Longer Retrieval Distances to the Automated External Defibrillator Reduces Survival After Out-of-Hospital Cardiac Arrest

Laura Sarkisian, M.D.1,2*, Laura.Sarkisian2@rsyd.dk
Hans Mickley, M.D., DMSc1, Hans.Mickley@rsyd.dk
Henrik Schakow, EMT3, schakow@pc.dk
Oke Gerke, MSc, PhD4,5, Oke.Gerke@rsyd.dk
Simon Michael Starck, M.D.1, simon.michael.starck@rsyd.dk
Jonas Junghans Jensen, M.D.1, JonasJunghansJensen@gmail.com
Jacob Eifer Møller, M.D., DMSc, PhD1, Jacob.Moeller1@rsyd.dk
Gitte Jørgensen, M.D.3, Gitte.Jorgensen@rsyd.dk
Finn Lund Henriksen, M.D., PhD1, Finn.L.Henriksen@rsyd.dk

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1Research Unit of Cardiology, Department of Cardiology, Odense University Hospital, J.B. Winsløws Vej 4, 5000 Odense C, Denmark (primary site of research).
2OPEN, Odense Patient data Explorative Network, Odense University Hospital, Odense, Denmark ( affiliation).
3Emergency Medical Services, Region of Southern Denmark, Damhaven 12, 7100 Vejle, Denmark
4Department of Nuclear Medicine, Odense University Hospital, J.B. Winsløws Vej 4, 5000 Odense C, Denmark.
5Research Unit of Clinical Physiology and Nuclear Medicine, Department of Clinical Research, University of Southern Denmark, J.B. Winsløws Vej 19, 5000 Odense C, Denmark.

* Corresponding author: Laura Sarkisian, phone no. +45 27 85 94 44, fax no. +45 65 41 30 02.
Abstract: (247 words)

**Aims:** To evaluate and compare survival after out-of-hospital (OHCA), where an automated external defibrillator (AED) was used, in densely, moderately and thinly populated areas. Also, to evaluate the association between AED retrieval distance and survival after OHCA.

**Methods:** From 2014 to 2018, AEDs used during OHCA in the region of Southern Denmark were systematically collected. OHCA were included if the OHCA address was known. OHCA at nursing homes were excluded. To evaluate population density, a map with 1000x1000 meter grid cells was used with each cell color-graded according to the number of inhabitants. Densely, moderately and thinly populated areas were defined as ≥200 inhabitants, 20-199 inhabitants and 0-19 inhabitants per km², respectively. Primary outcome was 30-day survival.

**Results:** A total of 423 cases of OHCA were included, of which 207 (49%) occurred in densely populated areas, while 78 (18%) and 138 (33%) occurred in moderately and thinly populated areas, respectively. AED retrieval distances were: densely populated 105 meters (IQR 5-450), moderately populated 220 meters (IQR 5-450) and thinly populated 350 meters (IQR 5-1500) (P<0.001). Thirty-day survival was 40%, 31% and 34%, respectively (P = 0.3). In a multivariable regression analysis, mortality increased with 10% per 100 meters an AED was placed further away from the site of OHCA.

**Conclusion:** Survival after OHCA, where an AED was used, did not seem to differ in thinly, moderately and densely populated areas. The length of the AED retrieval distance, however, was correlated with reduced survival after adjusting for other potentially explanatory variables.
Introduction

Out-of-hospital cardiac arrest (OHCA) is the third leading cause of death in Europe and remains a significant public health problem with only about 5% surviving to hospital discharge (1). Early cardiopulmonary resuscitation (CPR) and bystander defibrillation is pivotal for OHCA outcomes (2-4), and though bystander CPR has become widespread in recent years (5, 6), the rates of bystander defibrillation have remained relatively low at 2-10% (7-9). To improve the use of automated external defibrillators (AEDs), the European Resuscitation Council and the American Heart Association (AHA) have recommended public access defibrillation (PAD) programs where AEDs are placed “in public places with a high density and movement of citizens”, and where one OHCA can be expected per 2-5 years (10, 11). Accordingly, great effort has been put into identifying high-risk locations for AED placement in urban areas (12-14). Guidelines regarding AED placement in thinly populated areas remain scarce. In these areas, the response times for emergency medical services (EMS) are longer than in urban areas, which is associated with reduced survival after OHCA (7, 15-17). Also, the incidence of residential OHCA is higher in rural areas (16), making the effects of PAD in rural areas more uncertain. According to international guidelines, an AED is expected to cover an area reachable within 1-2 minutes of brisk walking (11), translated to a Euclidian distance of approximately 100 meters. However, in rural areas, distances to the nearest available AED may be longer (18), further inhibiting AED use, and the effects of longer AED retrieval distances on survival after OHCA remain unknown.

The aims of the study were 1) to evaluate and compare 30-day survival from OHCA, where an AED was used in densely, moderately and thinly populated areas, and 2) to evaluate the association between AED retrieval distance and 30-day survival after OHCA.

Methods

Study design and patient population

This is a retrospective cohort study. The AED data was collected prospectively. The 2014 Utstein recommendations for reporting resuscitation outcomes was used (19).
Patients were included from January 1st 2014 to December 31st 2018. The following inclusion criteria had to be fulfilled: 1) consecutive patients with OHCA in whom resuscitation by the EMS staff was attempted and an AED had been used before EMS arrival; and 2) the AED was subsequently transported to the AED-center at the Odense University Hospital for analysis. Exclusion criteria were: 1) OHCAs with signs of prolonged death, 2) OHCAs with unknown OHCA address, and 3) OHCAs occurring in outpatient clinics, hospitals and at nursing homes.

Definition of endpoint

The endpoint was 30-day survival after the index OHCA event.

Study settings

The study was conducted in the region of Southern Denmark, which is one of five politically controlled administrative units in Denmark. The region covers 12,191 km² and has 1.2 million inhabitants (21% of the Danish population, Statistics Denmark). It has 39 EMS stations, organized and dispatched by one Emergency Medical Dispatch Center (EMDC).

