Title: The incidence and outcomes of out-of-hospital cardiac arrest in metropolitan versus rural locations: A systematic review and meta-analysis

Authors: Ashlea Smith[1,2], Stacey Masters PhD[1], Stephen Ball PhD[1,2], Judith Finn PhD[1,2,3,4]

Affiliations:

[1]Prehospital, Resuscitation and Emergency Care Research Unit (PRECRU), Curtin School of Nursing, Curtin University, Bentley, Western Australia, Australia;

[2]St John Western Australia, Western Australia, Australia;

[3]Department of Epidemiology and Preventive Medicine, Monash University, Victoria, Australia;

[4] Emergency Medicine, Medical School, The University of Western Australia, Perth, Australia.

Corresponding Author: Ashlea Smith, PRECRU, Curtin School of Nursing, Curtin University, Perth, Western Australia; ORCID: 0000-0003-4319-4733; Email: ashlea.smith3@postgrad.curtin.edu.au

Funding: JF is funded by a National Health and Medical Research Council (NHMRC) Investigator Grant (#1174838), and AS receives a PhD Stipend Scholarship linked to this grant. SM is funded by the NHMRC Prehospital Emergency Care Centre for Research Excellence Grant (#1116453).

Word count:

Abstract- 246 words

Manuscript- 3985 words

Number of figures, tables and appendices:

Figures- 3

Tables- 2

Appendices- 4

References: 62

Abstract

Background/aims: Rurality poses a unique challenge to the management of out-of-hospital cardiac arrest (OHCA) when compared to metropolitan (metro) locations. We conducted a systematic review of published literature to understand how OHCA incidence, management and survival outcomes vary between metro and rural areas.

Methods: We included studies comparing the incidence or survival of ambulance attended OHCA in metropolitan and rural areas, from a search of five databases from inception until 9th March 2022. The primary outcomes of interest were cumulative incidence and survival (return of spontaneous circulation, survival to hospital discharge (or survival to 30 days)). Meta-analyses of OHCA survival were undertaken.

Results: We identified 28 studies (30 papers- total of 823,253 patients) across 13 countries of origin. The definition of rurality varied markedly. There was no clear difference in OHCA incidence between metro and rural locations. Whilst there was considerable statistical heterogeneity between studies, the likelihood of return of spontaneous circulation on arrival at hospital was lower in rural than metro locations (OR=0.53, 95% CI 0.40, 0.70; I^2=89%; 5 studies; 90,934 participants), as was survival to hospital discharge/survival to 30 days (OR= 0.52, 95% CI 0.38, 0.71; I^2=95%; 15 studies; 18,837 participants).

Conclusions: Overall, while incidence did not vary, the odds of OHCA survival were estimated to be approximately 50% lower in rural areas compared to metro areas. This suggests an opportunity for improvement in the prehospital management of OHCA within rural locations. This review also highlighted major challenges in standardising the definition of rurality in the context of cardiac arrest research.

Introduction

Out of hospital cardiac arrest (OHCA) is a significant public health issue,[1] with an average global incidence of approximately 55 adult cases per 100,000 person-years,[2, 3] and survival of less than 10%.[1] While average survival is low, there is evidence that OHCA survival and incidence varies between jurisdictions (i.e. between nations, provinces/states, or smaller government areas).[2-5] Such comparisons are important in highlighting potential opportunities for improvement in the various factors that have been identified as contributing to OHCA survival.[6-8] The early instigation of several modifiable factors have been shown to improve outcomes, including early recognition of cardiac arrest during emergency calls, bystander cardiopulmonary resuscitation (CPR), defibrillation, advanced life support and access to evidence based post resuscitation care.[8-11]

While a large focus of geographic comparisons of OHCA incidence and survival has been between jurisdictions, another geographic basis for comparison is between rural and metropolitan (metro) populations. Studies have suggested that rurality impacts the management and survival of OHCA[5, 12], however, the full impact has not yet been thoroughly explored. Rurality is known to be a major factor impacting on many health outcomes, including aspects of cardiac health. A systematic review by Butland et al[13] noted that compared to metro areas, patients in rural areas travel further to access medical resources, and are less likely to participate in prevention strategies, particularly programs targeting cardiac health. A review by Alanazy et al[14] reported that patients in rural areas experienced longer EMS (Emergency Medical Services) response times, longer transport times to health facilities and had poorer survival rates, across a range of health conditions. The aim of this systematic review was to compare the incidence, management, and survival outcomes of OHCA between rural and metropolitan locations.

Methods

This systematic review was conducted and reported in line with the Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) statement.[15] Prior to commencement, the systematic review methodology was registered in the International Prospective Register of Systematic Reviews (no. CRD42021270207).

Eligibility criteria

Papers were selected based on predetermined inclusion and exclusion criteria as per the PECOST framework[16], as follows:

P- The population of interest included adult/paediatric OHCA patients attended by EMS/ambulance in any location internationally. There was no restriction on age, sex, arrest aetiology, diagnostic criteria or witness status.

E- The exposure of interest was a rural/remote location. All definitions of “rural” (or variations of this term) were accepted. Where a population density scale was used, the “rural” exposure was considered met if the authors provided a definition of which population density range was considered to characterize “rural”. Where no such categorisation of rurality was clearly specified, the paper was excluded.

C- The comparator was metro/urban location, as specified by the study authors.

