of location addresses was undertaken. Geocoding is the process of assigning geographic coordinates to an address, following which the features can be entered into a GIS for spatial analysis and mapping purposes \textsuperscript{234}. Accurate geocoding depends on complete, precise and accurate address data \textsuperscript{145}. While every effort may be made to ensure the quality of address data, geocoding for areas that are sparsely populated are more prone to positional error and may be directly attributable to the proportion of rural cases in a dataset \textsuperscript{149,150}. Considering the rurality of Ireland, we were aware that this issue may affect the accuracy of our geocoding. In the scenario where precise geocoding is difficult, mapping data to the centroid of an aggregate area is possible. However, this pragmatic option leads to information loss at local level and may compromise cluster detection accuracy \textsuperscript{147}. Geocoding of our data was performed using the Irish mapping application ‘Health Intelligence Ireland’ \textsuperscript{235}. Cases where the location address recorded matched the address available in the Geodirectory were mapped to exact geographic coordinates. Matches for remaining addresses were searched for individually. Cases where location addresses were misspelled were mapped to exact coordinates. Addresses that were unavailable in the Geodirectory were geocoded using Google Maps \textsuperscript{236}. In cases where an exact match was not found, the address was matched to the centroid of the smallest administrative area possible, i.e., small area or ED. Cases that could not be matched to a small area or ED were classified as ‘unmatched’ if no matching options were available. A total of 94.5\% of cases (n=4734) were geocoded to at least ED level (see Figure 3.2). In order to assess whether bias might be introduced due to the exclusion of cases, comparison of the attributes of matched and unmatched cases was performed using a t-test for the continuous age variable and chi square analysis for categorical variables.
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Figure 3.2 Flowchart of Cases Included

Once geocoded, the address coordinates were mapped and analysed using the GIS software package ArcGIS10. Attribute data (including age, sex, bystander CPR, bystander defibrillation, call-response interval) for each case were linked to the corresponding point data to create a spatially-referenced OHCAR data file. A ‘shapefile’ containing ED level census data and an updated multi-class urban-rural index were also linked. To understand the rurality of a disease and its management, different aspects and dimensions of rurality must be considered in order to provide ‘an overarching classification’ (Teljeur and Kelly, 2008). The most remote rural class tends to be more prevalent in the western counties and along the Atlantic seaboard, and while there is still a large proportion of rural areas in the east of the country, these areas tend to be classified as rural (near), due to the higher prevalence of towns and cities. Figure 3.6 presents a map of the updated multi-class urban-rural classification along with a breakdown by urban-rural class for each county.

Once the urban-rural classification was linked to the ED-level database using the ‘Spatial Join’ function in ArcGIS, all relevant ED data was added to the OHCAR database. As the primary aim of analysis was to examine differences across the urban-rural spectrum, subsequent calculations were made for the total population and for each of the urban-rural classes, which facilitated an area analysis at urban-rural class level. Average age and the proportion of cases in each class were calculated for the following variables: male sex; initial recorded rhythm shockable; bystander witnessed collapse; OHCA occurring during working hours (9am to 5pm); public location of event. In addition, the following variables were generated and analysed for each class: cases with dispatch code ‘arrest’ at time of vehicle deployment (Arrest Recognition); cases that received bystander CPR (B-CPR); cases that received bystander...
defibrillation (B-Defib); cases with a call-response interval less than eight minutes (CRI less than eight minutes); cases where advanced EMS intervention was provided, i.e., advanced airway support given and/or epinephrine administered (Advanced EMS Intervention Provided). These derived aggregated variables were then used as markers for availability of the chain of survival at urban-rural class level. Furthermore, in order to provide an indication of the availability of EMS across the country, the travel distance to the nearest ambulance station from each ED centroid was calculated using the ArcGIS Network Analyst extension. This variable was also used as an additional marker of chain of survival availability (Ambulance Travel Distance).

Adult incidence of OHCA per 100,000 population per year in each urban-rural class was also calculated. To begin, the number of adults in each urban-rural class for each of the following groups was estimated from the 2011 census data: males aged under 65 years; females aged under 65 years; males aged 65 years or older; females aged 65 years or older. Incidence of OHCA per 100,000 adults per year for each of the four groups in every urban-rural class was calculated. The proportion of adults in each of the four groups was then calculated for the reference population, i.e., total number of adults enumerated in the 2011 census. For each class, the incidence in the four groups was adjusted to account for the proportion in the reference population and all four results were summed to give the total adult standardised incidence for each class. Standard errors generated in the calculations were used to calculate 95% confidence intervals for each standardised incidence result.

The overall characteristics of study cases were descriptively analysed using IBM SPSS database (Version 21.0 IBM Corporation). The Kruskal-Wallis test was used to test for inter-class differences in median age and median average ambulance travel times from ED centroids. The chi-squared test for linear trend was used to investigate if proportions in categorical variables changed with increasing rurality (cut-off p>0.05).
3.6 Results

Of the 5,889 cases available, those with missing age and gender information, children (i.e., those less than 18 years of age), cases with traumatic aetiology and cases where collapse was witnessed by EMS were excluded from analysis, leaving 5,011 cases (see Figure 3.2). Of these, 4,734 were geocoded to at least ED level and included in our final analysis. Table 3.1 presents an overview of the characteristics of these cases, both overall and by urban-rural class. The median age for the matched population was 68 years (inter-quartile range (IQR) 55-79 years). There was significant difference in ages across the urban-rural spectrum, with patients in the city and town tending to be younger than those in the most rural areas. As shown in Figure 3.3, however, despite being statistically significant, the actual variance in median age was relatively small across all categories. With regard to gender, over two thirds of patients were male (n=3184; 67%) and this proportion was significantly higher in rural areas and decreased with increasing urbanisation. Nearly a quarter of patients were in a shockable rhythm at the time of first rhythm analysis (n=1,106; 24%), with the proportion of patients in a shockable rhythm decreasing with increasing rurality. The majority of patients suffered a bystander-witnessed arrest (n=2,654; 58%) and a linear trend was observed with lower occurrence in city and town classes, increasing with increasing rurality. The percentage of OHCAs occurring during working hours was 42% overall and this did not vary significantly across the urban-rural spectrum. A higher proportion of OHCAs in a public place was observed in patients in city and town classes, declining with increasing remoteness. It should be noted here that comparative analysis showed that the proportion of males, shockable rhythm, bystander CPR and bystander witnessed cases was significantly higher in the unmatched group (results not presented here but available on request from the authors).
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Figure 3.3 Boxplots of Age categorised by Urban-Rural Class

Table 3.1 Characteristics of Study Cases by Urban-Rural Class

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>City</th>
<th>Town</th>
<th>Village (near)</th>
<th>Village (remote)</th>
<th>Rural (near)</th>
<th>Rural (remote)</th>
<th>p value</th>
<th>Overall</th>
<th>Missing Data</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, median (IQR)</td>
<td>69 (54-79)</td>
<td>66 (66-85)</td>
<td>66 (53-76)</td>
<td>71 (60-81)</td>
<td>70 (60-80)</td>
<td>69 (47-79)</td>
<td>0.000**</td>
<td>68 (55-79)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Males, No. (%)</td>
<td>1151 (65)</td>
<td>984 (67)</td>
<td>196 (65)</td>
<td>74 (71)</td>
<td>541 (70)</td>
<td>238 (73)</td>
<td>0.001***</td>
<td>3184 (67)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Initial Shockable Rhythm, No. (%)</td>
<td>411 (24)</td>
<td>375 (26)</td>
<td>73 (25)</td>
<td>22 (22)</td>
<td>161 (21)</td>
<td>64 (20)</td>
<td>0.018***</td>
<td>1106 (24)</td>
<td>102 (2)</td>
</tr>
<tr>
<td>Bystander Witnessed, No. (%)</td>
<td>930 (55)</td>
<td>826 (58)</td>
<td>175 (60)</td>
<td>61 (62)</td>
<td>471 (62)</td>
<td>190 (61)</td>
<td>0.001***</td>
<td>2654 (58)</td>
<td>171 (4)</td>
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<tr>
<td>During Working Hours, No. (%)</td>
<td>757 (44)</td>
<td>553 (40)</td>
<td>116 (41)</td>
<td>42 (43)</td>
<td>302 (40)</td>
<td>141 (46)</td>
<td>0.604***</td>
<td>4530 (42)</td>
<td>204 (4)</td>
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<tr>
<td>Public Location, No. (%)</td>
<td>342 (20)</td>
<td>306 (21)</td>
<td>53 (18)</td>
<td>10 (10)</td>
<td>98 (13)</td>
<td>43 (13)</td>
<td>0.000***</td>
<td>852 (18)</td>
<td>23 (0.5)</td>
</tr>
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</table>

*Kruskal-Wallis 1-way ANOVA
**Chi-square test for linear trend
Table 3.2 presents the adjusted incidence and percentage of each marker in the chain of survival for the whole population as well as for the urban-rural classes. The overall age and sex standardised incidence of OHCA was 46 per 100,000 adults per year. This incidence ranged from 35 to 51 across the six urban-rural classes with a statistically significant decreasing trend with increasing rurality (p=0.017) – see also Figure 3.4. The overall proportion of cases recognised as cardiac arrest at the time of EMS dispatch was 66%, with decreasing recognition with increasing rurality. Bystander CPR was performed during 66% of the cases which varied significantly across the urban-rural classes (p=0.000), with higher proportions in the rural classes decreasing with increasing urbanisation. The proportion of cases that had bystander defibrillation attempted also varied significantly with 7%, 11% and 8% of patients in the town, village (near) and rural (remote) classes having bystander defibrillation attempted, compared to only 4% in the city class. A trend was observed in the proportion of patients who received an EMS response in less than eight minutes, with a higher proportion of patients in both the city and town classes (29%), declining to 9% in the village (near) class, 6% in the rural (near) class, 4% in the village (remote) class and 2% in the rural (remote) class. (The proportion of patients who received an EMS response within eight minutes was significantly lower in the unmatched group.) The proportion of patients receiving advanced EMS intervention also varied significantly across the classes, with a smaller proportion of patients in the city class receiving advanced interventions than in all other classes. Finally, significant variation was also observed in average ambulance travel distances which were a lot shorter in the city class compared to all other classes – see also Figure 3.5.

Figure 3.4 Age and Sex Adjusted OHCA per 100,000 Adults per Year and associated Confidence Intervals by Urban-Rural Class
Figure 3.5 Boxplots of Median Ambulance Travel Distance from ED Centroid categorised by Urban-Rural Class

Table 3.2 Adjusted Incidence and Markers of Chain of Survival Availability in each Urban-Rural Class

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>City</th>
<th>Town</th>
<th>Village (near)</th>
<th>Village (remote)</th>
<th>Rural (near)</th>
<th>Rural (remote)</th>
<th>p value</th>
<th>Overall</th>
<th>Missing Data, No. (%)</th>
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</thead>
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<tr>
<td>OHCA cases, No. (%)</td>
<td>1761 (37)</td>
<td>1465 (31)</td>
<td>301 (6)</td>
<td>104 (2)</td>
<td>778 (16)</td>
<td>325 (7)</td>
<td>NA</td>
<td>4734 (100)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Adjusted incidence per 100,000 adults per year (95% CI)</td>
<td>51 (47-55)</td>
<td>51 (46-55)</td>
<td>48 (39-58)</td>
<td>44 (29-58)</td>
<td>35 (31-40)</td>
<td>35 (28-42)</td>
<td>0.017††</td>
<td>46 (44-48)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Arrest Recognition, No. (%)</td>
<td>1150 (68)</td>
<td>479 (67)</td>
<td>188 (66)</td>
<td>192 (63)</td>
<td>923 (64)</td>
<td>62 (61)</td>
<td>0.004††</td>
<td>2994 (66)</td>
<td>217 (5)</td>
</tr>
<tr>
<td>B-CPR, No. (%)</td>
<td>932 (55)</td>
<td>550 (69)</td>
<td>243 (78)</td>
<td>226 (79)</td>
<td>978 (73)</td>
<td>80 (77)</td>
<td>0.000††</td>
<td>3009 (66)</td>
<td>160 (3)</td>
</tr>
<tr>
<td>B-defib, No. (%)</td>
<td>65 (4)</td>
<td>47 (7)</td>
<td>25 (11)</td>
<td>31 (9)</td>
<td>100 (6)</td>
<td>9 (8)</td>
<td>0.005††</td>
<td>277 (6)</td>
<td>137 (3)</td>
</tr>
<tr>
<td>CRI less than eight mins, No. (%)</td>
<td>478 (29)</td>
<td>45 (23)</td>
<td>7 (9)</td>
<td>25 (4)</td>
<td>390 (6)</td>
<td>4 (2)</td>
<td>0.000††</td>
<td>949 (22)</td>
<td>376 (8)</td>
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<tr>
<td>Advanced EMS Intervention Provided No. (%)</td>
<td>1288 (75)</td>
<td>1118 (82)</td>
<td>226 (84)</td>
<td>82 (84)</td>
<td>589 (82)</td>
<td>256 (84)</td>
<td>0.000†</td>
<td>3559 (80)</td>
<td>171 (4)</td>
</tr>
<tr>
<td>Ambulance Travel Distance in kms, median (IQR)</td>
<td>3 (2-4)</td>
<td>4 (2-12)</td>
<td>16 (11-20)</td>
<td>16 (12-20)</td>
<td>15 (10-19)</td>
<td>17 (12-23)</td>
<td>0.000†</td>
<td>13668 (8757)</td>
<td>0 (0)</td>
</tr>
</tbody>
</table>
In conclusion, increasing urbanisation is associated with a lower proportion of bystander witnessed events and more events in a public location. Adult age and sex adjusted incidence decreases with increasing rurality, while bystander CPR, bystander defibrillation and advanced EMS intervention declined with increasing urbanisation. Ambulance travel time and distance were lower in more urban areas as expected.
3.7 Discussion

This paper has presented the very first multi-class urban-rural analysis of OHCA and the chain of survival in Ireland. Among the key findings are that the adjusted incidence of OHCA per 100,000 adults per year in the area where the event occurred declined with increasing rurality while, conversely, the proportion of events where bystander CPR was performed and bystander defibrillation was attempted increased with increasing rurality. The proportion of patients who received an EMS response within eight minutes was higher in urban areas, though the proportion of patients who received an advanced EMS intervention was lower in urban areas.

The majority of OHCA in adults is caused by heart disease and thus, an age profile with a median age of 68 years could be expected, since heart disease is particularly prevalent in the 60-70-year age group. The Irish median is in keeping with other international results: 67 years in Australia, 72 years in Denmark and 70 years in Sweden. The trend across the urban-rural classes is also not surprising as cities and towns tend to have younger populations compared to more rural areas. At 68%, the proportion of male patients was also similar to Victoria (68%), Sweden (68%) and Denmark (66%). Thus, the proportion of males is consistent across studies and again, as heart disease is the primary cause of OHCA and heart disease affects a higher proportion of males, this result is as expected.

The proportion of Irish patients with an initial shockable rhythm (24%) varied across the urban-rural spectrum, being highest in cities, towns and village (near) classes, and slightly lower in more rural classes. Considering the variation in travel distances across classes, this decrease in the proportion of shockable rhythm with increased rurality is not surprising. Patients who are in a shockable rhythm at the time of first rhythm analysis have a greater chance of survival, as they have either collapsed in the last five minutes or have received high quality CPR, which maintains a shockable rhythm. Maximising the proportion of patients in a shockable rhythm requires immediate high quality bystander CPR and rapid access to bystander or EMS defibrillation. The majority of Irish patients suffered a bystander witnessed arrest (58%), as was the case in a similar population in Denmark, and while there was variation across the classes, the actual range across classes was relatively small (55% to 62%). Although witnessed status cannot be influenced, patients who have a witnessed arrest are more likely to survive OHCA. The proportion of witnessed arrests in a population is indicative of the likelihood of survival, as the bystander can quickly call the EMS and commence CPR. With regard to the ‘time of day’, the proportion of patients who suffered an OHCA was relatively similar across the urban-rural classes at 42%. This was not the case for the proportion of cases that occurred in a public place, however, where a higher proportion of patients collapsed in a public place in the more urban classes. This finding reflects the fact that there are more people in more urban areas and therefore more opportunity to congregate than in sparsely populated areas, leading to a higher proportion of collapse in a public place.
The incidence of OHCA decreased significantly with increasing rurality. This is in line with previous studies which have also found a lower adjusted incidence of OHCA in more rural areas, including Nottinghamshire and South Korea. These studies only considered population density as a marker of rurality whereas our study also accounts for geographic characteristics associated with increasing rurality. Though incidence decreases as areas become more rural, it should be noted that there is still significant incidence of OHCA, even in more rural areas. This implies that pre-hospital resuscitation planning nationally should not be dramatically skewed towards urban areas in order to avoid inequitable provision of services.

The proportion of patients who received bystander CPR in our population is high at 66%, even compared to countries such as Sweden. While it is not currently possible to measure the quality and timeliness of bystander CPR, our results indicate a willingness among the Irish population to at least attempt CPR in the event of OHCA. Ways in which to capitalise on such willingness in terms of community CPR training programmes need to be supported in Ireland. It should be noted that a lower proportion of cases received bystander CPR in the cities compared to the other classes, which suggests that particular attention should be given to providing CPR training in city areas. Similarly, even though only 6% of patients had bystander defibrillation attempted, this is relatively high compared to other countries such as Denmark and North America (2% for both countries). There is a significant trend in the proportion of patients receiving bystander defibrillation across urban-rural classes, with a particularly low proportion in the city class. However, since the proportion of patients receiving an EMS response in less than eight minutes decreases with increasing rurality, this may be counteracted by decreasing EMS response interval and/or increasing the proportion of patients receiving bystander defibrillation. Also, it is interesting that while median ambulance travel distances increase with increasing rurality, the proportion of patients receiving an advanced EMS intervention also increases. Considering that advanced EMS interventions are available to all patients, regardless of rurality, this increase in interventions with increasing rurality suggests that patients in more rural areas are in a more deteriorated state by the time the EMS arrive and are therefore in need of more advanced interventions. It may seem obvious to decrease EMS response intervals by increasing the number of EMS ambulance stations nationwide, though the impact on outcomes and cost-effectiveness of this would need to be examined.

The reality is that the opportunity for successful intervention is narrow and relies primarily on an appropriate response within the first few minutes of collapse. In many areas, particularly rural areas, it is likely that patients will always be too far from ambulance services. OHCA data shows that, in the majority of cases, bystanders are willing to perform CPR. On an annual basis, approximately 65,000 people are trained in CPR and accredited by the Irish Heart Foundation. While this is a substantial number of people, it still represents a relatively small proportion of the overall population. This means that ways to instil and maintain the ability to perform CPR as a core life-skill in the Irish population should be found. In Norway, for example, resuscitation training is a mandatory part of the school curriculum. In Ireland, many ‘transition year’ students have received CPR training, and, indeed, have been
responsible for saving lives, suggesting that more widespread introduction of CPR training in schools should be introduced nationally. While school training would help to establish CPR training as an integral life-skill for young people, the majority of OHCAs occur in older age groups, at home, highlighting the need for adults and older members of the public also to have access to CPR training. CPR training as part of drivers’ licence applications is one option, and has been successfully introduced in Japan. Many rural communities set up community alert groups, and it may be possible that such groups could facilitate community CPR training.

Within local communities, there are also trained professionals, who are willing to participate in resuscitation in the event of OHCA. The Medical Emergency Responders Integration and Training (MERIT) project has trained large numbers of Irish General Practitioners (GPs) to manage life-threatening emergencies, including OHCA. GPs trained in the MERIT programme reported involvement in 272 events, 65% of which the GP was on scene before the ambulance. Fire service personnel receive regular resuscitation training and some fire brigades currently act as a first response to OHCA in their locale. Voluntary Community Responder groups, many of which involve off-duty members of the ambulance service, are proliferating nationwide. At present the evidence for widespread involvement of local fire services and community responder groups is limited, and further research is required to model which geographic areas are in most need of such first response schemes, so that tailored responses to local needs can be implemented.

Before reaching our conclusions, it is acknowledged that there are limitations to our data. Of particular note is the difficulty in estimating the correct incidence denominator. For this study, the underlying population of the area where the incidence occurred was used, but daily fluctuations in population could not be accounted for. Another issue was the fact that it was not possible to geocode all cases to at least ED level. Even though this only amounted to 6%, there were some differences in the attributes of the matched and unmatched subgroups which may have introduced bias to our results. With the introduction of centralised ambulance dispatch, it is hoped that centralised recording of ambulance GPS coordinates will be possible. Availability of this data will mean that more accurate recording of event locations will be possible in the future. There was missing data for a small number of patient characteristics and derived variables, though the proportion of missingness did not exceed 10% for any variable. It is also acknowledged that we did not address OHCA survival in this study, as survival is being examined in parallel research. A final limitation of note is that the number of years of annual data is limited to three at present, though the data currently available is very comprehensive and has created research opportunities in OHCA that were previously unavailable.

Overall, despite these caveats, in considering the spatial variation of OHCA across the urban-rural spectrum in the Republic of Ireland, our results suggest that the incidence of OHCA is significantly higher in urban areas, but not to an extent where services should be solely focussed on such areas. Differences also exist in availability of the chain of survival across the urban-rural spectrum, which presents opportunities for strengthening the chain including increased community CPR training, enhanced...
support of first responder defibrillation programmes and continued efforts to reduce EMS call-response intervals where possible. Repetition of our analysis with subsequent years’ data will improve the robustness of our findings and allow validation of our conclusions.

3.7.1 Acknowledgements
The authors wish to thank National Ambulance Service and Dublin Fire Brigade personnel who provide the clinical and dispatch data that has made this study possible, and the OHCAR Steering Group who encouraged and facilitated this research.
3.8 Supplementary Data

Figure 3.6 The Six Categories of Urban-Rural Classification
### Table 3.3 Distribution of Urban-Rural Classes by County

<table>
<thead>
<tr>
<th>County</th>
<th>City</th>
<th>Town</th>
<th>Village (Near)</th>
<th>Rural (Near)</th>
<th>Village (Remote)</th>
<th>Rural (Remote)</th>
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</table>

Note: Counties where majority of land space is occupied by a single class are underlined and highlighted in bold.
Key Points

- In chapter 3, differences in the incidence of OHCA in urban and rural settings were significant, however the extent to which ‘rurality’ affects incidence was not quantified.
- In this chapter, linear multilevel regression modelling will be used to quantify the impact of rurality on OHCA incidence, with adjustments made for area-level factors including deprivation and ambulance proximity.
- The impact of rurality and the concept of the urban-rural setting will be discussed both from an Irish and international perspective.
- The implications of results, and applicability of the methodology used in other countries and jurisdictions will be considered, together with opportunities for further geographical analysis.

Authors

Siobhán Masterson, Conor Teljeur, John Cullinan, Andrew W. Murphy, Conor Deasy and Akke Vellinga (2017)


(see Chapter 4 Appendix)
4.1 Abstract

**Purpose**: Variation in incidence is a universal feature of out-of-hospital cardiac arrest (OHCA). One potential source of variation is the rurality of the location where the OHCA incident occurs. While previous work has used a simple binary approach to define rurality, the purpose of this study was to use a categorical approach to quantify the impact of urban-rural classification on OHCA incidence in the Republic of Ireland.

**Methods**: The observed versus expected ratio of OHCA incidence where resuscitation was attempted for the period January 1, 2012, to December 31, 2014, was calculated for each of the 3,408 electoral divisions (ED). EDs were then classified into one of six urban-rural classes. Multilevel modelling was used to test for variation in incidence ratios (IR) across the urban-rural classes.

**Findings**: A total of 4,755 cases of adult OHCA, not witnessed by Emergency Medical Services, where resuscitation was attempted were included in the study. The number of EDs in each category was as follows: city (n = 477); town (n = 293); near village (n = 182); remote village (n = 84); near rural (n = 1,479); remote rural (n = 893). The IR per ED varied from 0 to 18.38 (EDs, n = 3,408). Multilevel modelling showed that 2.36% of variation in IR was due to urban-rural classification. This dropped to 0.45% when adjusted for ED deprivation score and median distance to an ambulance station. The addition of other explanatory variables did not improve the model.

**Conclusion**: OHCA variation in Ireland is limited and almost fully explained by area-level deprivation and proximity to ambulance stations.

**Key words**: emergency care systems, out-of-hospital cardiac arrest, pre-hospital care, remote and rural medicine, resuscitation incidence.
4.2 Introduction

In the United States and Europe, out-of-hospital cardiac arrest (OHCA) is estimated to account for almost 700,000 deaths annually. In Ireland in 2014, the unadjusted incidence of OHCA where resuscitation was attempted was 43 patients per 100,000 population per year. Incidence of OHCA varies internationally, both between and within countries. Most OHCAs have a cardiac aetiology, and for this reason, much of the variation reported can be explained by differences in individual patients, most notably age, gender, ethnicity, lifestyle, genetic/congenital factors and co-morbidities.

Event incidence may also have a geographic component, and clustering of OHCA cases in specific geographic areas has been demonstrated in previous studies. Statutory Emergency Medical Services (EMS) are tasked with ensuring equitable provision of pre-hospital resuscitation, regardless of the geographic location of the OHCA event, and poorer outcomes have been reported for rural-dwelling patients. This is a particular challenge in Ireland, where emergency response times have been shown to be significantly longer in more rural areas. In view of the disparity in outcomes, it is important to understand if there is a specific effect of rurality on the incidence of OHCA so that planning for resuscitation services accounts for differences at urban-rural level.

We have previously reported on marked differences between incidence in Irish urban and rural areas, where ‘urban’ was classified as a population cluster of 1,500 people or more. In OHCA research, the difference between urban and rural areas has often been defined in terms of population density. More recently, we have used a six category urban-rural ‘index’, which reflects the urban-rural spectrum by taking into account population density, settlement size, proximity to urban centres and land use. When adjusted for the age and gender profile of each category, while a significant difference in urban-rural incidence rates remained, the differences between Irish urban and rural incidence were reduced, if not fully explained. Building on our previous research, using this more nuanced rurality categorization, the aim of this study is to quantify the remaining difference in OHCA incidence between urban-rural categories using area-level variables derived from and based on Irish census data.
Chapter 4: The Effect of Rurality on Out-of-Hospital Cardiac Arrest Resuscitation Incidence: An Exploratory Study of a National Registry Utilising a Categorical Approach

4.3 Methods

This retrospective, cross-sectional study used data from the national Out-of-Hospital Cardiac Arrest Register (OHCAR), extracted for the period 1st January 2012 to 31st December 2014. The national OHCAR includes patients who experienced an OHCA, were attended by statutory EMS, and had resuscitation attempted. During the study period, pre-hospital cardiac arrest protocols followed the recommendations of the 2010 International Liaison Committee on Resuscitation (ILCOR). Specific circumstances existed under which the EMS were permitted not to attempt resuscitation, including recognition of death and the presence of a ‘do not resuscitate’ order. Patients aged less than eighteen years, events that were witnessed by the EMS, or that occurred as a result of a traumatic event were excluded from the study.

Each event address was geocoded using the Irish mapping application ‘Health Intelligence Ireland’. Geocoded addresses were mapped to their corresponding electoral divisions (EDs) using the geographic information system ArcGIS Software (Environmental Systems Research Institute [ESRI] Inc., Redlands, CA). Electoral divisions are legally defined areas for which small area population statistics are published by the Irish census and are similar to census tracts. Ireland is divided into 3,444 EDs, but aggregated to 3,409 to protect confidentiality in some small EDs.

Two ED-level explanatory variables were extracted from census data (i.e. proportions of persons living in one person households and self-reporting bad or very bad health (poor health)). The 2011 deprivation index (SAHRU), published by the Small Area Health Research Unit in Trinity College, Dublin, was also used as an explanatory variable. Deprivation reflects the level of disadvantage in an area, and thus is a multidimensional measure of the socioeconomic status of an area. A higher positive value indicates more severe deprivation. While the components may vary, the concept of material deprivation is similar to the concept of socioeconomic status used in the United States. The index comprises the following four indicators extracted from the 2011 Irish census: unemployment; low social class; no car; and type of housing tenure. Principal component analysis was to create a weighted combination of these factors. Material deprivation of individual EDs is expressed as deciles with 10 referring to the most deprived 10% of EDs.

Based on the location of ambulance services nationwide, the median distance from an ambulance station to each ED centroid was also calculated using the proximity toolset in ArcGIS.

In order to understand the rurality of disease, Teljeur and Kelly have argued that “different aspects and dimensions of rurality must be considered in order to provide an overarching classification”. For the purposes of this study, an updated version of their urban-rural classification was calculated with data from the 2011 Irish census. Finally, each ED was categorised into one of the resulting six urban-rural classes: city; town; near village; near rural; remote village and remote rural. The distinction between ‘near’ and ‘remote’ is on the basis of proximity to population centres which imply access to services and amenities.
does not reflect the daily population due to passenger throughput, it was excluded from analysis.

The total number of adult OHCA resuscitation cases for each ED was categorised into 5-year age bands by gender. The ED population data for a corresponding breakdown was extracted from census data for 2011. The incidence rate in each age band by gender nationally were calculated and then applied to ED population figures to calculate the expected number of adult OHCA resuscitation cases for each ED. The ratio of observed to expected OHCA resuscitation cases was calculated for each ED, providing the outcome of interest (Incidence Ratio (IR)).

Mixed effects multilevel linear regression modelling was performed to test for a random intercept (i.e. for significance of a differing effect across urban-rural classes for IR). Analysis was performed using the Stata Statistical Software (Statacorp 2013: Release 13. College Station, Texas). Likelihood ratio tests comparing the null single level model and the null multilevel model were used. In order to check whether the effect of urban-rural class could be explained by area-level variables, the ED-level explanatory variables were added to the null multilevel model (including interaction terms) and a likelihood ratio test was used to assess the effect of each variable on the model. No interactions between explanatory variables were found. The appropriateness of allowing for a random slope (i.e. differing effects of explanatory variables across urban-rural classes in the model) was also assessed. In order to ensure robust standard errors for regression coefficients, 1,000 bootstrapped resamples of the study population were performed. The bootstrap method of error estimation involves ‘resampling’ of the data to generate estimates of the data distribution from which robust confidence intervals can be derived, thus avoiding reliance on assumptions about data distribution that may not be valid, particularly when data are not normally distributed.
Chapter 4: The Effect of Rurality on Out-of-Hospital Cardiac Arrest Resuscitation Incidence: An Exploratory Study of a National Registry Utilising a Categorical Approach

4.4 Results

Of the 4,807 patients eligible for inclusion in the study, 4,781 cases (99.5%) were successfully geocoded to at least ED level. Following exclusion of cases that occurred in Dublin Airport ED, a total of 4,755 adult OHCA resuscitation cases were included in the analysis. Almost two thirds of patients were male (n=3,203; 64.7%). Patients ranged in age from 18 to 100 years, and the average age was 65.4 years (standard deviation 17.2 years). Over half (55%) of patients were aged 65 years or older.

As shown in Figure 4.1, OHCA resuscitation incidence ranged between 0 to 29 cases per ED, with cases occurring in just over half of EDs (n=1,713; 50.3%). The IR varied from zero to 18.38 across the 3,408 EDs included.

Figure 4.1 Cumulative Percentage of OHCA Resuscitation Cases per Electoral Division

The distribution of urban-rural classes across Ireland is presented in Figure 4.2. The most remote rural class tends to be situated along the western seaboard, while the near rural class tend to be clustered around the EDs classified as town or city (more prevalent in the east of the country). The near village class is situated in areas with relatively more near rural EDs. Conversely, the remote village class – the least common class – is more likely to be situated in areas with more remote rural EDs. In contrast, Figure 4.3 shows the ratio of observed:expected OHCA incidence as more randomly dispersed across EDs nationwide.
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Figure 4.2 Six Category Urban Rural Classification categorised by Electoral Division
Figure 4.3 Observed: Expected OHCA Resuscitation Incidence Ratio at Electoral Division Level

Characteristics of the study population and electoral divisions, categorised by urban-rural class are presented in Table 4.1.
Table 4.1 Characteristics of OHCA Resuscitation Cases and Electoral Divisions categorised by Urban-Rural Class

<table>
<thead>
<tr>
<th></th>
<th>City</th>
<th>Town</th>
<th>Near Village</th>
<th>Remote Village</th>
<th>Near Rural</th>
<th>Remote Rural</th>
<th>Overall</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>IR in each Urban-Rural classification</strong></td>
<td>1.09</td>
<td>1.12</td>
<td>1.04</td>
<td>0.96</td>
<td>0.79</td>
<td>0.76</td>
<td>0.99</td>
</tr>
<tr>
<td><strong>Electoral Divisions, n (%)</strong></td>
<td>477 (14%)</td>
<td>293 (8.6%)</td>
<td>182 (5.3%)</td>
<td>84 (2.5%)</td>
<td>1479 (43.4%)</td>
<td>893 (26.2%)</td>
<td>3408</td>
</tr>
<tr>
<td><strong>Mean number of adults per ED</strong></td>
<td>2,511</td>
<td>3,472</td>
<td>1,092</td>
<td>864</td>
<td>462</td>
<td>300</td>
<td>1,009</td>
</tr>
<tr>
<td><strong>Average ED Area (km²)</strong></td>
<td>2.0</td>
<td>17.1</td>
<td>23.2</td>
<td>25.8</td>
<td>22.3</td>
<td>28.0</td>
<td>20.6</td>
</tr>
<tr>
<td><strong>Adult population (per km²)</strong></td>
<td>1257</td>
<td>203</td>
<td>47</td>
<td>33</td>
<td>21</td>
<td>11</td>
<td>49</td>
</tr>
<tr>
<td><strong>EDs with IR greater than 1, n (%)</strong></td>
<td>247 (51.8%)</td>
<td>157 (53.6%)</td>
<td>88</td>
<td>34</td>
<td>448</td>
<td>240</td>
<td>1214</td>
</tr>
<tr>
<td><strong>Total Adult Population, n (%)</strong></td>
<td>1,196,863 (34.8%)</td>
<td>1,017,340 (29.6%)</td>
<td>198,756 (5.8%)</td>
<td>72,569 (2.1%)</td>
<td>682,712 (19.9%)</td>
<td>267,836 (7.8%)</td>
<td>3,436,076</td>
</tr>
<tr>
<td><strong>Number of patients, n (%)</strong></td>
<td>1,674 (35.2%)</td>
<td>1,470 (30.9%)</td>
<td>314 (6.6%)</td>
<td>109 (2.3%)</td>
<td>836 (1.7%)</td>
<td>352</td>
<td>4755</td>
</tr>
<tr>
<td><strong>SAHRU deprivation score, mean (SD)</strong></td>
<td>1.3 (2.9)</td>
<td>1.1 (1.8)</td>
<td>0.8 (1.1)</td>
<td>0.5 (1.2)</td>
<td>-0.6 (0.9)</td>
<td>-0.3 (1.0)</td>
<td>0.0 (1.6)</td>
</tr>
<tr>
<td><strong>Proportion of one person households, mean (SD)</strong></td>
<td>28.0 (9.9)</td>
<td>25.4 (8.3)</td>
<td>24.2 (5.6)</td>
<td>20.8 (5.2)</td>
<td>25.3 (6.2)</td>
<td>23.6 (7.2)</td>
<td>23.6 (7.2)</td>
</tr>
<tr>
<td><strong>Proportion of poor self-reported health, mean (SD)</strong></td>
<td>2.0 (1.0)</td>
<td>1.7 (0.7)</td>
<td>1.6 (0.7)</td>
<td>1.5 (0.6)</td>
<td>1.2 (0.6)</td>
<td>1.5 (0.9)</td>
<td>1.4 (0.8)</td>
</tr>
<tr>
<td><strong>Median distance (km) to ambulance station from ED centroid (IQR)</strong></td>
<td>3 (2-4)</td>
<td>4 (2-12)</td>
<td>16 (11-20)</td>
<td>16 (12-20)</td>
<td>15 (10-19)</td>
<td>17 (12-23)</td>
<td>13 (7-19)</td>
</tr>
</tbody>
</table>

Legend
- IR – Observed:Expected incidence ratio
- EDs – Electoral Divisions
- Km - Kilometers
- SAHRU - Small Area Health Research Unit
- SD – standard deviation
- IQR – inter-quartile range
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The multilevel null model was a superior fit to the single level model for IR (Likelihood ratio test statistic at 1 d.f.: 72.31 (p<0.001)), indicating variation at urban-rural level. The proportion of unexplained variance that was due to urban-rural class was 2.36% for the IR. Model fit improved significantly when adjusted for the SAHRU deprivation score. As shown in the final model (Table 4.2), increasing SAHRU score was positively associated with IR, and unexplained variance between urban-rural classes was reduced to 1.19% when adjusted for SAHRU score. The addition of median ambulance distance reduced unexplained variance to 0.45%. There was no evidence of a random slope (i.e. varying effect of deprivation across urban-rural classes for IR). Addition of other variables of deprivation from the census (i.e. proportions of persons living in one person households and self-reporting bad or very bad health (poor health)) did not improve the model.

Table 4.2 Multilevel Regression Analysis of Incidence Ratio across Urban-Rural Classes – Final Model

<table>
<thead>
<tr>
<th>Regression Coefficient</th>
<th>Incidence Ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>β</td>
</tr>
<tr>
<td>Constant</td>
<td>1.080</td>
</tr>
<tr>
<td><strong>ED level variables</strong></td>
<td></td>
</tr>
<tr>
<td>SAHRU Score 2011</td>
<td>0.092</td>
</tr>
<tr>
<td>Median ambulance distance</td>
<td>-0.011</td>
</tr>
</tbody>
</table>

Variance Explained by Final Models

<table>
<thead>
<tr>
<th></th>
<th>Variance</th>
<th>SE**</th>
</tr>
</thead>
<tbody>
<tr>
<td>Between Urban-Rural classes</td>
<td>0.007</td>
<td>0.013</td>
</tr>
<tr>
<td>Between EDs</td>
<td>1.614</td>
<td>0.003</td>
</tr>
</tbody>
</table>

Variance Partition Coefficient (%)*** 0.451

*95% Confidence Interval
** Bootstrap standard error
***0.007/(0.007+1.614)
4.5 Discussion

This study shows that in a national database of OHCA where resuscitation was attempted, after adjustment for age and gender, urban-rural area-level differences are almost fully explained by area-level deprivation and proximity to ambulance services. In 2017, Borders suggested that it is not sufficient to establish whether urban-rural disparities exist, but that it is necessary to explore the “potential mediators and moderators” of these differences. Since we first identified a difference in urban-rural OHCA incidence in Ireland, through subsequent studies we have tried to address each sub-component to understand the reason for urban-rural variation in Ireland. To the best of our knowledge, this is the first study to attempt to quantify and explain the effect of rurality on incidence of OHCA in a national population.

The definition of rurality varies greatly internationally. Since 1910, the United States census bureau has classified areas with a population of at least 2,500 within its boundaries as urban, with all other areas being considered rural. Internationally, definitions of rural range from settlements with fewer than 30,000 inhabitants in Japan to settlements with fewer than 200 people in Sweden. In the Irish urban-rural index used here, settlements containing more than 1,500 persons are almost universally considered towns. While most classifications rely on one indicator (i.e. population count or density), rurality may be considered as a larger concept; it has been theorised that characteristics such as agriculture, forestry, mining methods and water quality should be considered. Differing degrees and dimensions of rurality may pose differing challenges to health service provision.

Our study describes rurality in the context of the Republic of Ireland, using characteristics that may impact on the Irish OHCA population, such as settlement size, proximity to urban centres and land use. The distinction between ‘near’ and ‘remote’ is on the basis of a gravity model of proximity to settlements within 48km. Forty-four percent of ‘near’ EDs and 26% of ‘remote’ EDs are within 48km of one of the five cities in Ireland. With the exception of some of the islands, the most remote parts of the country are up to 160km (or over 2 hour’s drive) from one of the five cities (or to a city in Northern Ireland). Relative to other countries, this may not seem particularly remote. In the context of OHCA however, where rapid intervention is essential, the concept of ‘remote’ does not need to be on the basis of large distances.

Applying a localised urban-rural classification does however mean that our results may need adjustment to be applied to other countries. Once rurality is defined however, the methodology used in our study to quantify the effect of rurality on OHCA incidence is equally applicable in other countries, and will enable the generation of results that are appropriately localised to the area of study.

The urban-rural effect in our study adjusted for ED level deprivation score. In their study of participating centres in the Resuscitation Outcomes Consortium, Reinier et al. found that socioeconomic status was a predictor of incidence of sudden cardiac arrest. It is of note that the coefficient for this variable in our study was very stable.
throughout, even when the median ambulance travel distance was included in the model. Our study therefore supports the finding that OHCA resuscitation incidence is statistically significantly higher in more deprived populations, albeit — in the Irish context — that the size of the association is small. The concept of deprivation used (SAHRU) is closely aligned to the concept of socioeconomic status in the United States. Shavers observed that the components used to construct socioeconomic scores vary in health disparity research. For this reason — while the methodology used in this study can be applied elsewhere — it is hypothesised that the significance and strength of the association between rurality and deprivation will vary, depending on the context and the measure used.

One possible explanation for our finding that proximity to ambulance stations is associated with OHCA resuscitation incidence is that the more rurally located an OHCA patient, the less likely that the patient will have a resuscitation attempt. When an OHCA occurs in an area that is remote from an ambulance station, and if resuscitation is not commenced before ambulance services arrive, it may be more likely that resuscitation is deemed inappropriate when EMS personnel examine the patient. In the absence of national data on overall OHCA cases, it is not possible to confirm whether this is the case. Only recently, the consolidation of ambulance dispatch into a national operations centre has allowed the introduction of dynamic deployment of ambulance resources in Ireland. Our data predates this development, therefore it may be expected that dynamic deployment could have further decreased any disparities between urban and rural OHCA incidence. It should however be remembered that the actual effect found is very small.

Table 1, shows that 34% of all cases occurred in rural and village EDs, and 36% of the total adult population resides in these areas. The adult population density ranges from 11 adults per square kilometre in remote rural areas to 47 adults per square kilometre in near villages. Providing an adequately rapid ambulance response to these areas of low population density will remain a challenge, even with the introduction of dynamic deployment. Irish rural communities have a long history of reacting to this issue by providing a community response. Again, in recent years, the formation and deployment of Community First Responder groups in rural areas has been supported by the National Ambulance Service, and a national strategy which will attempt to address these challenges is being developed.

This study has a number of limitations. Firstly, almost half of EDs had an IR of zero, and approximately 72% of EDs had a predicted rate of less than one case. High numbers of zero values may be expected to lead to an underestimation of variance, though simulation studies have suggested that a sparse data structure has a limited effect on model robustness. Therefore we propose that the presence of zeros should not have affected the validity of our estimate. Such low incidence however, is likely to have contributed to unexplained variation at ED level, and a slight change in observed incidence may have a dramatic effect on IRs. To the best of our knowledge, this is the first time that multilevel modelling has been used to examine OHCA incidence across regions with remote rural areas and small or zero incidence counts. Ong et al. used multilevel modelling of similarly small geographical units in their study.
of incidence variation in Singapore. Singapore however is more uniformly metropolitan and densely populated than the Republic of Ireland and therefore small areas in Singapore are less prone to variation than Irish electoral divisions. In view of this issue, as subsequent years of OHCAR data become available, we intend to repeat our analysis in order to test the validity of our current findings. Further aggregation of data may also be an option. We explored the option of aggregating neighbouring EDs that were of the same urban-rural class and deprivation decile but this method had little impact on the number of units with little or no cases.

Secondly, events were geocoded to the location of arrest rather than patients’ residential addresses. Incidence rates were calculated using population data from the ED where the event occurred even though almost one third of cases occurred at a location other than a residential address. It is possible that geocoding based on patients’ home addresses may have affected the IRs.

Thirdly, this study includes only OHCA cases where resuscitation was attempted and does not fully reflect the burden of OHCA in the Irish population. Considering that the majority of cases included in our study would be presumed to have suffered an OHCA of cardiac aetiology, our finding of a ‘rural effect’ in relation to OHCA incidence may reflect a relationship with cardiovascular disease (CVD). While our finding suggests that OHCA resuscitation incidence tends to be lower with increasing rurality, Haraldsdottir et al. found a higher adjusted incidence of CVD mortality in the rural Icelandic population, while Kulshreshtha et al. found that high CVD mortality persisted in some subgroups, including rural populations. In contrast, our findings are in agreement with Ro et al., who found that OHCA where resuscitation was attempted increased with increasing urbanization. Our data relates specifically to OHCA where resuscitation is attempted, and should not be considered as a proxy measure for overall OHCA incidence.

In summary, this study suggests that there is significant urban-rural variation in OHCA incidence in Ireland, but that this variation is limited and almost fully explained by area-level deprivation and proximity to ambulance stations. The methodology used in this study has provided a national estimate of the effect of ED level factors in OHCA resuscitation incidence. The use of methods that allow area-level factors to be acknowledged while accounting for spatial variation at local level, such as Bayesian modelling, may be able to provide further explanation of more localised differences in OHCA resuscitation incidence that can help to inform pre-hospital resuscitation planning which is targeted at particular areas and communities.