According to Statistics Denmark, urban areas are defined as “built-up areas” with at least 200 inhabitants, and where the distance between the buildings is no more than 200 meters, unless due to e.g. parks or cemeteries facilities (20). The population density in urban areas is ≥200 inhabitants per km². Rural areas are defined as areas with <200 inhabitants per km². Sixteen percent of the population in the region (~200,000 inhabitants) live in rural areas, which comprise 94% of the entire area in the region (21).

In the last decade, the annual incidence of OHCAs in Denmark has been about 80 per 100,000 person-year (22, 23). According to the Danish Resuscitation Council, an AED was used during 11% of OHCAs in 2019 (22).

Emergency medical response during cardiac arrest
If the EMDC receives a call and suspects an OHCA, a two-tiered system is activated. The first tier involves an ambulance equipped with a defibrillator, and the second tier is an anesthesiologist-staffed emergency vehicle with means to provide advanced life support. Furthermore, health care professionals at the EMDC use a standardized protocol to phone-assist the bystander in performing CPR. If trained bystanders are present at the emergency site, the EMDC can choose to refer one bystander to the nearest available AED in accordance with international recommendations (10).

In rural parts of the region, trained volunteer first responders (VFRs) are dispatched to either perform CPR or collect a nearby publically available AED before approaching the emergency site. Three VFRs are geolocated and activated via a mobile phone application. The VFR system has been described in detail previously (24).

Data collection

AED data was collected from the AED-center at Odense University Hospital and the Danish national AED-network. Since 2014, the AED-center has collected AEDs used during OHCA in the region of Southern Denmark, which has previously been described (25). The Danish national AED-network was established in 2010 and is a voluntary based registry containing information regarding registered AEDs available for public use. The information is accessible via a homepage (www.hjertestarter.dk) and a smartphone application. Information regarding medical history and in-hospital treatment was collected from the medical records using each patients’ personal civil registration number (26). Information regarding the prehospital treatment was retrieved from the electronic Prehospital Patient Journals.

Geocoding, population density and AED retrieval distance

The exact addresses of OHCA sites, registered AEDs and AEDs used during OHCA were geocoded using the open source Quantum Geographic Information System (QGIS). An AED was defined as publically available, if it was registered at the AED network at the time of OHCA. Information regarding population density was retrieved from Statistics Denmark (27, 28) and integrated into QGIS, providing a map with 1000
x 1000 meter grid cells color-graded according to the number of inhabitants in each grid cell (Figure S1 in the Supplement).

Population density was defined as densely populated (≥200 inhabitants per km²), moderately populated (20-199 inhabitants per km²) and thinly populated (0-19 inhabitants per km²) areas according to the site of OHCA. Information regarding population density in the region was retrieved from Statistics Denmark using the 2014 GEOSTAT ‘New Degree of Urbanisation’ (27). Distance measurements for AED retrieval distance were obtained using Google Maps and represent the shortest one-way walking distance from AED location to OHCA site.

On-site AED use was defined as an AED retrieval distance of 0-5 meters and applied to cases where the OHCA and AED location had the same address.

Statistics

Categorical variables were presented as percentages and their respective frequencies. Categorical data were compared using either Pearson’s chi-squared test or Fisher’s exact test, depending on sample size.

Continuous variables were presented as means (± standard deviations) or medians (interquartile ranges), after visually inspecting for normal distribution. If normally distributed, two or more groups were compared using Student’s t-test or one-way analysis of variance (ANOVA), respectively. Non-normally distributed variables were compared using the non-parametric Mann-Whitney U test and the non-parametric Kruskall-Wallis test in cases of two or more group comparisons, respectively.

To evaluate aim 1) Pearson’s chi-squared test was used to compare survival in the three groups. To evaluate aim 2) we conducted a multivariable logistic regression analysis and the endpoint was regressed on AED retrieval distance, while adjusting for the following prognostic factors: Age, sex, cardiac cause of arrest, bystander witnessed OHCA, public place of arrest, shockable first rhythm, bystander defibrillation before EMS arrival, time of day, population density and EMS response time. Backward variable selection was applied with a p-stay of 0.4, while age and sex were kept in the model due to suspected prognostic value, irrespective of statistical significance.

Hypothesis tests were two-sided and the statistical significance level was set at 5%.
All statistical analyses were performed using Stata 15 (StataCorp LP, College Station, Texas).

Ethics and data protection

This study was approved by the Danish Safety Patient Authority (under Danish Health Authority) (no. 3-3013-2319/1 & 3-3013-2484/1) and the Danish Data Protection Agency (Journal no. 17/32047).

Results

Clinical characteristics and outcomes according to population density

During the 5-year period, an AED came into use in 621 cases of presumed OHCA. A total of 423 (68%) cases fulfilled the inclusion criteria (Figure 1). Of these, 207 (49%) took place in densely populated areas, while 78 (18%) and 138 (33%) occurred in moderately and thinly populated areas, respectively.

Table 1 shows patient characteristics and clinical outcomes. The groups were comparable in age, sex distribution, pre-arrest comorbidity and predictors of OHCA survival, including bystander witnessed arrest, bystander CPR and bystander defibrillation. In thinly populated areas, EMS response times were significantly longer (12 minutes (IQR 8-15) vs. 8 minutes (IQR 5-12), P<0.001) and residential OHCA s occurred more frequently than in densely populated areas (50% vs. 36%, P=0.01). AED retrieval distance became longer with declining population density (105 m (IQR 5-450) vs. 350 m (IQR 5-1500) in densely and thinly populated areas, respectively) (P<0.001). When evaluating 30-day survival, patients from densely populated areas appeared to have the most favorable outcome (40% versus 34% in thinly populated areas), but the result did not reach the level of statistical significance (Table 1) (P=0.3).