O- The outcomes of interest included cumulative incidence and any of the following survival outcomes: Return of Spontaneous Circulation (ROSC), Survival To Hospital Discharge (STHD) (%) or survival to 30 days (%) and survival to 1 year (%); or measures of effect (risk difference and risk ratio, or odds ratio). To be included, the paper was required to report at least one of these outcomes- incidence and/or survival.

S- All study types, including RCTs and observational studies, aside from grey literature and case reports, were included. No restrictions were placed on country of origin, or language, however abstracts were required to be in English.

T- No restrictions were placed on publication date

Search strategy and selection process

A search of the databases CINAHL, Scopus, EMBASE, Cochrane and Medline (from database inception) was initially conducted on the 24th August 2021, and updated on 9th March 2022. The search strategy, developed in conjunction with a Curtin University librarian, is shown in Appendix 1. Initial search results and screening was managed in Rayyan.[17] . The results were screened by two reviewers (AS and SM) independently, and any disagreements were resolved with consensus or arbitration by a third reviewer (JF). Conference abstracts that met the search criteria were included, with attempts made to source the published full text and contact the authors where full text papers were not found. All reference lists for selected studies were searched for additional studies.

Data extraction

Data were extracted from the selected studies using a pre-prepared data extraction spreadsheet. The data extracted included study characteristics (publication year, country, study inclusion criteria), participant characteristics (cohort/sample size, age range, sex), the definition of rurality, arrest characteristics (bystander witness status, bystander CPR provision, initial shockable rhythm presence, AED usage, aetiology of arrest and EMS response time) and outcomes (incidence and crude survival outcomes). The data extraction table was reviewed by JF and SM prior to data extraction, and data entry verified by SM.

Critical appraisal

Critical appraisal was performed independently by two reviewers (AS and JF) using the Joanna Briggs Institute (JBI) Critical Appraisal Tools.[18] The appropriate checklist was selected according to the type of study. A series of questions relevant to the specific study type were used to assess how the authors addressed bias and confounding, the validity of the study and statistical analysis, and methodological reliability. In relation to confounding, we focused on whether the study controlled for case mix, i.e., age, sex, aetiology and witness status. The responses to the questions included “yes” (indicating higher quality), “no” (indicating poorer quality) and “unclear”. Where disagreements arose, these were resolved by consensus, or arbitrated by a third reviewer. The assessments were tabulated and included in Appendix 2.

Synthesis of results

All patient and arrest characteristics, and outcomes of interest were summarised in tables. Due to different definitions of rurality between the studies, we regrouped the categories of some studies to enable a binary metro vs rural comparison. For example, with studies that separately reported results for ‘suburban’ and ‘metropolitan’ categories, we combined these as ‘metropolitan’. Similarly, with studies that separately reported results on ‘remote’, ‘very remote’ and ‘rural’ categories, we combined these as ‘rural’.

Cumulative incidence was presented for those studies that reported this variable. We produced forest plots using RevMan[19] of the effect of rurality on ROSC and STHD/survival to 30 days to display effect estimates and confidence intervals for both individual studies and summary effects - using the Mantel-Haenszel random effects model.[20] Decisions about the conduct of meta-analyses were based on assessment of clinical heterogeneity, methodological heterogeneity and statistical heterogeneity (I-squared statistic).[20]

Results

Study selection

From n=16,646 records identified in the search, 28 studies (30 papers) were selected as meeting the inclusion criteria (Figure 1). Title and abstract screening excluded the majority of the papers, primarily due to being unrelated to OHCA, or lacking a geographical location focus. At the full text screening phase, studies were excluded on the basis of the OHCA not being attended by EMS, no exposure of any participants to a clearly defined rural environment, no direct comparison between OHCA patients within metro and rural areas, and no reporting of OHCA incidence or survival outcomes. Two of the included studies[21, 22] were conference abstracts. Two studies[23, 24] had two reports published per study; a conference abstract[22, 25] and a peer-reviewed, published journal paper.[23, 26] For both cases, the data was extracted from the journal paper.[23, 26] A search of the reference lists of the included papers returned no further relevant studies.

In addition to the 30 included papers, 4 papers[27-30] were initially classified as meeting the inclusion criteria but subsequently excluded, for the reasons outlined in Appendix 3.

Study Characteristics

The included studies were conducted in different countries: four from Australia,[21, 24, 29, 31] five from the United States,[23, 26, 32-34] four from Ireland,[35-38] three from Taiwan,[39-41] two from Norway,[42, 43] three from South Korea,[44-46] two from Denmark,[47, 48] and one each from Canada,[49] the UK,[50] New Zealand,[51] Poland[52] and Finland.[53] The number of patients within the studies varied from 137[34] to 325,477.[23] Most studies reported on adult OHCA, with only two studies including both paediatric and adult arrests.[36, 46] The reported aetiology within the studies was predominantly "presumed cardiac", with some studies reporting medical aetiology,[22, 35, 37, 43] and some made no restriction based on aetiology.[36, 40, 46, 48, 51, 52] Four studies [24, 29, 32, 47] excluded cases on the basis of missing location of arrest, with 11 additional studies[23, 26, 34, 37, 39, 41, 43, 44, 46, 48, 53] excluding cases due to other missing patient/case data. Other case exclusion criteria specified in the studies were: arrests witnessed by EMS,[31, 32, 35, 37, 39, 43-45, 47] Do Not Resuscitate (DNR) orders in place or resuscitation not attempted,[31, 32, 36, 38, 39, 41, 43, 44, 49, 50, 53] traumatic or non-cardiac aetiology of arrest,[22, 23, 26, 31-33, 35, 37, 39, 41, 43, 44, 47] and patient age less than 18 years.[23, 24, 26, 29, 32, 33, 35, 37, 39, 41, 43-45, 47] Two studies[23, 48] excluded cases where OHCA occurred in health facilities, nursing homes or "transportation facilities" (e.g., airports and train stations). Four studies did not specify exclusion criteria.[21, 40, 42, 52]

