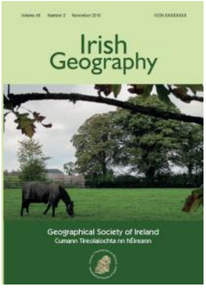

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The Spatial Distribution of Out-of-Hospital Cardiac Arrest and the Chain of Survival in Ireland: A Multi-Class Urban-Rural Analysis

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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

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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 OHCAs 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 care[1]. 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 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.,* (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

Category	**Description**
Medical	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
Traumatic:	Cardiac arrest directly caused by blunt, penetrating or burn injury
Drug overdose:	Evidence that the cardiac arrest was caused by deliberate or accidental overdose of prescribed medications, recreational drugs or ethanol
Drowning	Victim is found submersed in water without an alternative causation
Electrocution	Any case where electrocution is primary and obvious causes of arrest
Asphyxial	External causes of asphyxia, such as foreign-body airway obstruction, hanging or strangulation

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 aetiology 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 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 (Perkins *et al.,* 2015c). The introduction of CPR feedback technology has allowed the effect of CPR quality in EMS systems to be measured and Vadeboncoeur *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 OHCAs 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 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.,* (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.

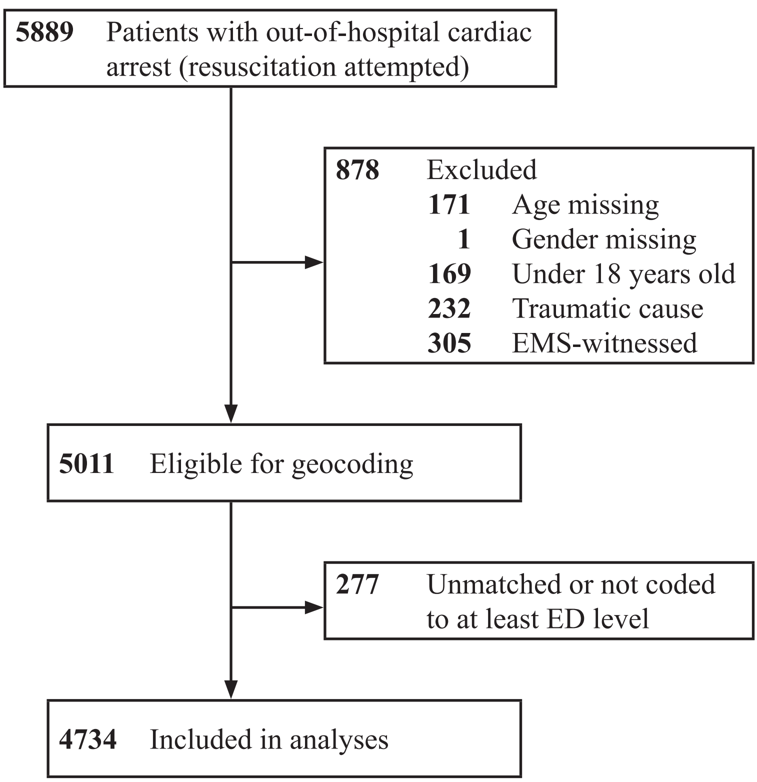
In summary, the studies described in this section show that while methodologies are transferable, local analysis of local data will often reveal unique results and also highlight the importance of correct geocoding in area-based studies. In this context, it is worth stressing that to date no study has 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 1st January 2012 to 31st 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



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; 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 (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 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 (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 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 $p>0.05$).