AED retrieval distance and survival outcome

In 348 out of 423 OHCA s (82%), the AED address was known, and AED retrieval distances were calculated. Figure 2 illustrates the distribution of four predictors of survival and the AED retrieval distance. It confirms that the proportion of residential OHCA s increases with higher AED retrieval distances, whereas the proportion of shockable first rhythm, witnessed OHCA s and OHCA s older than 65 years was unchanged. Figure 3 illustrates the cumulative distribution of AED retrieval distances. About one-third of AEDs were
collected on-site (Figure 3A) confirming that distances were longer in thinly populated areas compared with the two other groups (Figure 3B). Figure 4 shows that the number of OHCAs with ROSC at hospital arrival and the number of patients alive after 30 days decreased with longer AED retrieval distances.

Multivariable logistic regression

After adjusting for 10 clinically relevant variables (Table S1 in the Supplement), the variables ‘population density’, ‘public place of arrest’ and ‘bystander defibrillation before EMS arrival’ were excluded as part of the backward elimination process. This was done due to these variables’ high correlation with ‘EMS response time’ and ‘shockable first rhythm’, respectively, and due to the non-significant effect of these in the initial regression analysis (Table S1).

In the multivariable analysis, AED retrieval distance was regressed on 30-day survival adjusting for the remaining seven explanatory variables of interest (Table 2). The regression showed that mortality increased with 0.1% per meter (OR 1.0010 (95% CI 1.0004-1.0016)), corresponding to a 10% (95% CI 4-16%) increased mortality per 100 meters an AED was placed further away from the OHCA site. Younger age, bystander witnessed arrests and OHCAs with shockable first rhythms were associated with better survival outcomes.

Discussion

The present study involves consecutive patients with OHCA, where an AED was used before EMS arrival. The study had two main findings. Firstly; 30-day survival in thinly, moderately and densely populated areas were largely comparable, and secondly; increasing AED retrieval distances were significantly associated with increased mortality. More specifically, mortality increased with 10% per 100 meters an AED was placed further away from the site of OHCA.

Reducing time-to-shock has proven crucial for survival following OHCA (2-4). Despite many initiatives (29), research efforts and recommendations have mainly addressed urban centers and public places (10-14, 30). As a result, there is a knowledge gap concerning AED placement and use in rural areas (31). The region of Southern Denmark is a mixed rural-urban area, where the population majority live in urban areas, which
only comprises 6% of the total area (20). Despite this fact, we found that about half of OHCA cases, where an AED was used, occurred outside densely populated urban areas (216 of 423 cases). Masterson et al found similar results with a higher chance of bystander defibrillation in rural OHCAs (15). This may seem surprising as OHCAs occur more frequently in urban areas due to higher population densities (31). Perhaps the shorter EMS response times in urban areas makes it likely for the EMS to arrive before a bystander is able to collect and use an AED. Furthermore, numerous VFR systems have been established in rural parts of the region, as described previously (24). The results in Table 1 regarding VFR responses only demonstrated a small proportion of OHCAs, where a VFR arrived with an AED before EMS. However, the establishment of VFR systems could reflect a community awareness and a greater bystander willingness to put efforts into resuscitative care and AED use in rural areas, as the bystander is more likely to know the OHCA victim (15). Perhaps, this is the reason for increased AED use in rural areas. Previous studies have demonstrated that areas with low population density are associated with prolonged EMS response times, longer AED retrieval distances and higher rates of residential OHCAs (15, 16, 32, 33). The results of the present study confirm these earlier observations. However, we did not find a poorer 30-day survival in thinly versus densely populated areas. Perhaps the number of included OHCAs in the present study was too small to detect a true difference (type II error). Furthermore, a direct comparison between earlier all-comers OHCA studies (15, 16, 32, 33) and our selected AED-OHCA population should be done with caution. After all, despite longer AED retrieval distances, the rate of shockable first rhythm in the rural group was comparable with the two other groups, which may result from fewer interruptions in chest-compression due to AED voice prompts, or an indicator of younger and physically more able bystanders (6). Indeed, having an AED applied per se may be a marker of better outcome, as previously demonstrated by Weisfeldt and colleagues, even after adjusting for covariates and confounders (8). The survival benefits of on-site use of public AEDs within the first minutes after collapse are overwhelming (2, 4, 34). The impact of dispatched AEDs, however, and the effects of retrieval distances on survival are less clear. In a Dutch registry study, time-to-shock using a dispatched AED was significantly longer compared with use of on-site AEDs (8.5 minutes vs. 4.1 minutes, respectively), and accordingly, survival benefits of on-site AED use exceeded that of dispatched AEDs (50% vs. 17%, respectively) (35). However, the use of
dispatched AEDs was restricted to firefighters and police officers, making these observations difficult to compare with today’s widespread bystander use (35). It is likely that the AED retrieval distance is a proxy marker for the delay in time-to-shock. In a survival prediction model, Larsen and colleagues found that survival chances decreased by 7-10% per minute to defibrillation during OHCA (36). In thinly populated areas, we found a median AED retrieval distance of 350 meters (IQR 5-1500), and with an expected average walking speed of ≈1.5 m/sec (11), this can be translated into a delay in time-to-shock of ≈4 minutes. However, travel speed and retrieval distance are modifiable variables, as bystanders may choose to use motorized vehicles, or use shorter/longer walking routes to retrieve an AED. Also, if VFRs are dispatched for defibrillation purposes, AED retrieval distance could be further reduced (37-39), as they only travel a one-way distance and receive GPS-coordinates to rapidly geo-locate available AEDs. VFRs could therefore become an important link for increasing AED use in rural areas (24, 37, 40).

