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DISPATCH OF LAY RESPONDERS TO OUT-OF-HOSPITAL CARDIAC ARRESTS

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Cover image: "Le docteur Ure galvanisant le corps de l'assassin Clydsdale" from *Les merveilles de la science, ou Description populaire des inventions modernes*, 1867, by Louis Figuier. (Work in the public domain).

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Dispatch of lay responders to out-of-hospital cardiac arrests

THESIS FOR DOCTORAL DEGREE (Ph.D.)

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"The operation was almost finished, he said, when the anaesthetist informed the surgeon that pulse and blood pressure were not obtainable, and the patient was blue. The surgeon removed his gloves, went to a telephone in the corner of the room, and called the Fire Department Rescue Squad. When the firemen arrived, perhaps 15 minutes later, the oxygen mask and the 'Pul- motor' were applied vigorously but without effect, and eventually the patient was pronounced dead. Later he added, The experience left me with a conviction that we were not doing our best for the patient."

Story told to a group of students by Dr. Claude Beck from an incident during his internship as a surgeon in 1920 at Johns Hopkins Hospital in Baltimore [1]

ABSTRACT

Background and aim

Out-of-hospital cardiac arrest (OHCA) remains a major public-health problem affecting around 300 000 Europeans each year. If treatment is not started within a couple of minutes the chances of survival are slim. One important predictor of survival is the time from call to start of treatment. To reduce this time frame, different strategies, in addition to emergency medical services (EMS), such as widespread deployment of automated external defibrillators (AEDs) and dispatch of fire fighters and police officers have been implemented.

The aim of this thesis is to study the implementation and effects of a third additional resource, lay responders dispatched by the emergency dispatch center. The aim of **study 1** was to evaluate the technical function and performance of a lay responder system during a run-in phase. The aim of **study 2** was to measure the travelling speed and response time of the dispatched lay responders. In **study 3** the aim was to investigate the emotional response, both positive and negative, wellbeing and post-traumatic stress disorder, among dispatched lay responders. In **study 4** the aim was to investigate if lay responders instructed to fetch a public AED by using a smartphone application could increase the bystander use of AEDs before arrival of EMS, fire fighters and police officers.

Methods and results

In **study 1** data from the smartphone application were collected and linked to cardiac arrest data from the Swedish Register for Cardiopulmonary Resuscitation (SRCR). During six months in 2016 the system was activated 685 times. 224 of these cases were EMS treated OHCA. After exclusion of EMS-witnessed cases (n=11) and cases with missing survey data (n=15), 198 cases remained in the analytical sample. The results showed that dispatched lay responders reached the scene in 116 cases (58%), in 51 (26%) cases before the EMS. An AED was attached 17 times (9%) and defibrillated 4 times (2%). The median Euclidian distance to travel to perform CPR was 560 meters (IQR=332-860) compared with 1280 (IQR=748-1776) among for those who were directed to fetch an AED.

In **study 2**, data on lay responder movement were collected from the smartphone application. During the 7-month study period 1406 suspected OHCA were included. In these calls, 9058 lay responders accepted the mission and 2176 reached the scene of the

suspected cardiac arrest (the study population). Among all cases the median travelling speed was 2.3 meters/sec (IQR=1.4–4.0) while the response time was 6.2 minutes, and the travelling distance was 956 meters (IQR=480–1661). In the most densely populated areas the median travelling speed was 1.8 meters/sec compared with 3.1 in the least densely populated areas.

In **study 3** we included 886 unexposed and 1389 exposed lay-responders. The lay responders were divided into 3 groups; unexposed, exposed-1 (who tried, but failed to reach the scene before EMS) and exposed-2 (who either reached the scene before EMS or performed CPR). Using the two dimensions of the Swedish Core Affect Scales (SCAS), *valence* and *activation* the results suggested that exposed lay responders showed higher activation (Exp-1=7.5, Exp-2=7.6) than unexposed lay responders (7.0) ($p<0.001$). Exposed lay responders had lower valence (Exp-1=6.3, Exp-2=6.3) compared with unexposed lay responders (6.8) ($p<0.001$). PCL-6 mean scores were highest in the unexposed group (10.4) compared with the exposed group (Exp-1=8.8, Exp-2=9.2) ($p=0.007$). There were no differences in the WHO wellbeing index, (Un-Exp: 77.7; Exp-1: 77.8; Exp-2: 78.2) ($p=0.963$).

In **Study 4**, cases of suspected OHCA were randomly assigned to either an intervention group, where the majority of lay responders (4/5) were guided to the nearest AED, or to a control group, where all lay responders were directed to perform CPR. Data from the smartphone application system were linked to data from the SRCR. During the 13-month study period 2553 suspected OHCA were randomized. Among these, 815 (32%) were EMS-treated. The AED attachment rate was 13.2% in the intervention group compared with 9.4 in the control group ($p=0.087$). In both groups combined, 29.3% of all bystanders attached AEDs, and 35.3% of all cases of bystander CPR were performed by a dispatched lay responder.

Conclusions

The conclusion from the first run-in study (**study 1**) was that it is feasible to dispatch lay responders to suspected OHCA but that further system improvements are needed to reduce the time to defibrillation. The results from **study 2** suggested that lay responders travel faster than previously estimated and that the travelling speed is dependent on population density, information that may be used for simulation studies as well as in configurations in app-based systems. **Study 3** showed that lay responders rated the experience as high-energy and mostly positive. No indication of harm was seen, as the lay

responders had low post-traumatic stress scores and high levels of general wellbeing at follow-up. **Study 4** revealed that smartphone dispatch of lay responders to public AEDs did not increase the AED attachment rate before arrival of the EMS or first responders, versus smartphone dispatch to perform CPR. If dispatched lay responders arrived prior to the EMS, the likelihood of bystander AED use and CPR was increased.

LIST OF SCIENTIFIC PAPERS

- I. **Berglund E**, Claesson A, Nordberg P, Djärv T, Lundgren P, Folke F, Forsberg S, Riva G, Ringh M.
A smartphone application for dispatch of lay responders to out-of-hospital cardiac arrests.
Resuscitation. 2018 May;126:160-165.
- II. Jonsson M¹, **Berglund E**¹, Djärv T, Nordberg P, Claesson A, Forsberg S, Nord A, Tan HL, Ringh M.
A brisk walk – Real-life travelling speed of lay responders in out-of-hospital cardiac arrest.
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- III. **Berglund E**, Olsson E, Jonsson M, Svensson L, Hollenberg J, Claesson A, Nordberg P, Lundgren P, Högstedt Å, Ringh M.
Wellbeing, Emotional response and stress among lay responders dispatched to suspected out-of-hospital cardiac arrests.
Manuscript.
- IV. **Berglund E**, Hollenberg J, Jonsson M, Svensson L, Claesson A, Nord A, Nordberg P, Forsberg S, Rosenqvist M, Lundgren P, Högstedt Å, Riva G, Ringh M.
Use of automated external defibrillators by smartphone dispatched lay responders in out-of-hospital cardiac arrest.
Manuscript.

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LIST OF ABBREVIATIONS

AC/DC	Alternating Current/Direct Current
AED	Automated External Defibrillator
ALS	Advanced Life Support
AMI	Acute Myocardial Infarction
ANOVA	Analysis of Variance
BLS	Basic Life Support
CFR	Community First Responder
CI	Confidence Interval
CoSTR	Consensus on Science with Treatment Recommendation
CPP	Coronary Perfusion Pressure
CPR	Cardiopulmonary Resuscitation
DNR	Do Not Resuscitate
ECG	Electrocardiogram
ECMO	Extracorporeal Membrane Oxygenation
EMCC	Emergency Medical Communication Center
EMS	Emergency Medical Service(s)
ERC	European Resuscitation Council
EU	European Union
FR	First Responder
GDPR	General Data Protection Rule
GPS	Global Positioning System
GSM	Global System for Mobile communication
ICD	Implantable Cardioverter Defibrillator
ILCOR	International Liaison Committee on Resuscitation
IQR	Interquartile Range
LFR	Lay First Responder
MCCU	Mobile Coronary-Care Unit
NEJM	New England Journal of Medicine
OHCA	Out-of-Hospital Cardiac Arrest

OLS	Ordinary Least Square
OR	Odds Ratio
PAD	Public Access Defibrillation
PCI	Percutaneous Coronary Intervention
PCL	Post-traumatic stress disorder Checklist
PEA	Pulseless Electrical Activity
PTSD	Post-traumatic Stress Syndrome
pVT	Pulsless Ventricular Tachycardia
RCT	Randomized Controlled Trial
ROSC	Return of Spontaneous Circulation
SAMS	Small Area for Market Statistics
SCAS	Swedish Core Affect Scales
SMD	Standard Mean Deviation
SRCR	Swedish Register for Cardiopulmonary Resuscitation
TM	Text Message
VT/VF	Ventricular Tachycardia/Ventricular Fibrillation
WHO	World Health Organization
WMA	World Medical Association

1 PREFACE

Cardiac arrest is a lethal condition, which leads to death if not treated promptly within the first few minutes. Mostly, the victim is an individual without a previously known heart disease, and the most common place for the “sudden” nature of a cardiac arrest to appear is outside clinics, at home or in public areas. Historically, survival in out-of-hospital cardiac arrest (OHCA) has been low, and it is practically regarded as a condition equivalent to definite death.

A significant amount of research has addressed the problem with the aim to improve survival rates, and advances in treatment have nearly doubled survival in a 20-year perspective. Still, survival remains low worldwide, where only one in ten survives.

The big challenge for the healthcare system is to reach the patient *within a very short timeframe* from collapse. Internationally, different methods have progressed depending on the nature of underlying care systems, although at this time point several methods have reached consensus worldwide. One agreed-upon approach is the “chain-of-survival” which was introduced in 1991 by way of international guidelines for resuscitation. [2]

Concerning the short timeframe, a problem lies within the hands of a volunteering society, which can help shorten the response time with early recognition and knowledge of hands-on cardiopulmonary resuscitation, as well as bringing public automated external defibrillators (AEDs).

This thesis is about interventional research regarding the dispatch of volunteering lay responders to suspected OHCA, and their involvement in resuscitation.

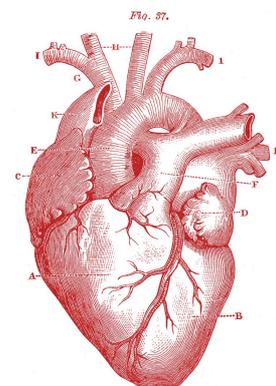


Figure 1. Joseph C Hutchinson
A Treatise on Physiology and Hygiene for Educational Institutions and General Readers, 1872
Work in the public domain.

2 HISTORY

2.1 APPARENTLY DEAD

The first reported effort to resuscitate an “apparently dead” person with electricity was carried out in 1774 by a Mr. Squires on a girl who had fallen from a window of a residential building. A called upon apothecary declared her dead, but a neighbour, Mr. Squires, was allowed to try electrical stimulation. He shocked different parts of her body and after a few shocks to the thorax a weak pulse was detected. She began to breathe and was fully recovered.[3] At the same time, Peter Christian Abildgaard, discovered the “countershock” by first shocking a hen in the head so that it appeared dead, and then giving a shock to the chest, which revived the hen. [4] Dr Charles Kite carried out the first comprehensive study in drowning and sudden death in 1788. [5] He was the first one to acknowledge the need to resuscitate immediately and out in-field, and sketched the first portable (Leyden Jar-) defibrillator. [6] In 1802 the Royal Humane Society in London proposed that electrical shocks should be used to distinguish between the apparently dead and the real dead. [7] During the 19th century’s galvanic and electrical discoveries the public fascination for electricity peaked and then fell in the hands of amateur quacksalvers.

2.2 DEFIBRILLATION AND CHEST COMPRESSIONS

Ventricular fibrillation (VF) was discovered with electrification. Carl Ludwig and Moritz Hoffa were the first to describe ventricular arrhythmia in 1849 as a “bizarre and chaotic action in the ventricles when exposed directly to electric current” and later Edme Vulpian named the action *fibrillation* and proposed that the arrhythmic movement was generated from the heart itself. Jean-Louis Prevost and Frederic Battelli continued his work with their study “La mort par les décharges électrique” (Death by electric discharges) from 1899. [8] They reported in 1899 that they had induced VF by a small shock over the chest, and in a footnote: that a larger shock reverted back the VF to normal rhythm. [8]

In 1933, funded by the Edison Electric Company, a research group at Johns Hopkins University Hospital under engineer William Kouwenhoven rediscovered defibrillation once again with a “counter shock” to the fibrillating heart of a dog. [9] Later, in 1958, they accidentally invented closed-chest CPR when pressing the pads firmly on the chest. [10] Carl J. Wiggers was first to explain mechanically the time window of VF and when successful resuscitation with electricity could be possible. He applied cardiac massage 30–60 seconds before the counter shock and could by this means extend the shock-treatable

period of VF from 3 minutes to 5–8 minutes. [11] He also invented the method of serial shocks. [12] The first physician to apply defibrillation to human VF was Dr Claude Beck in 1946 on a 14-year-old patient undergoing thoracic surgery. After open-chest cardiac massage and defibrillation the boy was resuscitated. [1, 13] Kouwenhoven and Beck's defibrillators were large and bulky (120 kg) and demanded an open-chest procedure and power connectors within the hospital walls.