The main study designs of the included studies were: cohort studies,[21-24, 26, 29, 32-34, 36, 38, 39, 41-43, 46-50, 52, 53] cross sectional studies[35, 37, 40, 44, 45, 51] and case series.[31] The majority of included studies [21, 23, 24, 26, 29, 31-33, 35-37, 39, 41, 42, 46, 47, 49, 50, 52, 53] had a primary aim of comparing OHCA incidence and/or survival outcomes in metro vs rural locations, while eight studies[34, 38, 40, 43-45, 48, 51] had a different primary aim, but reported metro/rural differences in their analyses. Some studies used overlapping cohorts (three Irish studies,[35-37] two Norwegian studies[42, 43] and two Australian studies[24, 29]). Each of these studies were included as they differed sufficiently in their study aims and the outcomes reported.

All of the included studies aside from two[32, 33] conducted an internal comparison between their metro and rural sub-cohorts, drawn from the same population. Kragholm et al[32] compared OHCA care and outcomes in urban versus non-urban in two states (North Carolina and Washington State). The Vukmir study[33] was a post-hoc analysis of OHCA patients included in a randomised controlled trial of sodium bicarbonate; comparing the survival outcomes and prognostic variables of OHCA cases across rural, suburban and urban locations.

The terminology describing the spectrum of rurality varied widely between studies (Table 1). "Metro" included urban, semi urban, town, city and near village; "rural" included remote or regional. While the studies had wide variation in their definitions of rurality (Table 1), most reported a comparison in a metro versus rural context.[21, 22, 26, 31, 32, 34, 36, 38, 39, 41, 43-45, 49, 52] Twelve studies[33, 38, 41-53] used population density as the basis for classifying rurality, with the threshold varying between studies. However, other studies compared three to a maximum of six subgroups across the spectrum of rurality.[23, 24, 29, 35, 40, 42, 47, 48, 50, 51, 53] For example, two Australian studies[24, 29] compared rurality across five categories (major cities, inner regional, outer regional, remote and very remote), and two Irish studies[35, 37] used six categories (city, town, near village, remote village, near rural and remote rural).

A number of studies[24, 29, 35, 37] used ordinal scales to classify the spectrum of rurality, developed through government derived classifications. The Australian studies[24, 29] used a geographical classification called the Australian Statistical Geographical Classification- Remoteness Areas (ASGC-RA)[54] (Table 1). This classification is applied to Census Collection Districts, derived from the use of Accessibility/Remoteness Index of Australia (ARIA), which uses a scoring-based system to indicate increasing remoteness and increasing distance to, and reduced access to amenities.[55] Two Irish studies[35, 37] used a similar scale to rank increasing rurality, using a 6-category urban-rural spectrum developed by Teljeur and Kelly[56] based on a similar premise as the ARIA scale. The United States also uses a government-developed rurality scale, called the Rural-Urban Commuting Area (RUCA) codes. This scale uses measures of population density, daily commuting and urbanization level to classify census tracts into 10 primary codes and a further 21 secondary codes to represent the metro to rural scale.[57] Two of the American studies[23, 25] also used the RUCA scale, however simplified this classification into five categories for their analysis. One other American study[26] also used this scale, however instead of comparing on an ordinal scale across 10 primary codes, they simplified this to a binary comparison of rural vs urban/suburban.

For the purposes of this review, we redefined geographic categories for eight studies[23, 29, 40, 42, 46-48, 53] as per Table 2. As Kragholm et al[32] reported two separate cohorts (North Carolina and Washington State) with a metro/rural comparison, these cohorts were analysed separately as we acknowledge that these cohorts were representative of two separate geographical areas.

Quality assessment

Given the observational design of all included studies, there was an inherent risk of bias.[58] Further assessment of the quality of the studies was conducted using the JBI quality assessment tools (Appendix 2). A number of studies[21, 33, 34, 38, 42, 50, 52] did not indicate adjustment for case mix or did not specify which variables were adjusted for. Three studies[37, 41, 46] acknowledged an exclusion of cases due to missing data, without addressing this or providing strategies to correct this. Two studies[21, 22] were conference abstracts, which did not provide specific details regarding how rurality was defined, how statistical analysis was performed, or whether confounding factors were adjusted for, and hence were considered to have a high risk of bias. No studies were excluded on the basis of their quality assessment.