4.5.1 Ethics Approval
Ethical approval for research using non-identifiable OHCAR data was obtained from the Research Ethics Committee, National University of Ireland, Galway.

4.5.2 Conflict of Interest
The authors declare that they have no conflict of interest.
Chapter 5  Out-of-Hospital Cardiac Arrest in the Home – Can Area Characteristics Identify At-Risk Communities in the Republic of Ireland?

Key Points

• The majority of OHCAs where resuscitation is attempted worldwide occur at home
• In this chapter the potential for identifying high risk areas for OHCA at home using Bayesian CAR modelling or spatial smoothing will be explored
• The effect of area-level variables, including urban-rural setting, self-reported health and, deprivation on the area-level risk of OHCA will be investigated
• Specific areas where the risk of OHCA is greater will be identified and the implications for pre-hospital resuscitation service planning will be discussed.

Authors

Siobhán Masterson, Conor Teljeur, John Cullinan, Andrew W Murphy, Conor Deasy and Akke Vellinga

(See Chapter 5 Appendix)
Chapter 5: Out-of-Hospital Cardiac Arrest in the Home – Can Area Characteristics Identify At-Risk Communities in the Republic of Ireland?

5.1 Abstract

**Background:** Internationally, the majority of out-of-hospital cardiac arrests where resuscitation is attempted (OHCAs) occur in private residential locations i.e. at home. The prospect of survival for this patient group is universally dismal. Understanding of the area-level factors that affect the incidence of OHCA at home may help national health planners when implementing community resuscitation training and services.

**Methods:** We performed spatial smoothing using Bayesian conditional autoregression on case data from the Irish OHCA register. We further corrected for correlated findings using area-level variables extracted and constructed from national census data.

**Results:** We found that increasing deprivation was associated with increased case incidence. The methodology used also enabled us to identify specific areas with higher than expected case incidence.

**Conclusions:** Our study demonstrates novel use of Bayesian conditional autoregression in quantifying area-level risk of a health event with high mortality across an entire country with a diverse settlement pattern. It adds to the evidence that the likelihood of OHCA resuscitation events is associated with greater deprivation and suggests that area deprivation should be considered when planning resuscitation services. Finally, our study demonstrates the utility of Bayesian conditional autoregression as a methodological approach that could be applied in any country using registry data and area-level census data.

**Keywords:** Out-of-hospital cardiac arrest; resuscitation; deprivation; residential characteristics; spatial smoothing; conditional autoregression

**Highlights:**
- The majority of OHCA where resuscitation is attempted worldwide occur at home
- We examined whether high risk areas for OHCA at home were identifiable using spatial smoothing
- Specific areas where case incidence was higher than expected were identified
- Greater deprivation was associated with higher than expected case incidence
5.2 Introduction

Cardiac arrest occurs when the heart suddenly stops or becomes incapable of pumping blood around the body, and is the ultimate cause of all deaths. Out-of-hospital cardiac arrest (OHCA) is the term ascribed to incidents that occur unexpectedly outside of an acute medical setting, and where the patient is attended by Emergency Medical Services (EMS). Survival from OHCA is almost entirely dependent on the initiation of ‘The Chain of Survival’. If the chain of survival is not activated within minutes of OHCA occurring, death is certain. The chain of survival is a sequence of resuscitation interventions, namely: early recognition of OHCA and immediate call for help to the EMS; high quality cardiopulmonary resuscitation (CPR); defibrillation within minutes of collapse; and effective advanced EMS and post-resuscitation care. Timely resuscitation that is correctly performed is extremely effective. It has been shown that defibrillation within 3-5 minutes of collapse can result in survival as high as 50-70%. Each minute of delay however reduces the likelihood of survival by 10-12%. For this reason, the ability to predict where OHCA events are most likely to occur can provide the opportunity to configure the provision of resuscitation training skills and services so that they are available in areas where they are most likely to be required.

The majority of OHCA events are located at home, geographic variation in OHCA incidence is consistently observed in OHCA epidemiological studies. One aspect of geography that should be taken into account when considering variation is spatial autocorrelation, “the ubiquitous phenomenon that two close areas are often more similar than those that are far apart”. Regression analyses that do not account for spatial autocorrelation are at risk of violating the assumption of independence which is generally necessary for regression analysis. The Bayesian conditional autoregression (CAR) model accounts for spatial autocorrelation in the error term, and has been shown to be particularly suited to modelling spatial phenomena strongly tied to a local context, ensuring a more realistic estimate of
relative area risks. From a health perspective, health behaviours tend to be clustered in individuals and some of this clustering may be linked to shared neighbourhood characteristics. This may also be the case for the occurrence of OHCA and attempted resuscitation.

In this study we aimed to estimate the underlying relative risk by small area of OHCA that occurred at home. Additionally we aimed to (1) identify underlying area-level factors that may increase the incidence of OHCA that occurs at home and (2) identify specific areas where the risk of OHCA at home is greatest in the Republic of Ireland. We also considered the influence of self-reported health, the rurality of a location, and the material deprivation of each ED on the incidence of OHCA in our analysis.
5.3 Methods

5.3.1 Setting
In the 2011 census the Republic of Ireland recorded a population of 4,588,252\(^{272}\). The country is divided into 3,409 small areas called Electoral Divisions (EDs)\(^{133}\). The average ED population was 1,346 (ranging from 73 to 36,057). At the time of the 2011 national census, 62% of the population lived in urban settlements of 1,500 people or more, accounting for 8% of total land mass. The remaining approximate 1.7million population were dispersed across the 65,000 square kilometres which constitute rural Ireland\(^{273}\).

The Irish National Ambulance Service is the sole provider of statutory Emergency Medical Services (EMS) outside of Dublin where the Dublin Fire Brigade (DFB) also provides the statutory EMS response. The Advanced Medical Priority Dispatch System (AMPDS\(^{26}\)) is used by both NAS and DFB to prioritise calls. Emergency ambulances and rapid response vehicles are tasked to OHCA incidents and are staffed by paramedics and advanced paramedics. Intermediate care vehicles may also be dispatched as first responders or to assist in the event of OHCA and are usually staffed by emergency medical technicians. In Dublin, fire tenders are staffed primarily by fire fighter paramedics and are routinely tasked to OHCA in the greater part of the city. Irish statutory EMS staff must be licensed and registered with the Irish Pre-Hospital Emergency Care Council (PHECC) and are required to comply with PHECC Clinical Practice Guidelines in their practice\(^{255}\).

5.3.2 Data
Data from the national Out-of-Hospital Cardiac Arrest Register (OHCAR) were extracted for the period 1\(^{st}\) January 2012 to 31\(^{st}\) December 2014\(^{253}\). OHCAR is a register of all patients who suffer an OHCA, are attended by the EMS, and have resuscitation attempted. In Ireland, as for the majority of countries where statutory resuscitation services are provided, specific circumstances exist under which the EMS are permitted to not attempt resuscitation, including recognition of death and the presence of a ‘do not resuscitate’ order\(^{274}\). OHCAR data are extracted from ambulance Patient Care Reports (PCRs) which are completed by EMS personnel during or directly after attending the OHCA event. Dispatch and time variables for each case are obtained from NAS and DFB ambulance control centres. Case validation and registration comprehensiveness is routinely performed to ensure the quality of OHCAR data\(^{87}\). Cases where no resuscitation was attempted are not recorded in OHCAR.

Patients 18 years or older, who suffered an event of non-traumatic aetiology and were not witnessed collapsing by the EMS, were included in the study. In European Union statistics on cardiovascular diseases, death at less than 65 years is considered ‘premature’\(^{275}\). Patients were therefore categorised into two age groups in order to check for a differing risk according to patient age i.e. less than 65 years and 65 years and older.
5.3.3 Geocoding and Data Preparation

Private residential event location addresses were geocoded to latitude and longitude using the application ‘Health Intelligence Ireland’. Coordinates were then allocated to EDs using ArcGIS (Environmental Systems Research 95 Institute [ESRI] Inc., Redlands, CA). Expected rates of OHCA by small area were computed using indirect standardisation based on 2011 census population figures. Standardisation was on the basis of sex and five year age bands. Standardised incidence ratios were also calculated for the two age categories separately (less than 65 years (Home U65) and patients aged 65 years or older (Home 65+)). Unsmoothed standardised incidence ratios that were greater than 1 where considered to be ‘high’ while those below 1 were considered to be ‘low’.

Three ED-level covariates were included: deprivation, urban-rural class and self-reported health. The deprivation index was based on four census indicators: unemployment, low social class, local authority housing, and car ownership. The indicators were selected based on the philosophy of the Townsend index developed in the UK. The four indicators are combined using principal components analysis, with the weights for the first three indicators being approximately equal, while a marginally lower weight applies to car ownership. The index is an estimate of material deprivation in an ED, and thus is a multidimensional measure of the socioeconomic status of an area. It can be expressed as a standardised score with higher positive values indicating greater deprivation, or as quintiles. While the latter results in regression coefficients that may be more interpretable, it does not capture the skewed nature of the measure, and the fact that highly deprived areas are more commonly located in city centres. We used a continuous score in the main analysis, and included a secondary analysis based on quintiles. Urban/rural classification was on the basis of a previously developed index with four levels: city; town; village; rural (Teljeur and Kelly, 2008, updated in Masterson et al. 2016). The classification combines information on population density, settlement size, land use, and proximity to other settlements. Higher rates of OHCA might be anticipated in areas where a high proportion of population report bad or very bad health. For this reason, a third variable indicating the proportion of people self-reporting bad or very bad health in each ED (Health) in the census 2011 was also calculated.

5.3.4 Exploratory Geographic Analysis

Before performing CAR analysis, a check for spatial autocorrelation in all Home cases, and the Home U65 and Home 65+ subgroups, was carried out using the Global Moran’s I statistic. Global Moran’s I is a z-score which describes the degree of spatial concentration or dispersion for a measured variable.

5.3.5 Spatial Smoothing

At the ED-level, OHCA is a relatively uncommon event, and therefore incidence rates are subject to substantial variability due to small numbers. Spatial smoothing provides a method to reduce noise due to random variation. The Bayesian CAR model was used.
to smooth the standardised incidence rates to adjust for small numbers and to allow the model to ‘borrow strength’ from observations in neighbouring areas. The model requires data on the spatial structure of observations. The neighbourhood matrix was determined using ‘first order queen contiguity’ i.e. EDs that share a boundary were considered neighbours. Artificial links were created for EDs that were otherwise not connected (e.g. islands).

The Bayesian CAR model was fitted using Markov Chain Monte Carlo algorithms with WinBUGS. The model is based on the assumption of a Poisson model for the spatial distribution of events. The model was given a burn-in run of 10,000 iterations followed by 40,000 iterations. Convergence was tested using the Gelman-Rubin test.

Initial models were created for all three groups without covariates. Models were also estimated for each covariate alone, all pairings of covariates and for all three covariates. Models were estimated separately for all cases and both age group-related subcategories. Model selection was conducted using the deviance information criterion (DIC), where a lower DIC suggested a better compromise between model fit and parsimony. A difference of less than 5 in model DIC is not considered sufficient to distinguish between two models. Where multiple models resulted in differences of less than 5 relative to the DIC of the best fitting model, preference was given to the model with the fewest covariates. Analysis was conducted on yearly data in order to assess the sensitivity of the overall results to yearly fluctuations in the spatial distribution of events. For ease of explanation, risk ratios were calculated for covariates included in the final models.
5.4 Results

Over a three year period (1st Jan 2012 to 31st December 2014), a total of 4,834 OHCAR cases were eligible for inclusion in the analysis, of which 3,388 cases were classified as ‘Home’ cases. Each Home case was successfully geocoded to the ED centroid level. A total of 41.6% of events occurred in patients aged less than 65 years (n=1,410). Table 5.1 describes the patient and ED characteristics of all Home cases.

Table 5.1 Summary Characteristics of Home Cases (n=3,388) compared to Irish Population (n=4,588,252, Irish census 2011 (Central Statistics Office, 2012c))

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Home Cases</th>
<th>Irish Population</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age in years (median (IQR))</td>
<td>68 (55-78)</td>
<td>36*</td>
</tr>
<tr>
<td>Age 65+years n(%)</td>
<td>1,978 (58.2%)</td>
<td>535,393 (11.7%)</td>
</tr>
<tr>
<td>Male n(%)</td>
<td>2,243 (66.0%)</td>
<td>2,272,699 (49.5%)</td>
</tr>
<tr>
<td>Number of EDs</td>
<td>1,512 (44.3%)</td>
<td>3,409 (100%)</td>
</tr>
<tr>
<td>Urban-Rural Classification of EDs</td>
<td></td>
<td></td>
</tr>
<tr>
<td>City n(%)</td>
<td>395 (26.1%)</td>
<td>478 (14.0%)</td>
</tr>
<tr>
<td>Town n(%)</td>
<td>253 (16.7%)</td>
<td>293 (8.6%)</td>
</tr>
<tr>
<td>Village n(%)</td>
<td>177 (11.7%)</td>
<td>266 (7.8%)</td>
</tr>
<tr>
<td>Rural n(%)</td>
<td>687 (45.4%)</td>
<td>2372 (69.6%)</td>
</tr>
<tr>
<td>Average proportion of people self-reporting bad or very bad health in each ED (Standard Deviation)</td>
<td>1.6% (1.4%)</td>
<td>1.4% (0.83%)</td>
</tr>
<tr>
<td>Average SAHRU deprivation score in each ED (Standard Deviation)</td>
<td>0.4 (2.0)</td>
<td>0.0 (1.6)</td>
</tr>
</tbody>
</table>

*Interquartile range not available
EDs – Electoral Divisions; IQR – Interquartile range; SAHRU – Small Area Health Research Unit

Unsmoothed SIRs ranged from 0-15.8 for all Home cases, and from 0-32.8 and 0-27.6 for the Home U65 and Home 65+ subgroups respectively. The Global Moran’s I statistic was calculated for the observed cases per ED. A z-score of 28.3 for all Home cases was highly significant. Similarly, z-scores of 18.7 and 26.3 for the Home U65 and Home 65+ subgroups respectively were also highly significant, confirming spatial autocorrelation in observed incidence.
### Table 5.2 Coefficients and Deviance Information Criteria for all Models

<table>
<thead>
<tr>
<th></th>
<th>Beta Coefficients (95% Confidence Intervals)</th>
<th>Deviance Information Criteria</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Deprivation</td>
<td>Health</td>
</tr>
<tr>
<td>All Home Cases</td>
<td></td>
<td></td>
</tr>
<tr>
<td>No Covariates</td>
<td></td>
<td></td>
</tr>
<tr>
<td>+ Deprivation*</td>
<td>0.10 (0.09, 0.12)</td>
<td></td>
</tr>
<tr>
<td>+ Urban-Rural</td>
<td></td>
<td>0.12 (0.07, 0.16)</td>
</tr>
<tr>
<td>+ Health</td>
<td></td>
<td></td>
</tr>
<tr>
<td>+ Deprivation &amp; Urban-Rural</td>
<td>0.10 (0.08, 0.12)</td>
<td></td>
</tr>
<tr>
<td>+ Deprivation &amp; Health</td>
<td>0.11 (0.08, 0.13)</td>
<td>-0.01 (-0.06, 0.04)</td>
</tr>
<tr>
<td>+ Urban-Rural &amp; Health</td>
<td>0.10 (0.06, 0.15)</td>
<td>0.25 (0.07, 0.43)</td>
</tr>
<tr>
<td>+ Deprivation &amp; Health &amp; Urban-Rural</td>
<td>0.10 (0.08, 0.13)</td>
<td>-0.01 (-0.06, 0.04)</td>
</tr>
<tr>
<td>Home cases &lt;65</td>
<td></td>
<td></td>
</tr>
<tr>
<td>No Covariates</td>
<td></td>
<td></td>
</tr>
<tr>
<td>+ Deprivation*</td>
<td>0.14 (0.12, 0.17)</td>
<td></td>
</tr>
<tr>
<td>+ Urban-Rural</td>
<td></td>
<td>0.23 (0.17, 0.29)</td>
</tr>
<tr>
<td>+ Health</td>
<td></td>
<td></td>
</tr>
<tr>
<td>+ Deprivation &amp; Urban-Rural</td>
<td>0.14 (0.11, 0.17)</td>
<td></td>
</tr>
<tr>
<td>+ Deprivation &amp; Health</td>
<td>0.13 (0.11, 0.16)</td>
<td>0.05 (-0.03, 0.13)</td>
</tr>
<tr>
<td>+ Urban-Rural &amp; Health</td>
<td>0.21 (0.14, 0.27)</td>
<td>0.20 (-0.03, 0.42)</td>
</tr>
<tr>
<td>+ Deprivation &amp; Health &amp; Urban-Rural</td>
<td>0.13 (0.10, 0.16)</td>
<td>0.05 (-0.03, 0.13)</td>
</tr>
<tr>
<td>Home cases 65+</td>
<td></td>
<td></td>
</tr>
<tr>
<td>No Covariates</td>
<td></td>
<td></td>
</tr>
<tr>
<td>+ Deprivation*</td>
<td>0.07 (0.05, 0.10)</td>
<td></td>
</tr>
<tr>
<td>+ Urban-Rural</td>
<td></td>
<td>0.05 (0.00, 0.11)</td>
</tr>
<tr>
<td>+ Health</td>
<td></td>
<td></td>
</tr>
<tr>
<td>+ Deprivation &amp; Urban-Rural</td>
<td>0.08 (0.05, 0.10)</td>
<td></td>
</tr>
<tr>
<td>+ Deprivation &amp; Health</td>
<td>0.09 (0.06, 0.12)</td>
<td>-0.05 (-0.12, 0.02)</td>
</tr>
<tr>
<td>+ Urban-Rural &amp; Health</td>
<td>0.04 (-0.02, 0.10)</td>
<td>0.29</td>
</tr>
<tr>
<td>+ Deprivation &amp; Health &amp; Urban-Rural</td>
<td>0.09 (0.06, 0.12)</td>
<td>-0.06 (-0.13, 0.01)</td>
</tr>
</tbody>
</table>

*Preferred Models
Table 5.2 shows the results of performing Bayesian conditional autoregression on all Home cases and both age subgroups, using all possible combinations of the three covariates. While there was limited difference in the DIC for some models, the beta coefficient for deprivation (i.e. magnitude of effect of deprivation on incidence) was largely unaffected by the inclusion of other covariates. The models including only the deprivation covariate therefore were best in terms of fit and parsimony for all cases and both age subgroups.

Table 5.3 Association of Deprivation with OHCA Incidence at Home

<table>
<thead>
<tr>
<th>Covariate</th>
<th>All Home Cases</th>
<th>Home U65</th>
<th>Home 65+</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>RR* (95% CI)</td>
<td>RR (95% CI)</td>
<td>RR (95% CI)</td>
</tr>
<tr>
<td>Deprivation</td>
<td>1.11 (1.09-1.13)</td>
<td>1.15 (1.13-1.18)</td>
<td>1.08 (1.05-1.10)</td>
</tr>
</tbody>
</table>

*RR = Relative Rate

Table 5.3 shows that higher ED deprivation scores were associated with higher incidence of all Home cases and both age subgroups. For all Home Cases, an increase of one point in Deprivation was associated with an 11% increased risk of OHCA (95% CI: 9%-13%). When expressed as quintiles, the risk difference between the 20% most deprived EDs and 20% least deprived EDs was 59%. The difference in deprivation was bigger for Home U65 compared to the Home 65+ category.
Figure 5.1 Relative Risk of OHCA incidence per Electoral Division, All Home Cases – Unsmoothed Rates
Figure 5.2 Relative Risk of OHCA incidence per Electoral Division, All Home Cases – Smoothed Standardised Incidence Rates
Chapter 5: Out-of-Hospital Cardiac Arrest in the Home – Can Area Characteristics Identify At-Risk Communities in the Republic of Ireland?

Figure 5.3 All Home Cases – Smoothed Standardised Incidence Rates – Dublin City and County Areas
Figure 5.4 All Home Cases – Smoothed Standardised Incidence Rates – Cork City
Figure 5.5 All Home Cases – Smoothed Standardised Incidence Rates – Limerick City
Table 5.4 Unsmoothed and Smoothed Standardised Incidence Ratios: Numbers of Electoral Divisions categorised by Significance

<table>
<thead>
<tr>
<th></th>
<th>All Home Cases</th>
<th>Home cases &lt;65</th>
<th>Home cases 65+</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Unsmoothed</td>
<td>Smoothed</td>
<td>Unsmoothed</td>
</tr>
<tr>
<td>High</td>
<td>1,122</td>
<td>108</td>
<td>717</td>
</tr>
<tr>
<td>Low</td>
<td>2,227</td>
<td>157</td>
<td>2,665</td>
</tr>
<tr>
<td>NS</td>
<td>60</td>
<td>3144</td>
<td>27</td>
</tr>
</tbody>
</table>

*NS – not significant

Figure 5.1 displays the number of EDs with higher and lower than expected incidence ratios i.e. observed:expected incidence ratio greater than 1 or less than 1 respectively, while Figure 5.2 displays the number of EDs with significantly high and low SIRs after spatial smoothing. Figures 5.3, 5.4 and 5.5 show three cities where clusters of a higher risk of OHCA were observed after applying smoothing. Table 5.4 presents the number of EDs in each category of significance before and after spatial smoothing. After spatial smoothing, 100 of the 108 EDs (93%) with a higher risk of OHCA were located in Cities. This was also the case for the Home U65 subgroup (99/119; 81%) and the 65+ subgroup (55/57; 96%).

5.4.1 Sensitivity Analysis

Analysis was repeated on yearly data in order to test the sensitivity of the final All Home cases model (results available as supplementary data). Only five EDs were significantly high across individual years and multi-year data. Deprivation was associated with greater incidence of attempted OHCA resuscitation in annual data. However, the addition of the deprivation covariate had less effect on the DIC than when multi-year data were used. The relative risk associated with a one point increase in deprivation appeared to decrease over time, from 23% (95% CI: 17% to 29%) in 2012 to 10% (95% CI: 7% to 14%) in 2014.
5.5 Discussion

5.5.1 Key Findings
Our study demonstrates the value of spatial smoothing in quantifying the area-level risk of a health event with high mortality across a whole country with a diverse settlement pattern (including adjustment for area-level factors). It also demonstrates novel application of Bayesian conditional autoregression to routinely collected health event registry data and area-level census data. Previous authors have demonstrated the value of this methodological approach in accounting for spatial clustering in infectious diseases including dengue fever \(^{138}\) and leprosy \(^{277}\). A previous Irish study used spatial smoothing to explain variation in the incidence of Amyotrophic Lateral Sclerosis (ALS), but did not attempt to provide area-level explanations for the variation observed \(^{166}\). We are aware of only one other study that has analysed OHCA incidence using this methodology, in the city-state of Singapore, a considerably more uniformly populated jurisdiction than Ireland \(^{165}\). Our study addresses some of the gaps in the existing literature by showing the utility of Bayesian conditional autoregression in providing a spatial analysis (adjusted for relevant area-level covariates) of a non-infectious disease event, across a whole nation with a diverse settlement pattern.

Our work adds to the evidence that the likelihood of OHCA resuscitation events – specifically in the home – is associated with greater deprivation and suggests that area deprivation should be considered when planning resuscitation services. Other covariates were not associated with OHCA incidence. By correcting for correlated findings between areas and using a methodology that accounts for spatial variation, our study considerably strengthens the evidence that deprivation is associated with a higher incidence of OHCA.

5.5.2 Choice of Area-Level Covariates
Our choice of area-level covariates was based on availability of data at ED level, robustness and relevance to the Irish population. In a study using a similar methodological approach, Ong et al. investigated spatial variation in OHCA incidence in the city-state of Singapore \(^{165}\). Ong et al. used a number of single measure variables including education, working status, and household size. They found no association between area-level measures and OHCA incidence and suspected that small sample size may have influence the lack of association found. We opted to use a robust composite deprivation variable in order to avoid the risk of multicollinearity between single measure variables and to ensure sufficient area-level data availability.

Previous studies of OHCA incidence have measured rurality as a direct function of population density and have observed reducing OHCA incidence with decreasing population density \(^{126,197,230}\). We chose to use a composite measure that was specifically designed to additionally account for the geographical qualities of an area, including population density, land use, proximity to an urban area and settlement size. In view of the fact that non-traumatic OHCA almost invariably occurs as the
result of an underlying disease, we believed that inclusion of an area-level health measure was essential in our analysis. As area-level statistics on morbidity were not available, self-reported health status was considered the most appropriate proxy measure for area-level health status.

In the United States, higher OHCA incidence has been observed in neighbourhoods with a higher proportion of black race\textsuperscript{278}. Associations between incidence and other ethnicities have not been observed. Only 1.4% of the Irish population was reported as black in the 2011 census, meaning area-level analysis of race and OHCA in the Irish context would be based on extremely sparse data and unlikely to be robust.

5.5.3 Association of Deprivation and OHCA Incidence

Our findings support those of Reinier et al.\textsuperscript{125,279} that there is an association between increased deprivation and increased OHCA incidence\textsuperscript{278}. While previous studies have found deprivation to be predictive of self-reported health\textsuperscript{280}, in our study population, deprivation appeared to be the more robust covariate, across all cases and both age subgroups. By using data from an OHCA register with national coverage, and accounting for spatial variation, our study lends support to the understanding that deprivation is associated with the incidence of OHCA incidents where resuscitation is attempted, regardless of age or geographical location.

It is important to keep in mind that deprivation is a relative concept to the country and/or circumstances in which it is measured. While individual components of a deprivation index may be stable across urban and rural areas, it cannot be assumed that an index will behave in as stable a manner as its constituent components\textsuperscript{181}. Additionally, deprivation measures that are centred on typical urban values are less likely to correctly identify deprivation in a rural setting\textsuperscript{282,283}. The index used here was developed to be applicable nationally, with only one indicator included (car ownership) that might be considered to bias towards urban areas. However, given the lower weight applied to that indicator, the influence it has on the deprivation score is moderated. The covariate coefficient for deprivation in the model is largely unchanged by the addition of the urban-rural index as a covariate, supporting the view that the index is not overly biased towards urban or rural areas. Area-level deprivation is not discrete. It is influenced by the deprivation level of surrounding areas\textsuperscript{284}, highlighting the importance of using analytical methods that account for spatial autocorrelation\textsuperscript{284}. Even when overall affluence increases, the relative association between deprivation and health inequalities remains\textsuperscript{285}.

Considering that the most common cause for non-traumatic adult OHCA is cardiovascular disease (CVD), and greater deprivation is associated with increased incidence of CVD, an association between OHCA and deprivation is consistent with expectations\textsuperscript{286,287}. As aging exerts an independent effect on CVD prevalence, the smaller influence of deprivation in the older age group can also be expected\textsuperscript{288}. In considering the impact of area-level deprivation, it is important to remember that deprivation affects morbidity and mortality, which in turn influence and/or limit the health choices that people can make\textsuperscript{289}. It is therefore ultimately individual factors,
such as pre-existing morbidity and health behaviours that account for the greater proportion of incidence risk. For example, for myocardial infarction – the most common CVD precursor to OHCA – nine individual-level modifiable risk factors were found to account for 90% of the Population attributable risk (PAR) in men and 94% of PAR in women.

5.5.4 Spatial Smoothing Changes the View of the Geography of OHCA Resuscitation

Spatial smoothing greatly reduced the number of EDs where incidence was higher or lower than expected, and enabled the identification of specific areas with significantly higher incidence. Areas with significantly higher incidence were primarily located in EDs that were classified as City. This was unexpected as 57% of Home Cases occur in EDs classified as either Rural or Village. According to the Irish census in 2011, only 36% of the general population were resident in Rural or Village EDs. Efforts to improve community first response tend to be focussed on more remote and rural areas. Our results suggest that certain city communities with greater deprivation should also be targeted.

5.5.5 Why do Patients who Collapse at Home have Poorer Survival than those who Collapse in a Public Place?

Various reasons for the difference in survival between collapsing at home have been suggested. Daya et al. found that in an American population, collapse in a public location was an independent predictor of OHCA survival, even after adjusting for known predictors of OHCA survival. In Ireland we have previously reported a strong adjusted association between survival and collapse in a public place. In contrast, Nakanishi et al. found that the influence of home as the incident location in Japan was eliminated when adjusted for ambulance call-response interval, performance of bystander cardiopulmonary resuscitation (CPR) and initial cardiac rhythm. An unmeasured but possible explanation for this difference may also be the higher prevalence of coronary heart disease in Western countries.

5.5.6 How these Findings Impact Service Provision

When cardiac arrest occurs, the heart becomes incapable of circulating blood around the body. In the absence of good quality cardiopulmonary resuscitation (CPR), the brain will become starved of oxygen within five minutes and cell death will begin to occur. The chances of patient survival therefore are largely determined by the actions of bystanders within the first few minutes of collapse. Home is the most common location of OHCA, and unless someone in the home is able to perform effective bystander CPR, the prospects of survival are severely limited. Previous studies have found an association between low income neighbourhoods and a reduced likelihood of bystander CPR being performed. At present, we do not know if the level of CPR training and knowledge of OHCA recognition in the general population in Ireland follows a socioeconomic gradient. Considering the association
between OHCA incidence and deprivation suggested in this study and previous studies, an understanding of the association between CPR knowledge and deprivation is an important area for further research.

In Ireland – as in other countries – EMS call-response intervals increase with increasing rurality of the event \(^{197}\). Communities in more rural locations have responded to this problem with the establishment of rapid response schemes and involvement of general practitioners in the emergency response \(^{203}\). Our study shows however, that the effect of urban-rural status on OHCA incidence reduces after adjusting for deprivation. We have also identified specific areas with significantly higher incidence – the majority of which are located in cities. Zijlstra et al. have shown the value of lay rescuers responding to OHCA events in densely populated residential areas \(^{294}\). Blom et al. have shown incremental improvement in OHCA survival with the introduction of police CPR training and the equipping of police vehicles with AEDs in the city of Amsterdam \(^{210}\). It can be suggested that similar interventions could be trialled in the deprived City EDs identified in our study as being at higher risk of OHCA.

### 5.5.7 Limitations
There are a number of limitations to our study. Firstly, OHCAR includes only OHCA where resuscitation was attempted and does not reflect the incidence of all Irish OHCA. Secondly, it was not possible in this study to consider the incidence of OHCA resuscitation which occurred at a location other than home as we could not determine a robust reference population for these cases. It is possible that areas with a low incidence of at home OHCA may have a high incidence of 'not home' OHCA, in which case different policy approaches may be necessary to ensure immediate, effective resuscitation is available for cases that occur in more public locations. Thirdly, our sensitivity analysis showed differences in the EDs that were identified on a year-to-year basis. The numbers of cases in the annual analyses were small and therefore not as robust as the multi-year analysis. Additionally, OHCA was a relatively rare event and sensitivity analysis shows that areas may change on a yearly basis, which may have resulted in the improved fit of the multi-year analysis. Fourthly, deprivation is right skewed and a quintile can encompass areas with a very broad range of scores. To assume that the effect of deprivation is equal across all areas within a quintile may be unreasonable, which is why we used the score itself. Scores are used for small area studies where relative rather than absolute difference is of particular interest \(^{284,295}\). The trade-off for using the score is that a one point change is difficult to interpret and cannot be readily considered in terms of quintiles. Finally, 1,897 (56%) of the total 3,409 EDs had zero Home cases – which may also have affected the robustness of our results.

### 5.5.8 Conclusions
In conclusion, we have shown that the likelihood of OHCA where resuscitation is attempted is likely influenced by deprivation, and have demonstrated a methodology that allows the identification of specific areas of high risk by correcting for correlated findings. Additionally, our study provides the opportunity to highlight that OHCA is...
not an event that happens to ‘others’ but rather an event that is most likely to occur at home, often in the presence of family or friends. While public policy should be targeted to at-risk communities, the universally greater risk of collapse at home must be communicated, regardless of geography.

5.5.9 Declarations

Ethical Approval
Ethical approval for research using non-identifiable data was obtained from the Research Ethics Committee, National University of Ireland, Galway (07-Sep-12).

Consent for Publication
Not applicable

Availability of Data and Materials
The data that support the findings of this study are available from the National Out-of-Hospital Cardiac Arrest Register Ireland (OHCAR) but restrictions apply to the availability of these data, which were used under license for the current study, and so are not publicly available. Data are however available from the authors upon reasonable request and with permission of the data controllers, the National Ambulance Service and Dublin Fire Brigade.

Competing Interests
The authors declare that they have no competing interests.

Funding
This study was completed with funding from the Health Research Board (HRB) Health Professionals Fellowship Grant, of which the first author is a recipient (HPF-2014-609). The HRB provided financial support to the first author for the conduct of the study, but did not have involvement in any aspects of study design, in the collection, analysis and interpretation of data; in the writing of the report; or in the decision to submit the article for publication.

Authors’ Contributions
SM conceived the study, performed geocoding and data preparation for statistical analysis, and drafted the manuscript. CT performed all conditional regression analyses. JC assisted with geocoding and data preparation and supervised SM in the conduct of geographic analysis. CD contributed to the discussion section of the study and advised on the clinical relevance of findings. AM contributed to the introduction and discussion sections of the manuscript. AV supervised SM in study design and manuscript preparation, and reviewed all manuscript drafts. All authors read and approved the final manuscript.
Acknowledgements
The authors wish to thank National Ambulance Service and Dublin Fire Brigade personnel who provided the data that has made this study possible, and the OHCAR Steering Group who encouraged and facilitated this research.
## 5.6 Supplementary Data

Table 5.5 Deviance Information Criteria, Beta Coefficients and Relative Rate for Annual All Home cases

<table>
<thead>
<tr>
<th></th>
<th>Deviance Information Criteria</th>
<th>Beta Coefficient (95% Confidence Intervals)</th>
<th>Relative Rate (95% Confidence Intervals)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>All Home cases 2012</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No covariates</td>
<td>4272.4</td>
<td></td>
<td></td>
</tr>
<tr>
<td>+ Deprivation</td>
<td>4244.5</td>
<td>0.21 (1.16-0.25)</td>
<td>1.23 (1.17-1.28)</td>
</tr>
<tr>
<td><strong>All Home cases 2013</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No covariates</td>
<td>4555.7</td>
<td></td>
<td></td>
</tr>
<tr>
<td>+ Deprivation</td>
<td>4530.2</td>
<td>0.14 (0.10-0.18)</td>
<td>1.15 (1.10-1.20)</td>
</tr>
<tr>
<td><strong>All Home cases 2014</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No covariates</td>
<td>4156.1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>+ Deprivation</td>
<td>4124.9</td>
<td>1.10 (0.07-0.13)</td>
<td>1.10 (1.07-1.14)</td>
</tr>
</tbody>
</table>
Chapter 6   Apples to Apples: Can Differences in Out-of-Hospital Cardiac Arrest Incidence and Outcomes between Sweden and Ireland be explained by Core Utstein Variables?

Key Points

- There is variation in the reported OHCA incidence and outcomes from different countries when aggregated data is compared.
- In this chapter, the proportion of variation between countries is examined using patient-level logistic regression analysis that includes core Utstein variables.
- The significant potential for the presence of unmeasured differences between countries is discussed.
- Finally, the implications for research and the development of national outcome targets are considered.

Authors

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Submitted to the Scandinavian Journal of Trauma, Resuscitation and Emergency Medicine
Chapter 6: Apples to Apples: Can Differences in Out-of-Hospital Cardiac Arrest Incidence and Outcomes between Sweden and Ireland be explained by Core Utstein Variables?

6.1 Abstract

Variation in reported incidence and outcome based on aggregated data is a persistent feature of out-of-hospital cardiac arrest (OHCA) epidemiology.

Objective: To investigate the extent to which patient-level analysis using core ‘Utstein’ variables explains inter-country variation between Sweden and the Republic of Ireland.

Methods: A retrospective cross-sectional comparative study was performed, including all Swedish and Irish OHCA cases attended by Emergency Medical Services (EMS attended OHCA) where resuscitation was attempted from 1st January 2012 to 31st December 2014. Incidence rates per 100,000 population were adjusted for age and gender. Two subgroups were extracted: (1) Utstein - adult patients, bystander witnessed collapse, presumed medical aetiology, initial shockable rhythm and (2) Emergency Medical Service (EMS)-witnessed events. Multivariable logistic regression analysis was used to identify predictors of survival following multiple imputations of data.

Results: Five thousand eight hundred eighty six Irish and 15,303 Swedish patients were included. Swedish patients were older than Irish patients (median age 71 vs. 66 years respectively). Adjusted incidence was significantly higher in Sweden compared to the Republic of Ireland (52.9 vs. 43.1 per 100,000 population per year). Proportionate survival in Sweden was greater for both subgroups and all age categories. Regression analysis of the Utstein subgroup predicted approximately 17% of variation in outcome, but there was a large unexplained ‘country effect’ for survival in favour of Sweden (OR 4.40 (95% CI 2.55–7.56)).

Conclusions: Using patient level data, a proportion of inter-country variation was explained, but substantial variation was not explained by the core Utstein variables. Researchers and policy makers should be aware of the potential for unmeasured differences when comparing OHCA incidence and outcomes between countries.

Key words: Out-of-hospital cardiac arrest; Utstein; incidence; outcomes; pre-hospital resuscitation

Key Questions
• What is already known about this subject?
  There is variation in the reported incidence and outcomes from out-of-hospital cardiac arrest when aggregated data is compared
• What does this study add?
  This study quantifies the proportion of variation between countries that can be explained using patient level analysis that includes core Utstein variables
• How might this impact on clinical practice?
  The significant potential for the presence of unmeasured differences between countries should be acknowledged, whether for research or for the development of national outcome targets.
6.2 Background

There is international variation in the reported incidence and outcome from out-of-hospital cardiac arrest (OHCA). Chamberlain and Eisenberg stated that in order to compare outcomes between different systems of care, it is necessary to have “a comparator that enables areas of weakness to be defined and addressed whether it be at local, national and international level”. The Utstein criteria were developed for this reason, and identify patients based on a number of indicators. International benchmarking is a highly desirable aspiration, and many notable studies and reviews have been carried out that compare the outcomes from OHCA across multiple countries and jurisdictions. To ensure that comparison is informative, it is essential that data is collected for the same purpose, data definitions and collection methodologies are similar, and that the population covered is equally representative. Assuring uniformity in OHCA data collection and reporting systems is essential, as differences in outcomes may well be attributable to differences in data availability and processing methodologies. This aim of this study was therefore to investigate the extent to which patient-level analysis using core ‘Utstein’ variables explains variation in OHCA incidence and outcome between two countries, namely Sweden and the Republic of Ireland.
Chapter 6: Apples to Apples: Can Differences in Out-of-Hospital Cardiac Arrest Incidence and Outcomes between Sweden and Ireland be explained by Core Utstein Variables?

6.3 Methods

6.3.1 Aim and Study Design
We conducted a retrospective analysis of a prospectively collected cohort of all Swedish and Irish cases of EMS-attended OHCA where resuscitation was attempted from 1\textsuperscript{st} January 2012 to 31\textsuperscript{st} December 2014, with the aim of examining the extent to which patient-level analysis using core ‘Utstein’ variables explains variation in OHCA incidence and outcome between Sweden and the Republic of Ireland.

6.3.2 Data Sources
Swedish OHCA registry data have been used to monitor national changes in OHCA incidence, management and outcome for more than 25 years\textsuperscript{111}. Ireland’s OHCA registry was established in 2007, modelled on the Swedish registry, and has had comprehensive national data collection since 2012\textsuperscript{197}. Both registries are hosted by universities, operate in collaboration with ambulance services, and are publicly funded. Irish data is transcribed by an external data management company from ambulance patient care reports while Swedish practitioners enter event data directly onto a web-based template that is forwarded to the registry. Dispatch data and patient outcome data is available directly from the dispatch centre and receiving hospitals in both countries. The availability of a unique patient identifier in Sweden means that status of the patient at thirty days can be obtained from Statistics Sweden. Both countries have systematic missing case identification procedures. This is performed centrally in Ireland and at county level in Sweden. Similarly, regular data quality assurance is performed, using the original patient care report (Ireland) or medical journal (Sweden) to validate data entered. A full description of the data collection comparison is available as a supplementary table. During the study period, clinical practice guidelines for EMS in both countries complied with the 2010 ILCOR recommendations\textsuperscript{297}. Irish and Swedish EMS practitioners are not required to start resuscitation in cases where definitive signs of death are present.

6.3.3 Study Setting
Sweden has a population of 9,995,153, occupying an area of 450,295 km\textsuperscript{2}\textsuperscript{298}. Approximately 85% of the Swedish population lives in cities. Ambulance provision is governed at county and municipal level, and vehicles are primarily staffed by nurses and paramedics. In some cities, physicians may also be part of the ambulance crew\textsuperscript{238}. Fire and police personnel are increasingly involved in providing a first response to OHCA in Sweden with public access defibrillators having been installed across the country\textsuperscript{199}.

The 2016 census showed that Ireland had a population of 4,757,976\textsuperscript{299}. Ireland is significantly smaller than Sweden (68,890 km\textsuperscript{2}) with approximately 63% living in urban areas. Statutory Emergency Medical Services (EMS) are provided by the National Ambulance Service (NAS). In Dublin city, Dublin Fire Brigade (DFB) also provides the statutory response. Paramedic and advanced paramedics are deployed to suspected
OHCA events. Emergency medical technicians may also be deployed as support crew or first responders to OHCA calls. Community first responder (CFR) volunteerism is becoming increasingly prominent in Ireland, with approximately 150 CFR schemes now established across the country. A more detailed description of the Irish EMS has been published elsewhere.

6.3.4 Data Processing
Register managers from both countries met to examine variables collected in both registries and identify which variables were comparable. Data were extracted from both registries, including original and derived variables. Variables with excessive missing values for either country (>25%) were excluded from further analysis (available as supplementary table).

Data were analysed using IBM SPSS Statistics v22.0© and STATA/IC 13.0 for Windows©. A subgroup was extracted based on the Utstein recommendations and included only adult patients with a bystander-witnessed collapse, with presumed medical aetiology and initial shockable rhythm. A second subgroup of EMS-witnessed events was also extracted.

6.3.5 Statistical Analysis
Variables were categorised into patient and event characteristics, interventions and outcomes. Where significant differences in variables were observed, further analysis of variables by five-year age groups was performed.

Sweden is divided into 21 administrative counties while the Republic of Ireland is composed of 34 (hereafter referred to as ‘admin areas’). For each admin area, crude incidence rates were calculated for all cases, both subgroups and for three age categories: children (under 18 years); adults (18-64 years); older people (65 years and over). Crude rates were adjusted to account for the proportion of the total population by gender in each age group at admin area-level. Swedish population figures were derived from Statistics Sweden data and were averaged for the years 2012-2014 for each admin area. Population estimates for the Republic of Ireland for each admin area were taken from the 2011 census. An average country value was calculated from admin area values for each age and gender group with their 95% confidence intervals. The analysis of variance method (ANOVA) was used to compare average incidence rates. A p-value of <0.05 was considered significant.

For key variables, missing data were imputed using a fully conditional specification (FCS) or chained equations imputation model. Imputation was performed separately for each country before data were merged for analysis.

Multivariable logistic regression analysis was used to identify predictors of the main outcome of interest (Discharge from hospital alive or alive at 30 days (Survival)). Models were estimated using original data (available as supplementary data) and imputed data. Potential explanatory variables were chosen based on previous
literature and clinical relevance. Both ‘epinephrine’ and ‘mechanical CPR’ were initially included but were dropped due to insignificance. Interactions between the variable ‘Country’ and all other variables were checked. Due to non-linearity, the call-response interval variable was transformed into a binary variable for the regression analysis. Interactions which changed the Odds Ratios (ORs) for any of the main variables by more than 10% were included in the final model.

Model fit was assessed using imputed estimates adjusted $R^2$, which were calculated using Harel’s method. Calibration of individual imputed models was assessed using the Hosmer and Lemeshow $\chi^2$ statistic ($p>0.05$).
6.4 Results

6.4.1 Patient, Event and Intervention Characteristics
A total of 5,886 Irish and 15,303 Swedish patients were included in the analysis. Swedish patients were significantly older than Irish patients for all cases and in both subgroups (Table 6.1). Only gender was shown to have a similar distribution. All other variables showed differences between the countries. There were differences in the three categories of witness status, particularly the proportion of patients who had an EMS-witnessed arrest (Sweden – 15.2% vs. the Republic of Ireland – 5.9%, Table 1).