In 1955, Paul Zoll became the first to report several successful closed-chest resuscitations with his external pacemaker/defibrillator. [14] But also his apparatus could only be wheeled in to the emergency room due to the heavy transformer. [7] In Russia Dr Lina Shtern and her student Naum Gurvich worked on safety, comparing AC & DC and found the thresholds for capacitance needed for closed-chest defibrillation without damaging the heart. [15] Gurvich invented the first biphasic waveform external defibrillator in 1952. Later, in the US, the biphasic defibrillator was reinvented by Lown-Berkowitz, in 1962, and it first came into use for VT patients followed by implantable cardioverter-defibrillators (ICDs). [16] Not until the 1990s did the biphasic waveform re-enter as the safe standard of the automated external defibrillators (AEDs) of today. [7]

2.3 EMS – FROM FIRE FIGHTERS AND DOCTORS TO PARAMEDICS

As early as in 1799 Charles Kite stated that resuscitation needed to be conducted instantly out in the field. This was also recognized by physician J. Frank Pantridge, and Geddes in the Belfast programme, Northern Ireland, in 1966. They developed a mobile coronary-care unit (MCCU) with a physician and a nurse from the cardiac department to monitor patients with suspected myocardial infarction. They brought out a heavy portable defibrillator plus two car batteries in the field.[17] Later, in 1971, Pantridge developed a smaller defibrillator. [18] The MCCU became the start of the era of all emergency medical services (EMS). William Grace adopted Pantridge's idea in the US in 1968 and copied the MCCU concept in New York. [19] Several mobile coronary-care units emerged in other areas. But, as stated in an editorial in NEJM in 1969, reports of successful resuscitations were mostly anecdotal and this type of high professional staffing would be costly and a logistical problem. [20]

However, Eugene Nagel in Miami began to train fire fighters and send them out with a radio and telemetry link as a legal extension of the physician. And shortly after, in 1970, Leonard Cobb started studies with the Seattle Fire department who early had

computerized data on first-aid runs. He developed a training program (Medic 1) to educate fire fighters, medical technicians and “paramedics” in CPR and defibrillation. He invented the tiered response system, where the medical technician first arrived and provided CPR, and after came the paramedic with defibrillator and intubation.

In Sweden, until the 80s, an ambulance was manned with two drivers, either fire fighters or taxi drivers without specific medical training. In 1978 the Swedish National Board of Health and Welfare instituted a compulsory 7- week course in basic pre-hospital care, and gradually the competence requirement increased to paramedic standards (a 20-week course). In 2005 it was required that at least one of the personnel was a nurse. Medical treatment was until then delegated under the direction of the pre-hospital senior physician. [21] It was not until 1985 that a manual defibrillator was added to the equipment and later replaced with semi-automatic monitors/defibrillators at the time of the millennium.

3 INTRODUCTION

3.1 DEFINITION

A cardiac arrest is “the cessation of cardiac mechanical activity as confirmed by the absence of signs of circulation” as defined by the “Utstein” template for resuscitation care. [22] “Sudden cardiac arrest/death is a condition that happens unexpectedly, within a very short time period of 1–2 hours from cause in a person without any known prior symptoms and can be the first manifestation of coronary heart disease. Sudden cardiac arrest death accounts for 15–20% of all natural deaths internationally. [23]

A cardiac arrest that appears outside clinics is called an out-of-hospital cardiac arrest (OHCA). These cases are registered by the emergency medical service (EMS) personnel by the definition “EMS-attended” or usually “EMS treated” in which a cardiac-arrest victim is not obviously dead, nor awake, but a case where the EMS have tried resuscitation. These cases of OHCA form the basis of for most research studies in this particular field.

3.2 INCIDENCE AND SURVIVAL DATA

Worldwide, approximately 300 000 persons per year suffer from OHCA. [24] The incidence of EMS-attended OHCA differs globally: (per 100 000 person years) Asia: 52.5, Europe: 86.4, North America: 98.1 and Australia: 111.9. [23]

In Sweden the incidence was 58/100 000 person years in 2018. Between the years 1992–2016 an increase in survival was seen from 4.5% to 11% leading to nearly 300 more survivors per year. [25]

3.3 THE UTSTEIN TEMPLATE

As in all research, comparing intervention counts and results between different areas and disciplines is a difficult task. The Utstein template was developed after a multidisciplinary meeting in the Utstein Abbey outside Stavanger, Norway, in 1990, with the aim of finding a consensus for terms and definitions in out-of-hospital resuscitation research. It has been revised twice, most recently in 2014. [26] Most registers use this template in reporting OHCA's.

Ambulance personnel register all OHCA-treated patients in the Swedish cardiac-arrest register (SRCR) directly after resuscitation. Some measures are best guesses (e.g. etiology) since their work is early in the diagnosis.

3.4 ETIOLOGY AND PATIENT CHARACTERISTICS

Sudden cardiac arrests are mainly related to coronary heart disease (70–75%). [27] For the most part, the OHCA occurs at home (65–75%), and otherwise in public areas. [28–30] The median age in Sweden is 71 years old and it is more common in males (69%). Females are older when they suffer from OHCA. [25]

3.4.1 Medical and non-medical

The updated Utstein template characterizes the cause into medical and non-medical. The true cause of an OHCA can be difficult to ascertain, especially in the pre-clinical setting, and post mortem analysis typically only reveals structural diseases. [23] The diagnosis and treatment of a cardiac arrest is assembled around these symptomatology.

3.4.1.1 Medical

Medical cases are typically of cardiac origin such as acute myocardial infarction or arrhythmia due to structural heart disease. Medical cases also include OHCA due to hypoxia caused by pulmonary diseases, or OHCA due to circulatory failure caused by sepsis, bleeding or other excessive serious conditions or sudden dehydration. Other medical causes include electrolyte disturbances such as hypo or hyperkalemia, pulmonary embolism or cardiac tamponade, where blood and fluids pile up in the pericardium.

3.4.1.2 Non medical

Traumatic cases can be a result of blunt or penetrating violence directly affecting the heart and lungs or through massive bleeding and tension pneumothorax. They can also be due to intoxication from fumes or gas, but mostly due to drug overdose (opiates). They can be caused by asphyxia from drowning, foreign-body airway obstruction, hanging, electrocution accidents and hypothermia from massive refrigeration due to cold weather or water. [31]

3.4.2 Shockable and not shockable

As mentioned above, sudden cardiac arrests are mainly related to coronary heart disease (70–75%) and the most usual pathophysiological cascade is acute myocardial ischemia that triggers ventricular arrhythmia of pulseless ventricular tachycardia (VT) and/or ventricular fibrillation (VF), which in time deteriorates to asystole. [27] Other first-registered ECG patterns seen in cardiac arrest include Pulseless Electrical Activity (PEA).

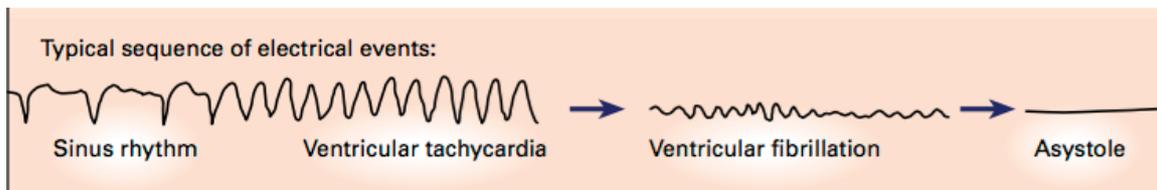


Figure 2. The typical sequence of electrical events, adapted from Huikuri et al. [27] Reproduced with permission from NEJM, Copyright Massachusetts Medical Society.

3.4.2.1 Not shockable

Asystole is the total absence of electrical activity in the heart, whereas in PEA, there is electrical activity without meaningful mechanical contractions of the heart. Asystole and PEA constitute 75% of all ECG patterns in OHCA and cannot be converted to meaningful contractions that restore circulation by means of applying an electrical shock (defibrillation) to the chest. These rhythms are therefore named “not shockable” and hence survival is very low in these cases. Reported survival in the SRCR register was 1% in 1992 (n=2500) and in 2016 it was 4.6% (n=5300) for not-shockable OHCA.

3.4.2.2 Shockable

VT and VF can be converted to normal heart rhythm by means of defibrillation and are therefore named “shockable rhythms”. Approximately 25% of all OHCA cases present with VF/VT on first ECG. However, the incidence of VF/VT is strongly time-dependent. If the victim is reached very early in the course of the arrest there is a higher probability of VF/VT. Cases with VT/VF have the highest survival rates. [32, 33] In 1992, 35% of cases were found in VF and the survival was 12%. In 2016, 21% were found in VF and the survival rate was increased to 33%. [30]

3.4.2.3 Ventricular fibrillation

The incidence of VF was 35% in Sweden in 1992 and 21% in 2015. Internationally, there has been a decline in the proportion of VF and possibly a rise in PEA during that period. Proposed factors contributing to this include advancement in medical interventions such as PCI and ICD, and medicine (beta blockers), [34] but also an aging population. [23] Recent studies have shown that the decline in VF in OHCA in residential areas seems to have leveled and there were no signs of decline in the OHCA in public places. [35]

The crucial part is the presumed frequency of VF early in the arrest process. We know that the odds of revival are very high by means of defibrillation during VF [32, 33] yet we have

difficulties to reach the patients as the cardiac arrest appears suddenly and most often outside clinics. We have to rely on immediate on-call responses.

3.5 KNOWN FACTORS THAT IMPROVE SURVIVAL

Herlitz et al. studied factors associated with increased survival in a sample of 33 453 OHCA with cardiac etiology treated but not witnessed by the EMS according to the Swedish SRCR register. [36] They listed six important factors for survival:

3.5.1.1 Ventricular fibrillation

The presence of ventricular fibrillation or pulseless ventricular tachycardia (VT) was the strongest predictor (OR: 5.3) of survival. In this group, 30% survive with good neurological outcome. [37] If a patient in VF is found and defibrillated within 3–5 minutes as many as 70–50% can survive. [38, 39]

3.5.1.2 EMS response times

A short EMS response time of ≤ 6 min showed an odds ratio of 3.6 for survival. Similar results independent of other factors such as CPR were seen in a Scottish study. [40] A German study comparing faster and slower EMS response times showed a linear decrease in survival independent of bystander CPR. [41]

3.5.1.3 Public place

OHCA victims found in public places have a double advantage compared with patients found in their homes. This is true even if controlled for other important factors such as bystander CPR, witnessed status, age and response time. Possible reasons could be unknown factors such as time till an emergency call (a 112-call in Sweden) or bystander-CPR quality. On a group level, persons walking outdoors might be more fit than persons staying inside.

3.5.1.4 Witnessed status

If a cardiac arrest is witnessed the odds of survival are doubled. This can be due to shorter time until a 112-call and early onset of CPR.

3.5.1.5 Bystander CPR

A stable predictor of survival is the presence of a bystander or a layperson performing CPR. In a Swedish study, 30 381 witnessed OHCA were matched according to bystander

CPR status before EMS arrival and there was a difference in 30-day survival of 4% vs. 10.5% (OR 2.15, 95% CI 1,88–2,45).

3.5.1.6 Age

An unmodifiable factor is age. The older you get the smaller the chance of survival. Herlitz found that someone with an age under the median (73 years) had higher odds of survival.

A newly investigated difference is also seen in sex. Females have a lower chance of survival than men. This could partly be because they live longer and therefore are older, and possibly older people stay more at home alone, without any witness to a cardiac arrest. When controlled for these factors a lower proportion of VF cases remained and could explain the sex difference. [42]

3.6 THREE PHASES OF RESUSCITATION

Myron et al. proposed a three-phase model based on time from collapse to intervention, where the treatment should be guided by the predominant dysfunction: the first phase of 0–5 min: electrical, the second phase of 4–10 min: circular, and a third phase of more than 10 min: metabolic. CPR was beneficial as regards survival in the circular phase, but not in the electrical phase. [43]

3.6.1 Defibrillation

Defibrillation is the only way to treat VT/VF. By applying an electrical shock to the heart, the fibrillating conduction system can reorder and restart to a normal pace.