Results of individual studies

Table 2 summarises the patient and arrest characteristics and incidence/survival outcomes by rural/metro area for each study. The main reported outcomes were ROSC and STHD, with 17 studies[21-23, 26, 31, 32, 36, 39-41, 43, 44, 46-49, 52] comparing ROSC between rural and metro areas and 16 studies[23, 31, 32, 34, 36, 38, 39, 41-46, 49, 50, 53] comparing STHD. Only four studies reported survival to 30 days[24, 40, 47, 48] and three reported survival to one year.[24, 34, 53] We present data for STHD and survival to 30 days as alternative measures of survival (Table 2), with recent evidence of these being interchangeable.[59] Visual inspection of forest plots (Appendix 4) showed consistency in the direction of effect across most of the studies. We decided to undertake meta-analyses to produce a summary estimate of effect – however these results should be interpreted cautiously due to high I-squared values. Some studies were excluded from the meta-analysis due to clinical and methodological heterogeneity, with the specific reasons for exclusion described under the respective outcome below.

Incidence

Incidence rates for EMS attended OHCA were reported in 13 studies,[21, 24, 29, 31, 35-37, 41, 43, 46, 50, 51, 53] with nine of those studies[24, 31, 35-37, 41, 43, 50, 53] reporting EMS attended and treated OHCA. Two of these studies[41, 53] only providing overall incidence for the cohort rather than comparing metro and rural (Table 2). There was wide variation among studies in the association between rurality and incidence. Within their cohorts, three studies[21, 46, 51] reported higher incidence rates of OHCA in rural areas; whereas five studies[31, 35-37, 50] reported higher incidence of OHCA in metro areas.

Return Of Spontaneous Circulation

The crude odds ratios (ORs) for studies[21, 31, 36, 44, 47] reporting ROSC in rural vs metro areas at ED are presented in a forest plot (Figure 2). There was a high level of statistical heterogeneity between studies; however, the meta-analysis showed that the crude odds of ROSC at ED were lower in rural locations by 47% when compared to metro locations across five included studies (OR=0.53, 95% CI 0.40, 0.70; I^2=89%; 5 studies; 90,934 participants) (Figure 2). Despite reporting ROSC at ED, the Sarkisian study[48] was excluded from the meta-analysis, as only cases with an AED applied prior to EMS arrival were included. The Pemberton study[29] was excluded from the meta-analysis as it reported standardised relative risk ratios of ROSC at ED. A sensitivity analysis (Supplementary Table 1) was conducted after removing the Munot study[21], a conference abstract, with only a minor effect observed (OR=0.49, 95% CI 0.35, 0.67; I^2=82%; 4 studies; 75,027 participants).

Survival To Hospital Discharge/Survival to 30 days

A meta-analysis showed the crude odds of STHD/survival to 30 days was lower in rural locations by 48% when compared to metro locations (OR= 0.52, 95% CI 0.38, 0.71; I^2=95%; 15 studies; 18,837 participants) (Figure 3). For the majority of the studies, the crude odds of STHD/survival to 30 days were significantly lower in rural areas than metro. However, five studies[34, 38, 39, 41, 53] had 95% CIs that included one. Three studies reporting STHD/30 day survival were excluded from the meta-analysis due to methodological heterogeneity: Sarkisian et al[48] due to only including cases with AED application prior to EMS arrival; Wang et al[40] due to only including cases with CPR or mechanical ventilation on arrival at ED; and Grubic et al[23] due to only including patients with an EMS response time of less than 60 minutes. A funnel plot was conducted to assess small trial effects (Supplementary Table 2), which showed no clear evidence of publication bias.

Other metro vs rural differences

In addition to the reporting of survival outcomes, Table 2 shows other metro/rural differences. A high proportion of patients across the studies were male, with males generally representing a larger proportion of the cases in rural areas than metro.[22, 23, 31, 34, 41, 43, 48, 49, 52] The average age of the participants across all studies and areas was approximately 60-70 years. EMS response time was shorter in metro areas than rural areas for all 13 reporting studies.[22, 23, 31, 32, 38, 39, 41, 43, 44, 46-49, 52]

Of the 17 studies[21, 23, 32, 34, 36-39, 42-49, 52] comparing bystander witness rates between rural and metro areas, nine studies[23, 32, 34, 37-39, 42, 49, 52] reported higher rates in rural areas than metro; seven studies[21, 36, 44-48] reported higher bystander witness rates in metro areas, with one paper[43] reporting that rates were equal in metro and rural areas. The rate of bystander CPR across the studies varied widely. Of the 19 studies that reported bystander CPR rates,[21, 23, 26, 31, 32, 34, 36-39, 41, 43-49, 52] 11 studies[23, 31, 36-38, 41, 43, 45, 47, 48, 52] reported higher rates in rural areas than metro. Kragholm et al[32] reported mixed findings, with higher rates of bystander CPR in metro areas of the North Carolina cohort, and higher rates in rural areas of the Washington cohort.

Of the studies[23, 26, 31, 32, 34, 36-39, 41-50, 52, 53] reporting the presence of initial shockable rhythm, little variation was noted between metro and rural areas. Twelve studies[21, 23, 32, 34, 36, 37, 39, 41, 44, 47-49] reported on AED usage, which was higher in rural areas in five studies.[34, 36, 39, 41, 44] Connolly et al[49] was the only study to report higher rates of AED use in metro areas. Four studies[23, 37, 47, 48] noted similar AED rates between metro and rural areas. Munot et al[21] reported an overall rate of approximately 10% usage across metro and rural areas combined. Kragholm et al[32] noted the rates of AED use varied between the two cohorts; the New Carolina cohort had higher rates of AED use in metro areas, whereas the Washington cohort had higher usage in rural areas.