There were differences between countries in who provided CPR. ‘Trained, may be dispatched by ambulance control’ included members of the community who had training in CPR i.e. community first responders, off-duty paramedics, nurses, doctors, other clinical personnel. While it is known that many of these individuals were dispatched to the event by ambulance control, it was not possible to accurately determine that proportion. In the Republic of Ireland, this category accounted for 33.5% of providers of CPR before ambulance arrival compared to 12.8% in Sweden. Conversely, in Sweden 28.2% of CPR before ambulance arrival was provided by the fire service compared with 2.8% in the Republic of Ireland. A greater proportion of Swedish patients received defibrillation before ambulance arrival, though the actual percentages in both countries were small (5.6% and 7.3%), and the median EMS call-response interval was significantly shorter in Sweden.
### Table 6.1 Comparison of Case Characteristics between Republic of Ireland and Sweden – All Cases, Utstein and EMS-Witnessed Subgroups

<table>
<thead>
<tr>
<th></th>
<th>All cases</th>
<th>Utstein subgroup***</th>
<th>EMS-witnessed subgroup</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Ireland</td>
<td>Sweden</td>
<td>Ireland</td>
</tr>
<tr>
<td>Number of patients</td>
<td>(n=5,886)</td>
<td>(n=15,303)</td>
<td>(n=920)</td>
</tr>
<tr>
<td>Patient and scene characteristics</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Median age in years (inter-quartile range)</td>
<td>66 (52-78)</td>
<td>71 (60-81)</td>
<td>65 (55-75)</td>
</tr>
<tr>
<td>Male (%)</td>
<td>67.9</td>
<td>66.6</td>
<td>78.8</td>
</tr>
<tr>
<td>Incident occurred outside home (%)</td>
<td>32.7</td>
<td>30.1</td>
<td>51.6</td>
</tr>
<tr>
<td>Presumed medical (%)</td>
<td>88.0</td>
<td>89.7</td>
<td>NA</td>
</tr>
<tr>
<td>Initial rhythm shockable (%)</td>
<td>23.7</td>
<td>23.7</td>
<td>NA</td>
</tr>
<tr>
<td>Witness status (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Not witnessed (%)</td>
<td>40.5</td>
<td>33.7</td>
<td>NA</td>
</tr>
<tr>
<td>Bystander (%)</td>
<td>53.5</td>
<td>51.1</td>
<td>NA</td>
</tr>
<tr>
<td>Crew (%)</td>
<td>5.9</td>
<td>15.2</td>
<td>NA</td>
</tr>
<tr>
<td>Interventions</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>CPR before ambulance arrival (%)*</td>
<td>66.3</td>
<td>68.8</td>
<td>79.6</td>
</tr>
<tr>
<td>Who started CPR before ambulance arrival (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bystander, not dispatched (%)</td>
<td>60.7</td>
<td>56.9</td>
<td>44.3</td>
</tr>
<tr>
<td>Trained, may be dispatched by ambulance control (%)</td>
<td>33.5</td>
<td>12.8</td>
<td>31.9</td>
</tr>
<tr>
<td>Fire service (%)**</td>
<td>2.8</td>
<td>28.2</td>
<td>1.9</td>
</tr>
<tr>
<td>Police or fire and police (%)</td>
<td>2.1</td>
<td>3.0</td>
<td>1.5</td>
</tr>
<tr>
<td>Defibrillation before ambulance arrival (%)*</td>
<td>5.6</td>
<td>7.3</td>
<td>22.8</td>
</tr>
<tr>
<td>EMS call-response interval in minutes (median)*</td>
<td>13 (8-20)</td>
<td>10 (6-15)</td>
<td>12 (8-18)</td>
</tr>
<tr>
<td>Epinephrine (%)</td>
<td>63.8</td>
<td>80.1</td>
<td>65.7</td>
</tr>
<tr>
<td>Mechanical CPR (%)</td>
<td>4.6</td>
<td>35.9</td>
<td>4.9</td>
</tr>
<tr>
<td>Transported to hospital</td>
<td>53.8</td>
<td>60.9</td>
<td>75.7</td>
</tr>
<tr>
<td>Outcomes</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Any ROSC</td>
<td>23.2</td>
<td>32.8</td>
<td>45.9</td>
</tr>
<tr>
<td>ROSC at hospital arrival or arrived at hospital alive</td>
<td>16.9</td>
<td>24.4</td>
<td>37.1</td>
</tr>
<tr>
<td>Discharged alive from hospital</td>
<td>6.0</td>
<td>UA</td>
<td>22.2</td>
</tr>
<tr>
<td>Alive at 30 days</td>
<td>UA</td>
<td>11.2</td>
<td>UA</td>
</tr>
<tr>
<td>Discharged alive or alive at 30 days</td>
<td>6.0</td>
<td>11.2</td>
<td>22.2</td>
</tr>
</tbody>
</table>

*For ‘All Cases’ this variable includes only cases NOT witnessed by EMS [Ireland n=5,342; Sweden n=12,335]; **Fire Service’ includes all city and county fire services EXCEPT Dublin Fire Brigade; ***The Utstein Subgroup includes patients who meet the following criteria – aged over 17 years, bystander-witnessed collapse, presumed medical aetiology, initial shockable rhythm; CPR, Cardiopulmonary Resuscitation; EMS, Emergency Medical Services; NA, Not applicable; ROSC, Return of Spontaneous Circulation; UA, Unavailable data
6.4.2 Differences in OHCA Incidence and Outcome Between Countries

The incidence of OHCA resuscitation attempts per 100,000 population per year was similar in both countries for the Utstein subgroup, despite the fact that the annual crude and adjusted incidence of OHCA was significantly higher in Sweden for all patients and for the EMS-witnessed subgroup (Table 6.2). This was also the case for all age categories for both genders, and for the EMS-witnessed subgroup.

<table>
<thead>
<tr>
<th></th>
<th>Ireland</th>
<th>Sweden</th>
</tr>
</thead>
<tbody>
<tr>
<td>Crude Incidence</td>
<td></td>
<td></td>
</tr>
<tr>
<td>All Cases</td>
<td>43.1 (39.8-46.3)*</td>
<td>52.9 (47.7-58.1)*</td>
</tr>
<tr>
<td>Utstein Subgroup</td>
<td>6.8 (6.1-7.4)</td>
<td>7.7 (6.5-8.9)</td>
</tr>
<tr>
<td>EMS-witnessed</td>
<td>2.6 (2.0-3.1)*</td>
<td>8.1 (7.1-9.2)*</td>
</tr>
</tbody>
</table>

**Adjusted Incidence**

<table>
<thead>
<tr>
<th></th>
<th>Ireland</th>
<th>Sweden</th>
</tr>
</thead>
<tbody>
<tr>
<td>All Cases</td>
<td>42.3 (39.6-45.1)*</td>
<td>50.7 (46.1-55.2)*</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Age Categories</th>
<th>Male</th>
<th>Female</th>
</tr>
</thead>
<tbody>
<tr>
<td>All Ages</td>
<td>28.7 (26.5-31.0)**</td>
<td>14.3 (13.1-15.5)§</td>
</tr>
<tr>
<td>U18</td>
<td>0.7 (0.6-0.9)</td>
<td>0.5 (0.3-0.7)</td>
</tr>
<tr>
<td>18-64</td>
<td>13.4 (12.2-14.6)</td>
<td>5.2 (4.6-5.8)</td>
</tr>
<tr>
<td>65+</td>
<td>14.1 (13.0-15.3)**</td>
<td>8.4 (7.6-9.3)§</td>
</tr>
</tbody>
</table>

The proportion of surviving patients was consistently higher in Sweden for all patients, the Utstein subgroup and the EMS-witnessed subgroup (Table 6.3). This significant differential in survival was persistent across both genders and all age categories.

<table>
<thead>
<tr>
<th></th>
<th>Ireland</th>
<th>Sweden</th>
</tr>
</thead>
<tbody>
<tr>
<td>n (%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>All cases</td>
<td>350 (6.0)*</td>
<td>1686 (11.2)*</td>
</tr>
<tr>
<td>Utstein Subgroup</td>
<td>200 (22.2)*</td>
<td>634 (31.7)*</td>
</tr>
<tr>
<td>EMS-witnessed</td>
<td>56 (16.8)*</td>
<td>436 (20.0)*</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Age Categories</th>
<th>Male</th>
<th>Female</th>
</tr>
</thead>
<tbody>
<tr>
<td>All ages</td>
<td>283 (7.2)**</td>
<td>67 (3.6)§</td>
</tr>
<tr>
<td>U18</td>
<td>9 (8.8)**</td>
<td>2 (3.2)§</td>
</tr>
<tr>
<td>18-64</td>
<td>164 (9.3)**</td>
<td>35 (5.8)§</td>
</tr>
<tr>
<td>65+</td>
<td>103 (5.3)**</td>
<td>30 (2.6)§</td>
</tr>
</tbody>
</table>

*Higher incidence in Sweden (p<=0.05)
**Higher incidence in Swedish males than Irish males (p<=0.05)
§Higher incidence in Swedish females than Irish females (p<=0.05)
EMS, Emergency Medical Services
6.4.3 Extent of Unmeasured Variation Between Countries

Variables independently associated with improved ORs for Survival were younger age, collapse at a location other than home, CPR and defibrillation before ambulance arrival and a shorter EMS call-response interval (Table 6.4). After adjustment for other variables and inclusion of interaction terms, the OR for Survival in Sweden was 4.28 (95% CI 2.51-7.30). Interactions included in the final model were country*gender and country*home location. There was no significant difference between results obtained from original or imputed data. The overall proportion of variation in Survival that is accounted for in the final model was relatively small (adjusted $R^2$ 17%).

Table 6.4 Multivariable Logistic Regression Analysis for the Outcome Survival in the Utstein Subgroup*

<table>
<thead>
<tr>
<th>Survival</th>
<th>Adjusted Odds Ratio (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Sweden</strong></td>
<td></td>
</tr>
<tr>
<td>Age (in years)</td>
<td>0.97 (0.96-0.97)</td>
</tr>
<tr>
<td>Male</td>
<td>1.60 (1.02-2.52)</td>
</tr>
<tr>
<td>Not at home</td>
<td>3.05 (2.16-4.30)</td>
</tr>
<tr>
<td>CPR before ambulance arrival</td>
<td>1.65 (1.30-2.10)</td>
</tr>
<tr>
<td>Defibrillation attempted before ambulance arrival</td>
<td>1.40 (1.13-2.74)</td>
</tr>
<tr>
<td>Call Response Interval 5 minutes or less</td>
<td>1.97 (1.61-2.40)</td>
</tr>
<tr>
<td>Model Fit</td>
<td></td>
</tr>
<tr>
<td>Nagelkerke $R^2$ adjusted</td>
<td>0.17</td>
</tr>
</tbody>
</table>

Hosmer and Lemeshow Test not significant for any imputations
*(adult, bystander-witnessed, initial rhythm, shockable, presumed medical aetiology)
6.5 Discussion

This patient-level analysis of three years of data from two well established national registries shows that the incidence of attempted resuscitation is similar for the Utstein subgroup in both countries, but that percentage survival is greater in Sweden than in the Republic of Ireland overall, for all age categories and both subgroups. Even when data from two countries has been collected using similar methods and rationale, the reasons for inter-country differences in outcome are not fully explained by the core Utstein variables used in this study.

Our study highlights that differences in OHCA outcomes between countries are not solely down to differences in patient age and gender profile or pre-hospital interventions. By using patient level data, this analysis serves to quantify the degree of variation that can be explained by inter-country comparison in a way that cannot be achieved with aggregate outcome data. The critical value of OHCA data collection is that it can focus national efforts on improving national outcomes. In the latest revision of the Utstein dataset, Perkins et al. advised on a range of core and supplemental OHCA elements that are likely to help explain a larger proportion of inter-country outcome variation, including pre-existing co-morbidities and in-hospital treatments and interventions. Implementation or improved systematic collection of these data elements is likely to explain substantial variation in outcome within and between countries.

There are clearly differences in the patient and intervention characteristics in both countries. On average, Swedish patients are older in all cases and in both subgroups, and the higher overall incidence of OHCA resuscitation is largely accounted for by the greater proportion of older OHCA patients in Sweden (Table 2). The explanation for this difference in age profile may lie in cultural attitudes and expectations surrounding death and morbidity in both countries. A survey of public attitudes to resuscitation in older people has not been previously carried out, but may help explain the significant difference in resuscitation incidence in this age category.

As also shown in Table 2, the incidence of Utstein subgroup cases is similar in both countries. This is likely to be largely driven by the fact that similar proportions of patients had an initial recorded shockable rhythm (23.7%). The ‘three phase model’ of cardiac arrest suggests that most patients will deteriorate into an asystole within five minutes without intervention. Considering the significantly shorter median EMS call response-interval in Sweden, it may have been expected that the proportion of Swedish patients with an initial recorded shockable rhythm would be greater than in the Republic of Ireland. One explanation may be the higher proportion of older people in the Swedish OHCA resuscitation population, as older people have been found to have a lower incidence of initial shockable rhythm. Additionally, a decline in the proportion of patients with an initial shockable rhythm has previously been observed in Sweden, despite efforts to improve call-to-shock times. It has been proposed that this decline may be due to a reduction in untreated ischaemic heart disease (IHD) in the Swedish population and that the proportion of cases with cardiac aetiology is less than presumed. Diagnosis of IHD continues to increase the
Republic of Ireland and what proportion of this increase is due to increasing prevalence or improved detection is unclear. Both registries primarily rely on the clinical impression formed by the attending ambulance crew to determine the aetiology of arrest. Previous work on validation of aetiology in paediatric OHCA has shown the potential value of adding coronial data to an OHCA registry. It is suggested that inclusion of coronial data in the Swedish and Irish registries may assure the validity of data on aetiology and ensure realistic expectations for the proportion of cases with an initial shockable rhythm.

The proportion of CPR provided by those who were ‘trained, may be dispatched by ambulance control’ in the Republic of Ireland is encouraging (Table 1). The Republic of Ireland already has an active and growing Community First Responder (CFR) network. While there is evidence that trained first responders can contribute to survival, the best model of CFR is not yet determined. The fire service plays a greater role in the provision of CPR in Sweden, suggesting there is potential for Irish Fire Services to participate more often in the OHCA response. It should be noted that – despite the fact that dual dispatch of ambulance and fire services in Sweden has been shown to have the greatest effect on response intervals in rural Swedish areas – survival benefit was most significant in densely populated areas. This suggests that there is a response interval beyond which any form of dual dispatch may not be of additional benefit to ambulance dispatch only.

Proportionate survival from OHCA is greater in Sweden for all patients, both subgroups and all age categories (Table 3). Patients who collapse in the presence of EMS are likely to receive good quality CPR and rapid defibrillation, which in turn is more likely to be immediately effective if performed soon after collapse. This is borne out in the relatively high proportion of survival in this subgroup in both countries, and partially explains the higher overall percentage survival in Sweden.

The multivariable logistic regression model of survival explains – at best – 17% of variation between countries, and includes a large ‘country effect’ in favour or Sweden that is not explained by the predictor variables (Table 4). Rather than suggesting that the chances of patients in the Utstein group surviving an OHCA are over four times greater in Sweden than in the Republic of Ireland, this result points to the large proportion of variation which is not explained by our Utstein predictor variables. The implication is that while improving the availability of important outcome predictors such as bystander CPR and defibrillation, and reducing EMS call response intervals is likely to increase survival in the Republic of Ireland, these measures alone are unlikely to achieve parity of outcomes with Sweden.
6.5.1 Limitations

Simplified coding was applied to many variables in order to facilitate systematic registry recording and inter-country analysis. Most notably, we created the variable ‘Survival’ using the different outcome measures used in Sweden and the Republic of Ireland. In the Republic of Ireland, the primary outcome is ‘discharged alive from hospital’. Patients are not included as OHCA survivors until discharged, regardless of the length of their acute hospital stay. In Sweden survivors are classified as those who are alive 30 days or more after the event, even if the patient has not been discharged from an acute facility. While it is possible that Irish patients who are discharged alive may not survive to 30 days, it is also possible that Swedish patients may remain as in-patients for 30 days or more. Both outcome measures have been used interchangeably in other national comparative studies, and the use of either outcome measure has been recommended in the Utstein guidelines. In general, it is not usual for studies to report both these outcomes. In cases where both outcomes have been reported, there is negligible difference in the number of surviving patients.

While the proportion of patients who had defibrillation attempted before ambulance arrival is similar for the Utstein subgroup in both countries, 14.8% of Swedish cases had missing data for this variable. Using the original data the adjusted OR for this variable in the logistic regression analysis was 1.41 (95% CI 1.11-1.78) compared to 1.40 (95%CI 1.13-2.74) using imputed data.

6.5.2 Conclusions

The ability to compare OHCA incidence and outcomes across countries and systems is essential to establishing international benchmarking. The use of patient-level data have highlighted the proportion of variation outside of the well-known predictors of OHCA outcome, something that is not possible in comparative studies that rely on aggregated data. We believe the approach used in this study is transferable to other comparative studies of OHCA national incidence and outcome, and that such an approach will improve the validity and value of inter-country comparison, whether for research or for the development of national outcome targets.

6.5.3 Declarations

Ethical Approval
Ethical approval for research using non-identifiable data was obtained from the Research Ethics Committee, National University of Ireland, Galway (07-Sep-12) and from the regional ethics committee in Gothenburg, Sweden (S392-00).

Consent for Publication
Not applicable

Availability
The data that support the findings of this study are available from OHCAR and the Swedish Registry of Resuscitation but restrictions apply to the availability of these
data, which were used under license for the current study, and so are not publicly available. Data are however available from the authors upon reasonable request and with permission of the contributing ambulance service providers.

**Competing Interests**
The authors declare that they have no competing interests

**Funding**
This study was completed using funding from the Health Research Board Health Professionals Fellowship Grant, of which the first author is a recipient (HPF-2014-609).

**Authors’ Contributions**
SM and AS conceived the idea for the study and prepared and extracted data for analysis. SM was responsible for data analysis and manuscript drafting. AS also contributed to manuscript discussion and drafting. AV and JC were responsible for supervising data analysis, commenting on manuscript drafting and approving the final draft. CD was responsible for contributing to and ensuring the clinical accuracy and relevance of the manuscript.

**Acknowledgements**
The authors wish to thank National Ambulance Service and Dublin Fire Brigade personnel who provided the data that has made this study possible, and the National Out-of-Hospital Cardiac Arrest (OHCAR) Steering Group who encouraged and facilitated this research. This study was supported by the Swedish Association of Local Authorities and Regions in Sweden, and was completed.
Chapter 6: Apples to Apples: Can Differences in Out-of-Hospital Cardiac Arrest Incidence and Outcomes between Sweden and Ireland be explained by Core Utstein Variables?

6.6 Supplementary Data

Table 6.5 Comparison of Irish and Swedish OHCA Resuscitation Registries

<table>
<thead>
<tr>
<th></th>
<th>Ireland</th>
<th>Sweden</th>
</tr>
</thead>
<tbody>
<tr>
<td>Managing Organisation</td>
<td>OHCAR is based in the HSE North West Department of Public Health and is carried out in collaboration with the National Ambulance Service, National University Institute Galway and the Pre-Hospital Emergency Care Council (PHECC). The OHCAR Steering Group is responsible for directing the project and includes representatives from each organisation.</td>
<td>The OHCA register is based in Gothenburg, the West Coast in Sweden and collaborates with the Emergency Ambulance Services (EMS) in all 21 counties. The OHCA Steering Group members are from several counties in Sweden but there is a working group situated in Gothenburg.</td>
</tr>
<tr>
<td>Funding</td>
<td>OHCAR is funded by the National Ambulance Service and the Pre-Hospital Emergency Care Council</td>
<td>The register is funded by The Swedish Association of Local Authorities and Regions</td>
</tr>
<tr>
<td>How is data collected?</td>
<td><strong>Patient and Event Variables</strong></td>
<td></td>
</tr>
<tr>
<td></td>
<td>In Ireland, statutory Emergency Medical Services use a standardised Patient Care Report (PCR) which contains a section dedicated to data collection for OHCAR. Specially designed OHCA envelopes have also been provided to each ambulance station. In the event of OHCA, practitioners place completed PCRs in OHCA envelopes. On a monthly or fortnightly basis, envelopes are collected together with all PCRs from each station. All PCRs are scanned and stored digitally and cases in OHCA envelopes are given priority in the scanning process to facilitate OHCAR. OHCAR variables are manually entered onto an electronic database. This database is then forwarded to OHCAR together with a scanned copy of each PCR for case-by-case validation.</td>
<td>There is a standard web template which will be documented in connection to a treated OHCA. The EMS crew is responsible for filling in the web template. All data is collected in a database.</td>
</tr>
<tr>
<td></td>
<td><strong>Time variables</strong></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Dispatch data (i.e. time variables) is collected directly from the ambulance dispatch centre by registry staff</td>
<td>The time variables are available from the dispatch centre and from the EMS medical journal.</td>
</tr>
<tr>
<td></td>
<td><strong>Outcome data</strong></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Outcome data is requested by registry staff from receiving hospitals</td>
<td>Outcome data is available from medical journals from EMS and in-hospital and also from Statistics Sweden.</td>
</tr>
</tbody>
</table>
### How are missing cases identified?

<table>
<thead>
<tr>
<th>Ireland</th>
<th>Sweden</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cases that are not placed in OHCA envelopes are not processed through the OHCAR data collection system and must be identified separately. Missing case identification is performed on a monthly basis and repeated on an annual basis to capture delayed reports. First, a search of the digital scanning archive is performed based on the ‘Chief Complaint’ field in the PCR using the word ‘arrest’. Reported cases are excluded from the results and then the digital scan of the PCR associated with each call found is viewed. Missed OHCAR cases are identified and captured during the viewing process. Next, emergency control data is filtered to identify all calls with an AMPDS© designation of ‘ECHO’ at the time of resource deployment. A further seventeen ‘DELTA’ codes that may signify arrest occurred are included in the filter. Reported calls are then excluded from the filtered list. PCRs on the filtered list are then viewed and remaining unreported OHCAR cases are identified.</td>
<td>The EMS crew makes regular retrospective observations with the aim of searching undocumented OHCA. The searching procedure is performed by a digital searching programme, and manually searching if medical journals have been documented in papers. Missed OHCA cases are identified and imported to the database. Missed OHCAs are labelled in order to identify them as retrospective data.</td>
</tr>
</tbody>
</table>

### How is data quality assured in the registry?

<table>
<thead>
<tr>
<th>Ireland</th>
<th>Sweden</th>
</tr>
</thead>
<tbody>
<tr>
<td>Data is received by OHCAR in an electronic database together with a scanned copy of each PCR. Each electronic entry is checked by OHCAR staff against the data in the PCR to ensure accuracy of manual data entry. Checked data is then forwarded to the OHCAR manager who performs a random check of cases before finally adding data to the master OHCAR database. For cases that are identified through the missing case identification process, data is extracted from the scanned PCR by OHCAR staff and manually entered onto an electronic database by OHCAR staff. The ‘missing' database is then forwarded to the OHCAR manager, who validates each entry using the corresponding scanned PCR. Once validation of the missing cases is complete, they are added to the master OHCAR database.</td>
<td>Registry data is compared to documented data in medical journals using variables such as incidence, place OHCA occurred, treatment and survival.</td>
</tr>
</tbody>
</table>
Table 6.6 Missing Data Items

<table>
<thead>
<tr>
<th>Variable Information</th>
<th>Ireland</th>
<th>Sweden</th>
</tr>
</thead>
<tbody>
<tr>
<td>Was OHCA identified by ambulance control at time of dispatch</td>
<td>Original**</td>
<td>270 (4.6)</td>
</tr>
<tr>
<td>Was dispatch assisted CPR offered</td>
<td>Original**</td>
<td>5886 (100.0)</td>
</tr>
<tr>
<td>Age</td>
<td>Original</td>
<td>171 (2.9)</td>
</tr>
<tr>
<td>Gender</td>
<td>Original</td>
<td>6 (0.1)</td>
</tr>
<tr>
<td>Who witnessed collapse</td>
<td>Original</td>
<td>209 (3.6)</td>
</tr>
<tr>
<td>OHCA location</td>
<td>Original</td>
<td>40 (0.7)</td>
</tr>
<tr>
<td>Home or not home location of collapse</td>
<td>Recode</td>
<td>40 (0.7)</td>
</tr>
<tr>
<td>CPR before ambulance arrival</td>
<td>Original</td>
<td>197 (3.3)</td>
</tr>
<tr>
<td>Who started CPR</td>
<td>Derived</td>
<td>197 (3.3)</td>
</tr>
<tr>
<td>Defibrillation before ambulance arrival</td>
<td>Recode</td>
<td>172 (2.9)</td>
</tr>
<tr>
<td>First monitored rhythm</td>
<td>Original</td>
<td>234 (4.0)</td>
</tr>
<tr>
<td>First monitored rhythm shockable or nonshockable</td>
<td>Recode</td>
<td>234 (4.0)</td>
</tr>
<tr>
<td>Presumed aetiology</td>
<td>Recode</td>
<td>0 (0.0)</td>
</tr>
<tr>
<td>Medical or non-medical aetiology</td>
<td>Recode</td>
<td>0 (0.0)</td>
</tr>
<tr>
<td>Call-Response interval***</td>
<td>Original</td>
<td>810 (15.2)</td>
</tr>
<tr>
<td>Call to defibrillation interval****</td>
<td>Original**</td>
<td>811 (39.1)</td>
</tr>
<tr>
<td>Epinephrine administered</td>
<td>Original</td>
<td>54 (0.9)</td>
</tr>
<tr>
<td>Airway control type</td>
<td>Original</td>
<td>505 (8.6)</td>
</tr>
<tr>
<td>Mechanical CPR</td>
<td>Original</td>
<td>343 (5.8)</td>
</tr>
<tr>
<td>Transported to hospital</td>
<td>Original</td>
<td>1 (0.0)</td>
</tr>
<tr>
<td>Any ROSC</td>
<td>Original</td>
<td>192 (3.3)</td>
</tr>
<tr>
<td>ROSC or alive on arrival at hospital</td>
<td>Derived</td>
<td>275 (4.7)</td>
</tr>
<tr>
<td>Discharged alive or alive at 30 days</td>
<td>Derived</td>
<td>64 (1.1)</td>
</tr>
<tr>
<td>CPC at discharge from hospital****</td>
<td>Original**</td>
<td>80 (22.9)</td>
</tr>
</tbody>
</table>

*Original (taken directly from national register), Derived (variables or variable lists from national register combined to create single study variable or similar options for both registries), Recode (number of variables options reduced to facilitate analysis)

**Variable excluded from study due to excess missing data in either or both countries

***Not EMS-witnessed cases (Ireland n=5342; Sweden n=12335)

****For cases where defib attempted (Ireland n=2072; Sweden n=5327)

*****For cases where survival to discharge or 30 days confirmed (Ireland = 350; Sweden = 1686)

Table 6.7 Logistic Regression Analysis for the Outcome Survival in the Utstein Subgroup using Original Data*

<table>
<thead>
<tr>
<th>Survival</th>
<th>Adjusted Odds Ratio (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sweden</td>
<td>3.60 (1.95 - 6.68)</td>
</tr>
<tr>
<td>Age (in years)</td>
<td>0.96 (0.96-0.97)</td>
</tr>
<tr>
<td>Male</td>
<td>1.79 (1.00-3.23)</td>
</tr>
<tr>
<td>Not at home</td>
<td>2.41 (1.96-2.97)</td>
</tr>
<tr>
<td>CPR before ambulance arrival</td>
<td>1.40 (1.06-1.84)</td>
</tr>
<tr>
<td>Defibrillation attempted before ambulance arrival</td>
<td>1.41 (1.11-1.78)</td>
</tr>
<tr>
<td>Call Response Interval 5 mins or less</td>
<td>2.25 (1.78-2.86)</td>
</tr>
</tbody>
</table>

*Model Fit

Nagelkerke R² adjusted 0.17

*Adult, bystander-witnessed, initial rhythm, shockable, presumed medical aetiology
Key Points

- The optimal OHCA survival that can be achieved in international airports is unknown
- In this chapter, a retrospective study of 800 cases of OHCA where resuscitation was attempted will be described in a passenger population of approximately 3.3 billion, and the impact of known study predictors of survival in this unique location will be investigated
- Estimation of OHCA survival that can be achieved in this relatively controlled, but real-life environment will add evidence to the setting of achievable goals for pre-hospital resuscitation
- Logistic multilevel modelling will be used to quantify and control for the impact of country and airport level grouping in the study population
- The importance of systematic data collection, particularly in international airports, to continually maximize activities to increase OHCA survival will be highlighted.

Authors


Published in Resuscitation 2018 Mar 14 pii: S0300-9572(18)30134-5. doi: 10.1016/j.resuscitation.2018.03.024. [Epub ahead of print]
Chapter 7: Out-of-Hospital Cardiac Arrest Survival in International Airports

7.1 Abstract

Background: The highest achievable survival rate following out-of-hospital cardiac arrest is unknown. Data from airports serving international destinations (international airports) provide the opportunity to evaluate the success of pre-hospital resuscitation in a relatively controlled but real-life environment.

Methods: This retrospective cohort study included all cases of out-of-hospital cardiac arrest at international airports with resuscitation attempted between January 1st, 2013 and December 31st, 2015. Crude incidence, patient, event characteristics and survival to hospital discharge/survival to 30 days (survival) were calculated. Mixed effect logistic regression analyses were performed to identify predictors of survival. Variability in survival between airports/countries was quantified using the median odds ratio.

Results: There were 800 cases identified, with an average of 41 per airport. Incidence was 0.024/100,000 passengers per year. Percentage survival for all patients was 32%, and 58% for patients with an initial shockable heart rhythm.

In adjusted analyses, initial shockable heart rhythm was the strongest predictor of survival (odds ratio, 36.7; 95% confidence interval [CI], 15.5 to 87.0). In the bystander-witnessed subgroup, delivery of a defibrillation shock by a bystander was a strong predictor of survival (odds ratio 4.8; 95% CI, 3.0 to 7.8). Grouping of cases was significant at country level and survival varied between countries.

Conclusions: In international airports, 32% of patients survived an out-of-hospital cardiac arrest, substantially more than in the general population. Our analysis suggested similarity between airports within countries, but differences between countries. Systematic data collection and reporting is essential to ensure international airports continually maximise activities to increase survival.
Chapter 7: Out-of-Hospital Cardiac Arrest Survival in International Airports

7.2 Introduction

The purpose of pre-hospital resuscitation systems is to optimise survival from out-of-hospital cardiac arrest (OHCA) by implementing the chain of survival. The first three links in the Chain – early recognition and call for help; immediate cardiopulmonary resuscitation (CPR); early defibrillation – must all be initiated immediately and effectively in the pre-hospital environment. Due to the variability in reported survival worldwide, a key question for policy makers and health care providers is, in an ‘ideal world’, what is the best survival from OHCA that can be achieved?

In 2015, the Cardiac Arrest Registry to Enhance Survival (CARES) in the United States collected data from twelve state-based registries and 50 community sites. It was estimated that the incidence of non-traumatic OHCA with resuscitation attempted was 57 per 100,000 population, with survival to discharge of 11%. In a one-month survey during October 2014, OHCA incidence across 27 European countries with resuscitation attempted ranged from 19 to 104 cases per 100,000 population with an average survival of 10% for at least 30 days or to hospital discharge. In airports serving international destinations (international airports) however, where the incidence of OHCA is low compared to passenger throughput, the proportion of survival is much higher than in the general OHCA population. International airports are unique environments. They are constructed similarly, are geographically discrete from the surrounding environs, and have a high public footfall. Under international aviation law, international airports are required to have on-site police, fire and rescue services. In an airport, it may be assumed that the majority of people who suffer OHCA believed themselves to be fit enough to go to work or to travel on that day. International airports therefore can be considered a natural laboratory to evaluate how successful pre-hospital resuscitation is in a relatively controlled real life situation.

The primary aim of this study was to determine survival from OHCA at international airports with resuscitation attempted. The study also aimed to estimate the incidence of OHCA at international airports and to identify the impact of known predictors of OHCA survival.
7.3 Methods

This was a retrospective cohort study of all cases of OHCA at international airports with resuscitation attempted over a 3-year period from the 1st of January 2013 to the 31st of December 2015. Thirty-four countries were requested to provide data. In 32 countries, data was requested by contacting individuals who had previously published using OHCA registry data in that country. These individuals then advised on the appropriate contact for international airport data in their country, or personally assisted with the provision of data, in line with ethical and data protection requirements in their jurisdiction. In two countries, OHCA data collection from international airports was not established, and therefore direct contact with international airports in both countries was attempted. Between October 2016 and February 2017 attempts were made to engage non-responding countries, using either repeat emails or by pursuing alternative contacts.

Data requested included patient age and gender; witnessed status (not witnessed/bystander/emergency medical services (EMS)); initial arrest rhythm (asystole/pulseless electrical activity/shockable/unspecified nonshockable); CPR before EMS arrival (bystander CPR) (yes/ no); shock delivered using an automated external defibrillator (AED) before EMS arrival (bystander AED defibrillation attempted) (yes/ no); interval in minutes from emergency call to emergency medical service arrival (EMS call-response interval); survival to hospital discharge (yes/no).

Participating countries were also requested to provide data on the passenger throughput of each international airport for each year of data provided. Country data was obtained based on the agreement that no airport or individual country was identified during the analysis or in the study results.

Overall crude incidence of OHCA with resuscitation attempted per 100,000 passengers per year was calculated and descriptive analyses of patients, event characteristics and outcome were performed. Survival to hospital discharge or survival at 30 days (survival) was calculated for the study population and for subgroups of each categorical variable.

Mixed effect logistic regression analyses were performed to identify predictors of survival. Predictors of survival were estimated for the entire study population.

In order to assess whether there was grouping of variables at airport and/or country level, null/empty single (patient level only), 2-level (patient and airport level; patient and country level) and 3-level (patient, airport and country level) logistic regression models for survival were compared using the likelihood ratio test, plots of random effects and the effect on resulting odds ratios (ORs). Plots of random effects were used to allow interpretation of differences in the mean residual effect or area (airport or country) level variance in survival before any predictor variables are added to the model. Due to multicollinearity, separate estimates of regression coefficients for survival were calculated for each known predictor of survival, with each model adjusted to account for patient age and gender, resulting in six final models. Coefficients were transformed into ORs to aid interpretation. To quantify the
variability between airports/countries in survival after OHCA, a median odds ratio was calculated using Larsen’s mOR\textsuperscript{160}. A mOR equal to one signifies no differences between airports/countries in the probability of survival from OHCA. As mOR is a measure of random effects, a Bayesian credible interval (cri) was calculated based on the distribution of the mOR to distinguish it from a fixed effects OR confidence interval (MLWiN version 2.35). Model fit was assessed using the deviance information criterion (DIC). A lower DIC suggested a better model fit, and a difference of less than 5 in model DIC is not considered sufficient to distinguish between two models\textsuperscript{163}.

The study was approved by the Research Ethics Committee of the National University of Ireland Galway (Ref: 16-Sep-18). Informed consent was not required as non-identifiable data was used. The corresponding author had full access to all the data in the study and takes responsibility for its integrity and the data analysis.
7.4 Results

Data on 800 OHCAs cases with resuscitation attempted were received from 70 airports in 9 countries. Data were requested from 34 countries in all: two were unable to participate due to data protection restrictions; nine did not participate because data were unavailable or insufficiently comprehensive; 14 countries did not respond. Data for the full study period (1st January 2013 and 31st December 2015) were available from 64 airport sites. Three sites provided data for 2013 and 2014, and the remaining three provided data for 2015 only.

A total of 32% of all patients survived to hospital discharge. The frequency of events across airports ranged from one to 72, with an average number of 41 cases per airport over the 3-year period (standard deviation, 19). The total denominator population was 3.3 billion passengers and the incidence of OHCA in airports with resuscitation attempted was 0.024/100,000 passengers per year.

Patients were predominantly male (Table 7.1). There was no difference in the average age of men and women (62.5 vs. 62.3 years respectively). Forty-two percent of patients had a shockable rhythm at the time of initial rhythm analysis. The majority of patients suffered a bystander-witnessed arrest (74%), and the majority of these patients had bystander CPR performed (77%). A significantly higher proportion of males had bystander AED defibrillation attempted compared to females (35% vs. 22%). Median EMS call-response interval was eight minutes, and 34% of patients received an EMS response in five minutes or less. Proportionate survival was significantly higher for patients who had bystander AED defibrillation attempted. The proportion of survivors was greater for males than females and also for patients who received an EMS response in five minutes or less, but this difference was not significant. There was a high proportion of survival in the unspecified nonshockable subgroup (27%). Patients who had a witnessed and initially shockable event had the highest proportion of survival (58%). A similar proportion of patients survived in the bystander-witnessed and EMS-witnessed group. Percentage missing data was below 10% for all variables except bystander AED defibrillation attempted (20%) and EMS call-response interval (24%).
Table 7.1 Patient, Event and Survival Characteristics

<table>
<thead>
<tr>
<th></th>
<th>n (%)</th>
<th>Percentage Crude survival (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Sex</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>580 (73)</td>
<td>34 (30-38)</td>
</tr>
<tr>
<td>Female</td>
<td>195 (27)</td>
<td>25 (20-32)</td>
</tr>
<tr>
<td><strong>Age in years</strong></td>
<td>64.2 (14.8)†</td>
<td>NA</td>
</tr>
<tr>
<td><strong>Initial heart rhythm</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Shockable</td>
<td>325 (42)</td>
<td>55 (49-60)</td>
</tr>
<tr>
<td>Unspecified nonshockable</td>
<td>114 (15)</td>
<td>27 (19-36)</td>
</tr>
<tr>
<td>Pulseless Electrical Activity</td>
<td>107 (14)</td>
<td>12 (7-21)</td>
</tr>
<tr>
<td>Asystole</td>
<td>220 (29)</td>
<td>4 (2-7)</td>
</tr>
<tr>
<td><strong>Witness status</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bystander witnessed</td>
<td>581 (74)</td>
<td>36 (32-40)</td>
</tr>
<tr>
<td>EMS witnessed</td>
<td>77 (10)</td>
<td>28 (19-40)</td>
</tr>
<tr>
<td>Not witnessed</td>
<td>125 (16)</td>
<td>12 (7-19)</td>
</tr>
<tr>
<td><strong>Bystander CPR§</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>439 (77)</td>
<td>37 (32-41)</td>
</tr>
<tr>
<td>No</td>
<td>131 (23)</td>
<td>33 (26-42)</td>
</tr>
<tr>
<td><strong>Bystander AED defibrillation attempted§</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>147 (32)</td>
<td>59 (51-67)</td>
</tr>
<tr>
<td>No</td>
<td>319 (68)</td>
<td>25 (21-30)</td>
</tr>
<tr>
<td><strong>EMS call-response interval 5 minutes or less ¶</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>183 (34)</td>
<td>37 (30-45)</td>
</tr>
<tr>
<td>No</td>
<td>354 (66)</td>
<td>27 (22-32)</td>
</tr>
<tr>
<td><strong>Discharged alive or 30 day survival</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>231 (32)</td>
<td>NA</td>
</tr>
<tr>
<td>No</td>
<td>497 (68)</td>
<td>NA</td>
</tr>
</tbody>
</table>

† Mean (standard deviation); § Bystander witnessed cases only; ¶ Excludes EMS witnessed; CPR, cardiopulmonary resuscitation; EMS, Emergency Medical Services

The likelihood ratio test suggested that there was variable grouping at both airport and country level. When compared to the 2-level patient and country-only model however, the use of the 3-level model (patient, airport and country) did not alter the mOR for country or the individual ORs for the predictor variables, suggesting that most of the group-level variability was at country level. Caterpillar plots of random effects at airport level and country level confirmed that most of the group-level variation observed was accounted for by country, with only one airport having a 95% confidence interval for residual effect that was significant (Figures 7.1 and 7.2). For this reason the less complex 2-level model was used to account for country-level grouping.
Figure 7.1 Caterpillar Plots of Mean Residual Effects for Airport

Figure 7.2 Caterpillar Plots of Mean Residual Effects for Country

Legend
Y-axis – Mean residual effect is a measure of the area (airport or country) level variance in survival prior to the addition of predictor variables to the model. If the error bars for the mean residual effect do not cross 0, that airport or country is significantly different to the other airports or countries.
Table 7.2 presents the mixed effect logistic regression models for each predictor variable. Male gender was a significant predictor of survival, while patient age showed no association (Model 1). All initial heart rhythms were strongly predictive of survival when compared to asystole, including the unspecified nonshockable category (Model 2). When compared to non-witnessed status, bystander witnessed and EMS witnessed status were similarly predictive of survival (Model 3). In the bystander-witnessed subgroup, bystander CPR did not influence patient survival however attempted bystander AED defibrillation was a strong predictor of survival (Models 4 & 5). In the subgroup of patients who did not have an EMS-witnessed collapse, EMS call-response interval was not associated with improved survival (Model 6). Addition of predictor variables significantly improved fit for all models.

The cluster effect or country level variance is presented as mOR and the higher the mOR the more pronounced the difference between countries. The lowest mOR for country level effect was 1.6 in the model with initial heart rhythm, and the highest mOR was 3.0 in the model with bystander AED defibrillation attempted.
## Table 7.2 Measures of Association between Individual and Area Characteristics and OHCA Survival

<table>
<thead>
<tr>
<th>Measures of Association</th>
<th>Model 1</th>
<th>Model 2</th>
<th>Model 3</th>
<th>Model 4</th>
<th>Model 5</th>
<th>Model 6</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of cases included</td>
<td>800</td>
<td>581</td>
<td>706</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Individual Level Variables (OR, 95% CI)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>1.6 (1.1-2.4)</td>
<td>0.9 (0.5-1.4)</td>
<td>1.6 (1.1-2.5)</td>
<td>1.7 (1.1-2.8)</td>
<td>1.1 (0.7-1.9)</td>
<td>1.3 (0.8-2.1)</td>
</tr>
<tr>
<td>Age centred on the mean (in years)</td>
<td>1.0 (1.0-1.0)</td>
<td>1.0 (1.0-1.0)</td>
<td>1.0 (1.0-1.0)</td>
<td>1.0 (1.0-1.0)</td>
<td>1.0 (1.0-1.0)</td>
<td>1.0 (1.0-1.0)</td>
</tr>
<tr>
<td>Initial heart rhythm (ref asystole)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Shockable</td>
<td>36.7 (15.5-87.0)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Unspecified nonshockable</td>
<td>9.2 (3.6-23.5)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pulseless Electrical Activity</td>
<td>4.1 (1.5-11.8)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Witness status (ref not witnessed)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bystander witnessed</td>
<td></td>
<td>4.3 (2.3-7.8)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>EMS witnessed</td>
<td></td>
<td>3.6 (1.6-8.2)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bystander CPR†</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>1.5 (0.9-2.4)</td>
</tr>
<tr>
<td>Bystander AED defibrillation attempted†</td>
<td></td>
<td></td>
<td></td>
<td>4.8 (3.0-7.8)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>EMS call-response interval 5mins or less‡</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>1.3 (0.8-2.1)</td>
</tr>
<tr>
<td><strong>Measure of Variation or Clustering</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>mOR for country (95% crl)</td>
<td>1.9 (1.3-4.4)</td>
<td>1.6 (1.1-3.7)</td>
<td>2.0 (1.4-4.8)</td>
<td>2.1 (1.4-5.2)</td>
<td>3.0 (1.6-14.3)</td>
<td>1.8 (1.3-5.1)</td>
</tr>
<tr>
<td>DIC</td>
<td>856.1</td>
<td>651.2</td>
<td>816.3</td>
<td>644.2</td>
<td>511.8</td>
<td>555.2</td>
</tr>
<tr>
<td>Difference between DIC and null model DIC§</td>
<td>27.0</td>
<td>231.9</td>
<td>66.8</td>
<td>29.0</td>
<td>161.4</td>
<td>231.5</td>
</tr>
</tbody>
</table>

†Bystander witnessed cases only
‡Excludes EMS witnessed cases
§DIC for null models. All cases = 883.1 (M1 – age and gender only; M2 – age, gender and initial heart rhythm; M3 - age, gender and witness status). Bystander witnessed cases only = 673.2 (M4 – age, gender and bystander CPR; M5 – age, gender and bystander AED defibrillation attempted). Excluding EMS witnessed cases = 786.7 (M6 – age, gender and EMS call-response interval 5mins or less)
CI, confidence interval; crl, credible interval; DIC, deviance information criteria - a lower DIC suggests a better model fit, and a difference of less than 5 between the null model and model DIC is not considered sufficient to distinguish between two models; EMS, Emergency Medical Service; mOR, median odds ratio; OR, odds ratio
7.5 Discussion

To the best of our knowledge, the proportion of OHCA survival observed in our study is among the highest achieved for any location worldwide. Systematic OHCA data collection and reporting in international airports can identify strengths and weaknesses in pre-hospital resuscitation interventions. These could then be acted upon as part of continual quality improvement in individual airports to sustain and maybe even increase overall airport OHCA survival rates.