Early defibrillators have progressed from a complicated open-chest apparatus only possible to use in a clinical setting, to smart and safe automated external defibrillators (AEDs) that can be maneuvered even by an untutored person. The AED is self-instructive and tells you what to do. Cummins and Eisenberg reported no difference in outcomes between semi-automated defibrillators and AEDs used by medical technicians and they concluded that AEDs have advantages in training, skill retention, and faster operation. [44] It was shown that the survival effect of an AED used by non-medically trained staff was beneficial, or even outstanding in controlled areas where the implementation had power to be fully executed, for example in flights and flight terminals, [39] or in casinos. [45]

If a case of VF is defibrillated within the first few minutes, directly without any CPR, as for example in implantable cardioverter defibrillators (ICDs), restoration to organized

electrical activity can be achieved immediately. In this early phase, in the field, the addition of CPR does not add any survival benefit. Cases of both VF with and without CPR survived at a rate of 53% if defibrillated the first 1-5 minutes. [46]

3.6.2 Cardio-pulmonary resuscitation (CPR)

If there is more than five minutes since collapse the combination of CPR and defibrillation is most successful. [46] Cardiopulmonary resuscitation –CPR – is recommended by international guidelines when a person is unconscious and not breathing normally. ERC guidelines [26] teach a loop of 30 compressions and two rescue breaths, continued until professionals take over. Rescue breaths oxygenate the lungs and chest compressions provide blood flow to the brain by building up cerebral and coronary perfusion pressure (CPP). Guidelines also stress continuity in chest compressions, to reach and maintain a functional cardiac output for good perfusion in the heart and brain. [26] It takes at least 30 seconds of high-quality CPR compressions to build up a functional CPP. During interruptions CPP falls and you have to start over again. A functional CPP is needed by the heart's conduction system to be susceptible to defibrillation. [47] In this way the combination of CPR and defibrillation results in a return of spontaneous circulation (ROSC).

CPR is easily taught. It can be disseminated through elementary schools, by school teachers to children, [48, 49] and in Sweden as many as 5 million courses have been attended. Telephone-assisted CPR consists of instructions executed by the 112-operator to calling witnesses. Simplified CPR (hands-only) can be conducted by persons with limited experience and training and may be lifesaving. [50]

4 LIFE SAVING RESOURCES

4.1 THE CHAIN OF SURVIVAL

Being a condition that needs to be attended immediately, some factors are critical in the endeavor to increase the low rate of survival. Firstly, the cardiac arrest has to be *witnessed* and *recognized* by someone and the witness/bystander has to *make a call* to an emergency dispatch center. Secondly, the dispatcher has to be able to *interpret the situation* as life-threatening and that there is a possible cardiac arrest. The dispatcher needs to identify the location indicated and send out the right *emergency resources* to the victim, and in the meantime he/she *instructs the bystander* in CPR. The emergency services then need to navigate fast through traffic and be prepared with a *defibrillator* and staff that can provide *defibrillation, chest compressions* and *ventilation*. To fully recover with good neurological outcome, *medical attendance* is needed. At hospital the physicians need to recognize the cause of the sudden arrest and provide treatment accordingly.

International guidelines call this the *chain of survival*, [2] where every part is equally important and dependent on each other for the succession to survival. But most of all it is a matter of *time*. Time until onset of resuscitation is also a factor for the rate of survival of patients found with pulseless ventricular tachycardia or ventricular fibrillation (pVT/VF).



Figure 2. The chain-of-survival. Reproduced with permission from Elsevier.

4.2 RECOGNITION AND SENSITIVITY

Recognition of an OHCA can be difficult and efforts are made in campaigns to guide the public by way of education in recognition and basic CPR. Dispatcher-assisted CPR is one way to shorten the time to chest compressions and CPR.

Recognition by the dispatcher at the EMCC who is the first professional to be reached by a caller is crucial in order to promptly recruit the EMS and other resources. Recognition can be difficult when the dispatcher has to rely on witness answers in order to make a decision. When to execute the dispatch varies in different countries. In a review the sensitivity was 14-83% and a median of 73.9%. [51] One reason for delayed recognition could be the presence of gasping or agonal breathing. [52] Gasping is a brainstem-induced reflex and frequent early after a cardiac arrest, although it decreases rapidly. [53] Survival rates are higher for persons found gasping. [54]

4.3 EMERGENCY RESOURCES

Emergency medical service systems vary across the world. Two types of organization have been distinguished and debated: the Anglo-American (load-and-go) and the Franco-German (stay-and-play). [55] These discrepancies stem from organizational factors such as tradition, number of vehicles and pre-hospital educational levels from medical technicians to anesthesia physicians. Across Europe we seem to have a mixture of them depending on resources in the country. [56] Discrepancies can also stem from studies in emergency medicine and depend on the type of priority call. Examples are the trauma emergency which leans more towards load-and-go (golden hour) and the medical emergency which leans more towards stay-and-play (period of VF). [57] There is no exact consensus on which system provides the best outcome, and efforts to have comparable data across countries have been made by the EU and the WHO. Two important measures are *number and types of responses*: basic life support and/or advanced life support, and *response times*, the measure from the emergency call to when the first unit arrives. [58]

As regards the OHCA patient, the *basic life support (BLS)* response concerns checking consciousness and agonal breathing, providing CPR with chest compressions, ventilation and defibrillation. The *advanced life support (ALS)* response is the same as BLS with the

addition of administration of medication, sedation and advanced airway management, i.e. intubation. [59] In some systems (i.e. Franco-German) if a patient has refractory VF the pre-hospital physicians (providing ALS) can start extracorporeal membrane oxygenation (ECMO), which means inserting a small heart-lung machine in large arteries or veins, at the place of arrest, out in the field. [60]

In Sweden, all ordinary ambulances are staffed with a paramedic and a nurse trained in ALS, and they carry a defibrillator as well as equipment for intravenous medication and assisted ventilation in form of (at least) a bag valve mask or a laryngeal mask. In Stockholm it is required that at least one person of the two in an ordinary ambulance is a nurse specialized in anesthesia or pre-hospital care with the skill of performing intubation.

In cases of a sudden cardiac arrest in Sweden an ordinary ambulance is dispatched as first tier at the earliest suspicion, which can be unspecified and indexed as “*serious medical condition*” or “*unconscious patient*”. As a second tier, when the suspected cardiac arrest is more verified as being “*unconscious and not breathing normally*” an advanced ALS vehicle with a physician and/or nurse anesthetist is dispatched. The ambulance response time for the first tier is 11 minutes.

4.3.1 EMS Response times

The survival rate in cases of OHCA drops linearly for every minute passed in shockable rhythm [61, 62] and is associated with EMS response times. This is also seen in Swedish registers (Figure 3).

The median response time for an ambulance to reach OHCA from the call to the dispatch center has increased from six minutes in 1992 to 11 minutes today. [30] The number of ambulance missions increased by 25% in the five years between 2009 and 2013. [63] One natural reason for this could be the steadily growing population in Sweden, from 8.5 million in 1992, to nearly 10 million in 2015, and it is possible that the EMS system has not increased in the same manner.

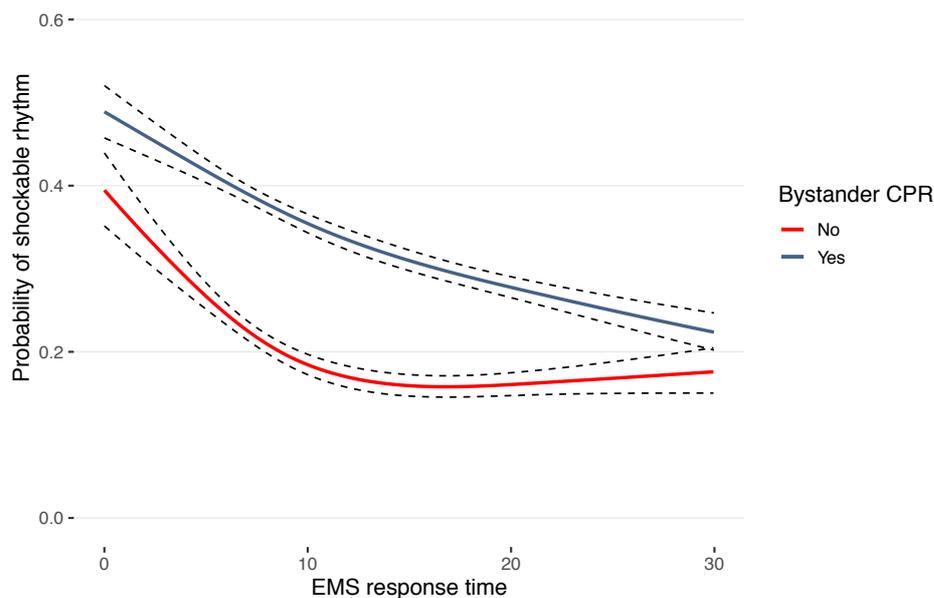


Figure 3. Relationship between EMS response time (X-axis) and the probability of having a shockable initial rhythm (Y-axis)

4.3.2 Two-tiered dispatch

The internationally most favored method of reaching an OHCA victim before declining VF occurs is a two-tiered solution, [55, 56, 64] with a first vehicle with at least BLS competence plus an AED [65], and a medical technician or paramedic as crew, and a second vehicle with ALS competence (either a specialist nurse or a physician as crew). The benefit of ALS itself has been discussed. [66] The OPALS study in Canada (an observational study) showed that the addition of ALS vehicles to a newly implemented BLS response did not increase the rate of survival. [67] However, a recent US study showed that ALS was important, when the ALS arrived either first alone, or after less than six minutes after BLS, survival rates was increased. [64, 65] In different arrondissements in Paris, the density of ALS (and BLS) vehicles also seems to have an impact on the rate of survival to discharge. [68]

4.3.3 Fire fighters and police

In an early study, Weaver et al. compared survival rates after shocks given by ordinary fire fighters with AEDs versus standard defibrillation by paramedics. In areas where paramedics had longer response times, fire fighters used AEDs. Survival to discharge in the fire-fighter/AED group was 30% versus 19% in the paramedic group. Another finding was that 15% of the AED-treated group had gained consciousness when the paramedics arrived. [69] During the 90s several programs emerged with the aim of giving instructions

to fire fighters and police officers, and AEDs were placed in their vehicles. In a review in 2013, Husain et al. calculated a pooled relative risk of survival of 1.4 (95% CI 1.3–1.6) when police applied an AED. [70] In a randomized study from the Netherlands, van Alem et al. concluded that there were no differences in survival, but a small increase in ROSC when fire fighters and police were dispatched. [71]

In most areas in Sweden an additional tier consisting of fire fighters and/or police is dispatched along with the second tier. In a nationwide Swedish study the additional dispatch of fire fighters and police to the conventional EMS was associated with a moderate increase in survival (conditional odds ratio 1.27 [95% CI 1.05–1.54]). [72]

4.3.4 Fire fighter and police response times

Time to recognition not only influences dispatch-assisted CPR but can also affect the total response time of resources by prolongation of the time it takes to alert resources. [73, 74] Whether or not additional BLS teams such as fire fighters and police officers as “first responders” are dispatched simultaneously with the EMS differs between settings, [70] and EMS systems with simultaneous dispatch show high rates of survival, and fast times to defibrillation. [75, 76]

In the Dutch study by van Alem et al., [71] in 75 cases the first responders came first in 75 cases of OHCA and in 85 cases the EMS came first. The delay from witness call to dispatch of the EMS was in median 120 seconds, and the delay to dispatch of the first responder was 180 seconds. The difference in total response time was small (decrease in call to defibrillation of 101 seconds) and there was no increase in survival. The small difference in response times was attributed to the delay during dispatch. In the study by Husain et al., the authors concluded that the use of the police force is beneficial, but they also acknowledged that challenges in implementing these programs are large, and dependent on the cooperation of decision-makers within different working fields (dispatch, police force, healthcare). They also stressed that if first responders and EMS are not dispatched simultaneously, the police will not arrive first at the scene. [70]

4.3.5 Community first responders

A particularly rarely studied group is that of “community first responders” (CFRs). [77–79] They have often emerged out of local trusts and are common in countries such as Great Britain. Community first responders are volunteers/professionals who can often be

dispatched in remote areas when the response time for the EMS is too long. They are usually locally based in the area of the victim and can be lay people [80] provided with a short course in first AID and CPR, and they can be equipped with first-aid materials, oxygen and AEDs. In some areas they are full- or part-time fire-fighter volunteers or medical personnel, [81] or on-duty regular fire fighters or community district nurses [79] or physicians. [78] The group is not easily defined, and is sometimes confused with other complementary responders in general, but they do serve as a complement to the EMS and are dispatched from the EDC according to different schemes across the world. Depending on the scheme they can respond while waiting for the EMS to arrive at cardiac events, providing CPR and/or defibrillation, and first aid. There are not many studies on this group, but the results of some qualitative studies have been summarized. [77] In Sweden we have CFRs who are called "In waiting for the ambulance" (IVPAs). [82] They have previously been part-time fire fighters and (more recently) home-care nurses. [79] One advantage of CFR systems is that individuals can be dispatched to all types of priority-1 calls, and therefore can often reach the victim before the EMS. [83] In some CFR systems communication is strong between the dispatch center and the CFRs.