Discussion

This systematic review identified 28 studies (30 papers) that examined the difference between rural and metro areas in the incidence and survival outcomes of OHCA. To our knowledge, this is the first systematic review to evaluate the effect of rurality specifically on OHCA survival outcomes. Our review covered studies from a variety of locations around the world, with varying methods for determining, and definitions of, rurality. We found that the incidence of OHCA varied between studies and across metro and rural areas. We also found that patients who experienced OHCA in rural areas had lower rates of ROSC and STHD/survival to 30 days when compared to patients in metro areas. Across the studies, the average patient age, relative percentages of male and female patients, initial shockable rhythm and bystander witness status were relatively similar between metro and rural areas. Rural areas also experienced longer EMS response times in comparison to metro areas. The findings from our review suggest that rurality has a much stronger effect on OHCA survival than it has on OHCA incidence. A possible reason for this, is that whereas incidence can only be influenced by factors that operate prior to the arrest (e.g. demographic composition and socio-economic factors), survival may be additionally influenced by factors that occur as part of the OHCA Chain of Survival.[60]

We observed a variety of means for identifying rurality internationally. The scales used to quantify rurality varied from ranges in population density to scales of road distance to amenities. Population density scales as a measure of rurality lacked information about distances to amenities, the availability of services, health services provision and the geography of the area that they covered.[61] The variation in terminology and definition made quantifying and comparing “metro” and “rural” challenging. While the binary division of metro vs rural was a common method of comparison across the studies, this division is inherently difficult in that it doesn’t consider extreme ends of either category or the variability across the two categories. However, given the potential for large differences in population, geography and available amenities, it is difficult to determine if a universal scale of rurality is feasible or would benefit health service planning or research, which was beyond the scope of this review.

There was wide variation in the incidence of OHCA across the studies. With less than half of the included studies reporting incidence rates, similar rates were observed across metro and rural areas. This variation could be reflective of differences in geography, population demographics, health services provision and capability across the locations of the included studies.

Meta-analysis was conducted for ROSC and STHD/survival to 30 days, demonstrating that the odds of survival in rural areas were lower than metro areas. All studies in the meta-analysis for ROSC showed lower odds of survival in rural areas. The meta-analysis for STHD/survival to 30 days showed a small number of studies with CI’s that crossed one, however still showed lower odds of survival in rural areas.

While there was a strong overall pattern of OHCA survival being lower in rural areas than metro areas, the meta-analyses showed a high level of heterogeneity between studies, with high I^2 values in all forest plots. For the purposes of comparison, we reclassified various definitions of “metro” and “rural” into a binary categories prior to meta-analyses to attempt to reduce methodological heterogeneity. Other factors, such as inclusion criteria for the cases, also introduced heterogeneity; we excluded studies from meta-analysis that differed significantly in their inclusion criteria. However, statistical heterogeneity was still noted, and these summary effects should be cautiously interpreted.

The provision of early CPR and defibrillation are factors known to be linked to improved survival in OHCA.[8, 10, 11] Notably, EMS response time for rural patients was generally longer, which is known to contribute to poorer survival rates.[12, 36, 62, 63] Interestingly, rural areas had lower survival rates despite higher rates of bystander CPR provision and AED usage. This suggests that there are other important factors that outweigh the positive effects of higher bystander CPR and AED use on survival in rural areas. One possibility is that the higher CPR and AED rates in rural areas are partly due to the longer rural response times, in providing more time prior to ambulance arrival in which CPR can be started, and in which AEDs can be accessed and used, albeit later after the arrest. It was beyond the scope of our review to assess this possibility Other factors that were not explored within this review that have been shown to contribute to lower survival rates in rural areas include the clinical capability of EMS crews in rural areas, access to tertiary level care in hospitals (e.g., access to cardiac catheterisation laboratories and intensive care units) and prolonged travel times to hospital.[6] In addition, there may aspects of the provision of bystander CPR and AED shocks that differ between rural and metro areas, such as the timing and quality of CPR provision, and the timing of AED shocks.

Limitations

We acknowledge that our search strategy was broad; this was intentionally developed to be sensitive rather than specific to minimise the risk of missing relevant studies. Given the variability in rurality definition, the assessment of the included literature required our judgement to combine some studies' rurality groups to enable comparisons. We reported crude numbers for survival outcomes for an overall affect due to the variable methods of adjustment between the studies. A high degree of methodological heterogeneity existed between the studies, limiting the inclusion of all studies in the meta-analyses, with some excluded because of clinical or methodological heterogeneity. The results of the meta-analysis should be interpreted cautiously due to high I^2 values.

Factors including EMS system composition and capability, hospital capability and comorbidities that may affect survival outcomes were not considered within this review. Due to the low number of paediatric cases included in the studies, we are unable to accurately assess the differences in paediatric survival outcomes in metro and rural areas.

Conclusion

Overall, while there was no clear difference in OHCA incidence between metro and rural areas, the crude odds of STHD are estimated to be approximately 50% lower in rural areas than metro areas . This suggests an opportunity for improvement in the prehospital management of OHCA within rural locations. This review also highlighted major challenges in standardising the definition of metro versus rural populations in the context of cardiac arrest research.