In international airports, the incidence of OHCA in relation to the passenger throughput is low, but the frequency of events is relatively high. In a state-wide study in Arizona over a 3-year period, Moon et al. identified the 'top' location types of OHCA incidents. These included 65 events across all public business/office/workplaces; 43 events across all outdoor recreation facilities and 39 events across all Arizona’s stores and malls. This compares to an average of 41 cases per airport across a 3-year period in our study. The population in an international airport is mobile and relatively healthy compared to the general population and a collapse is more likely to be observed by staff or a member of the public. The majority of events had the characteristics that determine survival: predominantly witnessed; a high proportion of initial shockable rhythms; a high proportion of bystander CPR and attempted bystander AED defibrillation.

Registries with nationwide coverage have reported OHCA survival of 5% in Japan, 6% in Ireland and 7% in England. After decades of quality improvement initiatives, survival in Denmark and Sweden has reached 11% and 14% in Norway. The large scale, collaborative databases of CARES and the Resuscitation Outcomes Consortium of North America (ROC) reported overall survival to discharge of 11% for non-traumatic OHCA in 2015 and 10% for 2010 respectively. Almost one in three patients who had an OHCA in international airports survived to hospital discharge, which is substantially better than in the general population. Despite the advantages of the airport environment however, the survival observed in our study has been equalled and bettered. For example, in 2002, Caffrey et al. observed an overall survival of 61% in the witnessed shockable subgroup, suggesting that there is potential for even higher survival in the airport environment. In the city of Rotterdam in the Netherlands, survival of 31% was reported between 1988 and 1994. In a study where security officers in US casinos were trained in both CPR and AED use, overall OHCA survival of 38% was achieved. In the casino study, 59% of patients who had a witnessed and initially shockable arrest survived. In our study, more than 20 years later, survival for the same subgroup was almost identical (59% vs. 58%).

As shown in Figures 7.1 & 7.2 and in the calculation of mORs, our analysis showed the importance of clustering of data at the country level over airport level. This suggests similarity between airports within countries, but differences between countries that can be considered substantial. To interpret the mORs it can be imagined that if a person having an OHCA in an airport in one country were to have had their OHCA at
an airport in another country with higher probability of survival (independent of individual factors), their chance of survival will (in median) increase 1.6 to 3.0 times. This finding invites further research and data collection on country/airport level characteristics to understand what explains this variance in survival after OHCA between countries.

Contrary to previous studies, we found little difference in the likelihood of survival between bystander-witnessed and EMS-witnessed patients. This finding, coupled with the lack of association with EMS call-response interval reinforces the value of rapid defibrillation, regardless of whether it is attempted by a bystander or EMS personnel. Similarly, the benefits of bystander CPR may also have been masked by availability of rapid defibrillation.

Our population had a higher proportion of shockable rhythms than is observed in the general OHCA population. Previous research has invariably shown that patients who are in a shockable rhythm have the best chance of survival and this conclusion is highlighted by our results. The high proportion of shockable rhythm is likely to be reflective of a short interval between collapse and attempted defibrillation. In our study, 59% of patients who had a bystander defibrillation attempt survived to hospital discharge. The ROC investigators recently reported percentage survival of 67% following a bystander defibrillation attempt for patients who had an observed, shockable OHCA. Both studies add to the evidence that lay responders can successfully use AEDs, which can in turn result in higher percentages of shockable rhythms and consequently greater survival. The likelihood of a relatively healthier travelling/working population with fewer of the comorbidities that are more likely to result in pulseless electrical activity (PEA) and asystole arrests, should also be acknowledged.

The frequency of OHCA in international airports is relatively high and the potential to save a life in an airport is greater than in the majority of locations where OHCA may occur. The need to continuously strive to improve survival by ensuring a strong and rapid sequence of pre-hospital resuscitation is as critical in international airports as in any other community or location. In fact, the airport location has many advantages over other locations due to the constant high volume of passengers and workers, and the large proportion of public spaces. Systematic OHCA data collection and reporting in the ‘Utstein style’ is an essential step, without which it cannot be assumed that an airport is maximising their improvement activities to increase survival.

Our study has a number of limitations. Firstly, only nine of the countries surveyed provided data and we have no information on airport survival in non-participating countries. However, to the best of our knowledge, our study is the most comprehensive analysis of OHCA incidence and outcomes in international airports to date. Secondly, data on defibrillation and EMS call-response interval was missing for 23% of cases which may limit interpretability of our results, as may the proportion of cases categorised as ‘unspecified, nonshockable’. In order to assess the impact of missing data, odds ratios for bystander AED defibrillation attempted and EMS call-response interval were generated using imputed data but did not differ significantly.
from ORs where original data was used. Thirdly, in 13% of cases, the initial cardiac rhythm was reported as unspecified nonshockable. This is likely to be a consequence of AED use by bystanders, where cases have been labelled as unspecified nonshockable because the AED code summary was not immediately available and/or not subsequently interpreted. Fourthly, we did not collect information on the advanced pre-hospital interventions and in-hospital treatment available to patients. Our study however accounts for the critical pre-hospital resuscitation interventions that largely determine survival, without which advanced care and hospital interventions would be futile 37. Finally, airport or country level variables were not collected, which means that inter-airport and inter-country differences could not be further explored.

In conclusion, our study demonstrated that in a public location where availability of defibrillation was high, bystanders attempted defibrillation in 59% of cases, 42% of patients were in an initial shockable rhythm and almost one in three patients survived. Our findings suggest that, while public access defibrillation is not the panacea for improving OHCA survival, it has a vital role to play when strategically used in appropriate locations such as international airports.

7.5.1 Conflicts of Interest
None to declare.

7.5.2 Acknowledgments
The authors wish to thank the airport and ambulance service staff who contributed to data collection and the following organizations and individuals:

- French national out of hospital cardiac arrest registry research group - Registre électronique des Arrêts Cardiaques (GR-RéAC), Lille, France
- Dr. Tatsuya Nishiuchi, Amagasaki Medical Centre, Japan; Mr. Nobuhiro Kimura, Sennshu-Minami-Kouiki Firefighting Headquarters, Japan; Dr. Hideharu Tanaka, Kokushikan University, Japan
- Hildigunnur Svavarsdottr, Akureyri Hospital Iceland and University of Akureyri, Iceland; EMS and Fire service, Reykjanesbaer, Iceland
Chapter 8   Drawing it All Together

This chapter presents a collective overview of the thesis, a summary of key findings, and a discussion of the drivers of OHCA variation. Strengths and limitations that affect interpretation, and the implications of findings for improving OHCA outcomes are explored, finishing with the personal account of an OHCA survivor.

8.1 Overview of Thesis

The aim of this thesis was to investigate the effect of area-level grouping and area-level characteristics on OHCA incidence and outcomes. Six objectives were defined and addressed in six analytical chapters, resulting in six peer-reviewed, national and international contributions to the literature:

Objective 1. Provided an up-to-date overview of OHCA where resuscitation is attempted in Ireland (Chapter 2)

Objective 2. Described the pattern of OHCA incidence and pre-hospital resuscitation interventions across the Irish urban-rural spectrum (Chapter 3)

Objective 3. Quantified the effect of urban-rural grouping on OHCA incidence in Ireland using multilevel linear regression (Chapter 4)

Objective 4. Used Bayesian CAR modelling to adjust for the effect of few cases when estimating OHCA incidence at small area level (Chapter 5)

Objective 5. Identified differences in adjusted OHCA incidence and outcome between Sweden and Ireland and quantify the extent of variation explained by common Utstein predictor variables using logistic regression analysis (Chapter 6)

Objective 6. Estimated best achievable OHCA outcomes following OHCA in international airports and quantify the impact of area-level grouping using multilevel logistic regression analysis (Chapter 7).

Chapter 2 provided a comprehensive overview of the first 2 years of Irish OHCA registry data, following a rigorous data quality assurance process (objective 1). Previous Irish studies investigated the incidence, management and outcomes from OHCA, starting with Margey et al.’s review of OHCA attended by Dublin Fire Brigade and Henry et al.’s study of OHCA attended by NAS in Cork, but data was limited to the Cork and Dublin areas. While results from the first year of nationwide OHCA data collection were published previously, chapter 2 enhanced understanding of OHCA incidence and outcomes in Ireland by providing age and sex adjusted incidence estimates and providing the first Irish analysis of outcomes in the Utstein subgroup.

Building on the foundation laid in chapter 2 and in recognition of the amount of resuscitation-related activity that took place in Ireland since the publication of the Sudden Cardiac Death Task Force Report in 2006, Chapter 3 provided the first spatial description of OHCA cases and the chain of survival for Ireland (objective 2).
Chapter 3 investigated the possibility of an urban-rural divide in Ireland by describing OHCA across an urban-rural categorisation that was constructed specifically to assist in health service planning, and accounts for both population and geography – a first in OHCA epidemiology.

Expanding on the urban-rural theme, Chapter 4 examined the effect of rurality on OHCA incidence in Ireland using multilevel linear regression modelling (objective 3). As part of chapter 4, the concept of rurality was discussed from both an Irish and international perspective. Chapter 4 demonstrated the first use of multilevel modelling to quantify the area-level effect of rurality on OHCA incidence, a technique that is equally applicable in other countries and jurisdictions.

The issue of area-level difference was further explored in Chapter 5, where the relative risk of OHCA in the home in Ireland at ED level was described using Bayesian CAR modelling (objective 4). Chapter 5 added a spatial dimension to the estimation of OHCA incidence, by using the geography of events as well as area-level characteristics to help predict risk. Bayesian CAR modelling also enabled the effect of area-level factors such as deprivation on OHCA incidence to be investigated in a way that was not possible using other techniques. Bayesian CAR modelling has rarely been applied in OHCA research, and chapter 5 presented the first use of the technique in OHCA research in a national population with a diverse settlement pattern.

The goal of improving OHCA survival requires the sharing of results and data beyond national borders, but an appreciation of how comparable data is between countries is critical to setting realistic goals. Chapter 6 used patient-level data to compare OHCA incidence and outcomes between Ireland and Sweden over a 3-year period using similar data definitions and data collection methodologies (objective 5). External validity of data was assessed, and single-level logistic regression was used to determine the proportion of variation between countries that was explained by core Utstein variables, thereby highlighting the need for unmeasured differences between countries to be acknowledged.

Chapter 7 demonstrated the capacity to share data across international boundaries to estimate best achievable OHCA outcomes (objective 6), while accounting for area-level difference in the outcomes reported. Despite the challenges of obtaining data, Chapter 7 provided the most comprehensive analysis of OHCA incidence and outcomes in international airports that has been published to date. It also demonstrated the application of multilevel logistic regression as a method for quantifying area level difference.
8.2 Key Findings

This thesis demonstrated area-level difference in OHCA incidence and outcomes, and used modelling techniques that contextualised these differences. In Ireland there was significant clustering of OHCA cases when grouped at urban-rural level, and deprivation was significantly associated with a higher risk of OHCA at ED level. Similarly, there was a significant ‘country effect’ on survival between Ireland and Sweden, and a country-level difference between outcomes in international airports. Chapters 3 to 7 showed statistically significant area-level differences in OHCA. The practical significance of these findings both within and between countries was quantified using single and multilevel regression modelling, and Bayesian CAR modelling techniques.

8.2.1 Small Area Level Differences

As stated above, small area level differences in OHCA incidence were statistically significant in Ireland, but the practical implications of these findings need to be considered. The description of the spatial distribution of OHCA in chapter 3 showed that in the subgroup of adults who suffered an OHCA of non-traumatic aetiology that was not EMS-witnessed, the overall age and gender-adjusted incidence of OHCA was higher in City and Town EDs (51/100,000 population per year [46-55]) than in Rural EDs (35/100,000 population per year [28-42]) (Objective 2). Using multilevel linear regression modelling, the exploratory analysis in chapter 4 showed that urban-rural clustering explained only 2% of variation in OHCA incidence (Objective 3). For patients who suffered OHCA at home, the use of Bayesian CAR modelling in chapter 5 suggested that the urban-rural characteristic did not explain higher than expected incidence. As a result of using Bayesian CAR modelling to smooth ED incidence rates, 108 EDs were identified with higher than expected OHCA incidence. The majority of these EDs were in cities (Objective 4). However, incidence in only five of these EDs was significantly higher across individual years and multi-year data. For the subgroup who suffered OHCA at home, area-level deprivation, and not urban-rural categorisation, contributed to explaining ED-level variation in OHCA incidence. A one-point increase in deprivation was associated with an 11% increase in the risk of OHCA. The influence of deprivation appeared to decrease over time from 24% in 2012 to 10% in 2014. The urban-rural divide identified in chapter 3 was further explained by the Bayesian CAR model which allowed for area-level deprivation. However, interpretation of the significance of the increase caused by a change in deprivation at ED-level should take into account that 50% of EDs had no cases, and at least 40% of EDs had four or fewer cases over a 3-year period. As the number of cases at ED level is low, potential differences in survival made by targeting more deprived EDs would be difficult to detect. In view of the fact that the actual number of cases per ED is low, even though deprivation was shown to be statistically significant, these findings do

*All values between square brackets [ ] are 95% Confidence Intervals unless otherwise stated.
not support changes in the implementation of pre-hospital resuscitation services based on area-level deprivation.

Results from logistic regression analysis in chapter 2 showed that early defibrillation was not an independent predictor of OHCA survival, though only 297 out of 3,701 patients received an early defibrillation attempt. A short EMS call-response interval is critical to achieving early defibrillation, and results in chapters 2 & 3 showed that the EMS were unable to reach the vast majority of patients on time to achieve this. The proportion of patients who received an EMS response in eight minutes or less ranged from an average of 2% in Remote Rural EDs to 29% in City and Town EDs. While there was a dramatic difference in proportions across urban-rural categories, even in City EDs, the capacity of the EMS to respond within a time frame when defibrillation was viable was limited. Chapter 7 provided an opportunity to evaluate defibrillation before EMS arrival and showed it to be the most significant independent predictor of survival. Chapter 3 showed that in Ireland, while a significantly greater percentage of patients in Remote Rural EDs had defibrillation attempted before EMS arrival compared to City EDs (8% vs. 4% respectively), the actual percentage was low, regardless of urban-rural category. In fact, chapter 6 showed that the issue is not exclusively an Irish problem, with only 7% of Swedish patients having defibrillation attempted before EMS arrival.

Overall, differences at small area-level in Irish OHCA incidence do not appear to be of a magnitude that should influence national initiatives to improve OHCA outcomes in Ireland. There was variation in the availability of key links in the chain of survival across the urban-rural spectrum, but no urban-rural category was sufficiently well served to suggest that efforts to improve the chain should be focused on particular categories at the expense of others. Finally, the techniques used to assess the magnitude of small area level effect have been previously used in OHCA research, but by applying these techniques to the Irish population, this thesis has shown that the techniques are fully generalisable to countries with disparate settlement patterns.

8.2.2 Country-Level Differences
Analysis of international OHCA registry data suggested that there was variation in incidence and outcomes between countries, but that routinely used registry variables explained only a small proportion of between-country variation. Different chapters have explained parts of this difference between countries, while other questions emerged.

Patient-level analysis in chapter 6 showed significant differences in OHCA incidence and outcomes between Ireland and Sweden. Overall incidence is a natural determinant of overall survival – the bigger the count of attempted OHCA

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*Patients were defined as having received early defibrillation if defibrillation was attempted by a bystander or if the EMS call-response interval was five minutes or less.
resuscitation, the bigger the total number of survivors. However, as well as having a bigger number of survivors, overall percentage survival was also greater in Sweden than in Ireland. Differences in population subgroups between both countries helped to account for some of the difference in overall percentage survival. The EMS-witnessed subgroup is often excluded from OHCA epidemiological analysis of survival, primarily because some links in the chain of survival do not apply to this group (i.e. OHCA recognition and call for help; activation of EMS; bystander CPR). Chapter 6 showed that the incidence of EMS-witnessed cases in Sweden was three times that of Ireland (8.1 [7.1–9.2]/100,000 population/year vs. 2.6 [2.0–3.1]/100,000 population/year respectively). Percentage survival in the Swedish and Irish EMS-witnessed subgroup differed significantly but not dramatically (Sweden 20% vs. Ireland 17%), suggesting a relatively similar prospect of survival for patients who had an EMS-witnessed arrest, regardless of the country in which OHCA occurred. However, EMS-witnessed patients made up a greater proportion of overall survivors in Sweden. Almost one in five Swedish survivors had an EMS-witnessed arrest compared to only one in ten Irish survivors. The reasons for the higher incidence of Swedish EMS-witnessed patients were not explained in chapter 6, but a substantial proportion of difference in overall percentage survival was attributable to the EMS-witnessed subgroup.

Unlike the EMS-witnessed subgroup, Utstein comparator incidence was similar in Sweden and Ireland (7.7 [6.5–8.9]/100,000 population/year vs. 6.8 [6.1–7.4] respectively). This supported an assumption of equivalent case ascertainment and validated between-country assessment of predictors of survival for this group. From the perspective of explaining difference, only 17% of survival variation between countries was predicted by the patient-level variables included in logistic regression analysis. Additionally, explained variation included a 4-fold ‘country effect’ in favour of Sweden.

The patients at international airports described in chapter 7 also represented a subgroup of national OHCA populations and, in common with the Utstein subgroup, included patients who were expected to benefit from efficient and effective activation of the chain of survival. Country-level differences were evident, ranging from a mOR of 1.6 (95% CrI 1.1-3.7) when adjusted for age, gender and initial rhythm type, to a mOR of 3.0 (95% CrI 1.6-14.3) when adjusted for age, gender and attempted bystander defibrillation. In this highly specific population, the likelihood of survival varied across countries, and highlighted the limitations of comparisons that use aggregated data, even for this contrived environment.

The between-country differences observed in OHCA incidence and outcome have practical implications for OHCA epidemiological research using registry data. The causes of country-level differences were not definable from the registry or area-level data available. However, the magnitude of between-country difference found using single-level and multilevel logistic regression analysis techniques highlight the importance of adjusting patient-level analysis to account for country-level grouping. The factors that constitute the country effect were not explained by this thesis. Findings in chapters 3, 4 and 5 showed the limited role of area-level factors in
explaining OHCA variation and suggested that the greater proportion of variance is explained by patient-level factors. In order to explain variation between countries, assuming Utstein incidence is similar, patient-level analysis with additional explanatory variables is needed. Possible contributors to unexplained variation will be discussed in the next section.
8.3 What Drives Out-of-Hospital Cardiac Arrest Variation?

The aim of this thesis was to investigate the effect of area-level grouping and area-level characteristics on OHCA incidence and outcomes. As well as helping to contextualise the role of area in OHCA incidence and outcomes, the registry data used in this thesis has helped to develop a greater understanding of the drivers of variation in OHCA incidence and outcomes.

8.3.1 Modifiable Patient Factors

Of the 3,701 Irish patients included in chapter 2, 86% had an OHCA of a presumed cardiac aetiology. Cardiac aetiology was either due to CAD, which developed over time, or due to a genetic predisposition present since birth (inherited cardiac disorder or arrhythmia). Area-level factors including air pollution 326 and deprivation 327,328 have been shown to be independently associated with the development of CAD. However, CAD risk is largely determined by individual behaviour and individual patient management. This was most clearly demonstrated by the INTERHEART study published in 2004, in which Yusuf and colleagues estimated that nine risk factors accounted for 90% of risk of CAD in men and 94% of risk in women, all of which were potentially modifiable at patient level 290. In the logistic regression model in chapter 6, it was estimated that of the 17% of outcome variation explained, the majority was attributable to the undefined country effect (14%). According to the results of chapters 3, 4 and 5 (and in accordance with Yusuf et al.) the country effect observed was most likely due to patient-level differences. This implies that improvements in pre-hospital resuscitation intervention will have a minor impact on OHCA survival, and that the individual risk profile of patients is the main predictor of OHCA outcome. Preventative measures to improve cardiac health and to reduce the risk of OHCA as a result of known inherited cardiac disorders can be part of public health policy. However, intervention and action must occur at individual patient level.

8.3.2 Area-Level Response to an Emergency Event

This thesis did not find a substantial association between area-level factors and OHCA incidence variation, though area-level variation has been found to be more important in other regions including Singapore 165 and Victoria, Australia 115. The mechanism whereby area-level factors might influence this variation is therefore worth consideration. While any association between area-level factors such as deprivation may be assumed to be a result of the role of deprivation in CAD aetiology, there is a difference between a condition (CAD) and an event (OHCA). Bayesian CAR analysis in chapter 5 suggested a statistically increased risk of OHCA in EDs with increased area-level deprivation, most of which were clustered in cities. Previous studies have found an association between greater area-level deprivation and increased use of emergency services by patients in inner-city areas in the UK 329,330. A similar effect in deprived areas of Irish cities may explain the small but significant area-level effect on OHCA incidence variation found in this thesis.
8.3.3 Method of Case Ascertainment

Unless similar case ascertainment methods are assured, a proportion of variation in incidence and outcome may be caused by differences in data collection methodologies. Estimates of incidence and outcome may be internally reliable i.e. the same method used nationally year-on-year, but lack of uniform case ascertainment methods across countries will undermine the validity of between-country comparisons. In the two main OHCA registries used in this thesis, primary case ascertainment was carried out by those who provided pre-hospital resuscitation care i.e. EMS practitioners. Additionally, the Swedish and Irish registries both operated systematic missing case identification procedures, and previous work in Sweden showed the value of actively searching for unreported cases. As demonstrated in chapter 6, similarity in case incidence for the Utstein comparator group confirmed the assumption of external validity, meaning consistency in case ascertainment methodologies allowed OHCA outcomes and incidence to be reliably compared between Sweden and Ireland, if not wholly explained. In contrast, the EuReCaONE study estimated that the crude incidence of OHCA where CPR was attempted was between 19 to 104 per 100,000 population per year across 27 countries, and wide variability in Utstein group incidence was also found. While findings in chapters 6 and 7 suggest that real differences in OHCA incidence and outcome between countries exist, in the EuReCaONE study “methods of data collection were not standardised between contributing countries and regions, and quality control was limited to queries to the N[ational] C[ooridinator]s”. It is likely that difference in case ascertainment methods also contributed to variation.

8.3.4 Patient Selection

Differences in OHCA incidence between patient subgroups can signpost differences in patient selection for resuscitation, but OHCA registry data used in this thesis did not explain those differences. The patient-level analysis in Chapter 6 showed that overall incidence of OHCA was higher in Sweden, and that this was mostly due to higher incidence of OHCA with attempted resuscitation in Swedish people aged over 65 years. The finding of lower incidence in the EMS-witnessed subgroup in Ireland highlights that the circumstances of arrest also affect patient selection. The reasons why more patients in Sweden had an EMS-witnessed arrest were not revealed by OHCA registry variables, but nonetheless, the more likely selection of this patient group in Sweden contributed to incidence and outcome variation between the countries. The location of the OHCA event may also affect patient selection. Of the 34 countries who were invited to contribute data for chapter 7, nine countries were unable to contribute because data from international airports was either not collected as part of OHCA registry data, or data was insufficiently comprehensive. This means that, in these countries, patients who suffer OHCA at international airports are routinely excluded from OHCA epidemiological analysis.
8.3.5 Resuscitation Intervention

The spatial description in chapter 3 showed differences in OHCA incidence and differences in availability in the chain of survival across the urban-rural classification. OHCA incidence and resuscitation intervention are not independent. Survival from OHCA is not possible without a resuscitation attempt, but availability of interventions is also part of what increases or decreases the chance of a patient becoming a ‘case’ on an OHCA registry. Chapter 3 showed that as EDs became more rural, OHCA incidence and the proportion of patients who received a call response interval in eight minutes or less decreased. Considering that 98% of patients in Remote Rural EDs did not receive an EMS response within eight minutes, it is possible that the lower incidence of OHCA where resuscitation was attempted was due to decreased availability of a timely intervention, resulting in death being declared on EMS arrival.

In a study from the ROC consortium, Brooks et al. observed a similar pattern in that the incidence of OHCA where resuscitation was attempted varied across EMS agencies and lower incidence was associated with longer response times.

As previously described, if there are more resuscitation attempts, there will be a bigger number of OHCA survivors. Chapter 6 showed that Sweden had a greater incidence of resuscitation and a higher count of survivors, but also that percentage survival was greater than in Ireland. This suggests that increasing the incidence of resuscitation in Ireland may increase overall percentage survival, but it is more likely that increased incidence is a consequence of increased awareness of OHCA and improvements in the chain of survival. A previous study in Sweden demonstrated that resuscitation incidence increased as national initiatives to improve the chain of survival were introduced, increasing from 27/100,000 population in 1992 to 52/100,000 population in 2011. These changes were accompanied by improved survival (from 5% in 1992 to 11% in 2011). A similar effect was observed by Kim et al., who assessed the effect of phased implementation of improvement programmes over a 10-year period in Korea. Resuscitation incidence increased from 18/100,000 population in 2006 to 41/100,000 population in 2015 and percentage survival increased from 3% in 2006 to 6% in 2015. These findings suggest that the target for Ireland should not be to increase the number of resuscitation attempts, but rather, efforts should be focussed on improving the chain of survival. As previously described however, expectations from improving the chain of survival should be tempered with the knowledge that only 3% of variation in OHCA outcomes in the Utstein subgroup for Sweden and Ireland could be accounted for by common Utstein predictor variables.

8.3.6 Rescuer Influence

When cardiac arrest occurs, the actions of those who attend the scene, particularly those who attend in a professional capacity, will determine whether resuscitation will be attempted. This in turn determines whether an event will be entered onto an OHCA registry. The identity and training level of the EMS practitioners or lay rescuers were not available in OHCA registry data used in this thesis but are also likely to have had an effect on OHCA incidence and outcomes. As described in chapter 1, in an earlier Irish study, it was found that when GPs attended an OHCA scene, they were
less likely to commence resuscitation and more likely to cease resuscitation on scene than their ambulance colleagues. Brooks et al. found a lower incidence of attempted resuscitation when advanced ambulance practitioners attended the scene, while Dyson et al. found that paramedics’ levels of exposure to OHCA were inversely related to the incidence of attempted resuscitation. These findings suggest that EMS practitioner exposure, experience and expertise all influence the likelihood of resuscitation being attempted, which in turn affect OHCA incidence and outcomes. There will also be emotional influences on the decision to commence or cease resuscitation, which are likely to particularly affect bystanders, such as prior knowledge of the patient, and the rescuer’s own emotional state at the time of collapse. However, these influences are subjective and may be difficult (if not impossible) to measure.
8.4 Strengths and Limitations

The strengths and limitations of individual chapters were included as part of each chapter’s discussion section. The additional issues addressed below are also important as they should be borne in mind when interpreting the key thesis findings, reflections and conclusions outlined in this chapter.

8.4.1 Existing Data Sources and the Value of Geocoding

A particular strength of this thesis is that it capitalised on existing available data, including OHCA registries, national census records and international airport statistics. It also demonstrated how sources of area-level data (i.e. census data) could be used to at least partially compensate for lack of patient-level data. While access to OHCA registry data required ethical approval and data controller permission, the other data sources were freely available and easy to access electronically. All data used was population-based (i.e. no sample data used), and collected from real-life circumstances rather than an experimental environment. The ability to link these data sources to individual cases was facilitated by the availability of geolocation data. Despite the lack of exact geo-coordinates for each OHCA, chapters 3, 4 and 5 showed how EDs could be used as units of measurement to directly link OHCA events to the population and area in which they occurred. Similarly, the value of accurate and precise location coding in OHCA registries was highlighted in chapter 7, as only countries that had included this location option in their OHCA registries were able to participate in the study.

8.4.2 Quantifying the Role of ‘Place’

A primary motivation for the aims and objectives outlined in this thesis was that area-level variation is an often observed factor in OHCA incidence and outcomes. The difficulty in exploring this observation was that OHCA was not a common event at small area level, meaning a change of one or two cases may potentially exert a disproportionate effect on incidence estimates. Individual chapters demonstrated how established statistical and geographical methodologies could be used to reduce the risk of small changes having an unbalanced influence on results, particularly by the use of Bayesian CAR modelling in chapter 5. While OHCA patients might be described as ‘contained’ units of measurement, patients themselves were not contained within the geographical units of measurement used in this study, and could move across ED borders, and the use of Bayesian CAR modelling acknowledged the spatial qualities of geographical units of measurement. Additionally, chapters 4, 6 and 7 demonstrated the usefulness of single and multilevel regression modelling for quantifying area-level differences, thereby adding context to findings that may be statistically significant, but are of questionable clinical importance.
8.4.3 Reinforcing Previous Knowledge from OHCA Epidemiology

As well as quantifying the role of place, findings reinforced the importance of patient-level factors in OHCA incidence and outcomes. OHCA is not a disease. It is a catastrophic event which occurs most often as a result of the presence of cardiac disease, or because of poor management of cardiac disease risk factors. As shown in chapter 7, once OHCA occurs, even in the most ideal of circumstances where the chain of survival is efficient and available, the chance of survival is approximately one in three. This means that the best way to avoid death from OHCA is not to have an OHCA in the first place, and while this fact makes intuitive and biological sense, it is rarely acknowledged as the most effective method for reducing death from OHCA.

The Utstein comparator subgroup may represent a small proportion of the overall OHCA population, but similar incidence in the Utstein subgroups in Sweden and Ireland verified that comparison between countries was feasible. Logistic regression analysis using the Utstein subgroup highlighted the degree of variation between countries in chapter 6 and enabled assessment of Irish pre-hospital resuscitation effectiveness in chapter 2.

A further finding that reinforced previous knowledge was the association between survival and attempted defibrillation before ambulance service arrival, with chapters 6 and 7 both showing it to be independently associated with survival (OR 1.4 [1.1-2.10] and OR 4.8 [3.0-7.8] respectively). The modified variable ‘early defibrillation’ in chapter 2 failed to achieve a significant association with survival (OR 1.4 [0.9-2.3]), but this may have been because the derived variable overestimated defibrillation availability.

8.4.4 Lack of a Cardiac Arrest Denominator Population

A particular limitation of this thesis is that OHCA incidence only included patients who were attended by ambulance services and who had resuscitation attempted. It may be argued that patients who do not receive a resuscitation attempt have no prospect of survival and therefore the outcome for this group cannot be affected. However, more information about the ‘no resuscitation’ group may have helped to resolve questions that were raised in the key findings. For example in chapter 3, the question of whether lower incidence in more rural EDs is related to EMS call-response interval may have been answered if the overall cardiac arrest incidence at ED level or urban-rural grouping level had been available. Knowledge of the overall cardiac arrest rate may also have helped explain the differences in patient selection between Sweden and Ireland in chapter 6. As already discussed, there are many factors that influence the decision to resuscitate when cardiac arrest occurs. Information on all cases of cardiac arrests that occur in the community may help explain the impact that these individual factors have on overall OHCA resuscitation rates.
8.4.5 Missing Data and Few Cases
As discussed in chapter 1, missing data was an expected issue in research using OHCA registries. Fortunately, the pattern of missing data was assessed to be at random, and multiple imputation could be used to verify results generated using original data (chapters 2 and 7) or to generate reported results (chapter 6). As stated in chapter 4, the issue of a small number of cases at ED level was more challenging. Additionally, while incidence at ED level was low, due to the rarity of survival at ED-level, planned area-level analysis of survival was not carried out. With regard to incidence, the fact that half of all EDs had no cases and 72% of EDs had a predicted OHCA rate of less than one may have potentially led to overestimation of incidence variance. While multilevel modelling and Bayesian CAR modelling techniques helped to adjust for this issue, sensitivity analysis in chapter 5 showed that the robustness of results was highly dependent on the fact that multi-year data was available. Repetition of analyses with more years of data may be the most effective way to assess the true impact of few cases on incidence variance.

8.4.6 Explanation of Variation Limited
Due to the use of existing data sources, this thesis had the major limitation that aims and objectives were limited by the available data, rather than research aims determining the data that was collected. Small area level grouping and small area level characteristics were shown to have minimal impact on OHCA incidence, but findings also showed that a large proportion of patient-level variation was not accounted for by the data that was routinely collected on OHCA registries. This particular limitation has consequences for future OHCA epidemiological research, which will be discussed in a later section.
8.5 Implications of Findings for Improving Out-of-Hospital Cardiac Arrest Outcomes

It has already been acknowledged that reducing the risk of cardiac disease is likely to have the greatest impact on death from OHCA, but this section will focus on describing ways in which the findings from this thesis can positively influence the rate of survival when OHCA occurs.

8.5.1 Compare
Collecting OHCA data may not in itself improve outcomes, but data collection facilitates comparison with what is assumed, what has happened previously, and what happened elsewhere. This in turn can help to motivate communities and health services to strive for further improvement. For example, in 2006 when the Report of the Taskforce on Sudden Cardiac Death was published, based on extrapolated data from 2002, the proportion of survival from sudden cardiac death was estimated to be 1%. When the chance of success is less than 1%, it has been suggested to be medically futile to intervene. The question of medical futility cannot be dealt with by universal application of a single quantitative measure, but such a low rate of survival did raise a question about the usefulness of OHCA resuscitation in Ireland. However, as reported in chapter 2, the first two years of national data collection showed that survival from OHCA where resuscitation was attempted was 6%, which was within a range where scope for improvement could be considered, and provided a baseline by which improvements can be measured internally. If internal comparison is to be meaningful, internal data validity must be assured. This means that maintaining internal data quality is a core and continuous process and it is recommended that national registries dedicate efforts and resources to the attainment and maintenance of data quality.

Chapters 6 and 7 demonstrated that international comparison should be performed in the knowledge that differences in OHCA incidence and outcomes are not fully explained by the variables routinely collected in OHCA registries, even where comparable data collection methodologies are used. For this reason, if international benchmarking is carried out, it is recommended that the comparability of countries should first be assessed (i.e. assure similar Utstein subgroup incidence), and that comparison of outcomes is focused on the Utstein comparator group, with adjustment for a ‘country effect’. International collaboration was the key to the successful production of the Utstein template and data definitions described in chapter 1. Many large OHCA data collection networks already exist including EuReCa, ROC, AusROC, CARES and PAROS, and it is recommended that aligning interpretation of data definitions and data collection methodologies could be substantially addressed through global collaboration between these networks. Additionally, and perhaps more significantly, there is an opportunity through these networks to develop simple, standardised reporting formats that could be used within countries to drive improvement in data quality and improve national OHCA outcomes, and ultimately increase overall international OHCA survival.
8.5.2 Explain
This thesis has shown that a large proportion of variation in OHCA incidence and outcome is not explained by routinely collected OHCA variables. Explaining these differences will require access to patient-level data. In Ireland, sources of individual-level data exist including: the civil register; patient medical records; hospital and primary care databases; and, exact geo-coordinate ambulance and event data from ambulance dispatch centres. However, linking data from different data sources may be prohibited, particularly since the adoption of the General Data Protection Regulation (GDPR) into national legislation across European Union countries on 25th May 2018 334.

GDPR requires a legal basis for the processing of personal data of living persons. In the case of the Irish OHCA registry, the legal basis for processing after GDPR introduction is ‘public interest’. Under GDPR, research using OHCA registry data will continue to be permissible, but only if data is fully anonymised (i.e. no way that individual patients can be retrospectively or prospectively identified from the data). This requirement would not have impeded the conduct of this thesis, but could impede future research that requires data linkage between existing patient-level data sources. Another possible legal basis for data processing under GDPR is the explicit and informed consent of the data subject. Consent will not be used as a legal basis for OHCA registry data processing as seeking individual consent would compromise the validity of results reported due to the risk of consent bias 335,336. For research purposes, as GDPR applies only to living persons, it may be possible to seek consent from surviving patients, but it is unlikely that ethical approval to treat patient data differently on the basis of patients’ status would be granted.

The alternative to this approach is that a unique citizen identifier is assigned to all individual-level data that is held by government agencies, and that data linkage is performed using this identifier, before data is anonymised for research purposes. In Denmark this approach is successfully used, as was demonstrated by Kragholm et al. in their study of the effect of bystander efforts on OHCA survival 76. They used the Danish Civil Personal Registration Number (CPRN) to combine data from the OHCA Registry, Cause of Death Register, National Patient Register and National Prescription Registry. In Ireland, attempts to use the existing Personal Public Services Number (PPSN) in the same way as the CPRN have been impeded by legal challenges 337.

In view of the existing difficulties with data linkage in Ireland, and in order to explain the variation in OHCA incidence and outcomes, it is recommended that OHCAR’s data collection process is broadened to encompass Utstein variables that are likely to enhance understanding of variation, particularly: diagnosed aetiology; comorbidities; hospital treatment; and quality of life after hospital discharge 67. If these data were part of routine OHCA data collection and data, the explanatory value of these factors could be fully investigated in subsequent anonymised research. A similar approach should be considered in other jurisdictions that do not have a unique citizen identifier.
8.5.3 Educate

When cardiac arrest occurs, there is no prospect of survival unless the chain of survival is activated, regardless of all other patient and event differences. However, as demonstrated in chapter 7, when the chain of survival was activated, the majority of patients did not survive, because of patient and event differences that were not fully explained in this thesis. The question of ‘who should receive a resuscitation attempt?’ is still unanswered. Based on survival observed in chapters 2 and 6, there is little doubt that within the Irish and Swedish OHCA population, there was a large cohort of patients who had a futile resuscitation attempt. Conversely, anecdotal accounts from the EMS suggest that there were people who may well have benefitted from resuscitation, but bystanders did not have the knowledge or skills to recognise cardiac arrest or react appropriately. Added to this is the fact that patients sometimes survive in rare, or seemingly impossible scenarios, and these are the cases that are most likely to pique media attention 338,339.

As demonstrated in this thesis, every VF does not survive, any CPR is not necessarily better than no CPR, and every citizen cannot save a life. The difficulty is that when an unexpected cardiac arrest occurs, bystanders are unlikely to be able to predict the patient’s outcome. For this reason, when the chain of survival is activated by a bystander, the EMS assume that survival is possible and resuscitation is appropriate, unless or until proven otherwise. With the adoption of dispatch-assisted CPR in ambulance control centres, bystanders are increasingly likely to be instructed to attempt CPR, even if they have no CPR training. In a recent observational study in Japan, which included 87,400 patients in a propensity analysis 340, Hagihara et al. reported a marginally negative association between survival and dispatch-assisted CPR when compared with bystander CPR without dispatch assistance (OR 0.81 [0.65-1.00]), and hypothesised that poor CPR quality was the reason for the difference observed. The EMS assumption that survival is possible is reasonable in the absence of evidence to the contrary, but in the absence of a bystander who is willing and able to provide effective CPR until defibrillation can be attempted, this assumption may be placing an unproductive burden on untrained bystanders. It is acknowledged that the EMS has a duty of care to patients for whom they are activated, but it may be argued that a duty of care is owed to those who make the emergency call. It is therefore recommended that introduction of dispatch-assisted CPR is accompanied by community-based, bystander CPR training to ensure bystanders have the skills and knowledge needed to improve survival.

Findings in this thesis support the assertion in the 2015 ERC Guidelines of, “the critical importance of the interactions between the emergency medical dispatcher, the bystander who provides CPR and the timely deployment of an AED. An effective, co-ordinated community response that draws these elements together is key to improving survival from out-of-hospital cardiac arrest” 24. Bystander CPR and defibrillation before ambulance arrival were associated with improved survival in chapters 2, 6 and 7. Improvements in survival cannot be achieved without community preparedness and willingness to contribute to the chain of survival. As part of community preparation, it is recommended that community education includes discourse on the inevitability of cardiac arrest as part of life, and the fact that the
chain of survival is not an absolute predictor of survival, even when properly implemented. The aim of this recommendation is to encourage communities to discuss with patients and family members whether resuscitation should be initiated in the event of cardiac arrest, and also to reinforce that death after a resuscitation attempt is not necessarily a failure in the chain of survival. In Ireland, less than one third of patients received an EMS response in eight minutes or less, and the median EMS call-response interval for Sweden and Ireland far exceeded the 5-minute window when defibrillation is most likely to influence survival (median EMS CRI in minutes [interquartile range]: Ireland 13 [8-20]; Sweden 10 [6-15]). These findings suggest that remote communities may need to be imaginative about how to ensure timely defibrillation. Drone dispatch of AEDs is an unproven methodology, but a simulation study by Claesson et al. in Sweden suggested that it has potential in rural areas. Unfortunately, communities may also need to be realistic about the prospect of survival. A recent study by Goto et al. suggested that in Japan, if bystander defibrillation was performed, the upper limit of EMS call-response times associated with neurologically survival was 13 minutes. This time limit may be equally applicable in other jurisdictions.

8.5.4 Research
This thesis showed minor impact of small area level grouping and factors on OHCA incidence, but the type of spatial analysis used was limited by the fact that OHCA locations were centred at ED level. Additionally, it was not possible to model survival due to the rarity of survival at ED level. Precise geo-location data for OHCA events and ambulance location at time of dispatch are used in emergency dispatch centres. Similarly, with the more widespread introduction of the location-specific Eircode, the accuracy and precision of patient address data has greatly improved. Availability of these variables for future OHCA spatial epidemiological analysis may allow more precise estimation of the role of geography in OHCA. Additional years of data would also improve the robustness of estimates of incidence risk. In this thesis, Bayesian posterior sampling using the Markov chain Monte Carlo (McMC) method was used to fit the Bayesian CAR model in chapter 5, and to generate 95% credible intervals for the mORs generated in chapter 7. This sampling method may also make it possible to model survival at area-level, particularly as additional years of data become available. It is also worth remembering that the finding of limited small area level effect is specific to Ireland. Countries that have more evident socioeconomic, health or racial disparities at area-level may find different results when applying the methodologies used in this thesis.

Differences between countries were a persistent finding in this thesis, and therefore it is recommended that future research that explores variation in international incidence and outcomes uses analytical techniques that adjust for country-level grouping. As previously discussed, in countries that have unique citizen identifiers, there is potential to link patient-level data and further explain variation in incidence and outcomes. This type of identification number is used in Sweden, Denmark and Norway, who all have national OHCA registries. Therefore, the potential for between-country analyses that explain a greater proportion of variation already exists. It is
important however that research into between-country differences does not detract from the primary function of national OHCA registries as an internal quality improvement tool. Therefore, between-country research which encourages a focus on complete case ascertainment and data quality is most likely to result in improved OHCA outcomes internationally.

It is also recommended that the work on location-specific outcomes is extended to locations other than international airports, as achieving substantial patient numbers may be difficult in one city or country. For example, Lee et al. carried out a study investigating survival following OHCA in ‘covered walkways’ in Toronto and identified 49 cases that met the criteria during a 10-year period with survival of 33% 343. Over 18 years in the Italian province of Piacenza, Aschieri et al. observed a total of 15 OHCA in the province’s sports centres that had on-site AEDs with 93% survival 344. In contrast, 800 OHCA patients were identified in international airports by combining data from nine countries. More international collaboration may help identify if survival rates reported for these locations in individual countries are replicated elsewhere.

8.5.5 Summary of Recommendations
In summary, the following recommendations are suggested for improving OHCA outcomes:

- National OHCA registries should dedicate efforts and resources to achieving and maintaining data quality. Between-country research should focus on improving case ascertainment and data quality in national registries, as a way of helping to improve international OHCA survival.
- Aligning interpretation of data definitions and data collection methodologies internationally should be addressed through collaboration between existing OHCA registry networks.
- In Ireland it is recommended that OHCAR’s data collection process is broadened to include variables that can enhance understanding of variation. In countries where unique identification numbers are used, the potential to link OHCA registries with other national registries of individual-level data should be explored.
- Research that explores variation in international incidence and outcomes should be focused on similar subgroups and use analytical techniques that adjust for country-level grouping.
- Improved estimates of best achievable survival in specific locations can be obtained by sharing data from similar locations across national boundaries, while acknowledging country-level differences.
- The expectation that bystanders will provide dispatch-assisted CPR should be supported by community-based, bystander CPR training to ensure the skills and knowledge needed to improve survival.
- Defibrillation before ambulance arrival is a critical predictor of survival. Communities should be engaged in finding ways to reduce time from collapse to defibrillation.
- Local communities are critical to improving outcomes. Community education should acknowledge the inevitability of cardiac arrest as part of life, and the fact that the chain of survival is not an absolute predictor of survival, even when properly implemented.
This thesis has shown how data from OHCA registries can help explain differences in OHCA incidence and outcomes, has suggested ways in which gaps in knowledge might be addressed, how OHCA registries might be used to improve international OHCA outcomes, and has acknowledged that there are aspects of OHCA incidence and management which cannot be measured. The chain of survival has limitations, but it offers the only prospect of survival when OHCA occurs. Monitoring the success of the chain of survival through good quality OHCA registry data is an important part of improving outcomes, both nationally and internationally.
8.6 A Story of Survival

Patient stories or cases in this thesis thus far were recorded from the perspective of the EMS personnel who were involved in resuscitation attempts, and the information collected was determined by predefined variables required for an OHCA registry. The following story is a personal account of OHCA, as told by a surviving patient.