4.4 ENGAGE SOCIETY

4.4.1 CPR courses for the public

Cobb was the first to include laypersons as an active part of the emergency system by educating the public in CPR in 1972. [84] In 1974 he reported his successful data [85] and Seattle still has one of the highest survival rates (16%) of EMS-treated OHCA's worldwide. [86][24] In Sweden by 1981, Stig Holmberg developed a national CPR education programme with the aim to disseminate CPR to the general population. By now, 5 million courses in basic CPR have been registered at the Swedish council for cardiopulmonary resuscitation (Chair Claesson A. personal communication). Sweden has a high rate (77%) of bystander CPR in general. [25]

4.4.2 AEDs, and AED-registers

In the 1990s the American Heart Association took on a task force to enhance engagement of civilians with CPR and early defibrillation by asking the medical industry to produce safe and easy-to-use AEDs at low cost for use by untrained laypersons. In 1993 the medical industry answered the question strongly and the market exploded all over the industrialized countries of the world. [87] Up to now, in Sweden, 44 000 AEDs have been

sold to working businesses, organized aid associations and private persons. [88] A Swedish national AED register was initiated in 2009 with the aim of increasing public awareness, and to make AEDs available. In 2019 the register covered almost 19 000 validated AEDs, mostly placed in offices and workplaces (43%), with others in shops, public buildings, and recreational facilities. Only 3% are placed in residential areas. [89, 90] A drawback of AED registers is the problem of accessibility. In Sweden, Fredman [91] showed a mismatch between AED placement and OHCA locations. A study in Denmark showed that bystander defibrillation of OHCA during opening hours was tripled compared with when AEDs were not easily accessible. [92]

4.4.3 Public access defibrillation

Public-access defibrillation (PAD) programs have emerged to engage laypersons, and studies followed. The programs needed extensive information campaigns, organizational plans, as well as education in CPR and the use of AEDs. [93] In an early prospective trial from 2004 by Hallstrom et al. [94] involving 19,000 volunteer responders in 993 community units in the US, units were randomized to either CPR responses with AEDs, or CPR only. 1600 AEDs were placed in public areas such as shopping centers and recreational facilities in the communities assigned to CPR/AED. The relative risk of survival to hospital discharge was favorable in the CPR/AED communities, with 30/128 survivors versus 15/107 ($p=0.03$; RR 2.0; 95% CI 1.07 to 3.77). Several international observational studies confirmed these results, with increased survival ranging from 4.4–51.0% for the PAD programs compared with no program (1.4–25.0%). [95]

The cost-effectiveness of PAD programs was regarded as good in areas with a high frequency of both cardiac arrests and CPR-trained civilians, but otherwise questioned. [96–98] Other discussions and problems that arose with the PAD programs included where the AEDs should best be placed for accessibility. [99] Should the shock be applied as soon as the AED was attached, or after a period of CPR? [100] What about persons that should not be resuscitated – terminal patients, and very old persons? [101] The “Do Not Resuscitate” (DNR) habit re-emerged from the 19th century in the form of chest tattoos, which have created dilemmas for medical attendants. [102, 103] But the major problem with the PAD programs was that they did not improve the survival rate in residential areas, where the majority of OHCA take place. [28, 104–106] Placing AEDs in the homes of cardiac patients did not change this either. In a large randomized trial of 7001 patients with previous

anterior-wall myocardial infarction, AEDs were placed in the homes of the intervention group but there was no significant improvement in mortality. An AED was used in 32 patients, of whom only 14 received a shock and four survived to hospital discharge. [107]

4.5 DISPATCH OF NEARBY LAY RESPONDERS VIA MOBILE PHONE

A possible solution to the problem arose in the modern era of global systems for mobile communication (GSM) and later, global positioning system(s) (GPS) as mobile phones became more and more advanced as well as common in society. The idea was early formulated in different parts of the world to engage volunteering laypersons (that had taken a course in CPR) for dispatch directly to the scene of an OHCA. [108, 109] This type of systems was early operational in Switzerland in the Ticino region in 2006, [110] the Dutch region of Twente in 2008, [111] and in North Holland in 2010, [112] as well as in Stockholm region in 2008. [113] In the US the smartphone application PulsePoint was launched in 2010. [114] Later app-based systems included those launched in Nordrhein-Westfalen in 2013 (Mobile Retter), London (GoodSAM), in 2015, [115, 116] Singapore, (myResponder), in 2015, [117] Copenhagen (Heartrunner) in 2017, [118] and Bologna, Italy (DAE ResponderR) in 2017, [119] and Paris (StayingAlive) 2017. [120] In Spain there is a pilot lay responder system with a smart watch, [121] although not clearly stated if it is dispatched by the dispatch center.

In Sweden the text message (TM) system was rebuilt as a smartphone application integrated with the national AED register in 2015. The new version (Heartrunner) operates in the study regions of Stockholm since 2015, and Västra Götaland since 2016. The same system is also newly integrated in regions of Blekinge, Kronoberg, Sörmland, Västmanland and Östergötland. In the latest version lay responders are located via smartphone GPS and dispatched and directed to go directly and perform CPR (1/5) or to bring a nearby AED (4/5). The same system also operates in region of Copenhagen, and was expanded to the whole Denmark in 2020. Run-in and trial data are presented in the results below. [88]

4.5.1 Principal functions

The lay responder downloads an app or registers in a text-messages system where the dispatcher at the local EMCC can send an alert in cases of a suspected OHCA. All systems basically have the same purpose: to summon volunteers to an OHCA via an alert from the EMCC.

Some differences are seen in the systems, which can be technical and configurational. These differences can involve GSM and text messages with a link, [112, 122] GPS and smartphone app notification, [88, 118] distance in search radius, number of lay responders located and alerted, and division of tasks (CPR/AED). Differences are also seen in having AED registers incorporated or not, route directions to selected AEDs [88, 118] or use of a general AED map [114, 123] and selective dispatched of lay responders to public places [114, 120] or to both public and residential areas. Regarding educational level, some systems have no requirements at all, [117, 119] others recruit only experienced personnel on free time, [81, 124, 125] and others offer education courses in first aid and BLS, which need to be completed before participation. [83] Most systems require a basic course in BLS/CPR. For some systems it is not at all clear if they solely recruit and summon laypersons, [126] and some systems dispatch both lay- and on-duty first responders in blue-light vehicles. [110] Some systems are more organized as community first-responder systems. [83, 127]

4.5.2 Lay responder outcomes

So far only observational data or descriptions of systems have been published, with the exception of one randomized study conducted here in Stockholm, Sweden, in 2012–2013. The study could show an increase in bystander CPR by 30% with the use of a text message (TM) system to locate and dispatch lay responders to nearby OHCA. [128]

Some important observational studies have been published. In the Netherlands, Zijlstra et al. investigated the TM system in North Holland and Twente, where dispatched laypersons used AEDs on OHCA victims in two regions of the Netherlands between 2010–2013 and they reported that lay responders attached AEDs in 12% (184 of 1536) of all OHCA and defibrillation was performed 2:39 min:sec earlier than EMS. Of these AEDs, 87.5% were brought to residential areas. [112] A later study in the same area concerned the densities of public AEDs and lay responders. Of 813 patients (45%) with shockable initial rhythm, 17% had the first shock delivered by a lay responder. In this group the density of public AEDs was associated with time to defibrillation, where an increase of AED density decreased the time from median 10:59 to 08:17 min:sec ($p < 0.001$). The density of lay responders was also associated with a decrease in time to defibrillation from median 10:59 to 08:20 min:sec ($p < 0.001$). [129]

Piljs et al. compared cases of OHCA where lay responders were and were not dispatched

in 2012–2014 in the region of Limburg. They found an increased odds ratio of survival to discharge in the lay-responder-dispatched group (adj. OR 2.82, 95% CI 1.52–5.24; $p=0.001$). [122] The TM system is still operational in the Netherlands although two apps are working but have not yet been evaluated. [130, 131]

In Seoul, Korea, CPR courses, an AED register and a lay-responder text-message system was launched in 2015, and in a “before and after” implementation study significant increases of bystander CPR (adj. OR 1.25 [1.08–1.44]) and survival to discharge were found (1.84 [1.29–2.63]), plus good neurological outcome (2.31 [1.44–3.70]). [132]

In Ticino, Switzerland, Caputo et al. compared a text-message system (2006 onwards) with smartphone app technology and found a brisker response time in the app group (3.5 [2.8–5.2] versus 5.6 [4.2–8.5] min, $p 0.0001$) as well as a greater proportion of first arrivals (70% versus 15%). [133] In a later geo-position study they found that lay responders travelled at a median speed of 6.9 m/s (IQR 4.5–9.8) over a distance of 1196 m (IQR 596–2314), and were assumed to be travelling by car. Only 4.4% showed a walking speed (< 1.5 m/sec). The median time it took for a lay responder to go directly to the site of an OHCA was 197 sec (IQR 120–306), and via an AED it was 275 sec (IQR 184–414) ($p < 0.001$). [134]

In Germany, Stroop et al. compared CPR performed by a) “mobile rescuers”, b) bystanders and c) EMS. They found that the response time was shorter (4 versus 7 min), the hospital discharge rate better (18% versus 7%), with better neurological outcome (11% versus 4%) in the mobile-rescuer group. There were no differences between the mobile-rescuer group and the bystander group. [126]

In a study from Copenhagen, Denmark, 42% of lay responders reached the OHCA before the EMS. Of the OHCA's reached by the lay responders, 80% were in residential areas. If a lay responder arrived first, there was a significant increase in bystander CPR (85.3%, OR 1.76 [1.07 to 2.91]) and bystander defibrillation (21.2%, OR 3.73 [2.04 to 6.84]) compared with first arrival of the EMS. [118]

In a study from Paris, OHCA's in public places where lay responders arrived ($n=46$) were propensity-score-matched ($n=42/72$) with OHCA's where lay responders did not arrive ($n=320$). As regards survival after hospital discharge the difference was a 35% versus 16% (adj. OR 5.9 [95% CI 2.12 to 16.54], $p < 0.001$) advantage for the lay-responder OHCA's. [120] A problem with this study was in the matching, where the places of arrest were

significantly different; there were more OHCA's out on the street in the interventional group, whereas the controls were more commonly inside public buildings.

In Denmark, on the island of Langeland, where distances for EMS are long, the community started a project in 2012 with education of volunteers in first aid and CPR and they were given a map of AEDs placed at strategic places over the island. In every case of priority-1 calls 185 volunteer FRs were alerted within 5000 meters. Of those who accepted, three responders were picked by the dispatcher, one to fetch an AED and two to go directly to the scene. Community lay responders arrived before EMS in 85% of all priority-1 cases (n=2662), and median response times were 4:46 min (IQR 3:16–6:52) as opposed to 10:13 min (6:14–13:41) for EMS ($p < 0.0001$). Lay responders who brought an AED arrived before EMS in 63% of the cases. The response times were gathered from the dispatch center (not stated how). There were only 112 OHCA's during the period 2012–2017. [83]

Two reviews have concerned the effects of mobile-phone-dispatched lay responders on bystander CPR, return of spontaneous circulation (ROSC), and 30-day survival.

Scquizzato et al. [135] reported combined ORs from three studies: [122, 128, 132] bystander CPR 1.7 (1.11–2.60), ROSC 1.50 (0.98–2.30) and 30-day survival 1.51 (1.24–1.84).

ILCOR guidelines for 2020 [136] reported adjusted RRs of bystander CPR of 1.27 (1.10–1.46) in the RCT by Ringh et al. [128] and 1.29 (1.20–1.37) in the “before-and-after” study by Lee et al., [132] plus an unadjusted pooled RR for ROSC of 0.97 (0.60–1.57). [122, 126, 132] and an adjusted pooled RR for 30 day survival of 1.7 (1.16–2.48). [110, 122, 126, 132]

In a statement in guidelines in 2015, mobile dispatch of responders was suggested. In 2020, the suggestion was raised to a clear recommendation that responder systems should be used. [136]

5 AIMS

The overall aim of this PhD project was to study implementation, improvement and refinement of lay-responder smartphone systems (Hearrunner, SMS-livräddare) so that an increase in use of AEDs hopefully will affect survival rates in cases of OHCA in Sweden. Specific aims were:

To investigate the performance of a new system adapted for smartphones for dispatch of lay responders to bring AEDs and perform CPR in cases of OHCA.

To calculate response times and pace of lay responders dispatched via a smartphone application to suspected OHCA's.

To investigate emotional responses, wellbeing and posttraumatic stress reactions among lay responders dispatched to suspected OHCA's.

To evaluate if a smartphone application with the addition of instructions to bring public AEDs could increase bystander use of AEDs in OHCA's before arrival of EMS, fire fighters and police.

6 ETHICAL CONSIDERATIONS

Research has the purpose, among other things, to improve therapeutic interventions and procedures. Evaluation of safety, efficiency and accessibility must be continually studied, even for the best-proven interventions. [137]

In these studies, the participants are unresponsive patients, where the ethics board has approved the study protocol and procedures. In Study IV, information about the study and General Data Protection Regulation was given to all survivors by mail. This ethics approval is based on the World Medical Association (WMA) Helsinki declaration, paragraph 30, in 2013, [137] which states that if the physical condition that prevents giving informed consent, in this case unconscious, is a necessary characteristic of the research, then the use of deferred consent is possible. Earlier studies from our research group concerning unconscious subjects have often been approved.