References

1. Yan S, Gan Y, Jiang N, Wang R, Chen Y, Luo Z, et al. The global survival rate among adult out-of-hospital cardiac arrest patients who received cardiopulmonary resuscitation: a systematic review and meta-analysis. Crit Care. 2020;24(1):61.
2. Berdowski J, Berg RA, Tijssen JG, Koster RW. Global incidences of out-of-hospital cardiac arrest and survival rates: Systematic review of 67 prospective studies. Resuscitation. 2010;81(11):1479-87.
3. Kiguchi T, Okubo M, Nishiyama C, Maconochie I, Ong MEH, Kern KB, et al. Out-of-hospital cardiac arrest across the World: First report from the International Liaison Committee on Resuscitation (ILCOR). Resuscitation. 2020;152:39-49.
4. Beck B, Bray J, Cameron P, Smith K, Walker T, Grantham H, et al. Regional variation in the characteristics, incidence and outcomes of out-of-hospital cardiac arrest in Australia and New Zealand: Results from the Aus-ROC Epistry. Resuscitation. 2018;126:49-57.
5. Nichol G, Thomas E, Callaway CW, Hedges J, Powell JL, Aufderheide TP, et al. Regional variation in out-of-hospital cardiac arrest incidence and outcome. JAMA. 2008;300(12):1423-31.
6. Dyson K, Brown SP, May S, Smith K, Koster RW, Beesems SG, et al. International variation in survival after out-of-hospital cardiac arrest: A validation study of the Utstein template. Resuscitation. 2019;138:168-81.
7. Huang JB, Lee KH, Ho YN, Tsai MT, Wu WT, Cheng FJ. Association between prehospital prognostic factors on out-of-hospital cardiac arrest in different age groups. BMC Emerg Med. 2021;21(1):3.
8. Sasson C, Rogers MA, Dahl J, Kellermann AL. Predictors of survival from out-of-hospital cardiac arrest: a systematic review and meta-analysis. Circ Cardiovasc Qual Outcomes. 2010;3(1):63-81.
9. Nolan JP, Neumar RW, Adrie C, Aibiki M, Berg RA, Bottiger BW, et al. Post-cardiac arrest syndrome: epidemiology, pathophysiology, treatment, and prognostication. A Scientific Statement from the International Liaison Committee on Resuscitation; the American Heart Association Emergency Cardiovascular Care Committee; the Council on Cardiovascular Surgery and Anesthesia; the Council on Cardiopulmonary, Perioperative, and Critical Care; the Council on Clinical Cardiology; the Council on Stroke. Resuscitation. 2008;79(3):350-79.
10. Hasselqvist-Ax I, Riva G, Herlitz J, Rosenqvist M, Hollenberg J, Nordberg P, et al. Early cardiopulmonary resuscitation in out-of-hospital cardiac arrest. N Engl J Med. 2015;372(24):2307-15.
11. Viereck S, Moller TP, Ersboll AK, Baekgaard JS, Claesson A, Hollenberg J, et al. Recognising out-of-hospital cardiac arrest during emergency calls increases bystander cardiopulmonary resuscitation and survival. Resuscitation. 2017;115:141-7.
12. Lyon RM, Cobbe SM, Bradley JM, Grubb NR. Surviving out of hospital cardiac arrest at home: a postcode lottery? Emerg Med J. 2004;21(5):619-24.

13. Butland M, Corones-Watkins K, Evanson AD, Cooke M. Health behaviours of rural Australians following percutaneous coronary intervention: a systematic scoping review. Rural Remote Health. 2019;19(2):4854.
14. Alanazy ARM, Wark S, Fraser J, Nagle A. Factors Impacting Patient Outcomes Associated with Use of Emergency Medical Services Operating in Urban Versus Rural Areas: A Systematic Review. Int J Environ Res Public Health. 2019;16(10).
15. Liberati A, Altman DG, Tetzlaff J, Mulrow C, Gotzsche PC, Ioannidis JP, et al. The PRISMA statement for reporting systematic reviews and meta-analyses of studies that evaluate healthcare interventions: explanation and elaboration. BMJ. 2009;339:b2700.
16. McKenzie JE, Brennan SE, Ryan RE, Thomson HJ, Johnston RV, Thomas J. Chapter 3: Defining the criteria for including studies and how they will be grouped for the synthesis. In: Higgins JPT, Thomas J, Chandler J, Cumpston M, Li T, Page MJ, Welch VA (editors). Cochrane Handbook for Systematic Reviews of Interventions version 6.3 (updated February 2022). Cochrane, 2022. Available from www.training.cochrane.org/handbook.
17. Ouzzani M, Hammady H, Fedorowicz Z, Elmagarmid A. Rayyan-a web and mobile app for systematic reviews. Syst Rev. 2016;5(1):210.
18. Moola S, Munn Z, Tufanaru C, Aromataris E, Sears K, Sfetcu R, Currie M, Lisy K, Qureshi R, Mattis P, Mu P. Chapter 7: Systematic reviews of etiology and risk. In: Aromataris E, Munn Z (Editors). JBI Manual for Evidence Synthesis. JBI, 2020. Available from https://synthesismanual.jbi.global. https://doi.org/10.46658/JBIMES-20-08.
19. Review Manager (RevMan) [Computer program]. Version 5.4, The Cochrane Collaboration. 2020.
20. Deeks JJ, Higgins JPT, Altman DG (editors). Chapter 10: Analysing data and undertaking meta-analyses. In: Higgins JPT, Thomas J, Chandler J, Cumpston M, Li T, Page MJ, Welch VA (editors). Cochrane Handbook for Systematic Reviews of Interventions version 6.3 (updated February 2022). Cochrane, 2022. Available from www.training.cochrane.org/handbook.
21. Munot S, Redfern J, Bray J, Marschner S, Von Huben A, Semsarian C, et al. 046 Bystander Cardiopulmonary Resuscitation (CPR) and use of Automated External Defibrillator (AED) for Out-of-hospital Cardiac Arrest (OHCA): Urban Versus Regional NSW. Heart Lung Circ. 2020;29:S58-S9.
22. Peters GA, Ordoobadi A, er, Cash RE, Panchal A. Cardiac arrest management in rural prehospital care. Circulation. 2020;142.
23. Grubic N, Peng YP, Walker M, Brooks SC. for the CARES Surveillance Group. Bystander-initiated cardiopulmonary resuscitation and automated external defibrillator use after out-of-hospital cardiac arrest: Uncovering disparities in care and survival across the urban-rural spectrum. Resuscitation. 2022;175:150-8.
24. Pemberton K, Franklin RC, Bosley E, Watt K. Long-term outcomes of adult out-of-hospital cardiac arrest in Queensland, Australia (2002-2014): incidence and temporal trends. Heart. 2021;107(16):1310-9.
25. Grubic N, Peng Y, Walker M, Brooks SC. Bystander cardiopulmonary resuscitation and automated external defibrillator use after out-of-hospital cardiac arrest: uncovering differences in care and survival across the urban-rural spectrum. Eur Heart J. 2021;42(SUPPL 1):659.
26. Peters GA, Ordoobadi AJ, Panchal AR, Cash RE. Differences in Out-of-Hospital Cardiac Arrest Management and Outcomes across Urban, Suburban, and Rural Settings. Prehospital Emergency Care. 2021:1-8.
27. Ringgren KB, Kragholm KH, Lindgren FL, Jacobsen PA, Jorgensen AJ, Christensen HC, et al. Out-of-hospital cardiac arrest: Does rurality decrease chances of survival? Resusc Plus. 2022;9:100208.
28. Nadeau A, Noording NAM, O'Neill G, Masterson S, Vellinga A. Outcomes and prevalence of adult out-of-hospital cardiac arrest (OHCA) by population density groups in the Republic of Ireland. Resuscitation. 2013;84:S51.