The gentleman whose story is described was 57 years old when he suffered an OHCA. A married man with a family in their teens and early twenties, he worked full time in a non-manual occupation, as well as being a part-time farmer on the family farm where he lived. At the time of his OHCA, he was involved in coaching amateur football. He had no previous history of heart disease. Prior to his OHCA, he attended annual medical check-ups and had a serum cholesterol level that was at the upper limit of normal, but was not found to have significant risk factors for cardiac disease.

“My cardiac arrest happened on a Sunday evening. I’d had a relaxing few days away from home, and was still taking it quite easy on the Sunday. I’d mowed the lawn, watched a bit of football, and then I went to check on grass growth on the farm about 5pm, planning to be back for dinner at 7pm. I measured grass for about 30 minutes, and then I drove a calf back to its mother, as the calf had managed to get into a different field. After chasing the cow and calf, I felt a strain in my chest, but I continued to measure grass in another two fields, ending up at a field outside my sister’s house. My brother-in-law asked me in for a drink. I declined due to time pressures, but spent 15 minutes chatting with him. I went back to the field across from sister’s house and then I felt the pain. I moved along the field, erecting poles for the electric fence. It was a light job, but I had to sit down and rest before I reeled out the electric wire. I felt like there was a ball pushing through a tube in the middle of my chest. I did not like the pain or its location, so then I shouted to my sister and her husband and called them over to the field. I started to feel worse and told them I felt weird. My sister suggested that she would call the out-of-hours GP service, but I said no, and told her to call an ambulance as I knew things were not okay. That shocked her, as I don’t like a fuss.

The ambulance was there within 18 minutes, and they were able to drive into the field as the gates were not locked, as they usually would be. I knew one of the paramedics and he told me afterwards that when he heard my name on the call, he knew it must be serious if I was calling an ambulance. They started working on me, and I don’t think I passed out, but I felt a sense of contentment and satisfaction. Even so, something told me I wasn’t ready to go, this was not my time. They got me into the ambulance, with my sister and a paramedic beside me. As we were backing out onto the road, on went the blue lights and sirens. The paramedic was discussing whether to take me to the emergency department or directly to coronary care.

Then, I don’t remember anything. My sister said the line on the screen above my head went flat. We haven’t really discussed what happened but I know that they shocked me at least two times. When I woke up 25 minutes later, there were four paramedics surrounding me (two more had arrived in separate vehicles), and there were IV lines
coming out of my arm. When I woke I said “hello” to my sister. I wasn’t agitated or upset, but I didn’t know what had happened. We raced in the road, and I remember being brought to the cath lab on the ambulance stretcher. There was such a crowd of doctors and nurses, and I kept apologising for ruining their Sunday evening. I remember one of the doctors commenting to the paramedics on the good job that they had done. I had two stents put in. The doctors told me that if I’d had a stress test or angiogram that morning, there was a good chance that my heart would have looked fine. I’ve no idea what it was that caused the plaque on my artery to break away and cause the blockage. My heart muscle was damaged that day. I have had atrial fibrillation since then. I’m expecting to have a procedure that will help to manage the atrial fibrillation soon. About nine months after the cardiac arrest I had an ICD fitted and it has fired once since then. I left the hospital a week after the cardiac arrest. I remember how it felt, even to bend down, when I got home, and it’s amazing how I’ve recovered. I know that I’m lucky. If the ambulance hadn’t arrived so quickly and if I’d been lying in the field when it happened, I don’t think I would be here today.

Not much in my life has changed. I stopped coaching football, but I did my time at that, so that’s fine. I don’t think that my family was greatly affected by what happened. I was always a person to enjoy the simple things in life, and aware of our beautiful environment and landscape. Even more so now, the simple and most pleasing thing of all is waking up in early morning after deep night’s sleep and knowing I have another beautiful day ahead of me.”
Chapter 1       Appendix


Complying with Utstein guidelines: Comprehensive case identification in the Irish national out-of-hospital cardiac arrest register

Resuscitation, 100, e3
Letter to the Editor

Complying with Utstein guidelines: Comprehensive case identification in the Irish national out-of-hospital cardiac arrest register

Sir,

The Utstein guidelines state that, "organisers of out-of-hospital cardiac arrest (OHCA) registries should implement monitoring and remediation for completeness of case capture" [1]. Additionally, as shown by Strömme et al., case underreporting may be an issue in OHCA registries [2]. We aim to describe how the issue of case comprehensiveness in the Irish OHCA registry (OHCAR) has been addressed in conjunction with the Irish National Ambulance Service (NAS).

In Ireland, statutory Emergency Medical Services use a standardised Patient Care Report (PCR) which contains a section dedicated to data collection for OHCA. Specially designed OHCA envelopes have also been provided to each ambulance station. In the event of OHCA, practitioners place completed PCRs in OHCA envelopes. On a monthly or fortnightly basis, envelopes are collected together with all PCRs from each station. All PCRs are scanned and stored digitally and cases in OHCA envelopes are given priority in the scanning process to facilitate OHCAR. OHCA variables are manually entered onto an electronic database. This database is then forwarded to OHCAR together with a scanned copy of each PCR for case-by-case validation.

Cases that are not placed in OHCA envelopes are not processed through the OHCA data collection system and must be identified separately. Missing case identification is performed on a monthly basis and repeated on an annual basis to capture delayed reports. First, a search of the digital scanning archive is performed based on the 'Chief Complaint' field in the PCR using the word 'arrest'. Reported cases are excluded from the result and then the digital scan of the PCR associated with each call found is viewed. Missed OHCAR cases are identified and captured during the viewing process.

Next, emergency control data is filtered to identify all calls with an AMPDSD designation of "ICHD" at the time of resource deployment. A further seventeen "BLDGA" codes that may signify arrest occurred are included in the filter. Reported calls are then excluded from the filtered list. PCRs on the filtered list are then viewed and remaining unreported OHCAR cases are identified.

Missing case identification was introduced to OHCAR during 2012 and 2013 and a full systematic process has been in operation since January 2014. In 2014, 1605 OHCA cases were reported. An additional 379 cases were identified through missing cases identification (19% of all cases). For 2014, approximately 5500 PCRs were viewed for the purposes of missing case identification. Of these, 7% (n = 379) were unreported OHCA cases. Missing case identification is labour intensive as PCRs in Ireland are currently paper-based. Plans are progressing to introduce an electronic PCR system to Ireland, which will obviate the effort currently expended on missing case identification. In the meantime, however, the current process ensures that we can have a high degree of confidence that OHCAR is a comprehensive register of OHCA cases attended by the NAS where resuscitation is attempted.

Conflict of interest

No conflicts of interest to declare.

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18 December 2015
22 December 2015
Masterson, S., J. Cullinan, B. McNally, C. Deasy, A. Murphy, P. Wright, M. O'Reilly & A. Vellinga (2016)

Out-of-hospital cardiac arrest attended by ambulance services in Ireland: first 2 years' results from a nationwide registry

Out-of-hospital cardiac arrest attended by ambulance services in Ireland: first 2 years’ results from a nationwide registry

Siobhán Masterson,1 John Cullinan,2 Bryan McNally,3 Conor Deasy,4,5 Andrew Murphy,1 Peter Wright,1 Martin O’Reilly,6 Akke Vellinga6

ABSTRACT

Background National data collection provides information on out-of-hospital cardiac arrest (OHCA) incidence, management and outcomes that may not be generalisable from smaller studies. This retrospective cohort study describes the first 2 years’ results from the Irish National Out-of-Hospital Cardiac Arrest Register (OHCAR).

Methods Data on OHCAcs attended by emergency medical services (EMS) where resuscitation was attempted (EMS-treated) were collected from ambulance services and entered onto OHCAR. Descriptive analysis of the study population was performed, and regression analysis was performed on the subgroup of adult patients with a bystander-witnessed event of presumed cardiac etiology and an initial shockable rhythm (Utstein group).

Results 3701 EMS-treated OHCAcs were recorded for the study period (1 January 2013–31 December 2015). Incidence was 39'/100,000 population/year. In the Utstein group (n=577), compared with the overall group, there was a higher proportion of male patients, public event location, bystander cardiopulmonary resuscitation (CPR) and early defibrillation. Median EMS call–response interval was similar in both groups. A higher proportion of patients in the Utstein group achieved return of spontaneous circulation (35% vs 17%) and survival to hospital discharge (22% vs 6%). After multivariate adjustment for the Utstein group, the following variables were found to be independent predictors of the outcome survival to hospital discharge: public event location (OR 3.1; 95% CI 1.9 to 5.0); bystander CPR (2.4; 95% CI 1.2 to 4.9); EMS response time of 8 min or less (2.2; 95% CI 1.3 to 3.6).

Conclusions This study highlights the role of nationwide registries in quantifying, monitoring and benchmarking OHCA incidence and outcome, providing baseline data upon which service improvement effects can be measured.

INTRODUCTION

While studies of single communities provide data on out-of-hospital cardiac arrest (OHCA) outcome, nationally representative data are essential in monitoring national trends in OHCA survival.1 In Europe and North America, over 573,000 cases of OHCA occur annually, and the clinical and societal impact of OHCA is such that the American Heart Association has recommended that it be classified as a reportable disease.2 In the absence of rapid recognition, good-quality cardiopulmonary resuscitation (CPR) and early defibrillation, there is a negligible prospect of survival from OHCA.3

Reported incidence of and outcomes from OHCA vary widely internationally. The reasons for this variation include: variation in age and gender distribution; levels of urbanisation; bystander CPR; availability of community defibrillators; and configuration of emergency medical services (EMS).3-5 Intercountry differences are affected by these factors and are also complicated by variation in study sample definition and denominator.3 This is despite the widespread acceptance and use of the Utstein criteria for OHCA data collection.6

The Irish National Out-of-Hospital Cardiac Arrest Register (OHCAR) was established in 2007 to provide data to estimate the incidence and survival of OHCA in Ireland, with the aspiration of improving it. OHCAR is funded by the National Ambulance Service and Prehospital Emergency Care Council. It is administered and academically supported by the National University of Ireland, Galway and hosted by the Department of Public Health Medicine in the Irish Health Service Executive. In 2012, OHCAR achieved comprehensive national data collection.7

Within this context, the aim of this paper is to provide an overview of the first 2 years of comprehensive Irish data collection and describe the incidence, key interventions and survival outcomes for OHCA attended by ambulance services where resuscitation was attempted (EMS-treated OHCA) in Ireland. In line with the Utstein guidelines and as recommended by Chamberlain and Eisenberg, we
focus our analysis on the subgroup of adult patients, with presumed cardiac arrestology, with a bystander-witnessed event and an initial shockable rhythm (Usenit group).15

METHODS
In Ireland, 62% of the total population of 4.6 million lives on 2.4% of the total land area.17 The remaining population is dispersed in low-density settlements across the country. In Dublin city and county, the National Ambulance Service (NAS) and the Dublin Fire Brigade (DFB) provide the statutory EMS response, while throughout the rest of the country, statutory ambulance services are solely provided by the NAS. All prehospital emergency practitioners who work for statutory ambulance services must be registered with the Pre-Hospital Emergency Care Council. Practitioners use clinical practice guidelines to inform decisions not to resuscitate or cease resuscitation.18 Emergency medical technicians and emergency first responders are trained in basic life support, including automated external defibrillator (AED) use. Paramedics can perform supraglottic airway placement and advanced paramedics are additionally trained to intubate in cardiac arrest situations, attempt manual defibrillation and administer cardiac resuscitation drugs. All ambulance vehicles are staffed with paramedics and/or advanced paramedics. For cardiac arrest calls, the DFB also deploy practitioners on fire engines. Community response to OHCA in Ireland varies. In some areas, the community response depends on the training and willingness of people to perform basic life support and the opportunistic availability of AEDs in the vicinity of the event. In other areas, the level of response is highly organised and coordinated by voluntary Community First Responder programmes. Irish general practitioners, primarily in some rural areas and some county fire services, also respond to OHCA at the request of the NAS.19

Statutory ambulance services in Ireland use a standardised Patient Care Report (PCR) which includes an ‘OHCA’ section for Usenit required data. For incidents attended by the DFB, all PCRs are received at a central location where PCRs for OHCA events are manually identified. Data from each OHCA incident are entered onto a Microsoft Access database. Each incident is electronically linked to corresponding dispatch data, and completed records are sent to OHCA on a quarterly basis. Data are then checked to ensure compliance with OHCA definitions as well as to avoid double entries.

In the rest of the country, immediately after attending an OHCA incident, NAS practitioners put completed PCRs for OHCA incidents in specially provided envelopes. These PCRs are digitally processed at a central location and then electronically forwarded to OHCA for case-by-case validation. Dispatch data are then added to all cases. A valid identification of cases that may not have been placed in envelopes, missing case searches are performed in the NAS digital PCR archive. Outcome data are also obtained for patients brought to hospital. Data for this study were anonymised and extracted from the OHCA database for the study period.

Ethical approval
Ethical approval for research using non-identifiable OHCA data was obtained from the Research Ethics Committee, National University of Ireland, Galway.

Statistical analysis
This is a retrospective cohort study of incidence, interventions and outcomes of EMS-treated OHCA in Ireland during 2012 and 2013. The reported population for 2012 and 2013 is described. To allow international comparisons and be in line with Usenit recommendations, a subgroup of patients was extracted, which includes only adult patients with a bystander-witnessed OHCA, of presumed cardiac arrestology and an initial shockable rhythm (Usenit group).21 To ensure our data can be compared with data from other national registries, incidences per 100,000 population per year for the total group and the Usenit subgroup were standardised for age and sex using the 2013 EUROSTAT population projections. In order to describe the difference in OHCA incidence according to age, age-adjusted incidence for the total group and Usenit subgroup is graphically presented. The key outcomes from our analysis are to calculate survival to discharge for the overall group and for the Usenit group, and to determine predictors of survival in the Usenit group.

An overview of differences between the total group and the Usenit group is presented. A variable was derived to represent the availability of early defibrillation using the following rule: (defibrillation attempted=yes AND (EMS response interval of 5 min or less OR defibrillation attempted before EMS arrival)). Analysis of predictors of survival was limited to the Usenit group only.

Logistic regression analysis was performed to identify predictors of the main outcome of interest, that is, survival to hospital discharge. Variables were entered into the model based on: at least moderate univariate associations (p<0.15); validation of significance in previous literature; clinical relevance to support inclusion. Continuous variables, that is, age and ambulance response times, were categorised for regression analysis. Calibration of the model was assessed using the Hosmer and Lemeshow Z statistic (p>0.05). In order to assess the potential effect of loss to follow-up, two potential scenarios were created: (i) assumed all missing cases had survived to hospital discharge; (ii) assumed all missing cases had died. Logistic regression analysis was repeated for both scenarios. Description and analysis of all cases of non-traumatic arrestology were also performed (see online supplementary tables S1 and S2).

RESULTS
A total of 3701 EMS-treated OHCA were recorded for the study period (1798 in 2012 and 1903 in 2013). The overall incidence of EMS-treated OHCA was 39/100,000 population/year. The Usenit group had an incidence of 6/100,000 population/year. Age-adjusted incidence was highest for overall cases in the 85+ age group, but peaked in the 70–74 year age category for the Usenit group (figure 1).

For the overall group, 853 cases were missing one or more descriptive variables (23%), including 30 patients who were lost to follow-up. In the Usenit group, nine patients were lost to follow-up. As shown in table 1, 6% of all patients survived to hospital discharge, compared with 22% of patients in the Usenit group. Median age for all cases was 67 years (IQR 52–78 years), with the majority of patients aged over 65 years. Over half of patients (54%) had a bystander-witnessed arrest, and 70% of these patients received bystander CPR. Most cases were presumed to be of a cardiac aetiology (86%). Trauma (including self-harm and road traffic accidents) accounted for 7% of cases. Other causes included submersion and drug or alcohol overdose. The Usenit group comprised 15% of all cases (n=577). Patients in this subgroup were similar in age and gender to the overall group, but had higher percentage survival to discharge (22%) and better secondary outcomes, that is, return of spontaneous circulation, than the overall group. The Usenit group also had higher proportions of publicly located


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Table 1 - Overview of the differences in descriptive variables and outcome between all cases and the Utstein group

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>All cases (n=3490)</th>
<th>Utstein group (n=577)</th>
<th>Missing variables n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age in years, mean (95% CI)</td>
<td>66 (52–79)</td>
<td>65 (55–75)</td>
<td>107 (2.0)</td>
</tr>
<tr>
<td>EMS Call*</td>
<td>12 (9–19)</td>
<td>12 (9–18)</td>
<td>235 (7.0)</td>
</tr>
<tr>
<td>Under 65 years</td>
<td>1002 (4.5)</td>
<td>278 (14.8)</td>
<td>167 (2.7)</td>
</tr>
<tr>
<td>Male</td>
<td>2479 (70.5)</td>
<td>577 (100)</td>
<td>8 (0.3)</td>
</tr>
<tr>
<td>Prescribed cardiac medication</td>
<td>3376 (96.6)</td>
<td>577 (100)</td>
<td>0 (0.0)</td>
</tr>
<tr>
<td>Urban setting</td>
<td>2208 (66.6)</td>
<td>321 (57)</td>
<td>90 (2.5)</td>
</tr>
<tr>
<td>Public location</td>
<td>812 (23.2)</td>
<td>239 (42)</td>
<td>28 (0.8)</td>
</tr>
<tr>
<td>Initial shockable rhythm</td>
<td>192 (5.5)</td>
<td>577 (100)</td>
<td>86 (2.3)</td>
</tr>
<tr>
<td>Bystander witnessed</td>
<td>1334 (50)</td>
<td>577 (100)</td>
<td>140 (3.0)</td>
</tr>
<tr>
<td>EMS witnessed</td>
<td>213 (6)</td>
<td>0 (0)</td>
<td>144 (3.0)</td>
</tr>
<tr>
<td>Bystander witnessed and bystander CPR attempted</td>
<td>1316 (10)</td>
<td>453 (88)</td>
<td>41 (2.5)</td>
</tr>
<tr>
<td>Defibrillation attempted</td>
<td>1302 (36)</td>
<td>575 (98)</td>
<td>104 (2.8)</td>
</tr>
<tr>
<td>Early defibrillation attempted</td>
<td>291 (8)</td>
<td>180 (31)</td>
<td>0 (0.0)</td>
</tr>
<tr>
<td>EMS Call 8 min or less*</td>
<td>549 (2.1)</td>
<td>175 (32)</td>
<td>235 (7.0)</td>
</tr>
<tr>
<td>Outcome</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ROSC at any stage (n (%)</td>
<td>814 (24)</td>
<td>245 (44)</td>
<td>156 (4.2)</td>
</tr>
<tr>
<td>ROSC on arrival at hospital (n %)</td>
<td>577 (100)</td>
<td>189 (35)</td>
<td>221 (4.6)</td>
</tr>
<tr>
<td>Survival to hospital discharge</td>
<td>216 (6)</td>
<td>124 (23)</td>
<td>30 (0.8)</td>
</tr>
</tbody>
</table>

*Excludes EMS-witnessed cases. All cases (n=3490); Utstein group (n=577).

†Includes only cases where the collapse was bystander witnessed. All cases (n=1854); Utstein group (n=577).

‡Patients were defined as having received early defibrillation if defibrillation was attempted in a bystander or if the EMS Call was 8 min or less. Includes only cases where defibrillation was attempted. All cases (n=3340); Utstein group (n=577).

§CPR, cardiopulmonary resuscitation; CI, confidence interval; EMS, emergency medical service; ROSC, return of spontaneous circulation.

As shown in figures 3, complete data were available for 502 of the 577 patients in the Utstein group. As shown in table 2, age under 85, collapse in an urban setting, collapse in a public location, bystander CPR, early defibrillation attempted and an EMS response of 8 min or less were all associated with patients' survival to discharge in the univariate analysis (model 1). In the logistic regression model (model 2), public location of the OHCA incident (OR 3.1; 95% CI 1.9 to 5.0), bystander CPR (OR 2.4; 95% CI 1.2 to 5.0) and EMS response time of 8 min or less (OR 2.2; 1.3 to 3.6) remained significant predictors of survival to discharge. Interactions between variables were not significant and omitted from the model. Data on outcome were missing for nine patients in the Utstein group. The analysis was repeated using the assumption that (1) all missing cases had survived or (2) all missing cases had died. In both models, adjusted ORs for all variables remained similar.

DISCUSSION

Ireland is one of the few countries in Europe where nationwide reporting of OHCA is currently possible and a system has been developed that allows routinely collected data to be used to build a national register of OHCA capable of providing meaningful risk-adjusted quality indicators. This paper provides a description of EMS-treated patients with OHCA and their outcome in Ireland during 2012 and 2013. Our paper highlights the value of quality registries in describing, benchmarking and highlighting where challenges arise in care delivery and solutions hypothesised.

The incidence of OHCA was 39/100,000 population/year. There is wide variation internationally in the reported incidence of OHCA, from 19 to 141 per 100,000 population per year, suggesting variation in the threshold to commence CPR. The total number of incidents was similar in 2012 and 2013, suggesting internal consistency in case identification and incidence. The proportion of incidents that occurred in urban areas reflects the proportion of the Irish population that resides in urban areas. The age and gender profile of patients was very similar to other large studies of OHCA, as was the difference in median male and female ages. 4 14 The proportion of patients presumed to have suffered an arrhythmia of cardiac origin is similar to North American data, but high compared with other population-based studies of EMS-treated OHCA.11 14 This may be explained by the fact that in Ireland cardiac arrhythmia is presumed in the absence of documented evidence of any other probable cause and may be considered analogous to 'unknown cause'.

While the proportion of patients in our study with an initial shockable rhythm was 24%, there is significant variation in population-based studies, from 8.7% in Japan to 36% in North America.11 14 Reported percentage survival to discharge globally varies from 0.8% to 25% in OHCA attended by ambulance services. At 6%,
Figure 2 Cumulative percentage of cases responded to by each emergency medical services (EMS) call—response interval. **Time in minutes from call pick-up to ambulance control centre to first EMS vehicle arrival at scene. EMS-witnessed cases excluded.

Figure 3 Cases included in logistic regression analysis. CPR, cardiopulmonary resuscitation; ROSC, return of spontaneous circulation.

percentage survival in Ireland is low, but many other studies are region-specific and do not reflect national survival. While there is considerable heterogeneity in the overall group, the Utstein subgroup includes patients who have been proven to benefit most from a resuscitation attempt, that is, adults, cardiac cause, bystander-witnessed and initial shockable rhythm.18 Survival in the Utstein subgroup was 22%, which is substantially lower than in other population-based studies where percentage survival of up to 52% has been achieved.17,18 Opportunities to strengthen the chain of survival in Ireland are being vigorously pursued.

In this study, we found that collapse in a public location, provision of bystander CPR and an EMS call—response interval (CR1) of 8 min or less were independent predictors of survival to hospital discharge. Our finding that collapse in a public location accounted for a threefold increase in survival is not surprising and has been reported in other large-scale registry-based studies.19,20


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The proportion of bystander CPR provided by bystander-witnessed cases was high at 70% and even more impressive in the Utrecht subgroup where bystander CPR was an independent predictor of survival. The proportion of bystander CPR provided is similar to the countries and regions where percentage survival is higher than that in Ireland.14-22 Reliability of bystander CPR measurement is an issue for all OHCA registers, but we believe that the nationwide introduction of dispatch-assisted CPR may help account for the high levels of bystander CPR observed in our study. Wiesenblatt et al.23 observed an association between improved OHCA survival in Denmark and increased bystander CPR rates following national initiatives to increase bystander interventions. Our results indicate willingness among the Irish population to attempt CPR and suggest that further extension of training initiatives may contribute to improve survival rates in Ireland.

An EMS CRI of 8 min or less was also an independent predictor of survival. Identifying ways in which to minimise this interval is essential to improving Irish OHCA outcomes. In 2013, the NAS introduced ‘ONELIFE’, an extensive programme to improve OHCA outcomes within the NAS.24 As part of ONELIFE, dynamic deployment of EMS vehicles has been implemented, and strategies to improve dispatcher OHCA recognition and incident location are currently being introduced. For this study, we derived a variable to represent early defibrillation and found that a minority of patients had access to early defibrillation. We had expected that early defibrillation would be a significant predictor of survival in multivariate analysis. The lack of significance may be because the derived variable underestimated the availability of early defibrillation, as we assumed that all defibrillation attempts before EMS arrival were made within minutes of collapse. This may not have been the case, particularly in more rural areas where travel times, even for first responders, may be prolonged. Blom et al.25 described how AED use was an independent predictor of survival in the Netherlands. In their study area, AED use was tripled as a result of policy measures, including: introduction of AED programmes for police teams (together with existing fire service response); implementation of a ‘6-min time zone’ and the introduction of a text alert system for registered volunteers. Structured AED programmes also have the advantage of efficiency as described by Ringh et al.26 They reported similar percentage survival as a result of 74 deployments from 911 public AEDs compared with 53 deployments out of a possible 135 first responder AEDs, suggesting that coordinated support of first responder programmes would be more cost-efficient than mass implementation of public AEDs. In Ireland, voluntary groups, general practitioners and county fire services already provide a community response to OHCA. Extension and support of such schemes is considered an important way in which to reduce time to defibrillation.

Limitations
A substantial percentage of data was missing for the overall group, most notably resulting in 75 cases being omitted from the logistic regression analysis. In order to assess the impact of missing data, missing data imputation was performed for all cases, and logistic regression analysis was repeated for the Utrecht group. The pooled results from regression analysis using imputed data did not differ significantly from the results found using original data (see online supplementary table S3).

Thirty patients were lost to follow-up. Most of these patients could not be traced due to unavailability of patient identification or poor legibility of PCBs. In our study, loss to follow-up did not significantly affect results, but it remains an issue for OHCA.

We presumed a cardiac cause in over 86% of OHCA cases. This presumption may have led to misclassification bias.27 Classification of cases as ‘presumed cardiac’ was originally proposed by the Utrecht Committee to create ‘case equivalency’; however, such classification can be highly subjective. Reporting of EMS-treated cases of non-traumatic aetiology is a suggested way in which to decrease subjectivity and improve comparability of registries worldwide (please see online supplementary data).

CONCLUSIONS
This study provides a nationwide description of EMS-treated OHCA in Ireland. The incidence and demography of OHCA is similar to other population-based studies. Initiatives to increase public education in CPR, support further implementations of community first responder programmes and continued quality improvement in the EMS are key to improving OHCA outcomes. This nationwide profile provides the dashboard by which improvements can be measured.

Acknowledgements
The authors wish to thank National Ambulance Service and Dublin Fire Brigade personnel who provided the clinical and dispatch data that have made this study possible.

Contributors
SM performed data analysis and drafted the text of the manuscript. IC, co-supervisor, SM wrote, read and revised manuscript drafts. CD contributed to the introduction and discussion sections. MD, contributed to the methods sections. PR, contributed to the discussion sections. SM, revised text and advised on data analysis. AV, contributed to the manuscript text, instructed on data analysis plan and checked results.

Funding
SM is funded by the Health Professionals’ Fellowship Award from the Health Research Board, Ireland (HHR-2014-0209).

Competing interests
EM reflects grants from American Red Cross, the American Heart Association, Medtronic,Philanthropy and Zoll Corporation, outside the submitted work.

Ethics approval
Research Ethics Committee, NUI Galway.

Provenance and peer review
Not commissioned; externally peer reviewed.
REFERENCES


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doi: 10.1136/emjmed-2015-205107

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The Spatial Distribution of Out-of-Hospital Cardiac Arrest and the Chain of Survival in Ireland: An Analysis across the Urban-Rural Spectrum

_Irish Geography_, 49, 1-27.
The Spatial Distribution of Out-of-Hospital Cardiac Arrest and the Chain of Survival in Ireland: A Multi-Class Urban-Rural Analysis

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The Spatial Distribution of Out-of-Hospital Cardiac Arrest and the Chain of Survival in Ireland: A Multi-Class Urban-Rural Analysis

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Abstract: Cardiac arrest occurs when the heart suddenly ceases to pump blood around the body. To optimise survival from out-of-hospital cardiac arrest (OHCA), knowledge of the spatial distribution of OHCA and the availability of resuscitation, or ‘Chain of Survival’, is required. Thus, this study aims to describe OHCA incidence and Chain of Survival availability in a manner that can help inform pre-hospital planning in the Republic of Ireland. In view of Ireland’s heterogeneous settlement pattern, we analyse the association between varying degrees of rurality, OHCA incidence and the availability of the Chain of Survival. In addition to population density, settlement size, proximity to urban centres and land use is taken into account which results in six classes: city; town; accessible village; remote village; accessible rural; remote rural. Results show that, when adjusted for age and sex, the incidence of adult OHCA decreases with increasing rurality. Furthermore, while distance to the nearest ambulance station and call-response interval is greater with increasing rurality, the lowest levels of bystander cardiopulmonary resuscitation occur in the most urban class. To the best of our knowledge, this is one of the very first whole-country geographic descriptions of OHCA to be performed internationally. It is also the first OHCA study to use a multi-class urban-rural classification that considers rurality as more than a function of population density.

Keywords: cardiac arrest; resuscitation; spatial distribution; rurality

*siobhan.masterson@nui galway.ie (Corresponding Author)
Introduction

The ultimate cause of all deaths is cardiac arrest, which occurs when the heart stops beating in a manner that interrupts blood circulation around the body (Paradis et al., 2007). The term ‘Out-of-Hospital Cardiac Arrest’ (OHCA) is used to describe incidents where cardiac arrest occurs unexpectedly and is responded to by statutory emergency medical services (EMS). The tragedy of OHCA has caught the public’s attention in recent years with the sudden deaths of a number of young athletes during participation in sport. In many of such cases, there tends to be a pre-existing heart abnormality. However, the vast majority of OHCA cases occur from middle-age onwards and are most commonly caused by coronary heart disease (Chugh et al., 2008). OHCA presumed to be caused by heart disease results in approximately 1,500 unexpected deaths every year in the Republic of Ireland (Irish National Out-of-Hospital Cardiac Arrest Register 2014). This compares to 554 deaths from suicide and 186 deaths in road traffic accidents. OHCA accounts for 5% of the approximately 30,000 deaths per annum in Ireland (Central Statistics Office 2014, RSA 2011). The societal and clinical impact of OHCA is such that the American Heart Association has recommended that it be classified as a reportable disease (Nichol et al., 2008).

Death from OHCA is frequent, though not inevitable, with the chances of survival relying on resuscitation being initiated within minutes of the patient’s collapse. In the case of OHCA, the term ‘resuscitation’ is used to describe a series of interventions that are used in an attempt to restore consciousness or other signs of life. The vital resuscitation interventions that improve survival from OHCA are collectively known as ‘The Chain of Survival’ and include: early recognition of OHCA and immediate call for help to the EMS; high quality cardiopulmonary resuscitation (CPR); defibrillation within minutes of collapse; and effective advanced EMS and post-resuscitation care1. Given the firm evidence that exists on how to improve survival, a Task Force to reduce deaths from OHCA was established in Ireland in 2006 (Department of Health and Children 2006). This taskforce has established effective resuscitation services including: standardised resuscitation training; documentation and equipment for all ambulance personnel; implementation of dispatch-assisted CPR protocols in ambulance control centres; accreditation of resuscitation training for lay people and occupational first aiders; protocols for establishing community first responder (CFR) programmes (HSE 2010). The need for data and surveillance was also highlighted in the 2006 report and, as a result, the National Out-of-Hospital Cardiac Arrest Register (OHCAR) was established (Irish National Out-of-Hospital Cardiac Arrest Register 2014).

Given the amount of resuscitation-related activity in recent years, an understanding of the spatial distribution of OHCA and the Chain of Survival is needed so that statutory services and community responses can be designed to optimise OHCA survival. OHCAR, with data on all OHCA incidents attended by the EMS where resuscitation was attempted, is available for the Republic of Ireland.

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1 While resuscitation guidelines are derived by consensus by the International Liaison Committee on Resuscitation (ILCOR), the European Resuscitation Council lists four key interventions and the American Heart Association includes five.
since January 2012. In an earlier study, Masterson et al., (2015) dichotomised OHCA events from the year 2012 into either an urban or rural setting, using a variable derived by the Central Statistics Office (2012). However, neither rural nor urban Ireland is homogenous. Indeed, for the former, there is a wide spectrum of settlement patterns, ranging from villages to one-off houses in isolated locations. Equally, urban settlements range from small towns to the city of Dublin, where almost one quarter of the national population resides (CSO 2012). Considering the range of differences in urban-rural living, the need for a different structure of services and a different response to OHCA according to the degree of rurality deserves consideration. Teljeur and Kelly (2008) developed an index of urban-rural classification at electoral division (ED) level, based on 2002 census data. As well as population density, the index also accounted for settlement size, proximity to urban centres and land use. The resulting index included six classes: city; town; accessible village; remote village; accessible rural; remote rural. These six classes reflect the range of disparate settlement patterns in the Republic of Ireland, making the index a useful tool for examining disease incidence and health service availability.

Within this context, this paper uses an updated version of the index developed by Teljeur and Kelly (2008) to explore the spatial distribution of OHCA incidence and availability of the Chain of Survival. More specifically, it examines whether the incidence of OHCA cases and availability of the Chain of Survival differs across the range of urban-rural classes classified in the index. The Republic of Ireland is one of three European countries along with Sweden and Denmark with long-established national OHCA registers. This paper is the first to present a whole-nation geographic description of OHCA in Europe. This is also the first study on OHCA that considers rurality as more than a function of population density.

The paper is structured as follows: in the next section, we describe the causes and demography of OHCA and provide an overview of the vital resuscitation interventions that make up the Chain of Survival with specific reference to the influence of potential spatial factors. We then review the literature that has considered the geography of OHCA in terms of incidence and resuscitation. The subsequent section describes data collection and processing, including a more detailed description of the national OHCAR, as well as the methods of analysis that are used. This is followed by a description of our results, a discussion of the relevance of our findings, and our conclusions.

Out-of-Hospital Cardiac Arrest and the Chain of Survival

Out-of-Hospital Cardiac Arrest

The primary cause of OHCA is coronary heart disease, with approximately 80% of OHCA's presumed to be of a cardiac aetiology. However, it has also been suggested that this may overestimate the proportion of cases due to cardiac cause, underestimating other causes. For example, Yoshida et al., (2011) analysed laboratory and post mortem results for 165 patients who were presumed to have an
OHCA of cardiac cause, and following investigation, 69 cases were re-classified as being of a non-cardiac cause. In fact, from a resuscitation perspective, there are six broad categories into which OHCA cause should be classified (see Figure 1).

**Figure 1: Classification of Causes of Out-of-Hospital Cardiac Arrest**

<table>
<thead>
<tr>
<th>Category</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Medical</td>
<td>Includes cases in which he cause of the cardiac arrest is presumed to be cardiac, other medical cause (e.g. - anaphylaxis, asthma, gastrointestinal bleed), and in which there is no obvious cause of the cardiac arrest</td>
</tr>
<tr>
<td>Traumatic:</td>
<td>Cardiac arrest directly caused by blunt, penetrating or burn injury</td>
</tr>
<tr>
<td>Drug overdose:</td>
<td>Evidence that the cardiac arrest was caused by deliberate or accidental overdose of prescribed medications, recreational drugs or ethanol</td>
</tr>
<tr>
<td>Drowning</td>
<td>Victim is found submersed in water without an alternative causation</td>
</tr>
<tr>
<td>Electrocution</td>
<td>Any case where electrocution is primary and obvious causes of arrest</td>
</tr>
<tr>
<td>Asphyxial</td>
<td>External causes of asphyxia, such as foreign-body airway obstruction, hanging or strangulation</td>
</tr>
</tbody>
</table>

While medical causes are the most common, trauma accounts for approximately 7-9% of OHCA cases and is a more significant cause in children and younger adults, accounting for almost one-third of cases (Deasy et al., 2013b). The true proportion of OHCA caused by drug overdose is less well documented, but Katz et al., (2015) found these patients to have comparable survival as other OHCA patients. Drowning is also a relatively minor cause of OHCA and is also associated with similar survival as other OHCA causes. Electrocution is rarely documented as a cause of OHCA, while hanging is a significant cause of asphyxial OHCA, with poorer outcomes than for other major causes of OHCA (Deasy et al., 2013a).

While treatment of patients may vary within category subgroups, broadly speaking, the basic sequence and approach to resuscitation is largely determined by the type of rhythm cardiac arrest has caused in the heart. Cardiac arrest rhythms are classified as ‘shockable’ and ‘non-shockable’. Shockable rhythms include ventricular fibrillation (VF) or pulseless ventricular tachycardia (pVT). When the heart is in a shockable rhythm it beats erratically, preventing blood from being pumped around the body. In the case of most cardiac or medical causes of OHCA, the heart is in a shockable rhythm for approximately five minutes, after which the rhythm stops entirely, becoming asystole. Another rhythm associated with OHCA.
is pulseless electrical activity (PEA), where the heart continues to pump but is unable to circulate blood due to an injury to the body. PEA is more commonly associated with non-cardiac causes of OHCA, including drowning, asphyxiation or severe blood loss.

In terms of demographics, OHCA occurs most commonly in adults aged over 65 years (Kitamura et al., 2014), a finding confirmed by Masterson et al., (2015) for Ireland. Significantly though, up to one third of cases occur in people aged 35-59 years old, highlighting that OHCA is not just a condition of older age. The incidence of OHCA in younger adults (aged less than 35 years) and children is lower, however, and the etiology is also more heterogeneous than in older adults (Deasy et al., 2011). This younger age group is the category most often affected by underlying heart abnormalities which can trigger heart rhythms that lead to OHCA. Females tend to comprise approximately one third of OHCA cases and this is a consistent finding across studies worldwide (Nichol et al., 2008, Lindner et al., 2011, Hiltunen et al., 2012, Henry et al., 2013).

In Ireland, the overall incidence of OHCA where resuscitation was attempted is 39/100,000/year, though estimates of OHCA incidence vary widely internationally (Masterson et al., 2015). In their systematic review of OHCA incidence and survival rates, Berdowski et al., (2010) reported that across four continents the incidence per 100,000 person-years of OHCA where resuscitation was attempted was as follows: America – 54.6; Europe – 35.0; Asia – 28.3; Australia – 44.0. Regional variability within countries has also been observed in North America, Japan, Finland and Victoria (Australia) (Nichol et al., 2008, Hasegawa et al., 2013, Hiltunen et al., 2012, Straney et al., 2015).

In summary, OHCA has a variety of causes, but in the majority of adults of middle and older age, the cause tends to be heart disease. Causes in the younger age groups are more varied, and the occurrence of OHCA is relatively rare. There is wide variation in OHCA incidence rates internationally, highlighting the importance of robust national data collection systems. Survival from OHCA also varies widely internationally. As reported by Berdowski et al., (2010), the proportion of survival in studies of OHCA where resuscitation was attempted ranged from 2% in Asia, to 11% in Australia (6% in America and 9% in Europe). The Irish proportion of survival for a similar population is approximately 6% (Masterson et al., 2015). While some variation may be due to differences in the underlying population and variations in data collection methodologies, it is universally recognised that improved survival can only be achieved through rapid and effective provision of each link in the Chain of Survival.

The Chain of Survival

The first link in the Chain of Survival is early recognition of the emergency and activation of the EMS system (Monsieurs et al., 2015). The inability to quickly recognise OHCA affects the chances of CPR being started, increases ambulance call-response interval and is associated with decreased survival (Axelsson et al., 2010, Berdowski et al., 2009). Some patients who have suffered OHCA may
continue to gasp and have intermittent and/or noisy intakes of breaths (agonal breathing). Agonal breathing is present in up to 40% of all OHCArs and reflects non-effective air intake and is a sign of imminent death. Rapid recognition of OHCA and immediate contact with emergency services expedites the arrival of EMS in the event of OHCA, and also allows ambulance dispatch staff to provide the caller with ‘pre-EMS arrival instructions’, most notably dispatch-assisted CPR (described below). It should be noted, however, that the likelihood and benefits of rapid recognition are mediated by the location of the event. The vast majority of incidents occur in one of the following places: in the home; in a residential institution; on a street or road; at an industrial place/premises; in a public building; at a sports facility or airport; in a GP surgery; or, in an ambulance. The likelihood of OHCA being witnessed increases in more public areas, and the likelihood of rapid recognition further increases in locations where personnel trained in resuscitation are available.

The next step in the Chain of Survival is the provision of early, good quality CPR. In the event of OHCA, the heart becomes incapable of pumping and blood circulation ceases. Additionally, the patient stops breathing. Within approximately four to five minutes without air intake and blood circulation, the body becomes starved of oxygen, and cell death begins. Good quality CPR compensates for the inability to breathe through manual ventilations, known as ‘rescue breaths’, and also compensates for the inability of the heart to pump blood by the use of ‘chest compressions’. Resuscitation guidelines advise that, for people trained in resuscitation, a cycle of thirty chest compressions to every two rescue breaths should be performed, with minimum interruptions between chest compressions. Guidelines also advise on the speed, depth and technique for good quality CPR (Perkins et al., 2015c).

The introduction of CPR feedback technology has allowed the effect of CPR quality in EMS systems to be measured and Vadboncoeur et al., (2014) have shown that compliance with guidelines for depth of chest compression improved OHCA survival. To maximise the chances of survival, CPR must be commenced immediately after a patient collapses. In most OHCA cases, this implies that members of the public must be willing to commence CPR, known as ‘bystander CPR’. Bystander CPR has long been recognised as a critical factor in OHCA survival and is proven to be an independent predictor of survival (Sasson et al., 2010). In Irish ambulance dispatch centres, when OHCA is recognised and reported, the call taker follows an algorithm to provide instructions to the caller on how to perform CPR, even if the caller is untrained in resuscitation. This is known as dispatch-assisted CPR and has been shown to increase the performance of bystander CPR (Wander, Fahrenbruch and Rea, 2014) and improve survival (Bohm et al., 2011). Spatial variation in the performance of bystander CPR has been found by Straney et al., (2015) in Australia, Ong et al., (2014) in Singapore, and Sasson et al., (2012b) in the United States (US).

In most cases of OHCA, the heart commonly goes through a five-minute interval where the rhythm of the heart is ‘shockable’. During this phase, a controlled
electrical shock can be applied to ‘shock’ the heart back into a normal rhythm through a process known as defibrillation. Good quality CPR must be followed up with prompt access to defibrillation to maximise the chances of survival from OHCA. In fact, defibrillation within three to five minutes of patient collapse can result in percentage survival as high as 50-70% and each minute of delay to defibrillation reduces the likelihood of survival by 10-12% (Perkins et al., 2015a). While defibrillation is a highly technical treatment, its application is simplified due to the availability of automated external defibrillators which can be used by trained and untrained people alike. In an Irish review of cost-effectiveness of a national public access defibrillation programme, Moran et al., (2015) estimated that there are between 8,000 and 10,000 functional AEDs available in Ireland, though few of these Irish AEDs had been used in the event of OHCA. Moon et al., (2015) found that the geographic location of AEDs in Phoenix, Arizona was weakly correlated with OHCA locations, mirroring the Irish finding that, despite proliferation of AED purchase, there is work to be done to ensure that these devices are located and deployed in the geographic locations where they are most needed.

The first three steps in the Chain of Survival are unequivocally linked to the likelihood of survival from OHCA. Evidence on the role of advanced care, however, is less concrete. For example, a variety of devices are used to ventilate unconscious patients, including advanced airway devices, but such methods are generally used with patients who are more seriously ill and, therefore, less likely to survive (Fouche et al., 2014). While devices can be used to support ventilation of a patient, the provision of chest compressions can also be performed mechanically. Mechanical chest compression devices can deliver uninterrupted compressions at a consistent rate and depth but, to date, have not been shown to be superior to manual chest compressions (Perkins et al., 2015b).

Survival from OHCA is largely dependent on pre-hospital resuscitation but studies also suggest that the facilities at the hospital can influence OHCA outcome. The full-time availability of cardiac catheterisation is associated with improved survival (Soholm et al., 2013). In summary, whatever the merits of advanced pre-hospital and post-resuscitation care, the main predictors of survival from OHCA are rapid recognition, good quality CPR and early defibrillation.

Spatial Analysis of Out-of-Hospital Cardiac Arrest

The response that occurs within the first few minutes of OHCA largely determines the likelihood of survival. In order to minimise response times and to target pre-hospital resources appropriately, the EMS need to know which communities are at highest risk of OHCA. Additionally, communities that are at higher risk of OHCA need to be targeted to ensure that the three first links in the Chain of Survival are optimised, i.e., OHCA recognition, good quality CPR and prompt defibrillation. In order to target services at more local levels, geographic information systems (GIS) can play a key role in the planning process. To this end, the American Heart Association has published a Science Advisory Statement recommending that
GIS be used to ‘enable researchers to explore the links between neighbourhood environments and bystander CPR’ (Sasson et al., 2013).