In a randomized controlled trial (RCT) study participants are randomly allocated into two different treatment groups. Ethically, a randomized study should not be planned if there is consensus in the treatment strategy. A randomized trial should preferably be performed if there are differences of opinion among peers, or no treatment consensus, i.e. equipoise.

There is a difference ethically (and statistically) whether you add (+) a new intervention to basic normal care, or if you want to question, or to withdraw (-) an already existing intervention. When you add you can use a superiority hypothesis (if better than normal care) and when you withdraw you need to do this with a non-inferiority hypothesis (if not worse than normal care). The difference is also seen in the number of study participants needed. If you have reason to believe that your new treatment is highly effective, you need fewer participants.

Another reason to carry out an RCT is if the study has the potential to promote health in future patients. In this case the principle of non-exploitation is valid, which states that a study participant is only harmed if the intervention makes them worse than before. [138] "Before" in this case is basic normal care. Withholding a new treatment does not make the patient worse than before. If a trial never could take place, due to the principle of not harming, patients would instead be harmed by the trial never taking place.

In Study IV we assessed a system of locating and alerting 40 000 volunteers to provide basic life support if, and only if, normal care does not get there in time. This could possibly

be unsafe and stressful to the volunteers, and if the system is not effective, useless for the patient. With a superiority (+) design, the most effective plan would have been to investigate the lay system + normal pre-hospital care compared with only normal pre-hospital care.

Our research group has already shown that the lay-responder system can increase bystander CPR in Stockholm. The ethical question in our case was if we could defend a policy of withholding CPR (and CPR has repeatedly been seen to be associated with increase survival) in order to have a clean control arm with only normal pre-hospital care.

On the other hand, with a possible twofold superior effect, the number of study participants could be kept low. Additionally, a negative (not statistically significant) study result could be interpreted as proof that the lay-responder system does not work, this leading to cancellation of such systems. In the long run this may lead to fewer saved lives in the future.

We concluded that it would be unethical in our study region to remove an existing treatment and the possibility of control cases to be treated by means of CPR by a trained lay responder. In 33% of cases the smartphone-dispatched CPR-trained lay responders provided CPR before arrival of the EMS and first responders, which is in line with previous data.

The question for future studies in other areas is to what degree a lay-responder system can be regarded as normal pre-hospital care. Is it normal care because the 2020 guidelines have made responder systems a clear recommendation that should be used [136]? Or is it dependent on the actual normal care provided in a study area?

It can be argued ethically that an RCT should be carried out when a first-responder system is being implemented and really is a + intervention adding to the existing pre-hospital system in the area. Countries and areas that are implementing the system, for instance in Lombardy, Italy, or in greater Copenhagen, Denmark, should use the opportunity to perform well planned randomized studies, which they very well are, and there is an ongoing randomized controlled study that also uses the Hearrunner system (ClinicalTrials.gov Identifier: NCT03835403). In this study there is no dispatch of lay responders in the control group, since there was no existing system prior to the start of the study.

7 METHODS

7.1 DATA SOURCES

7.1.1 Swedish register for cardiopulmonary resuscitation (SRCR)

The SRCR is a national quality register where EMS personnel report outcome data on OHCA cases such as treatment by the EMS. The register started in 1990 in Gothenburg and increased to 2010, covering all Swedish EMS agencies. In 2010 the full register was registered online. The register follows the Utstein template, and the EMS report treatment, response times, and factors at the scene such as witnessed status and place, and patient factors such as sex, age and etiology.

In 2015 the register extended the outcome variables to differentiate actions performed before the arrival of the EMS by fire fighters/police and civilian bystanders, such as *bystander performed CPR* and *bystander attached AED* and professional first responder CPR and attachment and defibrillation with an AED.

A case of OHCA is defined in the register as an EMS-treated patient, to avoid including obviously dead individuals, or conscious patients, such as epileptics.

7.1.2 Data from the national Swedish dispatch center

The national Swedish dispatch center SOS-alarm has a database containing all incoming calls along with their timestamps regarding: first-registered incoming call from witness, time to dispatch of EMS and additional resources (fire fighters and lay responders), and arrival times of EMS and fire fighters.

7.1.3 Data from lay-responder mission server and survey

The lay-responder database contains all data concerning the lay responders, and is based on the following sources:

- a) The lay-responder mission server containing alerts, coordinates, timestamps, assignments, technical confirmation, manual accepts and declines from all individual apps of the located lay responders during a mission.
- b) Data from when the lay responder registers in the system concerning county of habitat, age, gender, profession group, CPR course, smartphone device, registration date.

c) An online survey sent out 90 minutes after the alert to the dispatched lay responders regarding actions taken after the alert. The survey was built in 2016 and later improved in 2019. The responder states if they tried to fetch/succeeded in fetching and bringing an AED, if they arrived at the scene before EMS and on-duty responders, if they performed CPR, if they attached and defibrillated the patient.

For Study 3 an additional survey containing study-specific instruments was developed and added to the ordinary survey. (Please see Methods in Study 3.)

For Study 4 a study-specific validation in the form of a structured telephone interview took place, addressing lay responders who stated in the survey that they arrived before EMS and attached an AED. The purpose was to validate the primary outcome “lay responder attached AED” in Study 4.

7.2 SETTING

The studies were conducted in Stockholm region and Västra Götaland, which together contain approximately 40% of Sweden’s population, and were the first two regions to incorporate the lay-responder system. The EMS in the two areas are managed by dispatch center SOS-alarm.

The mobile-citizen system locates and alerts volunteers with BLS competence and directs them on a map to the suspected arrest and via a public AED. Of 30 located volunteers, approximately 5–11 accept the mission and reach the scene before EMS and fire fighters in 25–30% of the suspected cardiac arrests. If needed, the citizen responder then starts BLS with or without an AED, depending on vicinity and AED availability.

7.3 STUDY DESIGNS, OUTCOMES AND EXPOSURES

7.3.1 Study 1

In Study 1 we aimed to investigate the feasibility and performance of a new mobile lay-responder system.

Twenty lay responders were dispatched by the EMCC and automatically located via GPS signals. A smartphone application alerted the lay responder, who could either accept or decline the mission. The smartphone application was developed for iOS and Android and showed a map where the AED register was integrated. When alerted, the application provided instructions and guidance either directly to the suspected OHCA or via a specific

AED. The system was closed at night between 23:00 and 07:00. Dispatchers were instructed to activate the system in case of a suspected OHCA except for EMS-witnessed OHCA, traumatic cases and patients younger than eight years old.

The system measured two straight-line distances from each lay responder: one to the victim, and one via a specific AED. Lay responders were located within a distance of 1200 meters for CPR performers and 2400 m for AED retrievers. The lay responder was alerted via an alarm sound, and the text: "A suspected cardiac arrest has occurred in your vicinity. Are you available?"

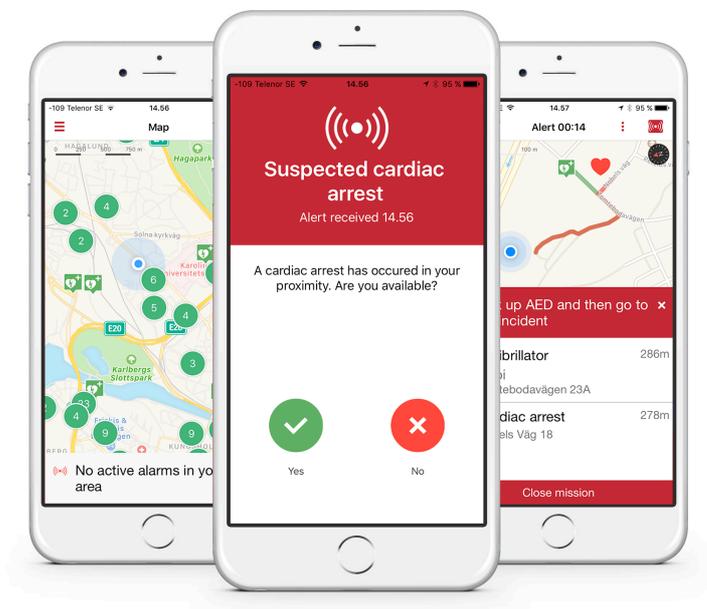


Figure 4. The lay responder smartphone application. Reproduced with kind permission from Heartrunner Sweden AB.

A survey was sent to the mobile phones of the activated lay responders after 90 minutes. The survey asked questions regarding the lay responder's actions: if they reached the victim before EMS, fire fighters and police, if they performed CPR, if they found and attached an AED and if the victim was defibrillated.

Recruitment of lay responders was done through e-mails, social media, in newspapers and via CPR-training companies. At the end of the run-in period the number of lay responders had increased from 17,206 to 23,097. When registering in to the application the lay responders gave their consent to be located, and to be part of a research project.

The response time of the lay responder was calculated, with an estimated pace of 4 m/second over a straight-line distance and compared with real response times of the first-arriving EMS units and professional first responders. The data were analyzed for descriptive purposes, with medians and interquartile ranges (IQRs). For analysis of response times Wilcoxon's rank sum was used, and the effect size (r) was calculated as $r=Z/\sqrt{N}$. Analysis was performed using STATA software, version 14.0 (StataCorp).

7.3.2 Study 2

After an extensive rebuild of the system techniques, and configurational changes concerning CPR and fetching an AED, for example, and a maximum of 30 lay responders located per case, we could continue studies of system performance. We also added a function to collect coordinates and timestamps after the alert so that we could see the paths the lay responders took.

In Study 2 we aimed to study the travelling speeds and response times of the lay responders. When a lay responder accepts a call, they are re-positioned every few seconds. These positions (coordinates) are recorded in the mission server, which enables measurement of the distance they actually travelled, the timestamp when they received the call, and the timestamp when they reached the scene of the suspected OHCA. When the dispatched lay responder was within 25 meters of the suspected OHCA we considered them to have reached the scene.



Figure 5. Example of dispatched lay responders. Red circle is a lay responder who runs directly to the suspected OHCA. Blue triangle is a lay responder who runs to fetch an AED before running to the suspected OHCA. Reproduced with permission from Elsevier.

The lay responder was instructed to either fetch an AED or run directly to perform CPR. Due to both non-compliance and contamination the groups were created by using the survey answers. If a lay responder answered that they tried to fetch an AED they were included in the AED group regardless of given instructions, and *vice versa* for the CPR group.

To study differences in travelling speed, distance and response time by population density we calculated the number of inhabitants per km². SAMS areas (Small Areas for Market Statistics) were used for these calculations.

Data were presented as counts and proportions for categorical data and medians with quartiles for continuous data. All statistical and geographical analyses were conducted using R version 3.6.0.

7.3.3 Study 3

This was an observational prospective cohort study. The aim was to investigate the emotional reactions among the lay responders after being dispatched to a suspected OHCA. Emotional reactions were measured after the cardiac arrest (within hours) and at follow-up 4–6 weeks later.

Three different study groups were constructed. The Un-Exposed (Un-Exp) group consisted of lay responders who were located but did not respond to the call. The majority of this group did not receive a call due to technical errors within the lay-responder system. In some cases (n=105) the lay responders received a call but stated that they did not take notice of the alert. To further reduce the possible effect of inactive lay responders, the question “if you had noticed the alert, would you have responded to the mission?” was added and those who answered “yes” formed the final control group.

Two exposed groups were created. Exposed group 1 (Exp-1) consisted of lay responders who tried, but did not reach the scene. Exposed group 2 (Exp-2) consisted of lay responders who either reached the scene before EMS/on-duty first responders or arrived after but helped perform CPR. To reduce the risk of recall bias all incoming alerts after the first recorded were excluded, as were answers by professional first responders alerted by the system.

Three different instruments were used to measure emotional reactions. In the primary analysis, the level of *emotional response* was measured with the *Swedish Core Affect Scales* (SCAS). [139, 140] The scales measure the state of mind using 12 pairs of items such as sad-glad or passive-active. The instrument can be reduced to two dimensions, namely *activation* and *valence*. Activation measures the level of strain (e.g. quietness–excitement), while the valence measure reflects a pleasant or unpleasant affect. High values of both

activation and valence could therefore be interpreted as a positive engaging event, while low values on both scales could be interpreted as a negative dull/slow event.

In addition to SCAS measures, *post-traumatic stress symptoms* were measured by using a 6-item PCL checklist. This checklist, [141] consists of five questions with values ranging from one to five, resulting in a maximum of 30 points. A score over 14 has been suggested to be associated with post-traumatic stress disorder symptoms.

The third instrument used was the WHO wellbeing index, [142] which consists of five questions with values ranging from one to five. The total number is then multiplied by four, which results in a maximum value of 100. A total value below 50 has previously been suggested as a cut-off when screening for depression.

All values were recorded using visual analog sliders with the middle value as default. If a lay responder did not answer any questions (e.g. all values were default values) they were excluded from the study.