29. Pemberton K, Bosley E, Franklin RC, Watt K. Epidemiology of pre-hospital outcomes of out-of-hospital cardiac arrest in Queensland, Australia. Emerg Med Australas. 2019;31(5):821-9.
30. Takei Y, Kamikura T, Nishi T, Maeda T, Sakagami S, Kubo M, et al. Recruitments of trained citizen volunteering for conventional cardiopulmonary resuscitation are necessary to improve the outcome after out-of-hospital cardiac arrests in remote time-distance area: A nationwide population-based study. Resuscitation. 2016;105:100-8.
31. Jennings PA, Cameron P, Walker T, Bernard S, Smith K. Out-of-hospital cardiac arrest in Victoria: rural and urban outcomes. Medical J Aust. 2006;185(3):135-9.
32. Kragholm K, Hansen CM, Monk L, Starks M, Jollis JG, Granger CB, et al. Care and outcomes of urban and non-urban out-of-hospital cardiac arrest patients during the HeartRescue Project in Washington state and North Carolina. Resuscitation. 2020;152:5-15.
33. Vukmir RB. The influence of urban, suburban, or rural locale on survival from refractory prehospital cardiac arrest. American journal of emergency medicine. 2004;22(2):90-3.
34. Layon AJ, Gabrielli A, Goldfeder BW, Idris AH, Hevia A. Utstein style analysis of rural out-of-hospital cardiac arrest [OOHCA]: Total cardiopulmonary resuscitation (CPR) time inversely correlates with hospital discharge rate. Resuscitation. 2003;56(1):59-66.
35. Masterson S, Murphy AW, Vellinga A, Teljeur C, Cullinan J, Deasy C. The Effect of Rurality on Out-of-Hospital Cardiac Arrest Resuscitation Incidence: An Exploratory Study of a National Registry Utilizing a Categorical Approach. J Rural Health. 2019;35(1):78-86.
36. Masterson S, Wright P, O'Donnell C, Vellinga A, Murphy AW, Hennelly D, et al. Urban and rural differences in out-of-hospital cardiac arrest in Ireland. Resuscitation. 2015;91:42-7.
37. Masterson S, Cullinan J, Teljeur C, Vellinga A. The spatial distribution of out-of-hospital cardiac arrest and the chain of survival in Ireland: A multi-class urban-rural analysis. Ir Geogr. 2016;49(2).
38. Henry K, Murphy A, Willis D, Cusack S, Bury G, O'Sullivan I, et al. Out-of-hospital cardiac arrest in Cork, Ireland. Emergency Medicine Journal. 2013;30(6):496-500.
39. Chen Y-C, Yu S-H, Chen W-J, Huang L-C, Chen C-Y, Shih H-M. Dispatcher-Assisted Cardiopulmonary Resuscitation: Disparity between Urban and Rural Areas. Emergency Medicine International. 2020;2020:9060472.
40. Wang C-Y, Wang J-Y, Teng N-C, Chen L, Chao T-T, Tsai S-L, et al. The secular trends in the incidence rate and outcomes of out-of-hospital cardiac arrest in Taiwan-A nationwide population-based study. PLoS ONE. 2015;10(4):e0122675.
41. Hsu YC, Wu WT, Huang JB, Lee KH, Cheng FJ. Association between prehospital prognostic factors and out-of-hospital cardiac arrest: Effect of rural-urban disparities. Am J of Emerg Med. 2021;46:456-61.
42. Mathiesen WT, Bjørshol CA, Søreide E. Survival after out-of-hospital cardiac arrest victims in urban, semi-urban and rural municipalities. Resuscitation. 2016;106:e65-e6.
43. Mathiesen WT, Bjorshol CA, Kvaloy JT, Soreide E. Effects of modifiable prehospital factors on survival after out-of-hospital cardiac arrest in rural versus urban areas. Critical Care. 2018;22(1):99.
44. Park JH, Ro YS, Shin SD, Song KJ, Hong KJ, Kong SY. Dispatcher-assisted bystander cardiopulmonary resuscitation in rural and urban areas and survival outcomes after out-of-hospital cardiac arrest. Resuscitation. 2018;123:1-7.
45. Jung E, Ro YS, Park JH, Ryu HH, Shin SD. Direct Transport to Cardiac Arrest Center and Survival Outcomes after Out-of-Hospital Cardiac Arrest by Urbanization Level. J Clin Med. 2022;11(4).
46. Ro YS, Cho S-I, Shin SD, Kim JY, Park CB, Suh GJ, et al. A trend in epidemiology and outcomes of out-of-hospital cardiac arrest by urbanization level: A nationwide observational study from 2006 to 2010 in South Korea. Resuscitation. 2013;84(5):547-57.
47. Moller SG, Rajan S, Moller-Hansen S, Kragholm K, Ringgren KB, Folke F, et al. Pre-hospital factors and survival after out-of-hospital cardiac arrest according to population density, a nationwide study. Resusc Plus.4:100036.