The utility of GIS methodologies in identifying spatial patterns in OHCA has been explored by many authors, starting with Mayer (1981). He plotted 525 OHCA to the census tract of occurrence and found that underlying population was the only variable that was predictive of OHCA incidence. Similarly, Soo et al., (2001) found variation in the spatial distribution of OHCA across the 191 electoral areas in Nottinghamshire, even when incidence was adjusted for age. They also investigated further and found that differences in OHCA incidence were in part explained by differences in deprivation across the electoral areas, thus highlighting that population density alone may be insufficient in explaining OHCA incidence. Instead of assigning cases to geographic areas, Lerner, Fairbanks and Shah (2005) used kernel density estimation (KDE) to identify areas where cases of OHCA were clustered and then derived census-defined ‘blocks’ so that associations between underlying population, demography and OHCA occurrence could be investigated. Despite the difference in approach, higher OHCA occurrence was also mainly linked to the population structure. This finding was confirmed by Ong et al., (2008) for Singapore. While these results suggest OHCA services should be planned around areas of high population density, this may not necessarily always be the case. For example, in a recent Australian paper, Straney et al., (2015) found that some of the most sparsely populated ‘local government areas’ in Victoria had the highest incidence of OHCA. In Japan, Yasunaga et al., (2011) found that planning services around areas of high population density augmented health inequalities due to prolonged ambulance response times and poorer survival. All these studies highlight that local geography plays an often-unseen role in OHCA incidence and outcomes.

Several methodologies for identifying areas of high OHCA incidence have been used. Sasson et al., (2012a) employed three different GIS methods, including Global Empirical Bayes rates (a form of smoothed adjusted rates), Local Moran’s I (hot spot identification), and the Spatial Scan statistic (identifies hot spots by comparing observed versus expected outcomes for an area). The three methods did not identify identical clusters, but five areas that were identified by all three were classified as ‘high risk’. The findings of Sasson et al. highlight that, even with precise data geocoding, the type of methodology used to identify clusters may affect results.

While precise geocoding of events is desirable, from a practical perspective it may in fact be more appropriate to consider the ‘area of action’, i.e., the geographical level at which changes that can influence OHCA incidence and outcomes can be made. Correctly estimating the OHCA population in the geographical area of interest is challenging given the fact that OHCA does not necessarily occur in the area of residence. For example, approximately 25% of OHCA occur in a location other than the patients’ home. One possibility is to geocode cases to patients’ home addresses. However, while home address data will be reliable for patients who collapsed at home, such data is not necessarily
available or wholly accurate for patients who collapse in other locations. Whether or not event location data or patient address data is used is also influenced by the research question. For example, Soo et al., (2001) used patient address data in their analysis of the influence of deprivation and cardiovascular disease incidence on OHCA occurrence. From a resuscitation perspective, it can be argued that the incidence rate for the area where the event occurs is of most interest, as it is desirable to strengthen the Chain of Survival where events are most likely to occur. For example, Sasson et al., (2012b) coded cases by incident location and used census tract data for those locations (similar to ED) to examine the relationship between likelihood of bystander CPR performance and neighbourhood characteristics, and found that income and race were predictors of bystander CPR performance across a population of 22 million people in the US.

In summary, the studies described in this section show that while methodologies are transferable, local analysis of local data will often reveal unique results and also highlight the importance of correct geocoding in area-based studies. In this context, it is worth stressing that to date no study has undertaken a detailed spatial analysis of OHCA in Ireland, a gap that is addressed in this paper using a unique dataset and innovative methods.

**Data and Methods**

This paper uses data from the OHCAR database for the period 1\textsuperscript{st} January 2012 to 31\textsuperscript{st} December 2014. In 2007, the OHCAR database project was implemented in response to a specific recommendation in the National Task Force on Sudden Cardiac Death Report (Department of Health and Children, 2006). OHCAR collects data on all OHCA cases where resuscitation is attempted and where the scene is attended by statutory EMS in Ireland. Cases are reported to OHCAR by the EMS and, since 2014, systematic missing case identification is also performed by the OHCAR office (Masterson and Jensen, 2016). Variables for each OHCAR case are extracted from individual ambulance Patient Care Reports (PCRs) which are completed by EMS practitioners who attend the patient. Information extracted includes patient and location details, description of the resuscitation attempt and treatment provided and the outcome at scene. Each case is then matched to the corresponding dispatch data including: time emergency call was received; time first emergency vehicle arrival at scene; time of arrival at hospital (if patient transported). As missing case identification was not systematically performed before 2014, a search of the National Ambulance Service (NAS) PCR archive was performed for 2012 to 2013 to ensure complete case capture.

Before analysis could be conducted, geocoding of location addresses was undertaken. Geocoding is the process of assigning geographic coordinates to an address, following which the features can be entered into a GIS for spatial analysis and mapping purposes (Laepple and Cullinan, 2012). Accurate geocoding depends on complete, precise and accurate address data (McElroy et al., 2003). While every effort may be made to ensure the quality of address data, geocoding for areas that are sparsely populated are more prone to positional error and may be
directly attributable to the proportion of rural cases in a dataset (Sonderman et al., 2012, Zandbergen et al., 2012). Considering the rurality of Ireland, we were aware that this issue may affect the accuracy of our geocoding. In the scenario where precise geocoding is difficult, mapping data to the centroid of an aggregate area is possible. However, this pragmatic option leads to information loss at local level and may compromise cluster detection accuracy (Ribeiro et al., 2014). Geocoding of our data was performed using the Irish mapping application ‘Health Intelligence Ireland’ (Health Intelligence Unit, 2015). Cases where the location address recorded matched the address available in the Geodirectory were mapped to exact geographic coordinates. Matches for remaining addresses were searched for individually. Cases where location addresses were misspelled were mapped to exact coordinates. Addresses that were unavailable in the Geodirectory were geocoded using Google Maps (Google, 2015). In cases where an exact match was not found, the address was matched to the centroid of the smallest administrative area possible, i.e., small area or ED. Cases that could not be matched to a small area or ED were classified as ‘unmatched’ if no matching options were available. A total of 94.5% of cases (n=4734) were geocoded to at least ED level (see Figure 2). In order to assess whether bias might be introduced due to the exclusion of cases, comparison of the attributes of matched and unmatched cases was performed using a t-test for the continuous age variable and chi square analysis for categorical variables.

Figure 2: Flowchart of Cases Included

5889  Patients with out-of-hospital cardiac arrest (resuscitation attempted)

878   Excluded

171   Age missing

1     Gender missing

169   Under 18 years old

232   Traumatic cause

305   EMS-witnessed

5011  Eligible for geocoding

277   Unmatched or not coded to at least ED level

4734  Included in analyses
Once geocoded, the address coordinates were mapped and analysed using the GIS software package ArcGIS10. Attribute data (including age, sex, bystander CPR, bystander defibrillation, call-response interval) for each case were linked to the corresponding point data to create a spatially-referenced OHCAR data file. A ‘shapefile’ containing ED level census data and an updated multi-class urban-rural index were also linked. To understand the rurality of a disease and its management, different aspects and dimensions of rurality must be considered in order to provide ‘an overarching classification’ (Teljeur and Kelly, 2008). The most remote rural class tends to be more prevalent in the western counties and along the Atlantic seaboard, and while there is still a large proportion of rural areas in the east of the country, these areas tend to be classified as remote (near), due to the higher prevalence of towns and cities. Appendix 1 presents a map of the updated multi-class urban-rural classification along with a breakdown by urban-rural class for each county.

Once the urban-rural classification was linked to the ED-level database using the ‘Spatial Join’ function in ArcGIS, all relevant ED data was added to the OHCAR database. As the primary aim of analysis was to examine differences across the urban-rural spectrum, subsequent calculations were made for the total population and for each of the urban-rural classes, which facilitated an area analysis at urban-rural class level. Average age and the proportion of cases in each class were calculated for the following variables: male sex; initial recorded rhythm shockable; bystander witnessed collapse; OHCAR occurring during working hours (9am to 5pm); public location of event. In addition, the following variables were generated and analysed for each class: cases with dispatch code ‘arrest’ at time of vehicle deployment (Arrest Recognition); cases that received bystander CPR (B-CPR); cases that received bystander defibrillation (B-Defib); cases with a call-response interval less than eight minutes (CRI less than eight minutes); cases where advanced EMS intervention was provided, i.e., advanced airway support given and/or epinephrine administered (Advanced EMS Intervention Provided). These derived aggregated variables were then used as markers for availability of the Chain of Survival at urban-rural class level. Furthermore, in order to provide an indication of the availability of EMS across the country, the travel distance to the nearest ambulance station from each ED centroid was calculated using the ArcGIS Network Analyst extension (Cullinan, Hynes and O’Donoghue, 2008). This variable was also used as an additional marker of Chain of Survival availability (Ambulance Travel Distance).

Adult incidence of OHCAR per 100,000 population per year in each urban-rural class was also calculated. To begin, the number of adults in each urban-rural class for each of the following groups was estimated from the 2011 census data (CSO 2012): males aged under 65 years; females aged under 65 years; males aged 65 years or older; females aged 65 years or older. Incidence of OHCAR per 100,000 adults per year for each of the four groups in every urban-rural class was calculated. The proportion of adults in each of the four groups was then calculated for the reference population, i.e., total number of adults enumerated in the 2011
census. For each class, the incidence in the four groups was adjusted to account for the proportion in the reference population and all four results were summed to give the total adult standardised incidence for each class. Standard errors generated in the calculations were used to calculate 95% confidence intervals for each standardised incidence result.

The overall characteristics of study cases were descriptively analysed using IBM SPSS database (Version 21.0 IBM Corporation). The Kruskal-Wallis test was used to test for inter-class differences in median age and median average ambulance travel times from ED centroids. The chi-squared test for linear trend was used to investigate if proportions in categorical variables changed with increasing rurality (cut-off p>0.05).

Results

Of the 5,889 cases available, those with missing age and gender information, children (i.e., those less than 18 years of age), cases with traumatic aetiology and cases where collapse was witnessed by EMS were excluded from analysis, leaving 5,011 cases (see Figure 2). Of these, 4,734 were geocoded to at least ED level and included in our final analysis. Table 1 presents an overview of the characteristics of these cases, both overall and by urban-rural class. The median age for the matched population was 68 years (inter-quartile range (IQR) 55-79 years). There was significant difference in ages across the urban-rural spectrum, with patients in the city and town tending to be younger than those in the most rural areas. As shown in Figure 3, however, despite being statistically significant, the actual variance in median age was relatively small across all categories. With regard to gender, over two thirds of patients were male (n=3184; 67%) and this proportion was significantly higher in rural areas and decreased with increasing urbanisation. Nearly a quarter of patients were in a shockable rhythm at the time of first rhythm analysis (n=1,106; 24%), with the proportion of patients in a shockable rhythm decreasing with increasing rurality. The majority of patients suffered a bystander-witnessed arrest (n=2,654; 58%) and a linear trend was observed with lower occurrence in city and town classes, increasing with increasing rurality. The percentage of OHCAs occurring during working hours was 42% overall and this did not vary significantly across the urban-rural spectrum. A higher proportion of OHCAs in a public place was observed in patients in city and town classes, declining with increasing remoteness. It should be noted here that comparative analysis showed that the proportion of males, shockable rhythm, bystander CPR and bystander witnessed cases was significantly higher in the unmatched group (results not presented here but available on request from the authors).
Figure 3: Boxplots of Age Categorised by Urban-Rural Class

Table 1: Characteristics of Study Cases by Urban-Rural Class

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>City</th>
<th>Town</th>
<th>Village (near)</th>
<th>Village (remote)</th>
<th>Rural (near)</th>
<th>Rural (remote)</th>
<th>p value</th>
<th>Overall</th>
<th>Missing Data, No. (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, median (IQR)</td>
<td>69 (54-79)</td>
<td>66 (60-85)</td>
<td>66 (53-76)</td>
<td>71 (60-81)</td>
<td>70 (60-80)</td>
<td>69 (47-79)</td>
<td>0.000†</td>
<td>68 (55-79)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Males, No. (%)</td>
<td>1151 (65)</td>
<td>984 (67)</td>
<td>196 (65)</td>
<td>74 (71)</td>
<td>541 (70)</td>
<td>238 (73)</td>
<td>0.001† †</td>
<td>3184 (67)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Initial Shockable Rhythm, No. (%)</td>
<td>411 (24)</td>
<td>375 (26)</td>
<td>73 (25)</td>
<td>22 (22)</td>
<td>161 (21)</td>
<td>64 (20)</td>
<td>0.018‡ †</td>
<td>1106 (24)</td>
<td>102 (2)</td>
</tr>
<tr>
<td>Bystander Witnessed, No. (%)</td>
<td>930 (55)</td>
<td>826 (58)</td>
<td>175 (60)</td>
<td>61 (62)</td>
<td>471 (62)</td>
<td>190 (61)</td>
<td>0.001† †</td>
<td>2654 (58)</td>
<td>171 (4)</td>
</tr>
<tr>
<td>During Working Hours, No. (%)</td>
<td>757 (44)</td>
<td>553 (40)</td>
<td>116 (41)</td>
<td>42 (43)</td>
<td>302 (40)</td>
<td>141 (46)</td>
<td>0.604† †</td>
<td>4530 (42)</td>
<td>204 (4)</td>
</tr>
<tr>
<td>Public Location, No. (%)</td>
<td>342 (20)</td>
<td>306 (21)</td>
<td>53 (18)</td>
<td>10 (10)</td>
<td>98 (13)</td>
<td>43 (13)</td>
<td>0.000‡ † †</td>
<td>852 (18)</td>
<td>23 (0.5)</td>
</tr>
</tbody>
</table>

*Kruskal-Wallis 1-way ANOVA

**Chi-square test for linear trend
Table 2 presents the adjusted incidence and percentage of each marker in the Chain of Survival for the whole population as well as for the urban-rural classes. The overall age and sex standardised incidence of OHCA was 46 per 100,000 adults per year. This incidence ranged from 35 to 51 across the six urban-rural classes with a statistically significant decreasing trend with increasing rurality (p=0.017) – see also Figure 4. The overall proportion of cases recognised as cardiac arrest at the time of EMS dispatch was 66%, with decreasing recognition with increasing rurality. Bystander CPR was performed during 66% of the cases which varied significantly across the urban-rural classes (p=0.000), with higher proportions in the rural classes decreasing with increasing urbanisation. The proportion of cases that had bystander defibrillation attempted also varied significantly with 7%, 11% and 8% of patients in the town, village (near) and rural (remote) classes having bystander defibrillation attempted, compared to only 4% in the city class. A trend was observed in the proportion of patients who received an EMS response in less than eight minutes, with a higher proportion of patients in both the city and town classes (29%), declining to 9% in the village (near) class, 6% in the rural (near) class, 4% in the village (remote) class and 2% in the rural (remote) class. (The proportion of patients who received an EMS response within eight minutes was significantly lower in the unmatched group.) The proportion of patients receiving advanced EMS intervention also varied significantly across the classes, with a smaller proportion of patients in the city class receiving advanced interventions than in all other classes. Finally, significant variation was also observed in average ambulance travel distances which were a lot shorter in the city class compared to all other classes – see also Figure 5.

Figure 4: Age and Sex Adjusted OHCA per 100,000 Adults per Year and Associated Confidence Intervals by Urban-Rural Class
Figure 5: Boxplots of Median Ambulance Travel Distance from ED Centroid categorised by Urban-Rural Class

Table 2: Adjusted Incidence and Markers of Chain of Survival Availability in each Urban-Rural Class

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>City</th>
<th>Town</th>
<th>Village (near)</th>
<th>Village (remote)</th>
<th>Rural (near)</th>
<th>Rural (remote)</th>
<th>p value</th>
<th>Overall</th>
<th>Missing Data, No. (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>OHCA cases, No. (%)</td>
<td>1761 (37)</td>
<td>1465 (31)</td>
<td>301 (6)</td>
<td>104 (2)</td>
<td>778 (16)</td>
<td>325 (7)</td>
<td>NA</td>
<td>4734 (100)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Adjusted incidence per 100,000 adults per year (95% CI)</td>
<td>51 (47-55)</td>
<td>51 (46-55)</td>
<td>48 (39-58)</td>
<td>44 (29-58)</td>
<td>35 (31-40)</td>
<td>35 (28-42)</td>
<td>0.017++</td>
<td>46 (44-48)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Arrest Recognition, No. (%)</td>
<td>1150 (68)</td>
<td>479 (67)</td>
<td>188 (66)</td>
<td>192 (63)</td>
<td>923 (64)</td>
<td>62 (61)</td>
<td>0.004++</td>
<td>2994 (66)</td>
<td>217 (5)</td>
</tr>
<tr>
<td>B-CPR, No. (%)</td>
<td>932 (55)</td>
<td>550 (69)</td>
<td>243 (78)</td>
<td>226 (79)</td>
<td>978 (73)</td>
<td>80 (77)</td>
<td>0.000++</td>
<td>3009 (66)</td>
<td>160 (3)</td>
</tr>
<tr>
<td>B-defib, No. (%)</td>
<td>65 (4)</td>
<td>47 (7)</td>
<td>25 (11)</td>
<td>31 (9)</td>
<td>100 (6)</td>
<td>9 (8)</td>
<td>0.005++</td>
<td>277 (6)</td>
<td>137 (3)</td>
</tr>
<tr>
<td>CRI less than eight mins, No. (%)</td>
<td>478 (29)</td>
<td>45 (29)</td>
<td>7 (9)</td>
<td>25 (4)</td>
<td>390 (6)</td>
<td>4 (2)</td>
<td>0.000++</td>
<td>949 (22)</td>
<td>376 (8)</td>
</tr>
<tr>
<td>Advanced EMS Intervention Provided No. (%)</td>
<td>1288 (75)</td>
<td>1118 (82)</td>
<td>226 (84)</td>
<td>82 (84)</td>
<td>589 (82)</td>
<td>256 (84)</td>
<td>0.000+</td>
<td>3559 (80)</td>
<td>171 (4)</td>
</tr>
<tr>
<td>Ambulance Travel Distance in kms, median (IQR)</td>
<td>3 (2-4)</td>
<td>4 (2-12)</td>
<td>16 (11-20)</td>
<td>16 (12-20)</td>
<td>15 (10-19)</td>
<td>17 (12-23)</td>
<td>0.000+</td>
<td>13668 (8757)</td>
<td>0 (0)</td>
</tr>
</tbody>
</table>
In conclusion, increasing urbanisation is associated with a lower proportion of bystander witnessed events and more events in a public location. Adult age and sex adjusted incidence decreases with increasing rurality, while bystander CPR, bystander defibrillation and advanced EMS intervention declined with increasing urbanisation. Ambulance travel time and distance were lower in more urban areas as expected.

Discussion
This paper has presented the very first multi-class urban-rural analysis of OHCA and the Chain of Survival in Ireland. Among the key findings are that the adjusted incidence of OHCA per 100,000 adults per year in the area where the event occurred declined with increasing rurality while, conversely, the proportion of events where bystander CPR was performed and bystander defibrillation was attempted increased with increasing rurality. The proportion of patients who received an EMS response within eight minutes was higher in urban areas, though the proportion of patients who received an advanced EMS intervention was lower in urban areas.

The majority of OHCA in adults is caused by heart disease and thus, an age profile with a median age of 68 years could be expected, since heart disease is particularly prevalent in the 60-70-year age group. The Irish median is in keeping with other international results: 67 years in Australia (VACAR 2016); 72 years in Denmark (Wissenberg et al., 2013) and 70 years in Sweden (Stromsoe et al., 2015). The trend across the urban-rural classes is also not surprising as cities and towns tend to have younger populations compared to more rural areas. At 68%, the proportion of male patients was also similar to Victoria (68%), Sweden (68%) and Denmark (66%). Thus, the proportion of males is consistent across studies and again, as heart disease is the primary cause of OHCA and heart disease affects a higher proportion of males, this result is as expected.

The proportion of Irish patients with an initial shockable rhythm (24%) varied across the urban-rural spectrum, being highest in cities, towns and village (near) classes, and slightly lower in more rural classes. Considering the variation in travel distances across classes, this decrease in the proportion of shockable rhythm with increased rurality is not surprising. Patients who are in a shockable rhythm at the time of first rhythm analysis have a greater chance of survival, as they have either collapsed in the last five minutes or have received high quality CPR, which maintains a shockable rhythm. Maximising the proportion of patients in a shockable rhythm requires immediate high quality bystander CPR and rapid access to bystander or EMS defibrillation. The majority of Irish patients suffered a bystander witnessed arrest (58%), as was the case in a similar population in Denmark (Wissenberg et al., 2013), and while there was variation across the classes, the actual range across classes was relatively small (55% to 62%). Although witnessed status cannot be influenced, patients who have a witnessed arrest are more likely to survive OHCA (Sasson et al., 2010). The proportion of
witnessed arrests in a population is indicative of the likelihood of survival, as the bystander can quickly call the EMS and commence CPR. With regard to the ‘time of day’, the proportion of patients who suffered an OHCA was relatively similar across the urban-rural classes at 42%. This was not the case for the proportion of cases that occurred in a public place, however, where a higher proportion of patients collapsed in a public place in the more urban classes. This finding reflects the fact that there are more people in more urban areas and therefore more opportunity to congregate than in sparsely populated areas, leading to a higher proportion of collapse in a public place.

The incidence of OHCA decreased significantly with increasing rurality. This is in line with previous studies which have also found a lower adjusted incidence of OHCA in more rural areas, including Nottinghamshire and South Korea (Soo et al., 2001; Ro et al., 2013; Masterson et al., 2015). These studies only considered population density as a marker of rurality whereas our study also accounts for geographic characteristics associated with increasing rurality. Though incidence decreases as areas become more rural, it should be noted that there is still significant incidence of OHCA, even in more rural areas. This implies thatprehospital resuscitation planning nationally should not be dramatically skewed towards urban areas in order to avoid inequitable provision of services.

The proportion of patients who received bystander CPR in our population is high at 66%, even compared to countries such as Sweden (Strömsoe et al., 2011). While it is not currently possible to measure the quality and timeliness of bystander CPR, our results indicate a willingness among the Irish population to at least attempt CPR in the event of OHCA. Ways in which to capitalise on such willingness in terms of community CPR training programmes need to be supported in Ireland. It should be noted that a lower proportion of cases received bystander CPR in the cities compared to the other classes, which suggests that particular attention should be given to providing CPR training in city areas. Similarly, even though only 6% of patients had bystander defibrillation attempted, this is relatively high compared to other countries such as Denmark (Wissenberg et al., 2013) and North America (Cardiac Arrest Registry to Enhance Survival 2015) (2% for both countries). There is a significant trend in the proportion of patients receiving bystander defibrillation across urban-rural classes, with a particularly low proportion in the city class. However, since the proportion of patients receiving an EMS response in less than eight minutes decreases with increasing rurality, this may be counteracted by decreasing EMS response interval and/or increasing the proportion of patients receiving bystander defibrillation. Also, it is interesting that while median ambulance travel distances increase with increasing rurality, the proportion of patients receiving an advanced EMS intervention also increases. Considering that advanced EMS interventions are available to all patients, regardless of rurality, this increase in interventions with increasing rurality suggests that patients in more rural areas are in a more deteriorated state by the time the EMS arrive and are therefore in need of more advanced interventions. It may seem obvious to decrease EMS response intervals
by increasing the number of EMS ambulance stations nationwide, though the impact on outcomes and cost-effectiveness of this would need to be examined.

The reality is that the opportunity for successful intervention is narrow and relies primarily on an appropriate response within the first few minutes of collapse. In many areas, particularly rural areas, it is likely that patients will always be too far from ambulance services. OHCAR data shows that, in the majority of cases, bystanders are willing to perform CPR. On an annual basis, approximately 65,000 people are trained in CPR and accredited by the Irish Heart Foundation (2012). While this is a substantial number of people, it still represents a relatively small proportion of the overall population. This means that ways to instil and maintain the ability to perform CPR as a core life-skill in the Irish population should be found. In Norway, for example, resuscitation training is a mandatory part of the school curriculum (Kanstad, Nilsen and Fredriksen, 2011). In Ireland, many ‘transition year’ students have received CPR training, and, indeed, have been responsible for saving lives (Byrne, 2016), suggesting that more widespread introduction of CPR training in schools should be introduced nationally. While school training would help to establish CPR training as an integral life-skill for young people, the majority of OHCAs occur in older age groups, at home, highlighting the need for adults and older members of the public also to have access to CPR training. CPR training as part of drivers’ licence applications is one option, and has been successfully introduced in Japan (Enami et al., 2010). Many rural communities set up community alert groups, and it may be possible that such groups could facilitate community CPR training.

Within local communities, there are also trained professionals, who are willing to participate in resuscitation in the event of OHCA. The Medical Emergency Responders Integration and Training (MERIT) project has trained large numbers of Irish General Practitioners (GPs) to manage life-threatening emergencies, including OHCA. GPs trained in the MERIT programme reported involvement in 272 events, 65% of which the GP was on scene before the ambulance (Bury et al., 2013). Fire service personnel receive regular resuscitation training and some fire brigades currently act as a first response to OHCA in their locale. Voluntary Community Responder groups, many of which involve off-duty members of the ambulance service, are proliferating nationwide. At present the evidence for widespread involvement of local fire services and community responder groups is limited, and further research is required to model which geographic areas are in most need of such first response schemes, so that tailored responses to local needs can be implemented.

Before reaching our conclusions, it is acknowledged that there are limitations to our data. Of particular note is the difficulty in estimating the correct incidence denominator. For this study, the underlying population of the area where the incidence occurred was used, but daily fluctuations in population could not be accounted for. Another issue was the fact that it was not possible to geocode all cases to at least ED level. Even though this only amounted to 6%, there were some differences in the attributes of the matched and unmatched subgroups which may
have introduced bias to our results. With the introduction of centralised ambulance
dispatch, it is hoped that centralised recording of ambulance GPS coordinates will
be possible. Availability of this data will mean that more accurate recording of
event locations will be possible in the future. There was missing data for a small
number of patient characteristics and derived variables, though the proportion of
missingness did not exceed 10% for any variable. It is also acknowledged that
we did not address OHCA survival in this study, as survival is being examined
in parallel research. A final limitation of note is that the number of years of
annual data is limited to three at present, though the data currently available is
very comprehensive and has created research opportunities in OHCA that were
previously unavailable.

Overall, despite these caveats, in considering the spatial variation of OHCA
across the urban-rural spectrum in the Republic of Ireland, our results suggest that
the incidence of OHCA is significantly higher in urban areas, but not to an extent
where services should be solely focussed on such areas. Differences also exist
in availability of the Chain of Survival across the urban-rural spectrum, which
presents opportunities for strengthening the chain including increased community
CPR training, enhanced support of first responder defibrillation programmes and
continued efforts to reduce EMS call-response intervals where possible. Repetition
of our analysis with subsequent years’ data will improve the robustness of our
findings and allow validation of our conclusions.

Acknowledgements
The authors wish to thank National Ambulance Service and Dublin Fire Brigade
personnel who provide the clinical and dispatch data that has made this study
possible, and the OHCAR Steering Group who encouraged and facilitated this
research.
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Figure A1: The Six Categories of Urban-Rural Classification
Table A1: Distribution of Urban-Rural Classes by County

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<thead>
<tr>
<th>County</th>
<th>City</th>
<th>Town</th>
<th>Village (Near)</th>
<th>Rural (Near)</th>
<th>Village (Remote)</th>
<th>Rural (Remote)</th>
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Note: Counties where majority of land space is occupied by a single class are underlined and highlighted in bold.

The Effect of Rurality on Out-of-Hospital Cardiac Arrest Resuscitation Incidence: An Exploratory Study of a National Registry Utilising a Categorical Approach.

The Effect of Rurality on Out-of-Hospital Cardiac Arrest Resuscitation Incidence: An Exploratory Study of a National Registry Utilizing a Categorical Approach

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Abstract

Purpose: Variation in incidence is a universal feature of out-of-hospital cardiac arrest (OHCA). One potential source of variation is the rurality of the location where the OHCA incident occurs. While previous work has used a simple binary approach to define rurality, the purpose of this study was to use a categorical approach to quantify the impact of urban-rural classification on OHCA incidence in the Republic of Ireland.

Methods: The observed versus expected ratio of OHCA incidence where resuscitation was attempted was calculated for each of the 3,408 electoral divisions (ED). EDs were then classified into 1 of 6 urban-rural classes. Multilevel modeling was used to test for variation in incidence ratios (IR) across the urban-rural classes.

Findings: A total of 4,735 cases of adult OHCA, not witnessed by Emergency Medical Services, where resuscitation was attempted were included in the study. The number of EDs in each category was as follows: city (n = 477); town (n = 293); near village (n = 182); remote village (n = 84); near rural (n = 1,479); rural remote (n = 493). The IR per ED varied from 0 to 18.38 (EDs, n = 3,408). Multilevel modeling showed that 2.36% of variation in IR was due to urban-rural classification. This dropped to 0.45% when adjusted for ED deprivation score and median distance to an ambulance station. The addition of other explanatory variables did not improve the model.

Conclusion: OHCA variation in Ireland is limited and almost fully explained by area-level deprivation and proximity to ambulance stations.

Key words emergency care systems, out-of-hospital cardiac arrest, prehospital care, remote and rural medicine, resuscitation incidence.

In the United States and Europe, out-of-hospital cardiac arrest (OHCA) is estimated to account for almost 700,000 deaths annually.1,2 In Ireland in 2014, the unadjusted incidence of OHCA where resuscitation was attempted was 43 patients per 100,000 population per year.3 Incidence of OHCA varies internationally, both between and within countries.4-9 Most OHCA have a cardiac etiology, and for this reason, much of the variation reported can be explained by differences in individual patients, most notably age, gender, ethnicity, lifestyle, genetic/congenital factors, and comorbidities.10-13 Event incidence may also have a geographic component, and clustering of OHCA cases in specific geographic areas has been demonstrated in previous studies.2,3,15

Statutory Emergency Medical Services (EMS) are tasked with ensuring equitable provision of prehospital
resuscitation, regardless of the geographic location of the OHCA event, and poorer outcomes have been reported for rural-dwelling patients. This is a particular challenge in Ireland, where emergency response times have been shown to be significantly longer in more rural areas. In view of the disparity in outcomes, it is important to understand if there is a specific effect of rurality on the incidence of OHCA so that planning for resuscitation services accounts for differences at the urban-rural level.

We have previously reported on marked differences between incidence in Irish urban and rural areas, where “urban” was classified as a population cluster of 1,500 people or more. In OHCA research, the difference between urban and rural areas has often been defined in terms of population density, more recently, we have used a 6-category urban-rural “index,” which reflects the urban-rural spectrum by taking into account population density, settlement size, proximity to urban centers, and land use. When adjusted for the age and gender profile of each category, while a significant difference in urban-rural incidence rates remained, the differences between Irish urban and rural incidence were reduced, if not fully explained. Building on our previous research, using this more nuanced rurality categorization, the aim of this study was to quantify the remaining difference in OHCA incidence between urban-rural categories using area-level variables derived from and based on Irish census data.

Methods

This retrospective, cross-sectional study used data from the national Out-of-Hospital Cardiac Arrest Register (OHCAR), extracted for the period January 1, 2012, to December 31, 2014. The national OHCAR includes patients who experienced an OHCA, were attended by statutory EMS, and had resuscitation attempted. During the study period, pre-hospital cardiac arrest protocols followed the recommendations of the 2010 International Liaison Committee on Resuscitation (ILCOR). Specific circumstances existed under which the EMS were permitted not to attempt resuscitation, including recognition of death and the presence of a “do not resuscitate” order. Patients under age 18, events that were witnessed by the EMS, or that occurred as a result of a traumatic event were excluded from the study.

Each event address was geocoded using the Irish mapping application, “Health Intelligence Ireland.” Geocoded addresses were mapped to their corresponding electoral divisions (EDs) using the geographic information system ArcGIS Software (Environmental Systems Research Institute [ESRI] Inc., Redlands, California). EDs are legally defined areas for which small area population statistics are published by the Irish census and are similar to census tracts. Ireland is divided into 3,444 EDs, but we aggregated to 3,409 to protect confidentiality in some small EDs.

Two ED-level explanatory variables were extracted from census data (ie, proportions of persons living in 1-person households and self-reporting bad or very bad health [poor health]). The 2011 deprivation index, published by the Small Area Health Research Unit (SAHRU) in Trinity College, Dublin, was also used as an explanatory variable. Deprivation reflects the level of disadvantage in an area, and thus it is a multidimensional measure of the socioeconomic status of an area. A higher positive value indicates more severe deprivation. While the components may vary, the concept of material deprivation is similar to the concept of socioeconomic status used in the United States. The index comprises the following 4 indicators extracted from the 2011 Irish census: unemployment; low social class; no car; and type of housing tenure. Principal component analysis was used to create a weighted combination of these factors. Material deprivation of individual EDs is expressed as deciles, with 10 referring to the most deprived 10% of EDs.

Based on the location of ambulance services nationwide, the median distance from an ambulance station to each ED centroid was also calculated using the proximity toolset in ArcGIS.

In order to understand the rurality of disease, Teljeur and Kelly have argued that “different aspects and dimensions of rurality must be considered in order to provide an overarching classification.” For the purposes of this study, and an updated version of their urban-rural classification was calculated with data from the 2011 Irish census. Finally, each ED was categorized into 1 of the resulting 6 urban-rural classes: city, town, near village, near rural, remote village, and remote rural (remote). The distinction between “near” and “remote” is on the basis of proximity to population centers, which implies access to services and amenities. As the census population of Dublin Airport ED does not reflect the daily population due to passenger throughput, it was excluded from analysis.

The total number of adult OHCA resuscitation cases for each ED was categorized into 5-year age bands by gender. The ED population data for a corresponding breakdown was extracted from census data for 2011. The incidence rate in each age band by gender nationally was calculated and then applied to ED population figures to calculate the expected number of adult OHCA resuscitation cases for each ED. The ratio of observed to expected OHCA resuscitation cases was calculated for each ED, providing the outcome of interest (incidence ratio [IR]).

Mixed effects multilevel linear regression modeling was performed to test for a random intercept (ie, for
significance of a differing effect across urban-rural classes for IR). Analysis was performed using the Stata Statistical Software (Release 13, 2013; StataCorp, LLC, College Station, Texas). Likelihood ratio tests comparing the null single-level model and the null multilevel model were used. In order to check whether the effect of urban-rural class could be explained by area-level variables, the ED-level explanatory variables were added to the null multilevel model (including interaction terms), and a likelihood ratio test was used to assess the effect of each variable on the model. No interactions between explanatory variables were found. The appropriateness of allowing for a random slope (i.e., differing effects of explanatory variables across urban-rural classes in the model) was also assessed. To ensure robust standard errors for regression coefficients, 1,000 bootstrapped resamples of the study population were performed. The bootstrap method of error estimation involves “resampling” of the data to generate estimates of the data distribution from which robust confidence intervals can be derived, thus avoiding reliance on assumptions about data distribution that may not be valid, particularly when data are not normally distributed.30

Results

Of the 4,807 patients eligible for inclusion in the study, 4,781 cases (99.5%) were successfully geocoded to at least ED level. Following exclusion of cases that occurred in Dublin Airport ED, a total of 4,755 adult OHCA resuscitation cases were included in the analysis. Almost two-thirds of patients were male (n = 3,203; 64.7%). Patients ranged in age from 18 to 100 years, and the average age was 65.4 years (standard deviation 17.2 years). Over half (55%) of patients were aged 65 years or older.

As shown in Figure 1, OHCA resuscitation incidence ranged between 0 and 29 cases per ED, with cases occurring in just over half of EDs (n = 1,713; 50.3%). The IR varied from 0 to 18.38 across the 3,408 EDs included (see Figure 2).

The distribution of urban-rural classes across Ireland is presented in Figure 3. The most remote rural class tends to be situated along the western seaboard, while the near rural class tend to be clustered around the EDs classified as town or city (more prevalent in the east of the country). The near village class is situated in areas with relatively more near rural EDs. Conversely, the remote village class—the least common class—is more likely to be situated in areas with more remote rural EDs. In contrast, Figure 2 shows the ratio of observed:expected OHCA incidence as more randomly dispersed across EDs nationwide.

Characteristics of the study population and ED, categorized by urban-rural class, are presented in Table 1.

The multilevel null model was a superior fit to the single-level model for IR (Likelihood ratio test statistic at 1 d.f.: 72.31 [P < .001]), indicating variation at the urban-rural level. The proportion of unexplained variance that was due to urban-rural class was 2.36% for the IR. Model fit improved significantly when adjusted for the SAHRU deprivation score. As shown in the final model (Table 2), increasing SAHRU score was positively associated with IR, and unexplained variance between urban-rural classes was reduced to 1.19% when adjusted for SAHRU score. The addition of median ambulance distance reduced unexplained variance to 0.45%. There was no evidence of a random slope (i.e., varying effect of deprivation across urban-rural classes for IR). Addition of other variables of deprivation from the census (i.e., proportions of persons living in 1-person households and self-reporting bad or very bad health [poor health]) did not improve the model.

Discussion

This study shows that in a national database of OHCA where resuscitation was attempted, after adjustment for age and gender, urban-rural area-level differences are almost fully explained by area-level deprivation and proximity to ambulance services. In 2017, Benders suggested that it is not sufficient to establish whether urban-rural disparities exist, but that it is necessary to explore the “potential mediators and moderators” of these differences.11 Since we first identified a difference in urban-rural OHCA incidence in Ireland, through subsequent studies we have tried to address each subcomponent to understand the reason for urban-rural variation in Ireland.16,22 To the best of our knowledge, this is the first study to attempt to quantify and explain the effect of rurality on incidence of OHCA in a national population.
The definition of rurality varies greatly internationally. Since 1910, the United States Census Bureau has classified areas with a population of at least 2,500 within its boundaries as urban, with all other areas being considered rural. Internationally, definitions of rural range from settlements with fewer than 30,000 inhabitants in Japan to settlements with fewer than 200 people in Sweden. In the Irish urban-rural index used here, settlements containing more than 1,500 persons are almost universally considered towns. While most classifications rely on 1 indicator (i.e., population count or density), rurality may be considered as a larger concept; it has been theorized that characteristics such as agriculture, forestry, mining methods, and water quality should be considered. Differing degrees and dimensions of rurality may pose differing challenges to health service provision. Our study describes rurality in the context of the Republic of Ireland, using characteristics that may impact on the Irish OHCA population, such as settlement size, proximity to urban centers, and land use.
between “near” and “remote” is on the basis of a gravity model of proximity to settlements within 48 km. Forty-four percent of “near” EDs and 26% of “remote” EDs are within 48 km of 1 of the 5 cities in Ireland. With the exception of some of the islands, the most remote parts of the country are up to 160 km (or over a 2-hour drive) from 1 of the 5 cities (or to a city in Northern Ireland). Relative to other countries, this may not seem particularly remote. In the context of OHCA, however, where rapid intervention is essential, the concept of “remote” does not need to be on the basis of large distances.

Applying a localized urban-rural classification does, however, mean that our results may need adjustment to be applied to other countries. Once rurality is defined, however, the methodology used in our study to quantify the effect of rurality on OHCA incidence is equally applicable in other countries, and it will enable the generation of results that are appropriately localized to the area of study.34

The urban-rural effect in our study adjusted for ED-level deprivation score. In their study of participating centers in the Resuscitation Outcomes Consortium, Reintier
Table 1: Characteristics of OHCA Resuscitation Cases and Electoral Divisions Categorized by Urban-Rural Class

<table>
<thead>
<tr>
<th></th>
<th>City</th>
<th>Town</th>
<th>Near Village</th>
<th>Remote Village</th>
<th>Near Rural</th>
<th>Remote Rural</th>
<th>Overall</th>
</tr>
</thead>
<tbody>
<tr>
<td>IR in each urban rural classification</td>
<td>1.09</td>
<td>1.12</td>
<td>1.04</td>
<td>0.96</td>
<td>0.79</td>
<td>0.76</td>
<td>0.99</td>
</tr>
<tr>
<td>Electoral divisions, n (%)</td>
<td>477 (14%)</td>
<td>293 (6.6%)</td>
<td>182 (5.3%)</td>
<td>84 (2.5%)</td>
<td>1,479 (43.4%)</td>
<td>893 (26.2%)</td>
<td>3,408</td>
</tr>
<tr>
<td>Mean number of adults per ED</td>
<td>2,511</td>
<td>3,472</td>
<td>1,092</td>
<td>864</td>
<td>462</td>
<td>300</td>
<td>1,009</td>
</tr>
<tr>
<td>Average ED area (km²)</td>
<td>20</td>
<td>17.1</td>
<td>23.2</td>
<td>25.8</td>
<td>22.3</td>
<td>28.0</td>
<td>20.6</td>
</tr>
<tr>
<td>Adult population (per km²)</td>
<td>1.257</td>
<td>203</td>
<td>47</td>
<td>33</td>
<td>21</td>
<td>11</td>
<td>49</td>
</tr>
<tr>
<td>EDs with IR greater than 1, n (%)</td>
<td>247 (91.6%)</td>
<td>157 (83.6%)</td>
<td>88 (44.3%)</td>
<td>34 (40.5%)</td>
<td>448 (89.9%)</td>
<td>240 (88.1%)</td>
<td>1,214 (90.6%)</td>
</tr>
<tr>
<td>Total adult population, n (%)</td>
<td>1,196,863 (54,850</td>
<td>1,017,340 (29,60)</td>
<td>198,756 (5,83)</td>
<td>72,569 (2.1%)</td>
<td>482,712 (19.1%)</td>
<td>267,836 (7.80)</td>
<td>3,436,076</td>
</tr>
<tr>
<td>Number of patients, n (%)</td>
<td>1,674 (35.20)</td>
<td>1,470 (30.99)</td>
<td>314 (6.61)</td>
<td>109 (2.33)</td>
<td>836 (17.91)</td>
<td>352 (7.40)</td>
<td>4,755</td>
</tr>
<tr>
<td>SAHRU deprivation score, mean (SD)</td>
<td>1.3 (2.9)</td>
<td>1.1 (1.8)</td>
<td>0.8 (1.1)</td>
<td>0.5 (1.2)</td>
<td>-0.6 (0.9)</td>
<td>-0.3 (1.0)</td>
<td>0.0 (1.6)</td>
</tr>
<tr>
<td>Proportion of 1-person households, mean (SD)</td>
<td>28.0 (9.9)</td>
<td>25.4 (8.3)</td>
<td>24.2 (5.6)</td>
<td>20.8 (5.2)</td>
<td>25.3 (6.2)</td>
<td>23.6 (7.2)</td>
<td>23.6 (7.2)</td>
</tr>
<tr>
<td>Proportion of poor self-reported health, mean (SD)</td>
<td>2.0 (1.6)</td>
<td>1.7 (0.7)</td>
<td>1.6 (0.7)</td>
<td>1.5 (0.6)</td>
<td>1.2 (0.6)</td>
<td>1.5 (0.9)</td>
<td>1.4 (0.8)</td>
</tr>
<tr>
<td>Median distance (km) to ambulance station from ED centroid (IQR)</td>
<td>3 (2-4)</td>
<td>4 (2-12)</td>
<td>16 (11-20)</td>
<td>16 (12-20)</td>
<td>15 (10-19)</td>
<td>17 (12-23)</td>
<td>13 (7-19)</td>
</tr>
</tbody>
</table>

IR, observed:expected incidence ratio; EDs, electoral divisions; km, kilometers; SAHRU, small area health research unit; SD, standard deviation; IQR, interquartile range.
and associates found that socioeconomic status was a predictor of incidence of sudden cardiac arrest. It is of note that the coefficient for this variable in our study was very stable throughout, even when the median ambulance travel distance was included in the model. Our study therefore supports the finding that OHCA resuscitation incidence is statistically significantly higher in more deprived populations, albeit—in the Irish context—that the size of the association is small. The concept of deprivation used (SAIRIU) is closely aligned to the concept of socioeconomic status in the United States. Shavers observed that the components used to construct socioeconomic scores vary in health disparity research. For this reason—while the methodology used in this study can be applied elsewhere—it is hypothesized that the significance and strength of the association between rurality and deprivation will vary, depending on the context and the measure used.

One possible explanation for our finding that proximity to ambulance stations is associated with OHCA resuscitation incidence is that the more rurally located an OHCA patient, the less likely that the patient will have a resuscitation attempt. When an OHCA occurs in an area that is remote from an ambulance station, and if resuscitation is not commenced before ambulance services arrive, it may be more likely that resuscitation is deemed inappropriate when EMS personnel examine the patient. In the absence of national data on overall OHCA cases, it is not possible to confirm whether this is the case. Only the recent consolidation of ambulance dispatch into a national operations center has allowed the introduction of dynamic deployment of ambulance resources in Ireland. Our data predate this development; therefore, it may be expected that dynamic deployment could have further decreased any disparities between urban and rural OHCA incidence. It should, however, be remembered that the actual effect found was very small.