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

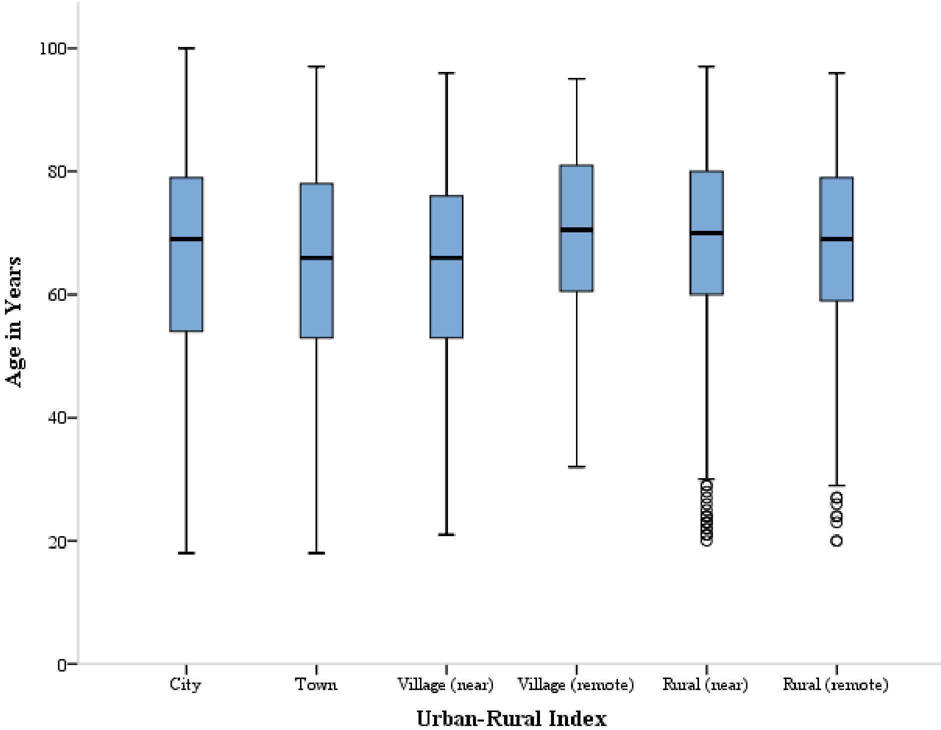


Table 1: Characteristics of Study Cases by Urban-Rural Class

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

†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

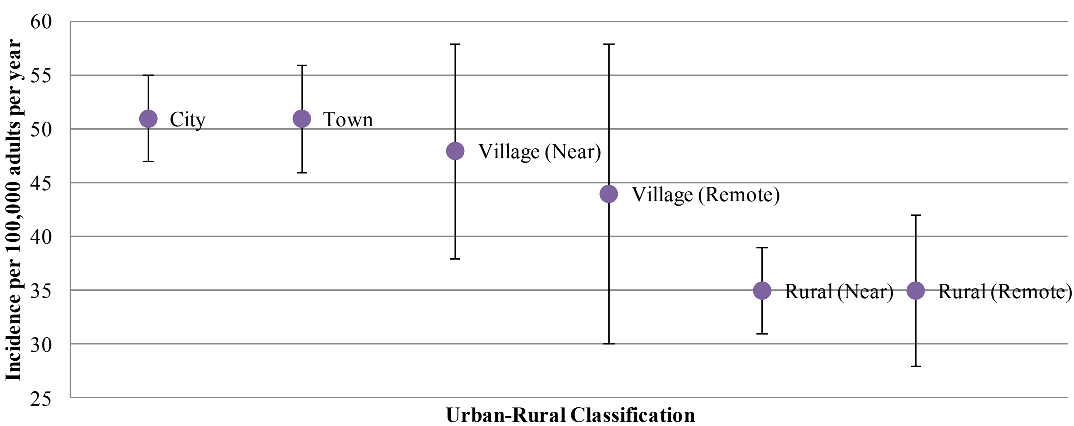


Figure 5: Boxplots of Median Ambulance Travel Distance from ED Centroid categorised by Urban-Rural Class

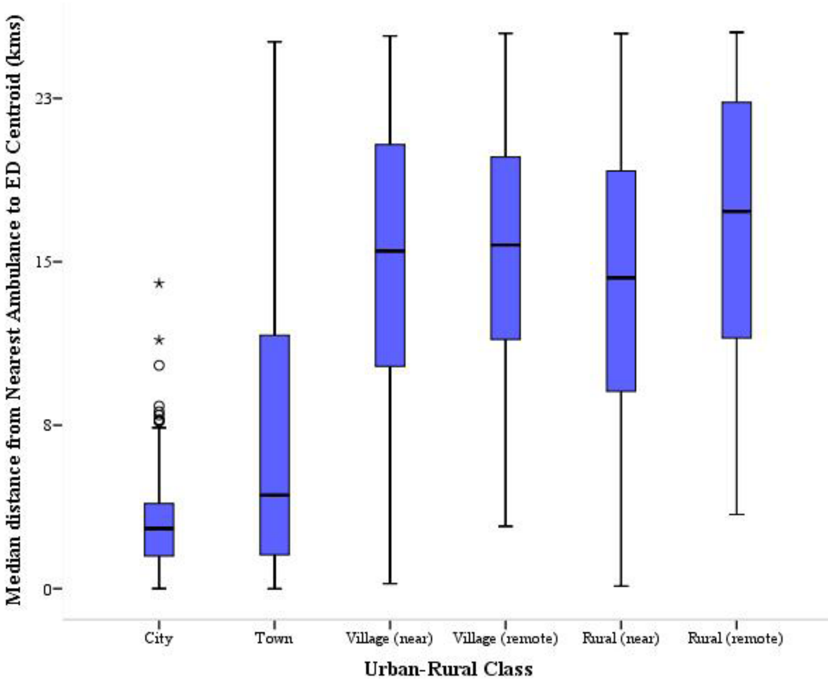


Table 2: Adjusted Incidence and Markers of Chain of Survival Availability in each Urban-Rural Class