The present study is the first to establish an adjusted correlation between AED retrieval distance and survival after OHCA. This observation may raise more questions than answers concerning AED placement in both high-risk urban and in low-risk rural areas. With the 10% survival reduction per 100 meter of retrieval distance in mind, it is critical to weigh all premises in order to decide which retrieval distance – as a proxy of mortality risk – is acceptable in a given situation. For example, in a rural setting with prolonged AED retrieval distances, when should a bystander be activated by the EMDC health care professional for AED retrieval, if the alternative is to ensure high-quality CPR by taking turns in chest-compression until EMS arrival? Likewise, when utilizing the one-way travel strategy for VFRs, it is crucial to establish the optimal retrieval distance for collecting and bringing an AED to the OHCA site, instead of directing the VFR directly to the emergency site to perform early CPR. The results of this study call for more research to establish what the optimal and acceptable distance between AEDs in high-density urban centers and low-density rural areas should be. Future guidelines should perhaps set forth separate strategies concerning AED use in urban vs. in rural areas, instead of setting forth uniform recommendation for all area types.

Limitations & strengths
This study has some limitations that must be addressed: 1) The data presented are limited by the observational study design. However, evaluating the effect of AED retrieval distance on survival can be addressed exclusively in an observational context; 2) OHCAs in nursing homes were excluded as these marked by age, comorbidity and prognosis compared with OHCAs outside of nursing homes (25, 41). Furthermore, in nursing homes, OHCA and AED location have the same address (25), which could affect the regression analysis, when evaluating survival in relation to AED retrieval distances; 3) the number of used AEDs that did not reach the AED-center is not available. However, in the event of AED deployment, the EMDC is required to inform both the AED-centre and EMS staff to ensure transportation to the AED-centre, which should limit this issue.

The present study is the first to establish an adjusted correlation between the AED retrieval distance and survival after OHCA. Earlier studies evaluating OHCA survival in relation to population density have used local, administrative units or geographical districts (15, 16, 32, 33, 42), resulting in varying rural-urban definitions that are difficult to reproduce. A strength of this study is that population density was evaluated by using the exact number of inhabitants in each km² grid cell (27). Another strength is the prospectively collected data material and the cross-linkage of information from EMS and hospital records using each patient’s personal identification number (26).

**Conclusion**

Patients with OHCA, where an AED was used before EMS arrival, had a favorable 30-day survival, which was comparable in densely, moderately and thinly populated areas. When evaluating the effect of AED retrieval distance on 30-day survival after OHCA, we found a 10% reduction in survival per 100 meters an AED was placed further away from the OHCA site. These results call for more research regarding the potential impact of AED retrieval distance on survival after OHCA. Ultimately, it may help guide future AED placement.


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Simon Michael Starck, M.D.1, simon.michael.starck@rsyd.dk
Jonas Junghans Jensen, M.D.1, JonasJunghansJensen@gmail.com
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Aims: To evaluate and compare survival after out-of-hospital (OHCA), where an automated external defibrillator (AED) was used, in densely, moderately and thinly populated areas. Also, to evaluate the association between AED retrieval distance and survival after OHCA.

Methods: From 2014 to 2018, AEDs used during OHCA in the region of Southern Denmark were systematically collected. OHCA were included if the OHCA address was known. OHCA at nursing homes were excluded. To evaluate population density, a map with 1000x1000 meter grid cells was used with each cell color-graded according to the number of inhabitants. Densely, moderately and thinly populated areas were defined as ≥200 inhabitants, 20-199 inhabitants and 0-19 inhabitants per km², respectively. Primary outcome was 30-day survival.

Results: A total of 423 cases of OHCA were included, of which 207 (49%) occurred in densely populated areas, while 78 (18%) and 138 (33%) occurred in moderately and thinly populated areas, respectively. AED retrieval distances were: densely populated 105 meters (IQR 5-450), moderately populated 220 meters (IQR 5-450) and thinly populated 350 meters (IQR 5-1500) (P<0.001). Thirty-day survival was 40%, 31% and 34%, respectively (P=0.3). In a multivariable regression analysis, the risk of mortality increased with 10% per 100 meters an AED was placed further away from the site of OHCA.

Conclusion: Survival after OHCA, where an AED was used, did not seem to differ in thinly, moderately and densely populated areas. The length of the AED retrieval distance, however, was correlated with reduced survival after adjusting for other potentially explanatory variables.
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Clinical characteristics and outcomes according to population density

During the 5-year period, an AED came into use in 621 cases of presumed OHCA. A total of 423 (68%) cases fulfilled the inclusion criteria (Figure 1). Of these, 207 (49%) took place in densely populated areas, while 78 (18%) and 138 (33%) occurred in moderately and thinly populated areas, respectively.

Table 1 shows patient characteristics and clinical outcomes. The groups were comparable in age, sex distribution, pre-arrest comorbidity and predictors of OHCA survival, including bystander witnessed arrest, bystander CPR and bystander defibrillation. In thinly populated areas, EMS response times were significantly longer (12 minutes (IQR 8-15) vs. 8 minutes (IQR 5-12), P<0.001) and residential OHCAs occurred more frequently than in densely populated areas (50% vs. 36%, P=0.01). AED retrieval distance became longer with declining population density (105 m (IQR 5-450) vs. 350 m (IQR 5-1500) in densely and thinly populated areas, respectively) (P<0.001). When evaluating 30-day survival, patients from densely populated areas appeared to have the most favorable outcome (40% versus 34% in thinly populated areas), but the result did not reach the level of statistical significance (Table 1) (P=0.3).

AED retrieval distance and survival outcome

In 348 out of 423 OHCA's (82%), the AED address was known, and AED retrieval distances were calculated. Figure 2 illustrates the distribution of four predictors of survival and the AED retrieval distance. It confirms that the proportion of residential OHCA's increases with higher AED retrieval distances, whereas the proportion of shockable first rhythm, witnessed OHCA's and OHCA's older than 65 years was unchanged. Figure 3 illustrates the cumulative distribution of AED retrieval distances. About one-third of AEDs were...
collected on-site (Figure 3A) confirming that distances were longer in thinly populated areas compared with the two other groups (Figure 3B). Figure 4 shows that the number of OHCAs with ROSC at hospital arrival and the number of patients alive after 30 days decreased with longer AED retrieval distances.