Categorical data were presented as counts and proportions, while continuous data were presented as means and standard deviations. Differences in categorical data were tested by using Chi²-tests and continuous data were tested by ANOVA. The results were analyzed by using ordinary least square (OLS) regression adjusting for age, gender, time since last CPR-course, professional group, region, month, acceptance ratio (accepts/alerts), years as lay responder and type of device (iOS/android). Sample-size calculation was based on detecting a small effect size (SMD = 0.2) with a power of 80% and an alpha value of 5%. For between-group differences a sample size of 784 cases was needed, and for within-group differences 199 cases were needed.

7.3.4 Study 4

In the fourth study we aimed to measure the effect of instructions to fetch an AED, using the lay-responder system. The study design was a randomized controlled trial with two treatment groups. In the intervention group the majority of lay responders were directed to fetch the nearest AED (four out of five received a map with directions to the nearest AED), while in the control group all lay responders were asked to run directly to the OHCA victim to perform CPR. In each case of suspected OHCA a maximum of 30 lay responders were alerted in a 1.8 km radius from the suspected OHCA. Each call was randomized 1:1 and was blinded to both researchers and dispatchers until the end of the study.

After the call all lay responders received a survey asking questions about the call. Examples of these questions were if they tried to fetch an AED, performed CPR and if they defibrillated the patient.

To detect a difference of six percentage points (from 3% to 9%) in AED attachment (primary endpoint) a sample size of 628 OHCAs was needed (beta=0.2, alpha=0.05). Secondary outcomes were the proportion of cases with CPR prior to arrival of EMS or on-duty first-responders, and the proportion of cases with bystander defibrillation prior to arrival of EMS or on-duty first responders. Cases that were not treated by EMS were excluded from the final analyses, as we did not have outcome data. In addition to these cases, those witnessed by EMS were also excluded.

Continuous variables were presented as medians (q1, q3) and categorical variables were presented as counts and proportions. The Chi²-test was used to test differences in proportions. All analyses were performed by using R version 4.0.0.

8 RESULTS

8.1 STUDY 1 - A SMARTPHONE APPLICATION FOR DISPATCH OF LAY RESPONDERS TO OUT-OF-HOSPITAL CARDIAC ARRESTS

During the study period between February and August 2016 the smartphone application was triggered in 685 cases of suspected OHCA, of which 224 were considered as EMS-treated in the SRCR register. In the analytic sample of 198 cases of OHCA, lay responders arrived at the scene in 58% (n=116) of the cases, prior to the EMS and on-duty responders in 26% (n=51) of the cases; they performed CPR in 27% (n=54), and attached an AED in 9% (n=17) of the cases. Of these, 23% (n=4) were defibrillated. Table 1 shows baseline data of cases in which the lay-responder system was activated, compared with cases not activated.

Table 1. Baseline data of OHCA cases where lay responders were and were not activated by the EMCC dispatcher.

		Not activated N=128	Activated by the EMCC N=252
OHCA, daytime,	n (%)	128 (33.7)	252 (66.3)
Age,	median (q25–q75)	71 (53–79.5)	73 (61–82)
Male sex,	n (%)	74 (58.3)	166 (65.9)
Witnessed by	Bystander, n (%)	61 (65.6)	132 (92.3)
	EMS, n (%)	32 (34.4)	11 (7.7)
Place	Home, n (%)	79 (63.2)	179 (71.3)
	Public, n (%)	46 (36.8)	72 (28.7)
Suspected aetiology	Presumed cardiac, n (%)	102 (79.7)	221 (91.3)
	Drug overdose, n (%)	5 (3.9)	6 (2.5)
	Trauma, n (%)	4 (3.1)	1 (0.4)
	Asphyxia, n (%)	10 (7.8)	9 (3.7)
	Suicide, n (%)	6 (4.7)	4 (1.6)
	Other non-medical, n (%)	1 (0.8)	1 (0.4)
First rhythm	VT/VF, n (%)	21 (18)	51 (22.3)
	PEA, n (%)	25 (39.3)	30 (13.1)
	Asystole, n (%)	71 (60.7)	148 (64.6)

The reported straight-line distance from the lay responder to the victim (assumed to have a pace of 4 m/sec) was a median of 560 meters (IQR 332–860) for lay responders

dispatched to perform CPR, and 1280 meters (IQR 748–1776) for lay responders dispatched to fetch an AED first.

The time from witness call to dispatch was a median of 2:02 minutes for EMS, 2:48 minutes for fire fighters and 2:54 minutes for lay responders. The total response time was 6:17 minutes (IQR 04:49–07:57) for CPR lay responders and 9:17 minutes (IQR 06:31–11:53) for AED responders.

8.2 STUDY 2 - A BRISK WALK - REAL LIFE TRAVELLING SPEED OF LAY RESPONDERS IN OUT-OF-HOSPITAL CARDIAC ARREST

During a nine-month period 2206 (22%) of 9058 accepting lay responders reached the scene of a suspected OHCA. After exclusions, 1430 (66%) lay responders who went directly to perform CPR, and 746 (34%) who tried to fetch an AED was analyzed. The median speed was 2.3 m/s (IQR 1.4–4.0), the median distance was 956 meters (IQR 480–1661) and the median response time was 6.2 minutes (IQR 4.3–9.2). The AED group had a longer distance to run (1087 meters) and a longer response time (7.0 minutes) compared with the CPR group (890 meters, 5.8 minutes).

There was a difference in speed according to population density. In highly populated areas (>8000 inhabitants/km²) the median travelling speed was 1.8 m/s (IQR = 1.2–2.5) were as in sparsely populated areas (0–1500 inhabitants/km²) the travelling speed was faster: 3.1 m/s (IQR 1.8–4.9).

Table 2 – Travelling speed, response time and distance travelled among lay responders reaching the scene of a suspected OHCA. Reproduced with permission from Elsevier.

	All n = 2176	CPR n = 1430	AED n = 746
All (n = 2176)			
Meters/second, median (Q1, Q3)	2.3 (1.4, 4.0)	2.3 (1.4, 3.9)	2.4 (1.5, 4.0)
Response time, median (Q1, Q3)	6.2 (4.3, 9.2)	5.8 (4.1, 8.2)	7.0 (4.8, 10.6)
Distance, median (Q1, Q3)	956 (480, 1661)	890 (450, 1568)	1087 (564, 1920)
Men (n = 1113)			
Meters/second, median (Q1, Q3)	2.6 (1.6, 4.3)	2.7 (1.6, 4.4)	2.6 (1.7, 4.2)
Time, median (Q1, Q3)	6.0 (4.2, 8.5)	5.5 (4.0, 7.6)	6.8 (4.6, 9.9)
Distance, median (Q1, Q3)	1030 (534, 1738)	977 (494, 1670)	1140 (600, 1948)
Women (n = 1051)			
Meters/second, median (Q1, Q3)	2.0 (1.3, 3.5)	2 (1.3, 3.4)	2 (1.4, 3.8)
Time, median (Q1, Q3)	6.5 (4.4, 9.9)	6.0 (4.2, 8.9)	7.6 (5.0, 11.8)
Distance, median (Q1, Q3)	889 (446, 1571)	808 (409, 1417)	1029 (517, 1908)
Population density			
8000 + /km² (n = 574)			
Meters/second, median (Q1, Q3)	1.8 (1.2, 2.5)	1.7 (1.1, 2.6)	1.9 (1.3, 2.4)
Time, median (Q1, Q3)	5.8 (4.1, 9.1)	5.3 (3.8, 7.9)	6.5 (4.6, 10.2)
Distance, median (Q1, Q3)	627 (376, 1108)	571 (330, 1014)	742 (452, 1195)
4000 – 7999/km² (n = 503)			
Meters/second, median (Q1, Q3)	2.4 (1.5, 4.1)	2.4 (1.4, 4.0)	2.4 (1.5, 4.1)
Time, median (Q1, Q3)	6.7 (4.5, 9.6)	5.8 (4.2, 8.4)	8.1 (5.7, 11.5)
Distance, median (Q1, Q3)	1057 (530, 1818)	983 (471, 1646)	1274 (711, 2067)
1500 – 4000/km² (n = 566)			
Meters/second, median (Q1, Q3)	2.5 (1.5, 4.1)	2.4 (1.5, 4.0)	2.7 (1.5, 4.2)
Time, median (Q1, Q3)	6.0 (4.2, 8.9)	5.8 (4.1, 7.7)	6.8 (4.4, 10.4)
Distance, median (Q1, Q3)	1003 (496, 1708)	958 (457, 1595)	1143 (565, 1956)
0 – 1500/km² (n = 533)			
Meters/second, median (Q1, Q3)	3.1 (1.8, 4.9)	3 (1.8, 4.8)	3.4 (2.0, 4.9)
Time, median (Q1, Q3)	6.4 (4.5, 9.0)	6.2 (4.3, 8.6)	6.8 (4.8, 10.0)
Distance, median (Q1, Q3)	1257 (693, 2015)	1125 (673, 1851)	1490 (740, 2382)

8.3 STUDY 3 – WELLBEING, EMOTIONAL RESPONSE AND STRESS AMONG LAY RESPONDERS DISPATCHED TO SUSPECTED OUT-OF-HOSPITAL CARDIAC ARREST

Altogether, 886 (26%) unexposed and 1389 (64%) exposed responders completed the survey. The dimension “activation” was elevated in the exposed groups: Un-Exp: 7.0 (SD 1.6), Exp-1: 7.5 (1.3) and Exp-2: 7.6 (1.3) ($p < 0.001$, SMD 0.287). The dimension “valence” was highest in the Un-Exp group: 6.8 (1.6), vs. Exp-1: 6.3 (1.6) and Exp-2: 6.3 (1.6) ($p < 0.001$, SMD 0.198). PCL-6 mean scores were highest in the Un-Exp group: 10.4 (5.4), vs. Exp-1: 8.8 (4.0) and Exp-2: 9.2 (4.9) ($p = 0.007$, SMD 0.226). There were no differences in the WHO wellbeing index: Un-Exp: 77.7 (16.8), Exp-1: 77.8 (17.2) and Exp-2: 78.2 (17.7) ($p = 0.963$, SMD 0.019).

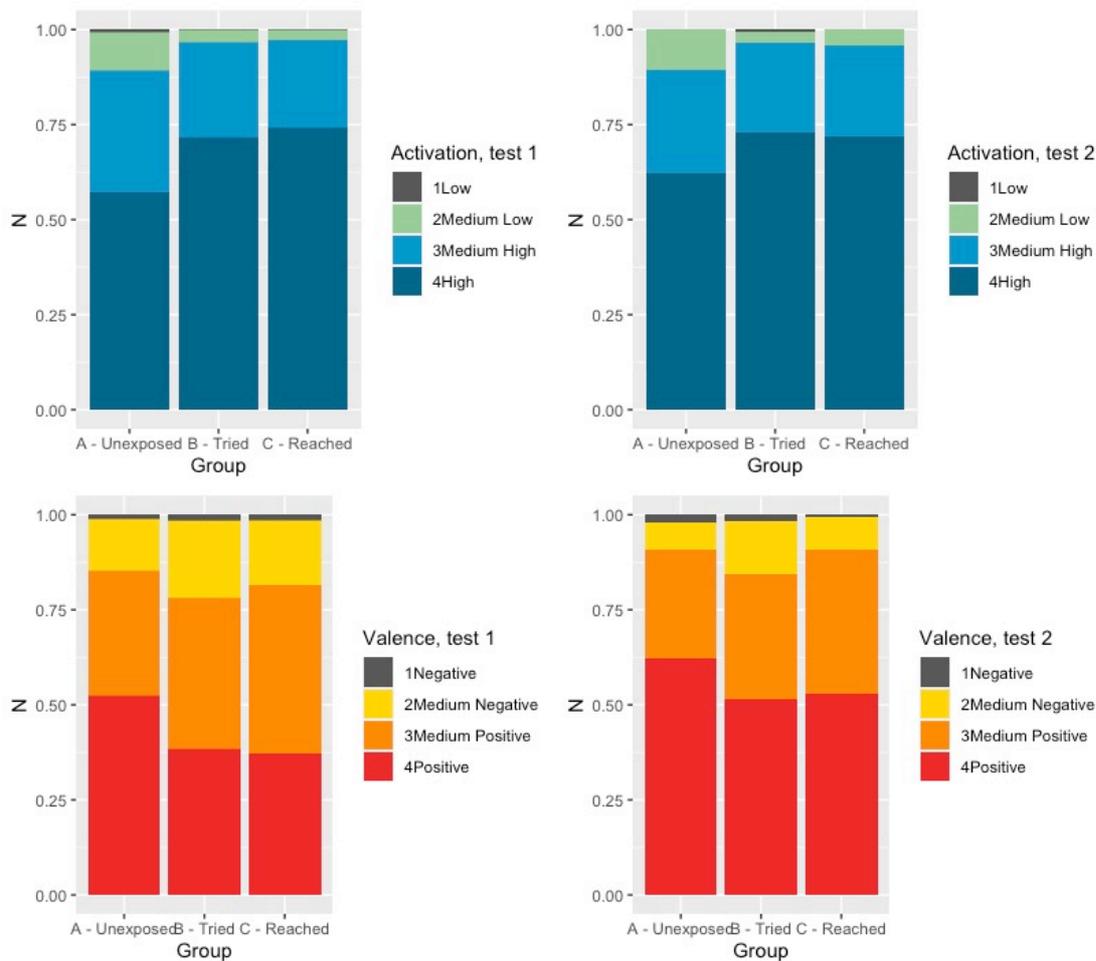


Figure 6. Lay responders' answers in an online survey according to activation (top row) and valence (bottom row). Column graphs to the left show results after the call while graphs on the right show results at follow-up.