Characteristic	City	Town	Village (near)	Village (remote)	Rural (near)	Rural (remote)	p value	Overall	Missing Data, No. (%)
OHCA cases, No. (%)	1761 (37)	1465 (31)	301 (6)	104 (2)	778 (16)	325 (7)	NA	4734 (100)	0 (0)
Adjusted incidence per 100,000 adults per year (95% CI)	51 (47-55)	51 (46-55)	48 (39-58)	44 (29-58)	35 (31-40)	35 (28-42)	0.017††	46 (44-48)	0 (0)
Arrest Recognition, No. (%)	1150 (68)	479 (67)	188 (66)	192 (63)	923 (64)	62 (61)	0.004††	2994 (66)	217 (5)
B-CPR, No. (%)	932 (55)	550 (69)	243 (78)	226 (79)	978 (73)	80 (77)	0.000††	3009 (66)	160 (3)
B-defib, No. (%)	65 (4)	47 (7)	25 (11)	31 (9)	100 (6)	9 (8)	0.005††	277 (6)	137 (3)
CRI less than eight mins, No. (%)	478 (29)	45 (29)	7 (9)	25 (4)	390 (6)	4 (2)	0.000††	949 (22)	376 (8)
Advanced EMS Intervention Provided No. (%)	1288 (75)	1118 (82)	226 (84)	82 (84)	589 (82)	256 (84)	0.000†	3559 (80)	171 (4)
Ambulance Travel Distance in kms, median (IQR)	3 (2-4)	4 (2-12)	16 (11-20)	16 (12-20)	15 (10-19)	17 (12-23)	0.000†	13668 (8757)	0 (0)

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 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 (Strömsöe *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.

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Figure A1: The Six Categories of Urban-Rural Classification