**Multivariable logistic regression**

After adjusting for 10 clinically relevant variables (Table S1 in the Supplement), the variables ‘population density’, ‘public place of arrest’ and ‘bystander defibrillation before EMS arrival’ were excluded as part of the backward elimination process. This was done due to these variables’ high correlation with ‘EMS response time’ and ‘shockable first rhythm’, respectively, and due to the non-significant effect of these in the initial regression analysis (Table S1).

In the multivariable analysis, AED retrieval distance was regressed on 30-day survival adjusting for the remaining seven explanatory variables of interest (Table 2). The regression showed that the risk of mortality increased with 0.1% per meter (OR 1.0010 (95% CI 1.0004-1.0016)), corresponding to a 10% (95% CI 4-16%) increased risk of mortality per 100 meters an AED was placed further away from the OHCA site. Younger age, bystander witnessed arrests and OHCAs with shockable first rhythms were associated with better survival outcomes.

**Discussion**

The present study involves consecutive patients with OHCA, where an AED was used before EMS arrival. The study had two main findings. Firstly; 30-day survival in thinly, moderately and densely populated areas were largely comparable, and secondly; increasing AED retrieval distances were significantly associated with increased mortality. More specifically, the risk of mortality increased with 10% per 100 meters an AED was placed farther away from the site of OHCA.

Reducing time-to-shock has proven crucial for survival following OHCA (2-4). Despite many initiatives (29), research efforts and recommendations have mainly addressed urban centers and public places (10-14, 30). As a result, there is a knowledge gap concerning AED placement and use in rural areas (31). The region of Southern Denmark is a mixed rural-urban area, where the population majority live in urban areas, which
only comprises 6% of the total area (20). Despite this fact, we found that about half of OHCA cases, where
an AED was used, occurred outside densely populated urban areas (216 of 423 cases). Masterson et al found
similar results with a higher chance of bystander defibrillation in rural OHCA (15). This may seem
surprising as OHCA occur more frequently in urban areas due to higher population densities (31). Perhaps
the shorter EMS response times in urban areas makes it likely for the EMS to arrive before a bystander is
able to collect and use an AED. Furthermore, numerous VFR systems have been established in rural parts of
the region, as described previously (24). The results in Table 1 regarding VFR responses only demonstrated
a small proportion of OHCA, where a VFR arrived with an AED before EMS. However, the establishment
of VFR systems could reflect a community awareness and a greater bystander willingness to put efforts into
resuscitative care and AED use in rural areas, as the bystander is more likely to know the OHCA victim (15).
Perhaps, this is the reason for increased AED use in rural areas. Previous studies have demonstrated that
areas with low population density are associated with prolonged EMS response times, longer AED retrieval
distances and higher rates of residential OHCA (15, 16, 32, 33). The results of the present study confirm
these earlier observations. However, we did not find a poorer 30-day survival in thinly versus densely
populated areas. Perhaps the number of included OHCA in the present study was too small to detect a true
difference (type II error). Furthermore, a direct comparison between earlier all-comers OHCA studies (15,
16, 32, 33) and our selected AED-OHCA population should be done with caution. After all, despite longer
AED retrieval distances, the rate of shockable first rhythm in the rural group was comparable with the two
other groups, which may result from fewer interruptions in chest-compression due to AED voice prompts, or
an indicator of younger and physically more able bystanders (6). Indeed, having an AED applied per se may
be a marker of better outcome, as previously demonstrated by Weisfeldt and colleagues, even after adjusting
for covariates and confounders (8).

The survival benefits of on-site use of public AEDs within the first minutes after collapse are overwhelming
(2, 4, 34). The impact of dispatched AEDs, however, and the effects of retrieval distances on survival are less
clear. In a Dutch registry study, time-to-shock using a dispatched AED was significantly longer compared
with use of on-site AEDs (8.5 minutes vs. 4.1 minutes, respectively), and accordingly, survival benefits of
on-site AED use exceeded that of dispatched AEDs (50% vs. 17%, respectively) (35). However, the use of
dispatched AEDs was restricted to firefighters and police officers, making these observations difficult to compare with today’s widespread bystander use (35). It is likely that the AED retrieval distance is a proxy marker for the delay in time-to-shock. In a survival prediction model, Larsen and colleagues found that survival chances decreased by 7-10% per minute to defibrillation during OHCA (36). In thinly populated areas, we found a median AED retrieval distance of 350 meters (IQR 5-1500), and with an expected average walking speed of ≈1.5 m/sec (11), this can be translated into a delay in time-to-shock of ≈4 minutes. However, travel speed and retrieval distance are modifiable variables, as bystanders may choose to use motorized vehicles, or use shorter/longer walking routes to retrieve an AED. Also, if VFRs are dispatched for defibrillation purposes, AED retrieval distance could be further reduced (37-39), as they only travel a one-way distance and receive GPS-coordinates to rapidly geo-locate available AEDs. VFRs could therefore become an important link for increasing AED use in rural areas (24, 37, 40).

The present study is the first to establish an adjusted correlation between AED retrieval distance and survival after OHCA. This observation may raise more questions than answers concerning AED placement in both high-risk urban and in low-risk rural areas. With the 10% survival reduction per 100 meter of retrieval distance in mind, it is critical to weigh all premises in order to decide which retrieval distance – as a proxy of mortality risk – is acceptable in a given situation. For example, in a rural setting with prolonged AED retrieval distances, when should a bystander be activated by the EMDC health care professional for AED retrieval, if the alternative is to ensure high-quality CPR by taking turns in chest-compression until EMS arrival? Likewise, when utilizing the one-way travel strategy for VFRs, it is crucial to establish the optimal retrieval distance for collecting and bringing an AED to the OHCA site, instead of directing the VFR directly to the emergency site to perform early CPR. The results of this study call for more research to establish what the optimal and acceptable distance between AEDs in high-density urban centers and low-density rural areas should be. Future guidelines should perhaps set forth separate strategies concerning AED use in urban vs. in rural areas, instead of setting forth uniform recommendation for all area types.