Table 2 shows that 34% of all cases occurred in rural and village EDs, and 36% of the total adult population resides in these areas. The adult population density ranges from 11 adults per square kilometer in remote rural areas to 47 adults per square kilometer in near villages. Providing an adequately rapid ambulance response to these areas of low population density will remain a challenge, even with the introduction of dynamic deployment. Irish rural communities have a long history of reacting to this issue by providing a community response. Again, in recent years, the formation and deployment of Community First Responder groups in rural areas has been supported by the National Ambulance Service, and a national strategy which will attempt to address these challenges is being developed.

**Table 2** Multilevel Regression Analysis of Incidence Ratio Across Urban-Rural Classes—Final Model

<table>
<thead>
<tr>
<th>Regression Coefficient</th>
<th>Incidence Ratio</th>
<th>95% CI*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Constant</td>
<td>1.080</td>
<td>1.000-1.154</td>
</tr>
<tr>
<td>ED-level variables</td>
<td></td>
<td></td>
</tr>
<tr>
<td>SAIRIU score 2011</td>
<td>0.092</td>
<td>0.064-0.121</td>
</tr>
<tr>
<td>Median ambulance distance</td>
<td>-0.011</td>
<td>-0.016-0.006</td>
</tr>
</tbody>
</table>

Variance explained by final models

| Between urban-rural classes | 0.007 | 0.013 |
| Between EDs                | 1.614 | 0.003 |
| Variance partition coefficient,%** | 0.451 |

*95% Confidence interval.
**Bootstrap standard error.
***0.007/0.007/1.614.

**Limitations**

This study has a number of limitations. First, almost half of EDs had an IR of 0, and approximately 72% of EDs had a predicted rate less than 1 case. High numbers of zero values may be expected to lead to an underestimation of variance, though simulation studies have suggested that a sparse data structure has a limited effect on model robustness. Therefore, we propose that the presence of zeros should not have affected the validity of our estimate. Such low incidence, however, is likely to have contributed to unexplained variation at the ED level, and a slight change in observed incidence may have a dramatic effect on IRs. To the best of our knowledge, this is the first time that multilevel modeling has been used to examine OHCA incidence across regions with remote rural areas and small or zero incidence counts. Ong and colleagues used multilevel modeling of similarly small geographical units in their study of incidence variation in Singapore. Singapore, however, is more uniformly metropolitan and densely populated than the Republic of Ireland, and therefore small areas in Singapore are less prone to variation than Irish ED. In view of this issue, as subsequent years of OHCAR data become available, we intend to repeat our analysis in order to test the validity of our current findings. Further aggregation of data may also be an option. We explored the option of aggregating neighboring EDs that were of the same urban-rural class and deprivation decile, but this method had little impact on the number of units with little or no cases.

Second, events were geocoded to the location of arrest rather than patients’ residential addresses. Incidence
rates were calculated using population data from the ED where the event occurred, even though almost one-third of cases occurred at a location other than a residential address. Our calculations assume that the majority of patients collapsed in the vicinity of their homes, as we were unable to obtain residential address data for all cases. It is possible that had geocoding been based solely on patients’ home addresses rather than event location, this may have affected the IRs obtained.

Third, this study includes only OHCA cases where resuscitation was attempted and does not fully reflect the burden of OHCA in the Irish population. Considering that the majority of cases included in our study would be presumed to have suffered an OHCA of cardiac etiology, our finding of a “rural effect” in relation to OHCA incidence may reflect a relationship with cardiovascular disease (CVD). While our finding suggests that OHCA resuscitation incidence tends to be lower with increasing rurality, Haraldsdottir and associates found a higher adjusted incidence of CVD mortality in the rural Icelandic population, while Kuhshreshta and colleagues found that high CVD mortality persisted in some subgroups, including rural populations.41,42 In contrast, our findings are in agreement with Ro and associates, who found that OHCA where resuscitation was attempted increased with increasing urbanization.16 Our data relates specifically to OHCA where resuscitation is attempted, and thus they should not be considered as a proxy measure for overall OHCA incidence.

Conclusion

In summary, this study suggests that there is significant urban-rural variation in OHCA incidence in Ireland, but that this variation is limited and almost fully explained by area-level deprivation and proximity to ambulance stations. The methodology used in this study has provided a national estimate of the effect of ED-level factors in OHCA resuscitation incidence. The use of methods that allow area-level factors to be acknowledged while accounting for spatial variation at local level, such as Bayesian modeling, may be able to provide further explanation of more localized differences in OHCA resuscitation incidence. Such further research could help to inform pre-hospital resuscitation planning that is targeted at particular areas and communities.43

References


Out-of-hospital cardiac arrest in the home: Can area characteristics identify at-risk communities in the Republic of Ireland?

*International Journal of Health Geographics, 17, 6*
Out-of-hospital cardiac arrest in the home: Can area characteristics identify at-risk communities in the Republic of Ireland?

Siobhán Masterson, Conor Teljeur, John Cullinan, Andrew W. Murphy, Conor Deasy and Akke Vellinga

Abstract

Background: Internationally, the majority of out-of-hospital cardiac arrests where resuscitation is attempted (OHCA) occur in private residential locations i.e. at home. The prospect of survival for this patient group is universally dismal. Understanding of the area-level factors that affect the incidence of OHCA at home may help national health planners when implementing community resuscitation training and services.

Methods: We performed spatial smoothing using Bayesian conditional autoregression on case data from the Irish OHCA register. We further corrected for correlated findings using area level variables extracted and constructed for national census data.

Results: We found that increasing deprivation was associated with increased case incidence. The methodology used also enabled us to identify specific areas with higher than expected case incidence.

Conclusions: Our study demonstrates novel use of Bayesian conditional autoregression in quantifying area level risk of a health event with high mortality across an entire country with a diverse settlement pattern. It adds to the evidence that the likelihood of OHCA resuscitation events is associated with greater deprivation and suggests that area deprivation should be considered when planning resuscitation services. Finally, our study demonstrates the utility of Bayesian conditional autoregression as a methodological approach that could be applied in any country using registry data and area level census data.

Keywords: Out-of-hospital cardiac arrest, Resuscitation, Deprivation, Residential characteristics, Spatial smoothing, Conditional autoregression

Background

Cardiac arrest occurs when the heart suddenly stops or becomes incapable of pumping blood around the body, and is the ultimate cause of all deaths [43]. Out-of-hospital cardiac arrest (OHCA) is the term ascribed to incidents that occur unexpectedly outside of an acute medical setting, and where the patient is attended by Emergency Medical Services (EMS). Survival from OHCA is almost entirely dependent on the initiation of “The Chain of Survival”. If the Chain of Survival is not activated within minutes of OHCA occurring, death is certain. The Chain of Survival is a sequence of resuscitation interventions, namely: early recognition of OHCA and immediate call for help to the EMS; high quality cardiopulmonary resuscitation (CPR); defibrillation within minutes of collapse; and effective advanced EMS and post-resuscitation care [34]. Timely resuscitation that is correctly performed is extremely effective. It has been shown that defibrillation within 3-5 min of collapse can result in survival as high as 50–70%. Each minute of delay however reduces the likelihood of survival by 10–12% [45]. For this reason, the ability to predict where OHCA events are most likely to occur can provide the opportunity to configure the provision of resuscitation training skills and services so that they are available in areas where they are most likely to be required.
The majority of OHCA's worldwide occur in private residential locations i.e. at home. The proportion of cases that occur at home range from 65.6% in Asia, 69.4% in Europe, 70.2% in Victoria (Australia), to 81.2% in the United States [18, 20, 42, 59]. Patient level factors have been reported to account for up to 89% of variability in OHCA outcome, including the location of collapse [8]. Whilst some of these factors cannot be affected by resuscitation services (e.g. age, gender, comorbidities), if geographic areas at higher risk of OHCA could be identified, there is potential to target these areas to improve the availability of modifiable predictors of survival at area level (e.g. bystander cardiopulmonary resuscitation (CPR) and availability of rapid defibrillation). This is particularly important when the event occurs at home, where the prospect of survival is poorer. Goh et al. [19] observed a three-fold difference in survival between home and non-residential locations (1 vs. 3% respectively). In an earlier study, Folke et al. [15] observed an even greater difference with only 3% of patients surviving at home compared with 14% in public locations. Given the proportion of OHCA that occurs at home, initiatives to narrow the gap between home and 'not home' survival are needed.

While the majority of OHCA events are located at home, geographic variation in OHCA incidence is consistently observed in OHCA epidemiological studies [20, 21, 38]. One aspect of geography that should be taken into account when considering variation is spatial autocorrelation, "the ubiquitous phenomenon that two close areas are often more similar than those that are far apart" [3]. Regression analyses that do not account for spatial autocorrelation are at risk of violating the assumption of independence which is generally necessary for regression analysis. The Bayesian conditional autoregression (CAR) model accounts for spatial autocorrelation in the error term, and has been shown to be particularly suited to modelling spatial phenomena strongly tied to a local context, ensuring a more realistic estimate of relative area risks [5, 28]. From a health perspective, health behaviours tend to be clustered in individuals and some of this clustering may be linked to shared neighbourhood characteristics [37, 51, 56]. This may also be the case for the occurrence of OHCA and attempted resuscitation.

In this study we aimed to estimate the underlying relative risk by small area of OHCA that occurred at home. Additionally we aimed to (1) identify underlying area-level factors that may increase the incidence of OHCA that occurs at home and (2) identify specific areas where the risk of OHCA at home is greatest in the Republic of Ireland. We also considered the influence of self-reported health, the rurality of a location, and the material deprivation of each ED on the incidence of OHCA in our analysis.

Methods

Setting
In the 2011 census the Republic of Ireland recorded a population of 4,588,252 [11]. The country is divided into 3409 small areas called Electoral Divisions (EDs) [13]. The average ED population was 1346 (ranging from 73 to 36,057). At the time of the 2011 national census, 62% of the population lived in urban settlements of 1500 people or more, accounting for 8% of total land mass. The remaining approximate 1.7million population were dispersed across the 65,000 square kilometres which constitute rural Ireland (Center for International Earth Science + Information Network—CIESIN—Columbia University [10].

The Irish National Ambulance Service is the sole provider of statutory Emergency Medical Services (EMS) outside of Dublin where the Dublin Fire Brigade (DFB) also provides the statutory EMS response. The Advanced Medical Priority Dispatch System (AMPDMS) is used by both NAS and DFB to prioritise calls. Emergency ambulances and rapid response vehicles are tasked to OHCA incidents and are staffed by paramedics and advanced paramedics. Intermediate care vehicles may also be dispatched as first responders or to assist in the event of OHCA and are usually staffed by emergency medical technicians. In Dublin, fire tenders are staffed primarily by fire fighter paramedics and are routinely tasked to OHCA in the greater part of the city. Irish statutory EMS staff must be licensed and registered with the Irish Pre-Hospital Emergency Care Council (PHECC) and are required to comply with PHECC Clinical Practice Guidelines in their practice (PHECC [46] 2012).

Data
Data from the national Out-of-Hospital Cardiac Arrest Register (OHCAR) were extracted for the period 1st January 2012 to 31st December 2014 [30]. OHCAR is a register of all patients who suffer an OHCA, are attended by the EMS, and have resuscitation attempted. In Ireland, as for the majority of countries where statutory resuscitation services are provided, specific circumstances exist under which the EMS are permitted to not attempt resuscitation, including recognition of death and the presence of a 'do not resuscitate’ order (PHECC [47] 2017). OHCAR data are extracted from ambulance Patient Care Reports (PCRs) which are completed by EMS personnel during or directly after attending the OHCA event. Dispatch and time variables for each case are obtained from NAS and DFB ambulance control centres. Case validation and registration comprehensiveness is routinely
performed to ensure the quality of OHCAR data [32]. Cases where no resuscitation was attempted are not recorded in OHCAR.

Patients 18 years or older, who suffered an event of non-traumatic aetiology and were not witnessed collapsing by the EMS, were included in the study. In European Union statistics on cardiovascular diseases, death at less than 65 years is considered ‘premature’ [58]. Patients were therefore categorised into two age groups in order to check for a differing risk according to patient age i.e. less than 65 years and 65 years and older.

Geocoding and data preparation
Private residential event location addresses were geocoded to latitude and longitude using the application ‘Health Intelligence Ireland’ (Health Intelligence Unit [22] 2015). Coordinates were then allocated to EDs using ArcGIS (Environmental Systems Research 95 Institute [ESRI] Inc., Redlands, CA). Expected rates of OHCAR by small area were computed using indirect standardisation based on 2011 census population figures. Standardisation was on the basis of sex and 5 year age bands. Standardised incidence ratios were also calculated for the two age categories separately (less than 65 years (Home U65) and patients aged 65 years or older (Home 65 +)). Unsmoothed standardised incidence ratios that were greater than 1 where considered to be ‘high’ while those below 1 were considered to be ‘low’.

Three ED-level covariates were included: deprivation, urban–rural class and self-reported health. The deprivation index was based on four census indicators: unemployment, low social class, local authority housing and car ownership [25]. The indicators were selected based on the philosophy of the Townsend index developed in the UK [62]. The four indicators are combined using principal components analysis, with the weights for the first three indicators being approximately equal, while a marginally lower weight applies to car ownership. The index is an estimate of material deprivation in an ED, and thus is a multidimensional measure of the socioeconomic status of an area. It can be expressed as a standardised score with higher positive values indicating greater deprivation, or as quintiles. While the latter results in regression coefficients that may be more interpretable, it does not capture the skewed nature of the measure, and the fact that highly deprived areas are more commonly located in city centres. We used a continuous score in the main analysis, and included a secondary analysis based on quintiles. Urban/rural classification was on the basis of a previously developed index with four levels: city; town; village; rural [61] updated in [31]. The classification combines information on population density, settlement size, land use, and proximity to other settlements. Higher rates of OHCA might be anticipated in areas where a high proportion of population report bad or very bad health. For this reason, a third variable indicating the proportion of people self-reporting bad or very bad health in each ED (Health) in the census 2011 was also calculated.

Exploratory geographic analysis
Before performing CAR analysis, a check for spatial auto-correlation in all Home cases, and the Home U65 and Home 65 + subgroups, was carried out using the Global Moran’s I statistic. Global Moran’s I is a z-score which describes the degree of spatial concentration or dispersion for a measured variable.

Spatial smoothing
At the ED-level, OHCA is a relatively uncommon event, and therefore incidence rates are subject to substantial variability due to small numbers. Spatial smoothing provides a method to reduce noise due to random variation. The Bayesian CAR model was used to smooth the standardised incidence rates to adjust for small numbers and to allow the model to ‘borrow strength’ from observations in neighbouring areas. The model requires data on the spatial structure of observations. The geographical matrix was determined using ‘first order queen contiguity’ i.e. EDs that share a boundary were considered neighbours. Artificial links were created for EDs that were otherwise not connected (e.g. islands).

The Bayesian CAR model was fitted using Markov Chain Monte Carlo algorithms with WinBUGS. The model is based on the assumption of a Poisson model for the spatial distribution of events. The model was given a burn-in run of 10,000 iterations followed by 40,000 iterations. Convergence was tested using the Gelman–Rubin test [27].

Initial models were created for all three groups without covariates. Models were also estimated for each covariate alone, all pairings of covariates and for all three covariates. Models were estimated separately for all cases and both age group-related subcategories. Model selection was conducted using the deviance information criterion (DIC), where a lower DIC suggested a better compromise between model fit and parsimony [23]. A difference of less than 5 in model DIC is not considered sufficient to distinguish between two models [27]. Where multiple models resulted in differences of less than 5 relative to the DIC of the best fitting model, preference was given to the model with the fewest covariates. Analysis was conducted on yearly data in order to assess the sensitivity of the overall results to yearly fluctuations in the spatial distribution of events. For ease of explanation, risk ratios were calculated for covariates included in the final models.
Results

Over a 3 year period (1st Jan 2012 to 31st December 2014), a total of 4834 OHCAR cases were eligible for inclusion in the analysis, of which 3388 cases were classified as ‘Home’ cases. Each Home case was successfully geocoded to the ED centroid level. A total of 41.6% of events occurred in patients aged less than 65 years (n = 1410). Table 1 describes the patient and ED characteristics of all Home cases.

Unsmoothed SIRs ranged from 0 to 15.8 for all Home cases, and from 0 to 32.8 and 0 to 27.6 for the Home U65 and Home 65 + subgroups respectively. The Global Moran’s I statistic was calculated for the observed cases per ED. A z-score of 28.3 for all Home cases was highly significant. Similarly, z-scores of 18.7 and 26.3 for the Home U65 and Home 65 + subgroups respectively were also highly significant, confirming spatial autocorrelation in observed incidence.

Table 2 shows the results of performing Bayesian conditional autoregression on all Home cases and both age subgroups, using all possible combinations of the three covariates. While there was limited difference in the DIC for some models, the beta coefficient for deprivation (i.e. magnitude of effect of deprivation on incidence) was largely unaffected by the inclusion of other covariates. The models including only the deprivation covariate therefore were best in terms of fit and parsimony for all cases and both age subgroups.

Table 3 shows that higher ED deprivation scores were associated with higher incidence of all Home cases and both age subgroups. For all Home Cases, an increase of one point in Deparvation was associated with an 11% increased risk of OHCA (95% CI: 9–13%). When expressed as quintiles, the risk difference between the 20% most deprived EDs and 20% least deprived EDs was 59%. The difference in deprivation was bigger for Home U65 compared to the Home 65 + category.

Figure 1a displays the number of EDs with higher and lower than expected incidence ratios i.e. observed/expected incidence ratio greater than 1 or less than 1 respectively, while Fig. 1b displays the number of EDs with significantly high and low SIRs after spatial smoothing. Figure 1c–e show three cities where clusters of a higher risk of OHCA were observed after applying smoothing. Table 4 presents the number of EDs in each category of significance before and after spatial smoothing. After spatial smoothing, 100 of the 108 EDs (93%) with a higher risk of OHCA were located in Cities. This was also the case for the Home U65 subgroup (99/119; 81%) and the 65 + subgroup (55/57; 96%).

Sensitivity analysis

Analysis was repeated on yearly data in order to test the sensitivity of the final All Home cases model (results available as Additional File 1: Table S1). Only five EDs were significantly high across individual years and multi-year data. Deprivation was associated with greater incidence of attempted OHCA resuscitation in annual data. However, the addition of the deprivation covariate had less effect on the DIC than when multi-year data were used. The relative risk associated with a one point increase in deprivation appeared to decrease over time, from 23% (95% CI: 17–29%) in 2012 to 10% (95% CI: 7–14%) in 2014.

Discussion

Key findings

Our study demonstrates the value of spatial smoothing in quantifying the area level risk of a health event with high mortality across a whole country with a diverse population.
Table 2  Coefficients and deviance information criteria for all models

<table>
<thead>
<tr>
<th>All home cases</th>
<th>Beta coefficients (95% CI)</th>
<th>Deviance information criteria</th>
</tr>
</thead>
<tbody>
<tr>
<td>No covariates</td>
<td></td>
<td></td>
</tr>
<tr>
<td>+ Deprivation*</td>
<td>0.10 (0.09, 0.12)</td>
<td>7197.8</td>
</tr>
<tr>
<td>+ Health</td>
<td>0.12 (0.07, 0.16)</td>
<td>7117.8</td>
</tr>
<tr>
<td>+ Urban-rural</td>
<td>0.10 (0.08, 0.12)</td>
<td>7190.3</td>
</tr>
<tr>
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<td>0.10 (0.08, 0.13)</td>
<td>-0.01 (-0.06, 0.04)</td>
</tr>
<tr>
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<td>0.25 (0.07, 0.43)</td>
</tr>
<tr>
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<td>0.10 (0.08, 0.13)</td>
<td>-0.01 (-0.06, 0.04)</td>
</tr>
<tr>
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<td></td>
<td></td>
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<td>+ Deprivation*</td>
<td>0.14 (0.12, 0.17)</td>
<td>4460.3</td>
</tr>
<tr>
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<td>0.23 (0.17, 0.29)</td>
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</tr>
<tr>
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<td>-0.01 (-0.24, 0.21)</td>
</tr>
<tr>
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<td>0.05 (-0.03, 0.13)</td>
</tr>
<tr>
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<td>0.13 (0.10, 0.16)</td>
<td>-0.02 (-0.25, 0.20)</td>
</tr>
</tbody>
</table>

Table 3  Association of deprivation with OHCA incidence at home

<table>
<thead>
<tr>
<th>All home cases</th>
<th>Home U6S</th>
<th>Home 65+</th>
</tr>
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<tbody>
<tr>
<td>Covariate</td>
<td>RR (95% CI)</td>
<td>RR (95% CI)</td>
</tr>
<tr>
<td>Depreciation</td>
<td>1.11 (1.09-1.13)</td>
<td>1.15 (1.13-1.18)</td>
</tr>
</tbody>
</table>

settlement pattern (including adjustment for area level factors). It also demonstrates novel application of Bayesian conditional autoregression to routinely collected health event registry data and area level census data. Previous authors have demonstrated the value of this methodological approach in accounting for spatial clustering in infectious diseases including dengue fever [29] and
Fig. 1  a-e Relative risk of OHCA incidence per electoral division, unsmoothed rates versus smoothed standardised incidence ratios.  
- a All home cases—unsmoothed rates  
- b All home cases—smoothed standardised incidence rates  
- c All home cases—Smoothed standardised incidence rates—Dublin City and County area  
- d All home cases—smoothed standardised incidence rates—Cork City  
- e All home cases—smoothed standardised incidence rates—Limerick City
Table 4 Unsmoothed and smoothed standardised incidence ratios: numbers of electoral divisions categorised by significance

<table>
<thead>
<tr>
<th></th>
<th>All home cases</th>
<th></th>
<th>Home cases &lt; 65</th>
<th></th>
<th>Home cases 65+</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Unsmoothed</td>
<td>Smoothed</td>
<td>Unsmoothed</td>
<td>Smoothed</td>
<td>Unsmoothed</td>
<td>Smoothed</td>
</tr>
<tr>
<td>High</td>
<td>1122</td>
<td>108</td>
<td>717</td>
<td>119</td>
<td>936</td>
<td>57</td>
</tr>
<tr>
<td>Low</td>
<td>2227</td>
<td>157</td>
<td>2665</td>
<td>204</td>
<td>2442</td>
<td>82</td>
</tr>
<tr>
<td>NS</td>
<td>60</td>
<td>3144</td>
<td>27</td>
<td>3086</td>
<td>31</td>
<td></td>
</tr>
</tbody>
</table>

NS: Not significant

A previous Irish study used spatial smoothing to explain variation in the incidence of Amyotrophic Lateral Sclerosis (ALS), but did not attempt to provide area level explanations for the variation observed [51]. We are aware of only one other study that has analysed OHCA incidence using this methodology, in the city-state of Singapore, a considerably more uniformly populated jurisdiction than Ireland [41]. Our study addresses some of the gaps in the existing literature by showing the utility of Bayesian conditional autoregression in providing a spatial analysis (adjusted for relevant area level covariates) of a non-infectious disease event, across a whole nation with a diverse settlement pattern.

Our work adds to the evidence that the likelihood of OHCA resuscitation events—specifically in the home—is associated with greater deprivation and suggests that area deprivation should be considered when planning resuscitation services. Other covariates were not associated with OHCA incidence. By correcting for correlated findings between areas and using a methodology that accounts for spatial variation, our study considerably strengthens the evidence that deprivation is associated with a higher incidence of OHCA.

Choice of area level covariates

Our choice of area level covariates was based on availability of data at ED level, robustness and relevance to the Irish population. In a study using a similar methodological approach, Ong et al. [41] investigated spatial variation in OHCA incidence in the city-state of Singapore. Ong et al. used a number of single measure variables including education, working status, and household size. They found no association between area level measures and OHCA incidence and suspected that small sample size may have influence the lack of association found. We opted to use a robust composite deprivation variable in order to avoid the risk of multicollinearity between single measure variables and to ensure sufficient area level data availability.

Previous studies of OHCA incidence have measured rurality as a direct function of population density and have observed reducing OHCA incidence with decreasing population density [33, 50, 57]. We chose to use a composite measure that was specifically designed to additionally account for the geographical qualities of an area, including population density, land use, proximity to an urban area and settlement size. In view of the fact that non-traumatic OHCA almost invariably occurs as the result of an underlying disease, we believed that inclusion of an area-level health measure was essential in our analysis. As area level statistics on morbidity were not available, self-reported health status was considered the most appropriate proxy measure for area level health status.

In the United States, higher OHCA incidence has been observed in neighbourhoods with a higher proportion of black race [16]. Associations between incidence and other ethnicities have not been observed. Only 1.4% of the Irish population was reported as black in the 2011 census, meaning area level analysis of race and OHCA in the Irish context would be based on extremely sparse data and unlikely to be robust.

Association of deprivation and OHCA incidence

Our findings support those of Reinier et al. [48, 49] that there is an association between increased deprivation and increased OHCA incidence. While previous studies have found deprivation to be predictive of self-reported health [63], in our study population, deprivation appeared to be the more robust covariate, across all cases and both age subgroups. By using data from an OHCA register with national coverage, and accounting for spatial variation, our study lends support to the understanding that deprivation is associated with the incidence of OHCA incidents where resuscitation is attempted, regardless of age or geographical location.

It is important to keep in mind that deprivation is a relative concept to the country and/or circumstances in which it is measured. While individual components of a deprivation index may be stable across urban and rural areas, it cannot be assumed that an index will behave in as stable a manner as its constituent components [17]. Additionally, deprivation measures that are centred on
typical urban values are less likely to correctly identify deprivation in a rural setting [2, 4]. The index used here was developed to be applicable nationally, with only one indicator included (car ownership) that might be considered to bias towards urban areas. However, given the lower weight applied to that indicator, the influence it has on the deprivation score is moderated. The covariate coefficient for deprivation in the model is largely unchanged by the addition of the urban–rural index as a covariate, supporting the view that the index is not overly biased towards urban or rural areas. Area level deprivation is not discrete. It is influenced by the deprivation level of surrounding areas, highlighting the importance of using analytical methods that account for spatial autocorrelation [7]. Even when overall affluence increases, the relative association between deprivation and health inequities remains [26].

Considering that the most common cause of non-traumatic adult OHCA is cardiovascular disease (CVD), and greater deprivation is associated with increased incidence of CVD, an association between OHCA and deprivation is consistent with expectations [1, 35]. As aging exerts an independent effect on CVD prevalence, the smaller influence of deprivation in the older age group can also be expected [40]. In considering the impact of area level deprivation, it is important to remember that deprivation affects morbidity and mortality, which in turn influence and/or limit the health choices that people can make [69]. It is therefore ultimately individual factors, such as pre-existing morbidity and health behaviours that account for the greater proportion of incidence risk. For example, for myocardial infarction—the most common CVD precursor to OHCA—nine individual-level modifiable risk factors were found to account for 90% of the Population Attributable Risk (PAR) in men and 94% of PAR in women [64].

Spatial smoothing changes the view of the geography of OHCA resuscitation

Spatial smoothing greatly reduced the number of EDs where incidence was higher or lower than expected, and enabled the identification of specific areas with significantly higher incidence. Areas with significantly higher incidence were primarily located in EDs that were classified as City. This was unexpected as 57.1% of Home Cases occur in EDs classified as either Rural or Village. According to the Irish census in 2011, only 36% of the general population were resident in Rural or Village EDs [12]. Efforts to improve community first response tend to be focussed on more remote and rural areas. Our results suggest that certain city communities with greater deprivation should also be targeted.

Why do patients who collapse at home have poorer survival than those who collapse in a public place?

Various reasons for the difference in survival between collapsing at home have been suggested. Daya et al. [14] found that in an American population, collapse in a public location was an independent predictor of OHCA survival, even after adjusting for known predictors of OHCA survival. In Ireland we have previously reported a strong adjusted association between survival and collapse in a public place [33]. In contrast, Nakashita et al. [56] found that the influence of home as the incident location in Japan was eliminated when adjusted for ambulance call-response interval, performance of bystander cardiopulmonary resuscitation (CPR) and initial cardiac rhythm. An unmeasured but possible explanation for this difference may also be the higher prevalence of coronary heart disease in Western countries [52].

How these findings impact service provision

When cardiac arrest occurs, the heart becomes incapable of circulating blood around the body. In the absence of good quality cardiopulmonary resuscitation (CPR), the brain will become starved of oxygen within 5 min and cell death will begin to occur [44]. The chances of patient survival therefore are largely determined by the actions of bystanders within the first few minutes of collapse [39]. Home is the most common location of OHCA, and unless someone in the home is able to perform effective bystander CPR, the prospects of survival are severely limited. Previous studies have found an association between low income neighbourhoods and a reduced likelihood of bystander CPR being performed [53, 54]. At present, we do not know if the level of CPR training and knowledge of OHCA recognition in the general population in Ireland follows a socioeconomic gradient. Considering the association between OHCA incidence and deprivation suggested in this study and previous studies, an understanding of the association between CPR knowledge and deprivation is an important area for further research.

In Ireland—as in other countries—EMS call-response intervals increase with increasing rurality of the event [33]. Communities in more rural locations have responded to this problem with the establishment of rapid response schemes and involvement of general practitioners in the emergency response [9]. Our study shows however, that the effect of urban–rural status on OHCA incidence reduces after adjusting for deprivation. We have also identified specific areas with significantly higher incidence—the majority of which are located in cities. Zijlstra et al. [65] have shown the value of lay responders responding to OHCA events in densely populated residential areas. Blom et al. [6] have shown incremental
improvement in OHCA survival with the introduction of police CPR training and the equipping of police vehicles with AEDs in the city of Amsterdam. It can be suggested that similar interventions could be trialled in the deprived City EDs identified in our study as being at higher risk of OHCA.

Limitations

There are a number of limitations to our study. Firstly, OHCAR includes only OHCA where resuscitation was attempted and does not reflect the incidence of all Irish OHCA. Secondly, it was not possible in this study to consider the incidence of OHCA resuscitation which occurred at a location other than home as we could not determine a robust reference population for these cases. It is possible that areas with a low incidence of at home OHCA may have a high incidence of ‘not home’ OHCAs, in which case different policy approaches may be necessary to ensure immediate, effective resuscitation is available for cases that occur in more public locations. Thirdly, our sensitivity analysis showed differences in the EDs that were identified on a year-to-year basis. The numbers of cases in the annual analyses were small and therefore not as robust as the multi-year analysis. Additionally, OHCA was a relatively rare event and sensitivity analysis shows that areas may change on a yearly basis, which may have resulted in the improved fit of the multi-year analysis. Fourthly, deprivation is right skewed and a quintile can encompass areas with a very broad range of scores. To assume that the effect of deprivation is equal across all areas within a quintile may be unreasonable, which is why we used the score itself. Scores are used for small area studies where relative rather than absolute difference is of particular interest [5, 55]. The trade-off for using the score is that a one point change is difficult to interpret and cannot be readily considered in terms of quintiles. Finally, 1897 (56%) of the total 3409 EDs had zero Home cases—which may also have affected the robustness of our results.

Conclusions

In conclusion, we have shown that the likelihood of OHCA where resuscitation is attempted is likely influenced by deprivation, and have demonstrated a methodology that allows the identification of specific areas of high risk by correcting for correlated findings. Additionally, our study provides the opportunity to highlight that OHCA is not an event that happens to ‘others’ but rather an event that is most likely to occur at home, often in the presence of family or friends. While public policy should be targeted to at-risk communities, the universally greater risk of collapse at home must be communicated, regardless of geography.

**Additional file**

**Additional file 1: Table S1.** Deviance information criteria, beta coefficients and relative rate for ALL Home cases categorised by year.

**Authors’ contributions**

SM conceived the study, performed geocoding and data preparation for statistical analysis, and drafted the manuscript. CT performed all conditional regression analyses. JC assisted with geocoding and data preparation and supervised SM in the conduct of geographic analysis. CD contributed to the discussion section of the study and advised on the clinical relevance of findings. AM contributed to the introduction and discussion sections of the manuscript. AV supervised SM in study design and manuscript preparation, and reviewed all manuscript drafts. All authors read and approved the final manuscript.

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**Acknowledgements**

The authors wish to thank National Ambulance Service and Dublin Fire Brigade personnel who provided the data that has made this study possible, and the OHCAR Steering Group who encouraged and facilitated this research.

**Competing interests**

The authors declare that they have no competing interests.

**Availability of data and materials**

The data that support the findings of this study are available from the National Out-of-Hospital Cardiac Arrest Register Ireland (OHCAR) but restrictions apply to the availability of these data, which were used under license for the current study, and so are not publicly available. Data were however available from the authors upon reasonable request and with permission of the data controllers, the National Ambulance Service and Dublin Fire Brigade.

**Consent for publication**

Not applicable.

**Ethical approval**

Ethical approval for research using non-identifiable data was obtained from the Research Ethics Committee, National University of Ireland, Galway (57, Sep-12).

**Funding**

This study was completed with funding from the Health Research Board (HRB) Health Professionals Fellowship Grant, of which the first author is a recipient (HFF-2014-9/09). The HRB provided financial support to the first author for the conduct of the study, but did not have involvement in any aspects of study design, in the collection, analysis and interpretation of data, in the writing of the report or in the decision to submit the article for publication.

**Publisher’s Note**

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**Received:** 12 October 2017 **Accepted:** 7 February 2018 **Published online:** 20 February 2018

**References**


Apples to apples: can differences in out-of-hospital cardiac arrest incidence and outcomes between Sweden and Ireland be explained by core Utstein variables?

Articles to apples: can differences in out-of-hospital cardiac arrest incidence and outcomes between Sweden and Ireland be explained by core Utstein variables?

Síobhán Masterson, Anneli Strömsoe, John Cullinan, Conor Deasy and Akke Vellinga

Abstract

Background: Variation in reported incidence and outcome based on aggregated data is a persistent feature of out-of-hospital cardiac arrest (OHCA) epidemiology.

Objective: To investigate the extent to which patient-level analysis using core 'Utstein' variables explains inter-country variation between Sweden and the Republic of Ireland.

Methods: A retrospective cross-sectional comparative study was performed, including all Swedish and Irish OHCA cases attended by Emergency Medical Services (EMS-attended OHCA) where resuscitation was attempted from 1st January 2012 to 31st December 2014. Incidence rates per 100,000 population were adjusted for age and gender. Two subgroups were extracted: (1) Utstein - adults patients, bystander-witnessed collapse, presumed medical aetiology, initial shockable rhythm and (2) Emergency Medical Service (EMS)-witnessed events. Multivariable logistic regression analysis was used to identify predictors of survival following multiple imputations of data.

Results: Five thousand eight hundred eighty-six (3,803 Swedish patients were included. Swedish patients were older than Irish patients (median age 71 vs. 66 years respectively). Adjusted incidence was significantly higher in Sweden compared to the Republic of Ireland (52.9 vs. 43.1 per 100,000 population per year). Proportionate survival in Sweden was greater for both subgroups and all age categories. Regression analysis of the Utstein subgroup predicted approximately 17% of variation in outcome, but there was a large unexplained 'country effect' for survival in favour of Sweden (OR 4.40 (95% CI 2.55–7.56)).

Conclusions: Using patient level data, a proportion of inter-country variation was explained, but substantial variation was not explained by the core Utstein variables. Researchers and policy makers should be aware of the potential for unmeasured differences when comparing OHCA incidence and outcomes between countries.

Keywords: Out-of-hospital cardiac arrest, Utstein, incidence, outcomes, pre-hospital resuscitation

Key questions

- What is already known about this subject?
  There is variation in the reported incidence and outcomes from out-of-hospital cardiac arrest when aggregated data is compared.

- What does this study add?
  This study quantifies the proportion of variation between countries that can be explained using patient level analysis that includes core Utstein variables.

- How might this impact on clinical practice?
  The significant potential for the presence of unmeasured differences between countries should be acknowledged, whether for research or for the development of national outcome targets.

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Background
There is international variation in the reported incidence and outcome from out-of-hospital cardiac arrest (OHCA). Chamberlain and Eisenberg stated that in order to compare outcomes between different systems of care, it is necessary to have "a comparator that enables areas of weakness to be defined and addressed whether it be at local, national and international level". The Utstein criteria were developed for this reason, and identify patients based on a number of indicators [1]. International benchmarking is a highly desirable aspiration, and many notable studies and reviews have been carried out that compare the outcomes from OHCA across multiple countries and jurisdictions [2–5]. To ensure that comparison is informative, it is essential that data is collected for the same purpose, data definitions and collection methodologies are similar, and that the population covered is equally representative [6]. Assuring uniformity in OHCA data collection and reporting systems is essential, as differences in outcomes may well be attributable to differences in data availability and processing methodologies [7]. This aim of this study was therefore to investigate the extent to which patient-level analysis using core 'Utstein' variables explains variation in OHCA incidence and outcome between two countries, namely Sweden and the Republic of Ireland.

Methods
Aim and study design
We conducted a retrospective analysis of prospectively collected cohort of all Swedish and Irish cases of EMS-attended OHCA where resuscitation was attempted from 1st January 2012 to 31st December 2014.

Data sources
Swedish OHCA registry data have been used to monitor national changes in OHCA incidence, management and outcome for more than 25 years [8]. Ireland’s OHCA registry was established in 2007, modelled on the Swedish registry, and has had comprehensive national data collection since 2012 [9]. Both registries are hosted by universities, operate in collaboration with ambulance services, and are publicly funded. Irish data is transcribed by an external data management company from ambulance patient care reports while Swedish practitioners enter event data directly onto a web-based template that is forwarded to the registry. Dispatch data and patient outcome data is available directly from the dispatch centre and receiving hospitals in both countries. The availability of a unique patient identifier in Sweden means that status of the patient at thirty days can be obtained from Statistics Sweden. Both countries have systematic missing case identification procedures. This is performed centrally in Ireland and at county level in Sweden. Similarly, regular data quality assurance is performed, using the original patient care report (Ireland) or medical journal (Sweden) to validate data entered. A full description of the data collection comparison is available as a supplementary table. During the study period, clinical practice guidelines for EMS in both countries complied with the 2010 ILCOR recommendations [10]. Irish and Swedish EMS practitioners are not required to start resuscitation in cases where definitive signs of death are present.

Study setting
Sweden has a population of 9,995,153, occupying an area of 450,295 km² [11]. Approximately 85% of the Swedish population lives in cities. Ambulance provision is governed at county and municipal level, and vehicles are primarily staffed by nurses and paramedics. In some cities, physicians may also be part of the ambulance crew [12]. Fire and police personnel are increasingly involved in providing a first response to OHCA in Sweden with public access defibrillators having been installed across the country [13].

The 2016 census showed that Ireland had a population of 4,757,976 [14]. Ireland is significantly smaller than Sweden (68,890 km²) with approximately 63% living in urban areas. Statutory Emergency Medical Services (EMS) are provided by the National Ambulance Service (NAS). In Dublin city, Dublin Fire Brigade (DFB) also provides the statutory response. Paramedic and advanced paramedics are deployed to suspected OHCA events. Emergency medical technicians may also be deployed as support crew or first responders to OHCA calls. Community first responder (CFR) volunteerism is becoming increasingly prominent in Ireland, with approximately 150 CFR schemes now established across the country. A more detailed description of the Irish EMS has been published elsewhere [9].

Data processing
Register managers from both countries met to examine variables collected in both registries and identify which variables were comparable. Data were extracted from both registries, including original and derived variables. Variables with excessive missing values for either country (> 25%) were excluded from further analysis (available as Additional file 1).

Data were analysed using IBM SPSS Statistics v22.0© and STATA/IC 13.0 for Windows®. A subgroup was extracted based on the Utstein recommendations and included only adult patients with a bystander-witnessed collapse, with presumed medical aetiology and initial shockable rhythm [1]. A second subgroup of EMS-witnessed events was also extracted.

Statistical analysis
Variables were categorised into patient and event characteristics, interventions and outcomes. Where significant
differences in variables were observed, further analysis of
variables by 5 year age groups was performed.

Sweden is divided into 21 administrative counties
while the Republic of Ireland is composed of 34 (here-
after referred to as 'admin areas'). For each admin area,
crude incidence rates were calculated for all cases, both
subgroups and for three age categories: children (under
18 years); adults (18–64 years); older people (65 years
and over). Crude rates were adjusted to account for the
proportion of the total population by gender in each age
group at admin area level. Swedish population figures
were derived from Statistics Sweden data and were aver-
aged for the years 2012–2014 for each admin area [15].
Population estimates for the Republic of Ireland for each
admin area were taken from the 2011 census [16]. An
average country value was calculated from admin area
values for each age and gender group with their 95% con-
fidence intervals. The analysis of variance method
(ANOVA) was used to compare average incidence rates.
A p-value of < 0.05 was considered significant.

For key variables, missing data were imputed using a fully
conditioned specification (FCS) or chained equations im-
putation model [17]. Imputation was performed separately
for each country before data were merged for analysis.

Multivariable logistic regression analysis was used to
identify predictors of the main outcome of interest (Dis-
charge from hospital alive or alive at 30 days (Survival)).
Models were estimated using original data (available as sup-
plementary data) and imputed data. Potential explanatory
variables were chosen based on previous literature and clin-
ic relevance. Both ‘epinephrine’ and ‘mechanical CPR’
were initially included but were dropped due to insignifi-
cance. Interactions between the variable ‘Country’ and all
other variables were checked. Due to non-linearity, the call-
response interval variable was transformed into a binary
variable for the regression analysis. Interactions which
changed the Odds Ratios (ORs) for any of the main vari-
ables by more than 10% were included in the final model.

Model fit was assessed using imputed estimates adjusted
R², which were calculated using Harel's method [18].
Calibration of individual imputed models was assessed
using the Hosmer and Lemeshow X² statistic (p > 0.05).

Results

Patient, event and intervention characteristics

A total of 5886 Irish and 15,030 Swedish patients were in-
cluded in the analysis. The median test showed that Swe-
dish patients were significantly older than Irish patients for
all cases and in both subgroups (Table 1). Only gender
was shown to have a similar distribution. All other vari-
ables showed differences between the countries. There
were differences in the three categories of witness status,
particularly the proportion of patients who had an EMS-
witnessed arrest (Sweden – 15.2% vs. the Republic of
Ireland – 5.9%, Table 1).

There were differences between countries in who pro-
vided CPR. 'Trained, may be dispatched by ambulance con-
trol' included members of the community who had training
in CPR i.e. community first responders, off-duty para-
medics, nurses, doctors, other clinical personnel. While it is
known that many of these individuals were dispatched to
the event by ambulance control, it was not possible to ac-
curately determine that proportion. In the Republic of
Ireland, this category accounted for 33.5% of providers of
CPR before ambulance arrival compared to 12.8% in
Sweden. Conversely, in Sweden 28.2% of CPR before ambu-
ance arrival was provided by the fire service compared with
2.8% in the Republic of Ireland. A greater proportion of
Swedish patients received defibrillation before ambulance
arrival, though the actual percentages in both countries
were small (5.6% and 7.3%), and the median EMS call-re-
response interval was significantly shorter in Sweden.

Differences in OHCA incidence and outcome between
countries

The incidence of OHCA resuscitation attempts per
100,000 population per year was similar in both coun-
tries for the Utstein subgroup, despite the fact that the
annual crude and adjusted incidence of OHCA was sig-
nificant higher in Sweden for all patients and for the
EMS-witnessed subgroup (Table 2). This was also the
case for all age categories for both genders, and for the
EMS-witnessed subgroup.

The proportion of surviving patients was consistently
higher in Sweden for all patients, the Utstein subgroup
and the EMS-witnessed subgroup (Table 3). This signifi-
cant differential in survival was persistent across both
genders and all age categories.