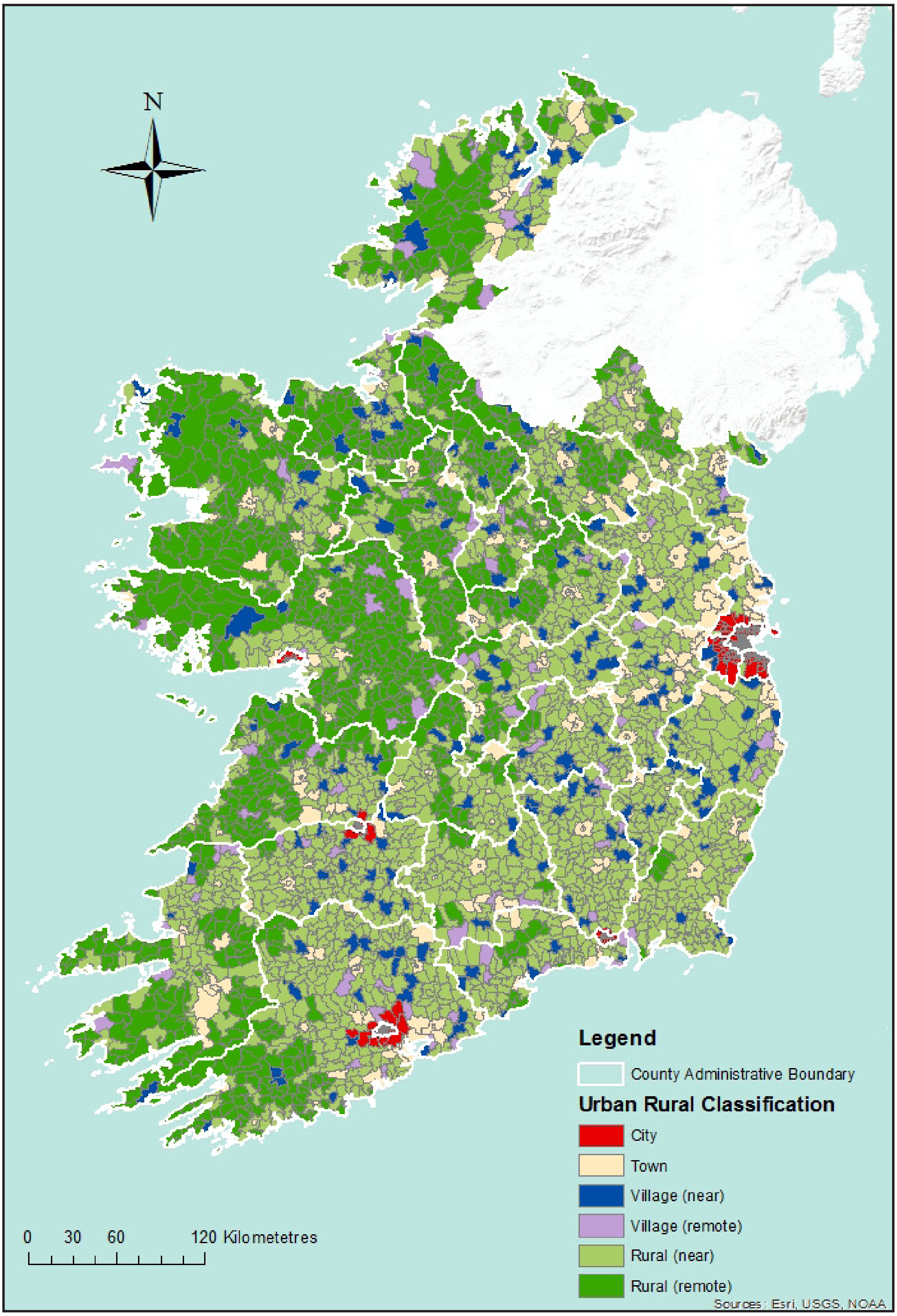

Table A1: Distribution of Urban-Rural Classes by County

County	**City**	**Town**	**Village (Near)**	**Rural (Near)**	**Village (Remote)**	**Rural (Remote)**
CARLOW		9.30%	14.80%	**74.10%**		1.90%
CAVAN COUNTY		9.00%	6.70%	40.40%	1.10%	42.70%
CLARE COUNTY	0.70%	7.90%	5.30%	36.40%	2.60%	47.00%
CORK CITY	**100.00%**					
CORK COUNTY	3.10%	10.20%	6.20%	**52.80%**	3.40%	24.40%
DONEGAL COUNTY		10.10%	8.10%	38.90%	4.00%	38.90%
DUBLIN CITY	**100.00%**					
DÚN LAOGHAIRE-RATHDOWN	**98.60%**			1.40%		
FINGAL	40.50%	40.50%	4.80%	14.30%		
GALWAY CITY	**100.00%**					
GALWAY COUNTY		4.20%	1.40%	17.80%	3.70%	**72.90%**
KERRY COUNTY		5.50%	1.20%	40.20%	4.30%	48.80%
KILDARE COUNTY		24.70%	10.10%	**61.80%**	3.40%	
KILKENNY COUNTY	0.90%	5.30%	8.80%	**81.40%**	3.50%	
LAOIS COUNTY		8.20%	8.20%	**73.20%**	3.10%	7.20%
LEITRIM COUNTY		1.40%	8.20%	21.90%	1.40%	**67.10%**
LIMERICK CITY	**100.00%**					
LIMERICK COUNTY	2.20%	3.70%	9.60%	**80.10%**	2.20%	2.20%
LONGFORD COUNTY		9.30%	3.70%	44.40%	5.60%	37.00%
LOUTH COUNTY		32.60%	7.00%	**51.20%**	2.30%	7.00%
MAYO COUNTY		6.60%	3.30%	24.30%	1.30%	**64.50%**
MEATH COUNTY		18.50%	7.60%	**71.70%**	1.10%	1.10%
MONAGHAN COUNTY		12.90%		**52.90%**	2.90%	31.40%
NORTH TIPPERARY		8.80%	6.30%	**53.80%**		31.30%
OFFALY COUNTY		9.30%	9.30%	**60.50%**	4.70%	16.30%
ROSCOMMON COUNTY		5.50%	4.50%	27.30%	3.60%	**59.10%**
SLIGO COUNTY		5.10%	8.90%	26.60%	2.50%	**57.00%**
SOUTH DUBLIN	**93.90%**	2.00%	4.10%			
SOUTH TIPPERARY		14.70%	3.20%	**71.60%**	3.20%	7.40%
WATERFORD CITY	**100.00%**					
WATERFORD COUNTY		9.80%	6.50%	**66.30%**	5.40%	12.00%
WESTMEATH COUNTY		9.50%	6.70%	**50.50%**	1.90%	31.40%
WEXFORD COUNTY		11.30%	3.20%	**78.20%**	1.60%	5.60%
WICKLOW COUNTY		18.30%	13.40%	**65.90%**	2.40%	

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