Limitations & strengths
This study has some limitations that must be addressed: 1) The data presented are limited by the observational study design. However, evaluating the effect of AED retrieval distance on survival can be addressed exclusively in an observational context; 2) OHCAs in nursing homes were excluded as these markedly differ regarding age, comorbidity and prognosis compared with OHCAs outside of nursing homes (25, 41). Furthermore, in nursing homes, OHCA and AED location have the same address (25), which could affect the regression analysis, when evaluating survival in relation to AED retrieval distances; 3) the number of used AEDs that did not reach the AED-center is not available. However, in the event of AED deployment, the EMDC is required to inform both the AED-centre and EMS staff to ensure transportation to the AED-centre, which should limit this issue.

The present study is the first to establish an adjusted correlation between the AED retrieval distance and survival after OHCA. Earlier studies evaluating OHCA survival in relation to population density have used local, administrative units or geographical districts (15, 16, 32, 33, 42), resulting in varying rural-urban definitions that are difficult to reproduce. A strength of this study is that population density was evaluated by using the exact number of inhabitants in each km² grid cell (27). Another strength is the prospectively collected data material and the cross-linkage of information from EMS and hospital records using each patient’s personal identification number (26).

**Conclusion**

Patients with OHCA, where an AED was used before EMS arrival, had a favorable 30-day survival, which was comparable in densely, moderately and thinly populated areas. When evaluating the effect of AED retrieval distance on 30-day survival after OHCA, we found a 10% reduction in survival per 100 meters an AED was placed further away from the OHCA site. These results call for more research regarding the potential impact of AED retrieval distance on survival after OHCA. Ultimately, it may help guide future AED placement.


### Population density at cardiac arrest site

<table>
<thead>
<tr>
<th></th>
<th>A) Densely populated (N=207)</th>
<th>B) Moderately populated (N=78)</th>
<th>C) Thinly populated (N=138)</th>
<th>All groups</th>
<th>A vs. B P value</th>
<th>B vs. C P value</th>
<th>A vs. C P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, year, mean (SD)</td>
<td>66 (14)</td>
<td>68 (14)</td>
<td>66 (11)</td>
<td>0.6(^1)</td>
<td>0.5(^2)</td>
<td>0.3(^2)</td>
<td>0.6(^2)</td>
</tr>
<tr>
<td>Male sex, % (n/valid cases)</td>
<td>78 (151/194)</td>
<td>77 (59/77)</td>
<td>83 (102/123)</td>
<td>0.5(^3)</td>
<td>0.8(^3)</td>
<td>0.3(^3)</td>
<td>0.3(^3)</td>
</tr>
<tr>
<td>Comorbidity, % (n/valid cases)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>- Known ischemic heart disease</td>
<td>24 (41/172)</td>
<td>20 (14/70)</td>
<td>23 (23/101)</td>
<td>0.8(^3)</td>
<td>0.5(^3)</td>
<td>0.7(^3)</td>
<td>0.8(^3)</td>
</tr>
<tr>
<td>- Congestive heart failure</td>
<td>16 (28/174)</td>
<td>7 (5/70)</td>
<td>12 (12/101)</td>
<td>0.2(^3)</td>
<td>0.06(^3)</td>
<td>0.3(^3)</td>
<td>0.3(^3)</td>
</tr>
<tr>
<td>- Prior stroke</td>
<td>10 (18/175)</td>
<td>11 (8/70)</td>
<td>7 (7/100)</td>
<td>0.6(^3)</td>
<td>0.8(^3)</td>
<td>0.3(^3)</td>
<td>0.4(^4)</td>
</tr>
<tr>
<td>- Diabetes</td>
<td>18 (31/175)</td>
<td>19 (13/70)</td>
<td>20 (20/101)</td>
<td>0.9(^3)</td>
<td>0.9(^3)</td>
<td>0.8(^3)</td>
<td>0.7(^3)</td>
</tr>
<tr>
<td>- COPD</td>
<td>15 (27/175)</td>
<td>24 (17/70)</td>
<td>6 (6/101)</td>
<td><strong>0.003(^3)</strong></td>
<td>0.1(^3)</td>
<td><strong>0.001(^4)</strong></td>
<td><strong>0.02(^3)</strong></td>
</tr>
<tr>
<td>- Malignancy</td>
<td>7 (12/175)</td>
<td>9 (6/70)</td>
<td>8 (8/100)</td>
<td>0.9(^3)</td>
<td>0.6(^3)</td>
<td>0.9(^3)</td>
<td>0.7(^2)</td>
</tr>
<tr>
<td>Cause of cardiac arrest, % (n/valid cases)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>- Cardiac(^a)</td>
<td>83 (146/176)</td>
<td>83 (53/64)</td>
<td>86 (103/120)</td>
<td>0.8(^3)</td>
<td>0.9(^3)</td>
<td>0.6(^3)</td>
<td>0.5(^3)</td>
</tr>
<tr>
<td>- Non-cardiac</td>
<td>10 (18/176)</td>
<td>17 (11/64)</td>
<td>6 (7/120)</td>
<td>0.05(^3)</td>
<td>0.1(^3)</td>
<td><strong>0.01(^3)</strong></td>
<td>0.2(^3)</td>
</tr>
<tr>
<td>- Trauma/suicide/accident</td>
<td>7 (12/176)</td>
<td>0 (0/64)</td>
<td>8 (10/120)</td>
<td><strong>0.04(^4)</strong></td>
<td><strong>0.03(^4)</strong></td>
<td><strong>0.02(^4)</strong></td>
<td>0.6(^3)</td>
</tr>
</tbody>
</table>