8.4 STUDY 4 - USE OF AUTOMATED EXTERNAL DEFIBRILLATORS BY SMARTPHONE DISPATCHED LAY RESPONDERS IN OUT-OF-HOSPITAL CARDIAC ARREST

During the study, 815 EMS-treated cases of OHCA were assessed (Figure 7). In the intervention group the AED attachment rate was 13.2% (n=53) versus 9.4% (n=39) in the control group (p=0.087). There were no in-group differences in the secondary outcomes (Table 3). Observational data concerning all bystander-attached AEDs showed that 29% of the attached AEDs were attached by a lay responder.

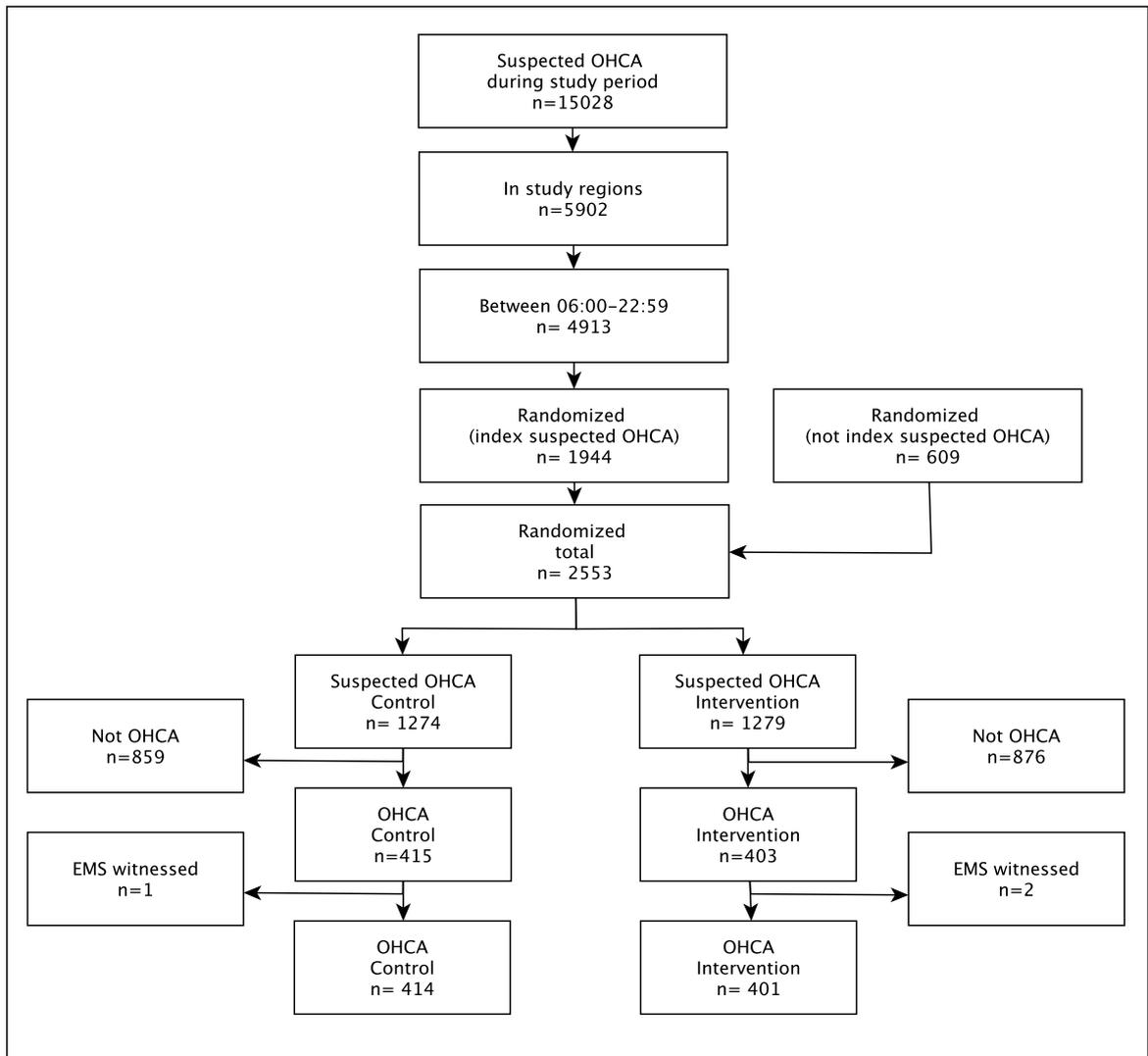


Figure 7. CONSORT diagram of enrollment in the SAMBA trial.

Table 3. Baseline characteristics of randomized patients in the SAMBA trial (n (%)). *Data from Emergency Medical System personnel (SRCR register), **Validated data from lay-responder survey, ***Data from lay-responder survey. SMD = Standardized Mean Difference.

	Control	Intervention	p	SMD
n	414	401		
<u>Primary outcome</u>				
Bystander attached AED* (%)	39 (9.4)	53 (13.2)	0.087	0.120
Lay responder attached AED** (%)	19 (4.6)	24 (6.0)	0.373	0.062
Lay responder & bystander attached (%)	11 (28.2)	16 (30.2)	0.836	0.044
<u>Secondary outcome</u>				
Bystander CPR* (%)	328 (79.2)	305 (76.1)	0.278	0.076
Lay responder CPR*** (%)	136 (32.9)	131 (32.7)	0.956	0.004
Lay responder & bystander CPR (%)	112 (34.1)	111 (36.4)	0.554	0.047
Bystander defibrillated* (%)	15 (3.6)	13 (3.2)	0.765	0.021
Lay responder defibrillated** (%)	11 (2.7)	8 (2.0)	0.531	0.044
Lay responder and & bystander defibr. (%)	4 (26.7)	4 (30.8)	0.811	0.091

Data from the lay-responder survey (Figure 8) showed that CPR performance was equally distributed in the two groups (32.9% versus 32.7%). As regards whether or not at least one lay responder tried to fetch an AED, the difference was significant: intervention 60.1% (n=241) versus control 42.5% (n=176) (p<0.001). The same applied as regards whether or not they succeeded in fetching an AED: intervention 35.7% (n=143) versus control 28.3% (n=117) (p<0.02).

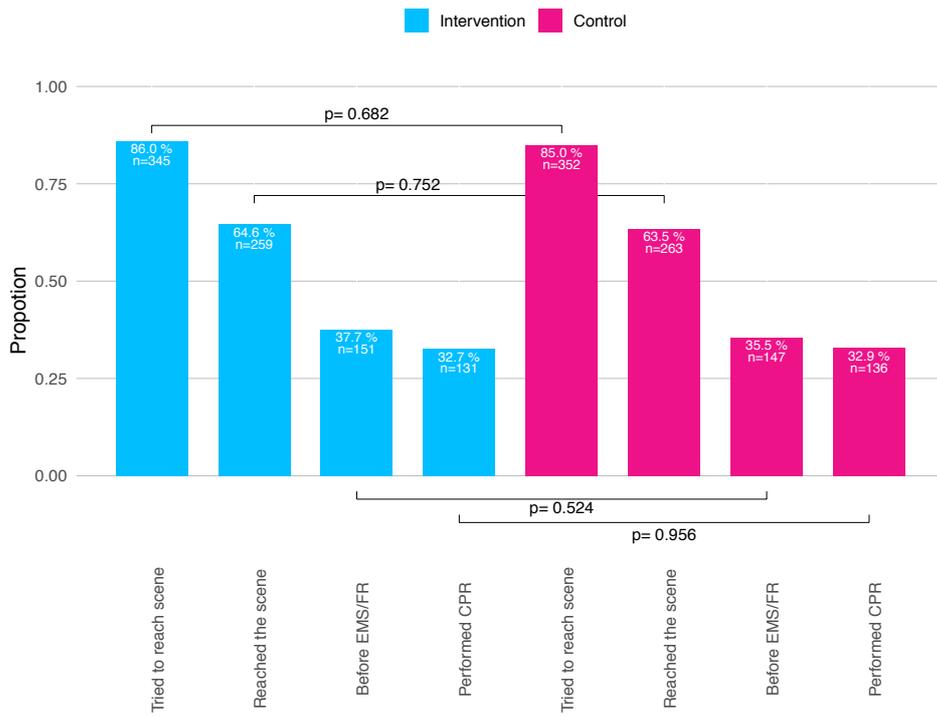


Figure 8. Survey answers from lay responders in the SAMBA trial. Blue bars represents the intervention group while pink bars represent the control group. The Y-axis indicates that at least one person during each mission answered “yes”.

9 DISCUSSION

9.1 FIRST RESPONDERS, WHO ARE THEY?

One problem when comparing and combining data for dispatched lay/first responders is that the different types are not clearly defined. Different studies use the same definitions but refer to various types, or some things have different names in different studies, and methods are not at all clear. [143] This calls for an Utstein-like agenda, to settle on an international template for what we are studying.

One method could be to include them all together. Indeed, some apps summon both traditional and lay responders. [110] In order to be able to compare outcomes of new strategies with normal pre-hospital care, a Cochrane report from 2019 compared studies of “community first responders” versus normal pre-hospital care. Two RCTs were reported. One concerned fire fighters and police, [71] and the other concerned lay responders. [128] In the review by Zcquizzato et al. [135] as well as in ILCOR and CoSTR recommendations, [136] systems involving both fire fighters and lay responders were included.

Most “lay first responder systems”, [112, 114, 118, 122, 132, 144] as well as the Swedish system described in this thesis, are based on laypersons with a minimal requirement of a CPR course, dispatched from the EMCC. A significant difference between lay-responder systems and traditional fire fighter/police first-responder systems [70, 71, 145] is the possibility for the latter to move quickly in cars with blue lights. Volunteer systems, especially in urban areas and city centers may rely on pedestrians, bikers or taxi drivers, or in remote areas cars, while fire fighters and police have the possibility to use alarms and blue-light vehicles.

Most importantly, in several areas the use of fire fighters in dispatch is a well-established function, and part of normal pre-hospital care. The distinction from normal pre-hospital care is important when measuring the effects of lay-responder systems. Some systems dispatch both professional first responders and lay responders via the same application. [110] Others do not clearly state how the professional first responders are engaged. [126] In some cases the system more closely resembles the “community responder system”, [78, 83, 146, 147] where either a local layperson with education greater than a CPR course, or a professional (fire fighter, nurse or general practitioner) with other responsibilities, can be hand-picked by the dispatcher and recruited in all cases of priority-1 calls. Systems where

the dispatcher can see the GPS signal from the app on a screen, and have at least some communication if necessary should be eligible for all systems. [79, 120, 147]

Studies concerning lay responders are with one exception all observational, mostly descriptive, few with comparisons. Only one of the studies is randomized. Due to the great variability in different apps across the world, ILCOR 2020 and ERC 2020 have announced that it should be a requirement to establish a uniform standard for these systems, not only for best practice but also to allow comparisons among different countries of system efficacy as regards clinical outcomes.