Extent of unmeasured variation between countries

Variables independently associated with improved ORs
for Survival were younger age, collapse at a location
other than home, CPR and defibrillation before ambu-
ance arrival and a shorter EMS call-response interval
(Table 4). Gender was not significantly associated
with Survival at a 5% level after controlling for interactions at
country level. After adjustment for other variables and
inclusion of interaction terms, the OR for Survival in
Sweden was 4.40 (95% CI 2.55–7.56). Interactions
included in the final model were country*gender and
country*home location. There was no significant differ-
ence between results obtained from original or imputed
data. The overall proportion of variation in Survival that
is accounted for in the final model was relatively small
(adjusted R² 17%).
Table 1  Comparison of case characteristics between Republic of Ireland and Sweden – all Cases, Utstein and EMS-witnessed subgroups

<table>
<thead>
<tr>
<th></th>
<th>All cases</th>
<th>Utstein subgroup^2</th>
<th>EMS-witnessed subgroup</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Ireland</td>
<td>Sweden</td>
<td>Ireland</td>
</tr>
<tr>
<td></td>
<td>(n = 5886)</td>
<td>(n = 15,303)</td>
<td>(n = 920)</td>
</tr>
<tr>
<td><strong>Patient and scene characteristics</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Median age in years (inter-quartile range)</td>
<td>66 (52–78)</td>
<td>71 (60–81)</td>
<td>65 (55–75)</td>
</tr>
<tr>
<td>Male (%)</td>
<td>67.9</td>
<td>66.6</td>
<td>82.3</td>
</tr>
<tr>
<td>Incident occurred outside home (%)</td>
<td>52.7</td>
<td>30.1</td>
<td>51.6</td>
</tr>
<tr>
<td>Presumed medical (%)</td>
<td>88.0</td>
<td>89.7</td>
<td>NA</td>
</tr>
<tr>
<td>Initial rhythm shockable (%)</td>
<td>23.7</td>
<td>23.7</td>
<td>NA</td>
</tr>
<tr>
<td>Witness status (%)</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>Not witnessed (%)</td>
<td>40.5</td>
<td>33.7</td>
<td>NA</td>
</tr>
<tr>
<td>Bystander (%)</td>
<td>53.5</td>
<td>51.3</td>
<td>NA</td>
</tr>
<tr>
<td>Crew (%)</td>
<td>5.9</td>
<td>15.2</td>
<td>NA</td>
</tr>
<tr>
<td><strong>Interventions</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>CPR before ambulance arrival (%)^3</td>
<td>66.3</td>
<td>68.8</td>
<td>79.6</td>
</tr>
<tr>
<td>Who started CPR before ambulance arrival (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bystander, not dispatched (%)</td>
<td>60.7</td>
<td>56.9</td>
<td>44.3</td>
</tr>
<tr>
<td>Trained, may be dispatched by ambulance control (%)</td>
<td>33.5</td>
<td>12.8</td>
<td>31.9</td>
</tr>
<tr>
<td>Fire service (%)^5</td>
<td>2.8</td>
<td>2.82</td>
<td>1.9</td>
</tr>
<tr>
<td>Police or fire and police (%)</td>
<td>2.1</td>
<td>3.0</td>
<td>1.5</td>
</tr>
<tr>
<td>Defibrillation before ambulance arrival (%)^6</td>
<td>5.6</td>
<td>7.3</td>
<td>22.8</td>
</tr>
<tr>
<td>EMS call-response interval in minutes (median)^7</td>
<td>13 (8–20)</td>
<td>10 (6–15)</td>
<td>12 (8–18)</td>
</tr>
<tr>
<td>Epinephrine (%)</td>
<td>63.8</td>
<td>80.1</td>
<td>65.7</td>
</tr>
<tr>
<td>Mechanical CPR (%)</td>
<td>4.6</td>
<td>35.9</td>
<td>4.9</td>
</tr>
<tr>
<td>Transported to hospital (%)</td>
<td>53.8</td>
<td>60.9</td>
<td>75.7</td>
</tr>
<tr>
<td><strong>Outcomes</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Any ROSC</td>
<td>23.2</td>
<td>32.8</td>
<td>45.9</td>
</tr>
<tr>
<td>ROSC at hospital arrival or arrived at hospital alive</td>
<td>16.9</td>
<td>24.4</td>
<td>37.1</td>
</tr>
<tr>
<td>Discharged alive from hospital</td>
<td>6.0</td>
<td>UA^1</td>
<td>22.2</td>
</tr>
<tr>
<td>Alive at 30 days</td>
<td>UA</td>
<td>11.2</td>
<td>UA</td>
</tr>
<tr>
<td>Discharged alive or alive at 30 days</td>
<td>6.0</td>
<td>11.2</td>
<td>22.2</td>
</tr>
</tbody>
</table>

CPR Cardiopulmonary Resuscitation, EMS Emergency Medical Services, NA Not applicable, ROSC Return of Spontaneous Circulation, UA Unavailable data
^1For All Cases this variable includes all cases NOT witnessed by EMS (Ireland n = 5342; Sweden n = 12,835)
^2For All Cases this variable includes only cases NOT witnessed by EMS (Ireland n = 5342; Sweden n = 12,835)
^3Fire Service includes all city and county fire services EXCEPT Dublin Fire Brigade
^4The Utstein subgroup includes patients who meet the following criteria – aged over 17 years, bystander-witnessed collapse, presumed medical etiology, initial shockable rhythm

**Discussion**

This patient-level analysis of 3 years of data from two well established national registries shows that the incidence of attempted resuscitation is similar for the Utstein subgroup in both countries, but that percentage survival is greater in Sweden than in the Republic of Ireland overall, for all age categories and both subgroups. Even when data from two countries has been collected using similar methods and rationale, the reasons for inter-country differences in outcome are not fully explained by the core Utstein variables used in this study.

Our study highlights that differences in OHCA outcomes between countries are not solely down to differences in patient age and gender profile or pre-hospital interventions. By using patient level data, this analysis serves to quantify the degree of variation that can be explained by inter-country comparison in a way that cannot be achieved with aggregate outcome data. The critical value of OHCA data collection is that it can focus national efforts on improving national outcomes [19, 20]. In the latest revision of the Utstein dataset, Perkins et al. advised on a range of core and supplemental OHCA elements that
Table 2. Incidence of out-of-hospital cardiac arrest resuscitation attempts per 100,000 population per year

<table>
<thead>
<tr>
<th></th>
<th>Ireland</th>
<th>Sweden</th>
</tr>
</thead>
<tbody>
<tr>
<td>Crude Incidence</td>
<td>48.1 (39.3–46.3)†</td>
<td>52.9 (47.7–58.1)†</td>
</tr>
<tr>
<td>Utstein Subgroup</td>
<td>68.6 (61.1–74.4)</td>
<td>77.7 (65.5–80.0)</td>
</tr>
<tr>
<td>EMS-witnessed</td>
<td>26.2 (20.2–31.1)†</td>
<td>81.7 (71.1–91.2)†</td>
</tr>
</tbody>
</table>

Adjusted Incidence:

<table>
<thead>
<tr>
<th></th>
<th>Male</th>
<th>Female</th>
</tr>
</thead>
<tbody>
<tr>
<td>All Cases</td>
<td>42.3 (39.6–45.1)†</td>
<td>50.7 (46.1–55.2)†</td>
</tr>
<tr>
<td>Age Categories</td>
<td></td>
<td></td>
</tr>
<tr>
<td>All Ages</td>
<td>28.7 (26.3–31.0)†</td>
<td>14.3 (13.1–15.5)‡</td>
</tr>
<tr>
<td>L8</td>
<td>0.7 (0.6–0.9)†</td>
<td>0.5 (0.3–0.7)‡</td>
</tr>
<tr>
<td>18–64</td>
<td>13.4 (12.2–14.6)†</td>
<td>5.2 (4.6–5.8)‡</td>
</tr>
<tr>
<td>65+</td>
<td>14.1 (13.0–15.5)†</td>
<td>8.4 (7.6–9.3)‡</td>
</tr>
</tbody>
</table>

EMS: Emergency Services
† Higher incidence in Sweden (p < 0.005)
‡ Higher incidence in Swedish males than Irish males (p < 0.005)
§ Higher incidence in Swedish females than Irish females (p < 0.005)

are likely to help explain a larger proportion of inter-country outcome variation, including pre-existing comorbidities and in-hospital treatments and interventions [21]. Implementation or improved systematic collection of these data elements is likely to explain substantial variation in outcome within and between countries.

There are clearly differences in the patient and intervention characteristics in both countries. On average, Swedish patients are older in all cases and in both subgroups, and the higher overall incidence of OHCA resuscitation is largely accounted for by the greater proportion of older OHCA patients in Sweden (Table 2). The explanation for this difference in age profile may lie in cultural attitudes and expectations surrounding death and morbidity in both countries. A survey of public attitudes to resuscitation in older people has not been previously carried out, but may help explain the significant difference in resuscitation incidence in this age category.

As also shown in Table 2, the incidence of Utstein subgroup cases is similar in both countries. This is likely to be largely driven by the fact that similar proportions of patients had an initial recorded shockable rhythm (23.7%). The ‘three phase model’ of cardiac arrest suggests that most patients will deteriorate into an asystole within 5 min without intervention [22]. Considering the significantly shorter median EMS call response-interval in Sweden, it may have been expected that the proportion of Swedish patients with an initial recorded shockable rhythm would be greater than in the Republic of Ireland. One explanation may be the higher proportion of older people in the Swedish OHCA resuscitation population, as older people have been found to have a lower incidence of initial shockable rhythm [23]. Additionally, a decline in the proportion of patients with an initial shockable rhythm has previously been observed in Sweden, despite efforts to improve call-to-shock times [24]. It has been proposed that this decline may be due to a reduction in untreated ischaemic heart disease (IHD) in the Swedish population and that the proportion of cases with cardiac aetiology is less than presumed [25]. Diagnosis of IHD continues to increase the Republic of Ireland and what proportion of this increase is due to increasing prevalence or improved detection is unclear [26]. Both registries primarily rely on the clinical impression formed by the attending ambulance crew to determine the aetiology of arrest. Previous work on validation of aetiology in paediatric OHCA has shown the potential value of adding coronal data to an OHCA registry [27]. It is suggested that inclusion of coronal data in the Swedish and Irish registries may assure the validity of data on aetiology and ensure realistic expectations for the proportion of cases with an initial shockable rhythm.

Table 3. Proportion of surviving patients categorised by country, gender and age group

<table>
<thead>
<tr>
<th></th>
<th>Ireland</th>
<th>Sweden</th>
</tr>
</thead>
<tbody>
<tr>
<td>n (%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>All cases</td>
<td>350 (64.6)†</td>
<td>1686 (11.2)†</td>
</tr>
<tr>
<td>Utstein Subgroup</td>
<td>210 (22.3)</td>
<td>634 (31.7)</td>
</tr>
<tr>
<td>EMS-witnessed</td>
<td>56 (16.8)†</td>
<td>436 (20.0)†</td>
</tr>
<tr>
<td>Age Categories</td>
<td>Male</td>
<td>Female</td>
</tr>
<tr>
<td>All ages</td>
<td>283 (72.7)†</td>
<td>67 (3.6)†</td>
</tr>
<tr>
<td>L8</td>
<td>9 (0.8)†</td>
<td>2 (2.2)†</td>
</tr>
<tr>
<td>18–64</td>
<td>164 (9.5)†</td>
<td>35 (5.0)†</td>
</tr>
<tr>
<td>65+</td>
<td>103 (8.3)†</td>
<td>32 (2.6)†</td>
</tr>
</tbody>
</table>

EMS: Emergency Services
† Higher incidence in Sweden (p < 0.005)
‡ Higher incidence in Swedish males than Irish males (p < 0.005)
§ Higher incidence in Swedish females than Irish females (p < 0.005)
The proportion of CPR provided by those who were ‘trained, may be dispatched by ambulance control’ in the Republic of Ireland is encouraging (Table 1). The Republic of Ireland already has an active and growing Community First Responder (CFR) network. While there is evidence that trained first responders can contribute to survival, the best model of CFR is not yet determined [28]. The fire service plays a greater role in the provision of CPR in Sweden, suggesting there is potential for Irish Fire Services to participate more often in the OHCA response. It should be noted that – despite the fact that that dual dispatch of ambulance and fire services in Sweden has been shown to have the greatest effect on response intervals in rural Swedish areas – survival benefit was most significant in densely populated areas [29]. This suggests that there is a response interval beyond which any form of dual dispatch may not be of additional benefit to ambulance dispatch only.

Proportionate survival from OHCA is greater in Sweden for all patients, both subgroups and all age categories (Table 3). Patients who collapse in the presence of EMS are likely to receive good quality CPR and rapid defibrillation, which in turn is more likely to be immediately effective if performed soon after collapse [30]. This is borne out in the relatively high proportion of survival in this subgroup in both countries, and partially explains the higher overall percentage survival in Sweden.

The multivariable logistic regression model of survival explains – at best – 17% of variation between countries, and includes a large ‘country effect’ in favour of Sweden that is not explained by the predictor variables (Table 4). Rather than suggesting that the chances of patients in the Utstein group surviving an OHCA are over four times greater in Sweden than in the Republic of Ireland, this result points to the large proportion of variation which is not explained by our Utstein predictor variables. The implication is that while improving the availability of important outcome predictors such as bystander CPR and defibrillation, and reducing EMS call response intervals is likely to increase survival in the Republic of Ireland, these measures alone are unlikely to achieve parity of outcomes with Sweden.

**Limitations**

Simplified coding was applied to many variables in order to facilitate systematic registry recording and inter-country analysis. Most notably, we created the variable ‘Survival’ using the different outcome measures used in Sweden and the Republic of Ireland. In the Republic of Ireland, the primary outcome is ‘discharged alive from hospital’. Patients are not included as OHCA survivors until discharged, regardless of the length of their acute hospital stay. In Sweden survivors are classified as those who are alive 30 days or more after the event, even if the patient has not been discharged from an acute facility. While it is possible that Irish patients who are discharged alive may not survive to 30 days, it is also possible that Swedish patients may remain as in-patients for 30 days or more. Both outcome measures have been used interchangeably in other national comparative studies, and the use of either outcome measure has been recommended in the Utstein guidelines [21]. In general, it is not usual for studies to report both these outcomes. In cases where both outcomes have been reported, there is negligible difference in the number of surviving patients [31, 32]. While the proportion of patients who had defibrillation attempted before ambulance arrival is similar for the Utstein subgroup in both countries, 14.8% of Swedish cases had missing data for this variable. Using the original data the adjusted OR for this variable in the logistic regression analysis was 1.41 (95% CI 1.11–1.78) compared to 1.40 (95% CI 1.13–2.74) using imputed data.

**Conclusions**

The ability to compare OHCA incidence and outcomes across countries and systems is essential to establishing international benchmarking. The use of patient-level data have highlighted the proportion of variation outside of the well-known predictors of OHCA outcome, something that is not possible in comparative studies that rely on aggregated data. We believe the approach used in this study is transferable to other comparative studies of OHCA national incidence and outcome, and that such an approach will improve the validity and value of inter-country comparison, whether for research or for the development of national outcome targets.
Additional file

Additional file 1: Table S1. Comparison of Irish and Swedish OHCAR resuscitation regimens. Table S2. Missing data items. Table S3. Logistic regression analysis for the outcome survival in the Utstein subgroup using original data (adult, bystander-witnessed, initial rhythms, shockable, presumed medical worksheet), 3 PDF (54 KB)

Acknowledgements

The authors wish to thank National Ambulance Service and Dublin Fire Brigade personnel who provided the data that has made this study possible, and the National Out-of-Hospital Cardiac Arrest (OHCA) Steering Group who encouraged and facilitated this research. This study was supported by the Swedish Association of Local Authorities and Regions in Sweden, and was completed with.

Funding

This study was completed using funding from the Health Research Board Health Professionals Fellowship Grant of which the first author is a recipient (HRF-2014-09).

Availability of data and materials

The data that support the findings of this study are available from OHCAR and the Swedish Registry of Resuscitations but restrictions apply to the availability of these data, which were used under license for the current study, and so are not publicly available. Data are however available from the authors upon reasonable request and with permission of the contributing ambulance service providers.

Authors’ contributions

SM and AS conceived the idea for the study and prepared and extracted data for analysis. SM was responsible for data analysis and manuscript drafting. AS also contributed to manuscript discussion and drafting. AV and JC were responsible for supervising data analysis, commenting on manuscript drafting and approving the final draft. CO was responsible for contributing to and ensuring the clinical accuracy and relevance of the manuscript. All authors read and approved the final manuscript.

Ethics approval and consent to participate

Ethical approval for research using non-identifiable data was obtained from the Research Ethics Committee, National University of Ireland, Galway (07/SEP/12) and from the regional ethics committee in Gothenburg, Sweden (S390-08).

Competing interests

The authors declare that they have no competing interests

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5 Received: 20 November 2017 Accepted: 25 April 2018

References


Table S1 Comparison of Irish and Swedish OHCA resuscitation registries

<table>
<thead>
<tr>
<th></th>
<th>Ireland</th>
<th>Sweden</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Managing Organisation</strong></td>
<td>OHCAR is based in the HSE North West Department of Public Health and is carried out in collaboration with the National Ambulance Service, National University Institute Galway and the Pre-Hospital Emergency Care Council (PHIECC). The OHCAR Steering Group is responsible for directing the project and includes representatives from each organisation.</td>
<td>The OHCA register is based in Gothenburg, the West Coast in Sweden and collaborates with the Emergency Ambulance Services (EMS) in all 21 counties. The OHCA Steering Group members are from several counties in Sweden but there is a working group situated in Gothenburg.</td>
</tr>
<tr>
<td><strong>Funding</strong></td>
<td>OHCAR is funded by the National Ambulance Service and the Pre-Hospital Emergency Care Council</td>
<td>The register is funded by The Swedish Association of Local Authorities and Regions</td>
</tr>
<tr>
<td><strong>Patient and Event Variables</strong></td>
<td>In Ireland, statutory Emergency Medical Services use a standardised Patient Care Report (PCR) which contains a section dedicated to data collection for OHCAR. Specially designed OHCA envelopes have also been provided to each ambulance station. In the event of OHCA, practitioners place completed PCRs in OHCA envelopes. On a monthly or fortnightly basis, envelopes are collected together with all PCRs from each station. All PCRs are scanned and stored digitally and cases in OHCA envelopes are given priority in the scanning process to facilitate OHCAR. OHCAR variables are manually entered onto an electronic database. This database is then forwarded to OHCAR together with a scanned copy of each PCR for case-by-case validation.</td>
<td>There is an standard web template which will be documented in connection to a treated OHCA. The EMS crew is responsible for filling in the web template. All data is collected in a database.</td>
</tr>
<tr>
<td><strong>Time variables</strong></td>
<td>Dispatch data (i.e. time variables) is collected directly from the ambulance dispatch centre by registry staff</td>
<td>The time variables are available from the dispatch center and from the EMS medical journal.</td>
</tr>
<tr>
<td><strong>Outcome data</strong></td>
<td>Outcome data is requested by registry staff from receiving hospitals</td>
<td>Outcome data is available from medical journals from EMS and in-hospital and also from Statistics Sweden.</td>
</tr>
<tr>
<td><strong>How are missing cases identified?</strong></td>
<td>Cases that are not placed in OHCA envelopes are not processed through the OHCAR data collection system and must be identified separately. Missing case identification is performed on a monthly basis and repeated on an annual basis to capture delayed reports. First, a search of the digital scanning archive is performed based on the 'Chief Complaint' field in the PCR using the word 'arrest'. Reported cases are excluded from the results and then the digital scan of the PCR associated with each call found is viewed. Missed OHCA cases are identified and captured during the viewing process. Next, emergency control data is filtered to identify all calls with an AMPDSS designation of 'ECHO' at the time of resource deployment. A further seventeen 'DELTAR' codes that may signify arrest occurred are included in the filter. Reported calls are then excluded from the filtered list. PCRs on the filtered list are then viewed and remaining unreported OHCA cases are identified.</td>
<td>The EMS crew makes regular retrospective observations with the aim of searching undocumented OHCA. The searching procedure is performed by a digital searching programme, and manually searching if medical journals have been documented in papers. Missed OHCA cases are identified and imported to the database. Missed OHCA cases are labelled in order to identify them as retrospective data.</td>
</tr>
</tbody>
</table>
### Table S1 Comparison of Irish and Swedish OHCA resuscitation registries (continued)

<table>
<thead>
<tr>
<th>How is data quality assured in the registry?</th>
<th>Sweden</th>
<th>Ireland</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Data is received by OHCAR in an electronic database together with a scanned copy of each PCR. Each electronic entry is checked by OHCAR staff against the data in the PCR to ensure accuracy of manual data entry. Checked data is then forwarded to the OHCAR manager who performs a random check of cases before finally adding data to the master OHCAR database. For cases that are identified through the missing case identification process, data is extracted from the scanned PCR by OHCAR staff and manually entered onto an electronic database by OHCAR staff. The “missing” database is then forwarded to the OHCAR manager, who validates each entry using the corresponding scanned PCR. Once validation of the missing cases is complete, they are added to the master OHCAR database.</td>
<td>Registry data is compared to documented data in medical journals using variables such as incidence, place OHCA occurred, treatment and survival.</td>
</tr>
<tr>
<td>Variable Information</td>
<td>Ireland Missing Data n(%)</td>
<td>Sweden Missing Data n(%)</td>
</tr>
<tr>
<td>----------------------------------------------------------</td>
<td>----------------------------</td>
<td>--------------------------</td>
</tr>
<tr>
<td>Was OHCA identified by ambulance control at time of dispatch</td>
<td>270 (4.8)</td>
<td>15303 (100.0)</td>
</tr>
<tr>
<td>Was dispatch assisted CPR offered</td>
<td>5886 (100.0)</td>
<td>8386 (54.8)</td>
</tr>
<tr>
<td>Age</td>
<td>171 (2.9)</td>
<td>484 (3.2)</td>
</tr>
<tr>
<td>Gender</td>
<td>6 (0.1)</td>
<td>3 (0.0)</td>
</tr>
<tr>
<td>Who witnessed collapse</td>
<td>200 (3.8)</td>
<td>757 (4.9)</td>
</tr>
<tr>
<td>OHCA location</td>
<td>40 (0.7)</td>
<td>322 (2.1)</td>
</tr>
<tr>
<td>Home or not home location of collapse</td>
<td>Recode</td>
<td></td>
</tr>
<tr>
<td>CPR before ambulance arrival</td>
<td>197 (3.3)</td>
<td>803 (5.2)</td>
</tr>
<tr>
<td>Who started CPR</td>
<td>197 (3.3)</td>
<td>842 (5.5)</td>
</tr>
<tr>
<td>Defibrillation before ambulance arrival</td>
<td>Recode</td>
<td>2973 (19.4)</td>
</tr>
<tr>
<td>First monitored rhythm</td>
<td>234 (4.0)</td>
<td>1555 (10.2)</td>
</tr>
<tr>
<td>First monitored rhythm shockable or nonshockable</td>
<td>234 (4.0)</td>
<td>1555 (2.5)</td>
</tr>
<tr>
<td>Presumed aetiology</td>
<td>0 (0.0)</td>
<td>0 (0.0)</td>
</tr>
<tr>
<td>Medical or non medical aetiology</td>
<td>Recode</td>
<td>0 (0.0)</td>
</tr>
<tr>
<td>Call-Response interval***</td>
<td>810 (15.2)</td>
<td>1030 (8.4)</td>
</tr>
<tr>
<td>Call to defibrillation interval****</td>
<td>811 (39.1)</td>
<td>801 (15.0)</td>
</tr>
<tr>
<td>Epinephrine administered</td>
<td>54 (0.9)</td>
<td>314 (2.1)</td>
</tr>
<tr>
<td>Airway control type</td>
<td>505 (8.6)</td>
<td>9868 (64.5)</td>
</tr>
<tr>
<td>Mechanical CPR</td>
<td>343 (5.8)</td>
<td>1938 (12.7)</td>
</tr>
<tr>
<td>Transported to hospital</td>
<td>1 (0.0)</td>
<td>118 (0.8)</td>
</tr>
<tr>
<td>Any ROSC</td>
<td>192 (3.3)</td>
<td>892 (5.8)</td>
</tr>
<tr>
<td>ROSC or alive on arrival at hospital</td>
<td>275 (4.7)</td>
<td>240 (1.6)</td>
</tr>
<tr>
<td>Discharged alive or alive at 30 days</td>
<td>64 (1.1)</td>
<td>289 (1.9)</td>
</tr>
<tr>
<td>CPC at discharge from hospital****</td>
<td>80 (22.9)</td>
<td>795 (47.2)</td>
</tr>
</tbody>
</table>

*Original (taken directly from national register), Derived (variables or variable lists from national register combined to create single study variable or similar options for both registries), Recode (number of variables options reduced to facilitate analysis)

**Variable excluded from study due to excess missing data in either or both countries

***Not EMS-witnessed cases (Ireland n=5,342; Sweden n=12,335)

****For cases where defibr attempted (Ireland n=2,072 ; Sweden n=5,327)

*****For cases where survival to discharge or 30 days confirmed (Ireland = 350; Sweden = 1,886)
<table>
<thead>
<tr>
<th>Survival</th>
<th>Adjusted Odds Ratio (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sweden</td>
<td>3.60 (1.95-6.68)</td>
</tr>
<tr>
<td>Age (in years)</td>
<td>0.96 (0.86-0.97)</td>
</tr>
<tr>
<td>Male</td>
<td>1.79 (1.00-3.23)</td>
</tr>
<tr>
<td>Not at home</td>
<td>2.41 (1.96-2.97)</td>
</tr>
<tr>
<td>CPR before ambulance arrival</td>
<td>1.40 (1.05-1.84)</td>
</tr>
<tr>
<td>Defibrillation attempted before ambulance arrival</td>
<td>1.40 (1.78-2.88)</td>
</tr>
<tr>
<td>Call Response Interval 5 minutes or less</td>
<td>2.25 (1.78-2.86)</td>
</tr>
</tbody>
</table>

**Model Fit**

Nagelkerke R² adjusted 0.17

Hosmer and Lemeshow Test not significant for any imputations
Chapter 7  Appendix


Out-of-hospital cardiac arrest survival in international airports

*Resuscitation, 127:58-62*
Clinical paper

Out-of-hospital cardiac arrest survival in international airports*

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A R T I C L E   I N F O

Keywords:
Out-of-hospital cardiac arrest
Resuscitation
International epidemiology
survival

A B S T R A C T

Background: The highest achievable survival rate following out-of-hospital cardiac arrest is unknown. Data from airports serving international destinations (international airports) provide the opportunity to evaluate the success of pre-hospital resuscitation in a relatively controlled but real-life environment.

Methods: This retrospective cohort study included all cases of out-of-hospital cardiac arrest at international airports with resuscitation attempted between January 1st, 2013 and December 31st, 2015. Cardiac arrest, patient, event characteristics and survival to hospital discharge/survival to 30 days (survival) were calculated. Multivariable logistic regression analyses were performed to identify predictors of survival. Variability in survival between airports/countries was quantified using the mean odds ratio.

Results: There were 800 cases identified, with an average of 40 per airport. Incidence was 0.024/100,000 passengers per year. Percentage survival for all patients was 22%, and 58% for patients with an initial shockable heart rhythm.

In adjusted analyses, initial shockable heart rhythm was the strongest predictor of survival (odds ratio, 30.7; 95% confidence interval [CI], 15.5-67.0). In the bystander-witnessed subgroup, delivery of a defibrillation shock by a bystander was a strong predictor of survival (odds ratio 4.8; 95% CI, 3.0-7.8). Grouping of cases was significant at country level and survival varied between countries.

Conclusions: In international airports, 32% of patients survived an out-of-hospital cardiac arrest, substantially more than in the general population. Our analysis suggested similarity between airports within countries, but differences between countries. Systematic data collection and reporting are essential to ensure international airports continually maximise activities to increase survival.

Introduction

The purpose of pre-hospital resuscitation systems is to optimise survival from out-of-hospital cardiac arrest (OHCA) by implementing the Chain of Survival [1]. The first three links in the Chain – early recognition and call for help, immediate cardiopulmonary resuscitation...
(CPR) early defibrillation – must all be initiated immediately and ef-
fectively in the pre-hospital environment. Due to the variability in re-
ported survival worldwide, a key question for policy makers and health
 caregivers is, in an 'ideal world', what is the best survival from
OHCA that can be achieved?
In 2015, the Cardiac Arrest Registry to Enhance Survival (CARES) in
the United States collected data from 12 state-based registries and 50
community sites. It was estimated that the incidence of non-traumatic
OHCA with reanimation attempted was 57 per 100,000 population, with
survival to discharge in 9% [1]. In a one-month study during October
2014, OHCA incidence across 27 European countries with re-
animation attempted ranged from 39 to 104 cases per 100,000 popu-
lation with an average survival of 10% for at least 30 days or to hospital
discharge [2]. In airports serving international destinations (interna-
tional airports) however, where the incidence of OHCA is low compared
to passenger throughputs, the proportion of survival is much higher than
in the general OHCA population [4-6]. International airports are un-
ique environments. They are constructed similarly, are geographically
discrete from the surrounding environs, and have a high public footfall.
Under international aviation law, international airports are required to
have on-site police, fire and rescue services [7]. In an airport, it may be
assumed that the majority of people who suffer OHCA believed them-
selves to be fit enough to go to work or to travel on that day. Inter-
national airports therefore can be considered a natural laboratory to
evaluate how successful pre-hospital resuscitation is in a relatively
controlled real life situation.
The primary aim of this study was to determine survival from OHCA at
international airports with resuscitation attempted. The study also
aimed to estimate the incidence of OHCA at international airports and
to identify the impact of known predictors of OHCA survival.
Methods
This was a retrospective cohort study of all cases of OHCA at in-
ternational airports with resuscitation attempted over a 3-year period
from the 1st of January 2013 to the 31st of December 2015. Thirty-
four countries were requested to provide data. In 32 countries, data
was requested by contacting individuals who had previously published
using OHCA registry data in that country. Those individuals then ad-
vanced to distribute a request for international airport data in their
country, or personally assisted with the provision of data, in line with
ethical and data protection requirements in their jurisdiction. In 2 coun-
tries, data was not established, and therefore direct contact with international airports in
both countries was attempted. Between October 2016 and February
2017 attempts were made to approach countries in which data was
available, excluding airports in China, using either repeat emails or by pursuing alternative contacts.
Data requested included patient age and gender, witnessed status
(not witnessed/bystander/emergency medical services (EMS)), initial
arrest rhythm (asystole/pulseless electrical activity/shockable/un-
specifiable nonshockable), CPR before EMS arrival (bystander CPR (yes/-
nos)), shock delivered using an automated external defibrillator (AED)
before EMS arrival (bystander AED defibrillation attempted (yes/no));
interval in minutes from emergency call to emergency medical services
arrival (EMS call-response interval); survival to hospital discharge (yes/
no). Participating countries were also requested to provide data on the
passenger throughput of each international airport for each year of data
provided. Country data was obtained based on the agreement that no
airport or individual country was identified during the analysis or in the
study results.
Overall crude incidence of OHCA with resuscitation attempted per
100,000 passengers per year was calculated and descriptive analyses of
patients, event characteristics and outcome were performed. Survival to
hospital discharge or survival at 30 days (survival) was calculated for the
study population and for subgroups of each categorical variable.
Mixed effect logistic regression analyses were performed to identify
predictors of survival. Predictors of survival were estimated for the
entire study population.
In order to assess whether there was grouping of variables at airport
and/or country level, null empty single (patient level only), 2-level
(patient and airport level: patient and country level) and 3-level (pa-
tient, airport and country level) logistic regression models for survival
were compared using the likelihood ratio test, plots of random effects
and the effect on resulting odds ratios (ORs) [8]. Plots of random effects
were used to allow interpretation of differences in the mean residual
effect or area (airport or country) level of the model before any predictor variables are added to the model [9]. Due to multilateralism,
separate estimates of regression coefficients for survival were calcu-
lated for each known predictor of survival, with each model adjusted to
account for patient age and gender, resulting in 6 final models. Coef-
ficients were transformed into ORs to aid interpretation. To quantify the
variability between airports/countries in survival, the adjusted model with
all predictor variables in the models was used to calculate an odds
ratio for each known predictor of survival. A C statistic equal to one
signifies no differences between airports/countries in the probability of
survival from OHCA. As a OR is a measure of random effects, a Baye-
sian credible interval (CI) was calculated based on the distribution of
the OR to distinguish it from a fixed effects OR confidence interval
(MLwiN version 2.35). Model fit was assessed using the deviance in-
formation criterion (DIC). A lower DIC suggested a better model fit, and
a difference of less than 5 in model DIC is considered sufficient to
distinguish between two models [10].
The study was approved by the Research Ethics Committee of the
National University of Ireland Galway (Ref: 16-EPH-18). Informed
consent was not required as non-identifiable data was used. The cor-
responding author had full access to all the data in the study and taken
responsibility for its integrity and the data analysis.
Results
Data on 800 OHCA cases with resuscitation attempted were re-
cieved from 70 airports in 9 countries in all. Of cases: 1) 174
cases (22%) were not witnessed by bystander; 2) 74 cases
(9%) were bystander witnessed but not attended by AED;
3) 364 cases (45%) were bystander witnessed and attended
by AED; 4) 108 cases (14%) were EMS witnessed but not
attended by AED; 5) 19 cases (2%) were EMS witnessed and
attended by AED; 6) 6 cases (1%) were EMS witnessed and
attended by bystander AED; 7) 9 cases (1%) were EMS
witnessed and attended by bystander CPR. A total of 59 cases
(7%) were EMS witnessed and attended by bystander CPR,
but not attended by AED. A total of 31 cases (4%) were EMS
witnessed and attended by bystander CPR and bystander
AED. Of the 800 cases, 726 (91%) were witnessed and 74
(9%) were not witnessed. Of the 74 non-witnessed cases,
63 (85%) were EMS attended but not witnessed. In total,
772 (97%) were witnessed and 28 cases (3%) were not
witnessed.
The incidence of OHCA in the 38 countries for which data was
available is presented in Table 1. In total, 105 (13%) of all
800 OHCA cases were witnessed by bystander, and 695
(86%) were witnessed by EMS. In total, 772 (97%) were
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witnessed and 28 cases (3%) were not witnessed.
Table 1: Patient, event and survival characteristics.

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>n (%)</th>
<th>Percentage 5-year survival (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>580 (73)</td>
<td>24 (20-28)</td>
</tr>
<tr>
<td>Female</td>
<td>195 (27)</td>
<td>25 (20-32)</td>
</tr>
<tr>
<td>Age in years</td>
<td></td>
<td></td>
</tr>
<tr>
<td>≥ 65</td>
<td>442 (44.8)</td>
<td>NA</td>
</tr>
<tr>
<td>Initial heart rhythm</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Shockable</td>
<td>325 (42)</td>
<td>55 (49-60)</td>
</tr>
<tr>
<td>Unspecified nonshockable</td>
<td>114 (18)</td>
<td>27 (19-38)</td>
</tr>
<tr>
<td>Palpable Electrical Activity</td>
<td>187 (14)</td>
<td>12 (7-21)</td>
</tr>
<tr>
<td>Asystole</td>
<td>200 (29)</td>
<td>4 (2-7)</td>
</tr>
<tr>
<td>Witness status</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bystander witnessed</td>
<td>581 (74)</td>
<td>26 (22-30)</td>
</tr>
<tr>
<td>EMS witnessed</td>
<td>77 (10)</td>
<td>26 (19-36)</td>
</tr>
<tr>
<td>Not witnessed</td>
<td>125 (16)</td>
<td>12 (7-19)</td>
</tr>
<tr>
<td>Bystander CPR?</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>450 (77)</td>
<td>57 (53-61)</td>
</tr>
<tr>
<td>No</td>
<td>153 (23)</td>
<td>55 (28-62)</td>
</tr>
<tr>
<td>Bystander AED defibrillation attempted</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>147 (14)</td>
<td>56 (51-61)</td>
</tr>
<tr>
<td>No</td>
<td>319 (30)</td>
<td>25 (23-30)</td>
</tr>
<tr>
<td>EMS call-response interval</td>
<td></td>
<td></td>
</tr>
<tr>
<td>≤ 5 minutes or less</td>
<td>183 (14)</td>
<td>37 (20-30)</td>
</tr>
<tr>
<td>&gt; 5 minutes</td>
<td>205 (46)</td>
<td>27 (23-32)</td>
</tr>
<tr>
<td>Discharged alive or 30-day survival</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>221 (32)</td>
<td>NA</td>
</tr>
<tr>
<td>No</td>
<td>498 (68)</td>
<td>NA</td>
</tr>
</tbody>
</table>

CPR, cardiopulmonary resuscitation; EMS, Emergency Medical Services.

* Mean (standard deviation).
* Bystander witnessed cases only.
* Excludes EMS witnessed.

(20%).

The likelihood ratio test suggested that there was variable grouping at both airport and country level. When compared to the 2-level patient and country-only model however, the use of the 3-level model (patient, airport and country) did not alter the mOR for country or the individual Ols for the predictor variables, suggesting that most of the group-level variability was at country level. Catterpillar plots of random effects at airport level and country level confirmed that most of the group-level variation observed was accounted for by country, with only one airport having a 95% confidence interval for residual effect that was significant (Fig. 3a & b). For this reason the less complex 2-level model was used to account for country-level grouping.

Table 2 presents the mixed effect logistic regression models for each predictor variable. Male gender was a significant predictor of survival, while patient age showed no association (Model 1). All initial heart rhythms were strongly predictive of survival when compared to asystole, including the unspecified nonshockable category (Model 2). When compared to non-witnessed status, bystander witnessed and EMS witnessed status were similarly predictive of survival (Model 3). In the bystander-witnessed subgroup, bystander CPR did not influence patient survival however attempted bystander AED defibrillation was a strong predictor of survival (Models 4-6). In the subgroup of patients who did not have an EMS-witnessed collapse, EMS call-response interval was not associated with improved survival (Model 6). Addition of predictor variables significantly improved fit for all models.

The cluster effect or country level variance in presented as mOR and the higher the mOR the more pronounced the difference between countries. The lower mOR for country level effect was 1.8 in the model with initial heart rhythm, and the highest mOR was 2.6 in the model with bystander AED defibrillation attempted.

Discussion

To the best of our knowledge, the proportion of OHCA survival observed in our study is among the highest achieved for any location worldwide. Systematic OHCA data collection and reporting in international airports can identify strengths and weaknesses in pre-hospital resuscitation interventions. These could then be acted upon as part of continual quality improvement in individual airports to sustain and maybe even increase overall airport OHCA survival rates.

In international airports, the incidence of OHCA in relation to the passenger throughput is low, but the frequency of events is relatively high. In a state-wide study in Arizona over a 3-year period, Moon et al identified the 'top' loction types of OHCA incidents [1-2]. These included 65 events across all public business/office/workplaces; 42 events across all outdoor recreation facilities and 39 events across all Arizona's stores and malls. This compares to an average of 41 cases per airport across a 3-year period in our study. The population in an international airport is mobile and relatively healthy compared to the general population and a collapse is more likely to be observed by staff or a member of the public. The majority of events had the characteristics that determine survival: predominantly witnessed; a high proportion of initial shockable rhythm; a high proportion of bystander CPR and attempted bystander AED defibrillation.

Registries with nationwide coverage have reported OHCA survival of 5% in Japan, 6% in Ireland and 7% in England. After decades of quality improvement initiatives, survival in Denmark and Sweden has reached 11% and 14% in Norway [13-18]. The large scale, collabora-

Fig. 1a & b Catterpillar plots of mean residual effects for (a) airports and (b) country.

Y-axis = Mean residual effect is a measure of the area (airport or country) level variance in survival prior to the addition of predictor variables to the model. If the error bars for the mean residual effect do not cross 0, that airport or country is significantly different to the other airports or countries.

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Table 3: Measures of association between individual and scene characteristics and OHCA survival.

<table>
<thead>
<tr>
<th>Measure of Association</th>
<th>Model 1</th>
<th>Model 2</th>
<th>Model 3</th>
<th>Model 4</th>
<th>Model 5</th>
<th>Model 6</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hazard ratio (HR)</td>
<td></td>
<td></td>
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<td></td>
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</tr>
<tr>
<td>Overall Survival</td>
<td>1.4 (1.2-2.4)</td>
<td>1.0 (0.8-1.3)</td>
<td>1.6 (1.0-2.7)</td>
<td>1.7 (1.2-2.5)</td>
<td>1.7 (1.2-2.5)</td>
<td>1.5 (1.0-2.5)</td>
</tr>
<tr>
<td>Age (years)</td>
<td>1.6 (1.2-2.1)</td>
<td>1.0 (0.8-1.1)</td>
<td>1.0 (0.8-1.2)</td>
<td>1.1 (0.8-1.5)</td>
<td>1.1 (0.8-1.5)</td>
<td>1.0 (0.8-1.5)</td>
</tr>
<tr>
<td>Location radius (km)</td>
<td>1.0 (0.8-1.2)</td>
<td>1.0 (0.8-1.1)</td>
<td>1.0 (0.8-1.2)</td>
<td>1.0 (0.8-1.5)</td>
<td>1.0 (0.8-1.5)</td>
<td>1.0 (0.8-1.5)</td>
</tr>
<tr>
<td>Scene type (Ambulance)</td>
<td>1.6 (1.2-2.0)</td>
<td>1.0 (0.8-1.0)</td>
<td>1.0 (0.8-1.2)</td>
<td>1.1 (0.8-1.5)</td>
<td>1.1 (0.8-1.5)</td>
<td>1.0 (0.8-1.5)</td>
</tr>
<tr>
<td>Bystander witnessed</td>
<td>4.0 (2.5-6.7)</td>
<td>3.0 (1.8-4.2)</td>
<td>3.0 (1.8-4.2)</td>
<td>3.0 (1.8-4.2)</td>
<td>3.0 (1.8-4.2)</td>
<td>3.0 (1.8-4.2)</td>
</tr>
<tr>
<td>EMS witnessed</td>
<td>4.0 (2.5-6.7)</td>
<td>3.0 (1.8-4.2)</td>
<td>3.0 (1.8-4.2)</td>
<td>3.0 (1.8-4.2)</td>
<td>3.0 (1.8-4.2)</td>
<td>3.0 (1.8-4.2)</td>
</tr>
<tr>
<td>Distance [km]</td>
<td>4.0 (2.5-6.7)</td>
<td>3.0 (1.8-4.2)</td>
<td>3.0 (1.8-4.2)</td>
<td>3.0 (1.8-4.2)</td>
<td>3.0 (1.8-4.2)</td>
<td>3.0 (1.8-4.2)</td>
</tr>
</tbody>
</table>

Our population had a higher proportion of shockable rhythms than is observed in the general OHCA population. Previous research has invariably shown that patients who are in a shockable rhythm have the best chance of survival and this conclusion is highlighted by our results. The high proportion of shockable rhythms is likely to be reflective of a short interval between collapse and attempted defibrillation. In our study, 59% of patients who had a bystander defibrillation attempt survived to hospital discharge. The ROC investigation recently reported percentage survival of 65% following a bystander defibrillation attempt for patients who had an observed, shockable OHCA [27]. Both studies add to the evidence that lay responders can successfully use AEDs, which can in turn result in higher percentages of shockable rhythms and consequently greater survival. The likelihood of a relatively travel-time travelling/working population with fewer of the considerations that are more likely to result in pulseless electrical activity (PEA) and asystolic arrests, should also be acknowledged [29,30].

The frequency of OHCA in international airports is relatively high and the potential to save a life in an airport is greater than in the majority of locations where OHCA may occur. The need to continuously strive to improve survival by ensuring a strong and rapid sequence of pre-hospital resuscitation is critical in international airports as in any other community or location. In fact, the airport location has many advantages over other locations due to the constant high volume of passengers and workers, and the large proportion of public spaces. Systematic OHCA data collection and reporting in the ‘Vennus style’ is an essential step, without which it cannot be assumed that an airport is maximizing their improvement activities to increase survival [30,31].

Our study has a number of limitations. Firstly, only 9 of the countries surveyed provided data and we have no information on airport survival in non-participating countries. However, to the best of our knowledge, our study is the most comprehensive analysis of OHCA incidence and outcomes in international airports to date. Secondly, data on defibrillation and EMS call-response interval was missing for 20% of cases which may limit interpretability of our results, as may the
proportion of cases categorised as 'unspecified, nonstockable'. In order to assess the impact of missing data, odds ratios for bystander AED defibrillation attempted and EMS call-response interval were generated using imputed data but did not differ significantly from ORs where original data was used. Thirdly, in 13% of cases, the initial cardiac rhythm was reported as unspecified nonstockable. This likely is to be a consequence of AED use by bystanders, where cases have been labelled as unspecified nonstockable because the AED code summary was not immediately available and/or not subsequently interpreted. Fourthly, we did not collect information on the advanced pre-hospital interventions and in-hospital treatment available to patients. Our study however accounts for the critical pre-hospital resuscitation interventions that largely determine survival, without which advanced care and hospital interventions would be futile [32]. Finally, airport or country level variables were not collected, which means that inter-airport and inter-
country differences could not be further explored.

In conclusion, our study demonstrated that in a public location where availability of defibrillation was high, bystanders attempted defibrillation in 59% of cases, 42% of patients were in an initial shockable rhythm and almost one in three patients survived. Our findings suggest that, while public access defibrillation is not the panacea for improving OHCA survival, it has a vital role to play when strategically used in appropriate locations such as international airports.

Conflicts of interest

None to declare.

Acknowledgements

This first author is the recipient of the Health Professions Fellowship Award from the Health Research Board (HFR-2014-609). The authors wish to thank the airport and ambulance service staff who contributed to collection and processing of the data and the passengers and individuals:
- French national out of hospital cardiac arrest registry research group – Registre electronique des Arrêts Cardiaques (REAC-IRMM), Lille, France.
- Dr. Tatuya Nishihara, Amagasaki Medical Center, Japan; Mr. Nobuhiko Kimura, Hyogo Children’s Medical School, Japan; Dr. Hiroshi Tanaka, Kansai University, Japan.
- Hildurgunn Svaravsdottir, Alæyri Hospital Iceland and University of Akureyri, Iceland; EMS and Fire service, Reykjavik, Iceland.
- Coriolen de Vries, Emergency Response Advisor and Niels Bakker, Senior Safety Advisor, Schiphol airport, the Netherlands.

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