\(^a\) Includes trauma, suicide, and accidental cardiac arrest.
<table>
<thead>
<tr>
<th>Time of day, % (n/valid cases)</th>
<th>63 (127/202)</th>
<th>65 (48/74)</th>
<th>59 (78/132)</th>
<th>0.7³</th>
<th>0.8³</th>
<th>0.4³</th>
<th>0.5³</th>
</tr>
</thead>
<tbody>
<tr>
<td>Day (8 am to 3.59 pm)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Evening (4 pm to 11.5 pm)</td>
<td>28 (56/202)</td>
<td>27 (20/74)</td>
<td>30 (39/132)</td>
<td>0.9³</td>
<td>0.9³</td>
<td>0.7³</td>
<td>0.7³</td>
</tr>
<tr>
<td>Night (12 pm to 7.59 am)</td>
<td>9 (19/202)</td>
<td>8 (6/74)</td>
<td>11 (15/132)</td>
<td>0.7³</td>
<td>0.7³</td>
<td>0.5³</td>
<td>0.6³</td>
</tr>
</tbody>
</table>

| Bystander witnessed, % (n/valid cases) | 71 (143/202) | 71 (53/75) | 66 (84/128) | 0.6³ | 0.9³ | 0.5³ | 0.3³ |

| Bystander CPR, % (n/valid cases) | 99 (202/205) | 100 (77/77) | 100 (132/132) | 0.3³ | 0.3⁴ | 0.9⁴ | 0.2³ |

| AED with shockable first rhythm, % (n/valid cases) | 59 (110/186) | 46 (29/63) | 55 (69/125) | 0.2³ | 0.07³ | 0.2³ | 0.5³ |

| Bystander defibrillation, % (n/valid cases) | 56 (104/186) | 49 (31/63) | 59 (72/122) | 0.07³ | 0.4³ | 0.2³ | 0.6³ |

| Bystander defibrillation and ROSC before EMS arrival, % (n/valid cases) | 24 (47/197) | 16 (12/76) | 22 (29/130) | 0.3³ | 0.1³ | 0.3³ | 0.7³ |

| Volunteer first responder with AED, % (n/valid cases) | 3.5 (7/201) | 3.9 (3/77) | 6 (8/130) | 0.5⁴ | 0.6⁴ | 0.8⁴ | 0.3³ |

<table>
<thead>
<tr>
<th>AED registered at AED-network, % (n/valid cases)</th>
<th>75 (154/205)</th>
<th>81 (62/77)</th>
<th>74 (101/137)</th>
<th>0.5³</th>
<th>0.3³</th>
<th>0.3³</th>
<th>0.8³</th>
</tr>
</thead>
<tbody>
<tr>
<td>Available 24/7</td>
<td>67 (103/154)</td>
<td>85 (53/62)</td>
<td>77 (78/101)</td>
<td><strong>0.01³</strong></td>
<td><strong>0.006³</strong></td>
<td>0.2³</td>
<td>0.08³</td>
</tr>
</tbody>
</table>

| No. of AEDs in grid cell of cardiac arrest, median (IQR) | 3.5 (2.0-7.5) | 1.0 (1.0-2.0) | 0.0 (0.0-1.0) | <0.001³ | <0.001⁶ | <0.001⁶ | <0.001⁶ |

<p>| AED one-way retrieval distance one-way, median (IQR) | 105 (5-450) | 220 (5-450) | 350 (5-1500) | &lt;0.001³ | 0.1⁶ | <strong>0.04³</strong> | &lt;0.001⁶ |</p>
<table>
<thead>
<tr>
<th>EMS response time, minutes, median (IQR)</th>
<th>8 (5-12)</th>
<th>11 (8-14)</th>
<th>12 (8-15)</th>
<th>&lt;0.001&lt;sup&gt;f&lt;/sup&gt;</th>
<th>&lt;0.001&lt;sup&gt;f&lt;/sup&gt;</th>
<th>0.5&lt;sup&gt;f&lt;/sup&gt;</th>
<th>&lt;0.001&lt;sup&gt;f&lt;/sup&gt;</th>
</tr>
</thead>
</table>

<table>
<thead>
<tr>
<th>Location of cardiac arrest, % (n/valid cases)</th>
<th>36 (71/199)</th>
<th>48 (37/77)</th>
<th>50 (62/125)</th>
<th>0.03&lt;sup&gt;3&lt;/sup&gt;</th>
<th>0.06&lt;sup&gt;3&lt;/sup&gt;</th>
<th>0.8&lt;sup&gt;3&lt;/sup&gt;</th>
<th>0.01&lt;sup&gt;3&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td>Residential area</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Public place</td>
<td>34 (67/199)</td>
<td>32 (25/77)</td>
<td>24 (30/125)</td>
<td>0.2&lt;sup&gt;3&lt;/sup&gt;</td>
<td>0.8&lt;sup&gt;3&lt;/sup&gt;</td>
<td>0.2&lt;sup&gt;3&lt;/sup&gt;</td>
<td>0.06&lt;sup&gt;3&lt;/sup&gt;</td>
</tr>
<tr>
<td>Mixed group&lt;sup&gt;b&lt;/sup&gt;</td>
<td>31 (61/199)</td>
<td>19 (15/77)</td>
<td>26 (33/125)</td>
<td>0.2&lt;sup&gt;3&lt;/sup&gt;</td>
<td>0.06&lt;sup&gt;3&lt;/sup&gt;</td>
<td>0.3&lt;sup&gt;3&lt;/sup&gt;</td>
<td>0.4&lt;sup&gt;3&lt;/sup&gt;</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>ROSC at hospital arrival, % (n/valid cases)</th>
<th>50 (102/203)</th>
<th>43 (33/77)</th>
<th>36 (47/130)</th>
<th>0.04&lt;sup&gt;3&lt;/sup&gt;</th>
<th>0.3&lt;sup&gt;3&lt;/sup&gt;</th>
<th>0.3&lt;sup&gt;3&lt;/sup&gt;</th>
<th>0.01&lt;sup&gt;3&lt;/sup&gt;</th>
</tr>
</thead>
</table>