48. Sarkisian L, Mickley H, Schakow H, Gerke O, Starck SM, Jensen JJ, et al. Longer retrieval distances to the automated external defibrillator reduces survival after out-of-hospital cardiac arrest. Resuscitation. 2022;170:44-52.
49. Connolly MS, Goldstein PJP, Currie M, Carter AJE, Doucette SP, Giddens K, et al. Urban-Rural Differences in Cardiac Arrest Outcomes: A Retrospective Population-Based Cohort Study. CJC Open. 2022;4(4):383-9.
50. Soo L, Huff N, Gray D, Hampton JR. Geographical distribution of cardiac arrest in Nottinghamshire. Resuscitation.48(2):137-47.
51. Dicker B, Swain A, Wong S, Smith T, Todd V, Garrett N, et al. Relationship between socioeconomic factors, distribution of public access defibrillators and incidence of out-of-hospital cardiac arrest. Resuscitation. 2019;138:53-8.
52. Cebula GM, Osadnik S, Wysocki M, Dyrda M, Chmura K, Nowakowski M, et al. Comparison of the early effects of out-of-hospital resuscitation in selected urban and rural areas in Poland. A preliminary report from the Polish Cardiac Arrest Registry by the Polish Resuscitation Council. Kardiol Pol. 2016;74(4):356-61.
53. Hiltunen P, Kuisma M, Silfvast T, Rutanen J, Vaahersalo J, Kurola J, et al. Regional variation and outcome of out-of-hospital cardiac arrest (ohca) in Finland - the Finnresusci study. Scand J Trauma Resusc Emerg Med. 2012;20:80.
54. Australian Institute of Health and Welfare 2004 18 May 2021 Available from: https://www.aihw.gov.au/reports/rural-remote-australians/guide-to-remoteness-classifications/contents/table-of-contents.
55. Commonwealth Department of Health and Aged Care. Measuring Remoteness: Accessibility/Remoteness Index of Australia (ARIA) Revised Edition. 2001. Accessed on: 18 May 2021 from: .
56. Teljeur C, Kelly A. An urban–rural classification for health services research in Ireland. Ir Geogr. 2008;41:295-311.
57. USDA. USDA Economic Research Service- Urban Influence Codes. 2019. [cited 11 May 2022]. Available from: https://www.ers.usda.gov/data-products/urban-influence-codes/. [
58. Grimes DA, Schulz KF. Bias and causal associations in observational research. Lancet. 2002;359(9302):248-52.
59. Majewski D, Ball S, Bailey P, McKenzie N, Bray J, Morgan A, et al. Survival to hospital discharge is equivalent to 30-day survival as a primary survival outcome for out-of-hospital cardiac arrest studies. Resuscitation. 2021;166:43-8.
60. Nolan J, Soar J, Eikeland H. The chain of survival. Resuscitation. 2006;71(3):270-1.
61. Moeller SG, Rajan SR, Folke FF, Malta Hansen CMH, Karlsson LK, Gislason GG, et al. Population density and survival after out-of-hospital cardiac arrest. European Heart Journal. 2016;37:968-9.
62. Stiell IG, Wells GA, Field BJ, Spaite DW, De Maio VJ, Ward R, et al. Improved out-of-hospital cardiac arrest survival through the inexpensive optimization of an existing defibrillation program: OPALS study phase II. Ontario Prehospital Advanced Life Support. Jama. 1999;281(13):1175-81.
63. Vukmir RB. Survival from prehospital cardiac arrest is critically dependent upon response time. Resuscitation. 2006;69(2):229-34.

Rural, regional and remote health: a guide to remoteness classifications. AIHW cat. no. PHE 53. Canberra: AIHW