<table>
<thead>
<tr>
<th>30-day survival, % (n/valid cases)</th>
<th>40 (82/203)</th>
<th>31 (24/77)</th>
<th>34 (44/128)</th>
<th>0.3&lt;sup&gt;3&lt;/sup&gt;</th>
<th>0.2&lt;sup&gt;3&lt;/sup&gt;</th>
<th>0.6&lt;sup&gt;3&lt;/sup&gt;</th>
<th>0.3&lt;sup&gt;3&lt;/sup&gt;</th>
</tr>
</thead>
</table>

<table>
<thead>
<tr>
<th>Cerebral Performance Category Score 1-2 at discharge, % (n/valid cases)</th>
<th>98 (79/81)</th>
<th>100 (23/23)</th>
<th>98 (44/45)</th>
<th>0.7&lt;sup&gt;3&lt;/sup&gt;</th>
<th>0.9&lt;sup&gt;4&lt;/sup&gt;</th>
<th>0.5&lt;sup&gt;4&lt;/sup&gt;</th>
<th>0.9&lt;sup&gt;4&lt;/sup&gt;</th>
</tr>
</thead>
</table>

<sup>1</sup>One-way ANOVA.  <sup>2</sup>Student’s t-test.  <sup>3</sup>Pearson’s chi-square test.  <sup>4</sup>Fisher’s exact test.  <sup>5</sup>Kruskall-Wallis test.  <sup>6</sup>Non-parametric Wilcoxon rank sum test.

<sup>a</sup>Includes OHCAs with presumed, confirmed and unknown cause of cardiac arrest.  <sup>b</sup>Mixed group: Company/workplace, institutions, health clinic and sports facility/recreational.

Table 2: Multivariable logistic regression of 30-day survival after the index OHCA event on AED retrieval distance and other prognostic factors

<table>
<thead>
<tr>
<th></th>
<th>Odds Ratio</th>
<th>95% CI</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>AED retrieval distance</td>
<td>1.0010</td>
<td>1.0004-1.0016</td>
<td><strong>0.001</strong></td>
</tr>
<tr>
<td>Age</td>
<td>1.070</td>
<td>1.034-1.11</td>
<td><strong>&lt;0.001</strong></td>
</tr>
<tr>
<td>Male sex</td>
<td>0.82</td>
<td>0.30-2.25</td>
<td>0.7</td>
</tr>
<tr>
<td>Cardiac cause of arrest</td>
<td>0.48</td>
<td>0.10-2.27</td>
<td>0.4</td>
</tr>
<tr>
<td>Bystander witnessed</td>
<td>0.16</td>
<td>0.05-0.58</td>
<td><strong>0.005</strong></td>
</tr>
<tr>
<td>Shockable first rhythm</td>
<td>0.06</td>
<td>0.02-0.19</td>
<td><strong>&lt;0.001</strong></td>
</tr>
<tr>
<td>EMS response time</td>
<td>1.065</td>
<td>0.99-1.15</td>
<td>0.09</td>
</tr>
</tbody>
</table>

Time of day
- Day (8 am to 3.59 pm)          | 1          | -          | -       |
- Evening (4 pm to 11.5 pm)      | 1.41       | 0.61-3.27  | 0.4     |
- Night (12 pm to 7.59 am)       | 2.15       | 0.54-8.49  | 0.3     |

Figure 2. Shows the relative percentages of residential OHCAs (2A), shockable first rhythms (2B), bystander witnessed OHCAs and >65 year-olds according to the AED retrieval distance.
Figure 4 shows the proportion of OHCAs that had ROSC at hospital arrival and were alive after 30 days in relation to the AED retrieval distance.
**Figure 1.** Flow-chart showing the inclusion-exclusion
Figure 3. 3A shows the cumulative distribution of AED retrieval distance, and 3B shows the cumulative distribution of AED retrieval distance according to population density.
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Supplemental files for online publication only
Table S1.docx
Conflicts of interest:

Doctor Møller has received grants and personal fees from Abiomed, and personal fees from Orion Pharma and Novartis. All other authors declared no conflict of interests.
Credit Author Statement

**CRediT Author statement:**

**Laura Sarkisian:** Conceptualization, Methodology, Validation, Formal Analysis, Investigation, Data Curation, Writing – Original Draft, Writing – Review & Editing, Visualization, Project Administration, Funding Acquisition.

**Hans Mickley:** Conceptualization, Methodology, Validation, Formal Analysis, Writing – Original Draft, Writing – Review & Editing, Supervision, Project Administration, Funding Acquisition.

**Henrik Schakow:** Conceptualization, Methodology, Investigation, Resources, Data Curation, Writing – Review & Editing.

**Oke Gerke:** Conceptualization, Methodology, Validation, Formal Analysis, Writing – Review & Editing, Supervision.

**Simon Michael Starck:** Methodology, Validation, Investigation, Data Curation, Writing – Review & Editing.

**Jonas Junghans Jensen:** Methodology, Validation, Investigation, Data Curation, Writing – Review & Editing.

**Jacob Eifer Møller:** Conceptualization, Methodology, Validation, Writing – Review & Editing, Supervision.

**Gitte Jørgensen:** Methodology, Validation, Investigation, Resources, Writing – Review & Editing.

**Finn Lund Henriksen:** Conceptualization, Methodology, Validation, Formal Analysis, Investigation, Resources, Data Curation, Writing – Original Draft, Writing – Review & Editing, Supervision, Project Administration, Funding Acquisition.