9.2 FIRST RESPONDERS, ARE THEY FIRST?

First responders have their name because they supposedly reach the victim first, to offer BLS. In the early days, evolution started from the fire brigade to finally become a full EMS system. In this instance the first responders were fire fighters who took a brief course to become medical technicians. They were greater in number and started off offering CPR (BLS) while waiting for a paramedic to assist with defibrillation and medication. As soon as defibrillators became safer the task was moved down to first line in order to gain time (BLS+AED).[69]

9.2.1 Witness call to dispatch

Today, in systems implementing laypersons, fire fighters and police officers as first responders, the instruction is to have cases of suspected OHCA more strongly confirmed before dispatch. [70, 71, 145] How this turns out during dispatch is seen in unpublished data from Stockholm and Gothenburg (Figure 9). Here, the EMS (ALS) is dispatched *first*, at earliest suspicion. Later, when the OHCA is more confirmed, the fire fighters, police and lay responders (BLS+AED) as well as one more EMS (ALS) team are dispatched. This results in a delay of more than one minute for the additional responders, and a total response time similar to that for the first-dispatched EMS. In other words, many resources arriving at the same time, but too late. It is hard to say that the first responders are first. To overcome this problem the dispatch should be simultaneous in order to gain time. Husain et al. and van Alem et.al. also stress that if the first responders and EMS are not dispatched simultaneously, the first responders will not arrive first at the scene. [70, 71] In the Copenhagen study, they had shorter time frames at the EMCC. The call to dispatch time for EMS was 00:45–00:47 seconds. In cases where lay responders arrived first, the lay

responder only had an addition of 00:23 seconds before dispatch. In cases where the lay responders did not come first the additional time for dispatch was 00:51 seconds. [118]

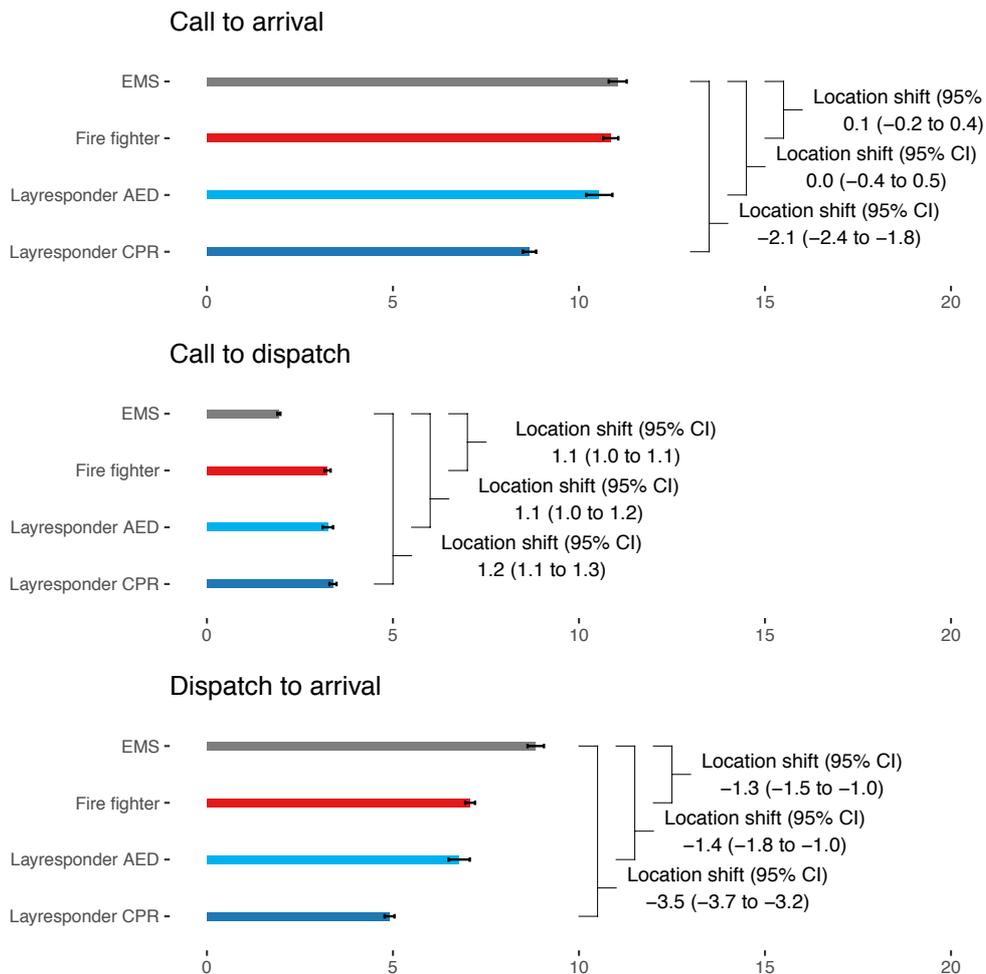


Figure 9. Time intervals for different responders. The top row represents the total response time, the middle row the call to dispatch time and the bottom row the time from dispatch to arrival at the scene.

Earlier dispatch would increase the sensitivity of finding an actual OHCA, but also result in far more alerts being sent to the first responders, which could at worst result in fatigue effects among the dispatched lay responders. As regards the group of lay responders the difference could result in one OHCA in 10 dispatches instead of three in 10 today (see Table 4). On the other hand, in a system with a high density of lay responders the individual difference might not be so apparent. In addition, if the system adds some minor

communication between the dispatcher and lay responder during the alert, it could contribute to specificity and smartness. In some CFR systems [79, 146, 147] the locations of lay responders are visible to the dispatcher, and in Stockholm a new function has been implemented, the cancel/update function. It was developed from the need for the dispatcher to be able to 1) cancel an alert if the need for assistance is no longer present or the situation is unfit for lay responders, and 2) update the mission with additional information concerning the location and/or how to get there, i.e. door codes, floor plan or fresh coordinates etc.

Table 4. Data from run-in, 2016. Sensitivity of finding a real OHCA after dispatch of lay responders to suspected OHCA between 07:00 and 23:00 during the run-in period. When lay responders were activated the sensitivity was 66% (252/380), with a positive predictive value (PPV) of 34% (252/752) and a false-alarm rate of 66% (500/752). In comparison, sensitivity after the dispatch of EMS to suspected OHCA under the index code of “Unconscious adult” was 79% (299/380), with a PPV of 11% (299/2807) and a false-alarm rate of 89% (2508/2807). The index code “unconscious adult” covered 89% (427+240)/752 of the activations of lay responders.

<u>Suspected OHCA (more confirmed)</u>				
	Lay Activated	Lay Not activated	Total	
OHCA	252	128	380	Sensitivity: 66%
Not OHCA	500	-	-	Specificity: -
All	752	-	-	
PPV (%)	34%			
<u>Index as Unconscious (not specified)</u>				
	Yes	No	Total	
OHCA	299	81	380	Sensitivity: 79%
Not OHCA	2508	-	-	Specificity: -
All	2807	-	-	
PPV (%)	11%			

A related problem during dispatch is finding the address of the scene of the victim, which can be time delaying. This could be improved with GPS locations sent from the witness' smartphones, but at least in Sweden there have been legal concerns resulting from GDPR.

9.3 BEST PRACTICE FOR LAY RESPONDING?

Once dispatched, all additional responders seem to have an advantage over the EMS (Figure 9). There is reason to believe that these systems have the possibility to reach the

OHCA in a reasonable time and even increase survival outcomes in future. However, there are still some discrepancies in the different lay-responder systems.

Although many applications show points of access to AEDs, some lay-responder systems do not direct the responder to a specific task of either CPR or fetching an AED, [110, 114, 115, 119] while others specifically indicate an AED location via a text message [122, 132, 148] or an app. [88, 149]

At present our lay-responder system directs responders either to go directly and start CPR or to go via an AED location and fetch an AED. In the first version (Study 1) the division of missions was 10 for CPR and 10 for AED out of a maximum of 20 located responders/case. The distances to an AED were also sometimes extremely long for the fewer lay responders as a result of this and other technical miscalculations. We could see that this was a problem since the lay responders directed via an AED often did not arrive in time, or chose to go directly instead. In an effort to increase the attachment rate of AEDs in the later version we changed the proportions so that the fraction was one for CPR and five for fetching an AED, with a maximum of 30 lay responders located per case. This resulted in the outcome that the number of lay responders who tried and succeeded to fetch an AED nearly doubled, and other measurements of effort, such as trying to reach and succeeding in reaching the victim also increased. In Study 4 we saw that lay responders very much chose the best option for them in the specific alert. The purpose of directing a lay responder to go directly to an AED can be discussed and should be investigated, but in our experience the guidance given at least increased the effort in trying to fetch an AED.

It is not clearly stated in other systems, but our application locates lay responders and measures the distance to the case in a straight line (euclidian distance). A more correct way would be to measure the actual route and distance according to a street map. [150] Another problem with a straight-line radius is that it does not take into account the walkability, for example, several people can be located over impassable areas such as water or gated parts. It was shown in a PulsePoint study from Philadelphia that an increase in radius did not improve the numbers of persons located and thereby increase walkability. [151]

In Study 2 we measured the actual distances for lay responders from the initial location to the victim and could conclude that the median travelling speed was 2.3 meters/second. This, together with distance calculations from a street map, would give more accurate

estimates of the time it will take for each individual lay responder to reach the victim. Configurations for recruitment could be improved.

In Study 2 the travelling speed was shown to change according to population density, suggesting pedestrian travel in cities, and in sparsely populated areas (with longer distances and response times) faster transportation such as a bike or car. It is reasonable to suggest that distance calculations should be based on actual route distance and density of lay responders, and be configurable according to place of arrest.

One problem in first responder systems can be delays in redirection between caretakers. Data from the lay-responder system shows that automatic triggering of the app, which includes technical time (including repositioning) and manual time until the lay responder accepts is short (see Figure 10). Validation of the lay-responder survey answers in Study 4 suggests that police officers on duty (who also have the app) are reached faster by the app alert rather than through radio communication channels.

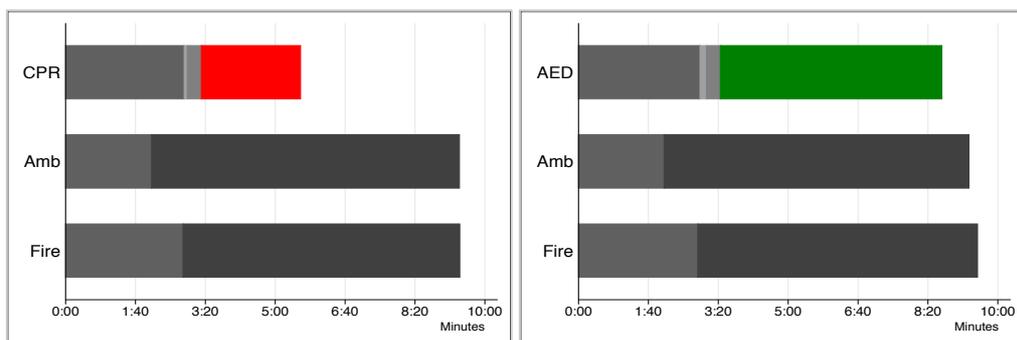


Figure 10. Delay times between alerting and accepting. Median 25 seconds for lay responders assigned to the CPR group and 29 seconds for lay responders assigned to the AED group. Reproduced with permission from Elsevier.

Another problem in different countries could be legislation and laws against use of AEDs by the public and lack of insurance for Good Samaritans (i.e. Good-Samaritan laws). [152, 153] In the US the PulsePoint app is restricted by perceived safety issues and legal concerns and lay responders are recruited to public places only. One attempt to deal with this was the verified responder project, involving a special squad of off-duty safety professionals to be recruited to the more private residential areas. The verified responders were notified in only 7% of cases and involved in just 2% of 475 cases of residential OHCA. [124] However in a representative public-opinion survey (Ipsos), 89% of Canadians and 85% of Americans had no objection to receiving help from lay responders in private residential settings. [154]

9.4 IS IT SAFE FOR LAY RESPONDERS?

The safety of the lay responder is an important factor frequently questioned by peers and health authorities. In a Danish survey of lay responders one person out of 1630 was injured (lower extremity fracture) while running to an OHCA, and 2% reported that the resuscitation had a severe psychological impact. [118] Dispatched lay responders in the Netherlands were asked to grade the psychological impact of attended resuscitation on a 3-grade scale (mild, bearable, severe). Soon after the event, 13% reported a severe psychological impact. [155] The questions asked by the Danish and Dutch investigators did not have a distinct positive or negative direction. Our results (Study 3) indicate that lay responders involved in resuscitation have increased emotional responses directly after the event in the dimension of “activation” and a small decrease in the dimension “valence” compared with an unexposed group of lay responders. In other words, the lay responders were highly activated (i.e. peppy, awake, active, interested, engaged, optimistic) and largely without negative emotions (i.e. sad, depressed, displeased, anxious, tense and nervous). Negative stress would have been indicated by high activation combined with negative valence, which was not the case. We interpreted this combination of activation and valence as a general adrenaline rush, due to the engagement.

Our study showed that the proportion of persons with PTSD symptoms was highest among the unexposed controls. This was a rather unexpected finding. Zijlstra et al. also carried out follow-up, with use of an impact-of-event scale (IES). At follow-up after 4–6 weeks none of the exposed subjects reported symptoms related to PTSD. The study covered 30% of all dispatched responders, and there was no comparison group. [156]

Scores in the wellbeing (WHO) index were high and uniform among the three groups, and higher than the mean in the Swedish general population. [157] In the present study 98% of the respondents stated that they would act as lay responders again.

Very similar results in the state of “activation” at an individual level at two time points indicate an overall high level of activation in the exposed groups, which could be a sign of an emotional trait. The most exposed group had accepted and acted on previous alerts, prior to the study period, more frequently than the other groups. In summary, these results indicate a largely willing and dedicated crowd of volunteers. The data supports results in qualitative studies, where basically trained community first-responders have been reported to show personal satisfaction in retaining a role as a CFR, reflecting altruistic

attitudes, such as helping the community, [158] and they were reported to have high degrees of resilience to stress. [159]

9.5 DO WE HAVE ENOUGH RESOURCES FOR INCREASED SURVIVAL?

The density of professional resources is crucial for survival. The density and availability of professional pre-hospital responders influences the response time, and thereby the possibility to resuscitate a patient in OHCA. [68] The study areas in the present work have a very different density of serving fire-fighter stations than in one of the most successful areas, King County in Seattle, where the overall OHCA survival rate is 16% (Figure 11).

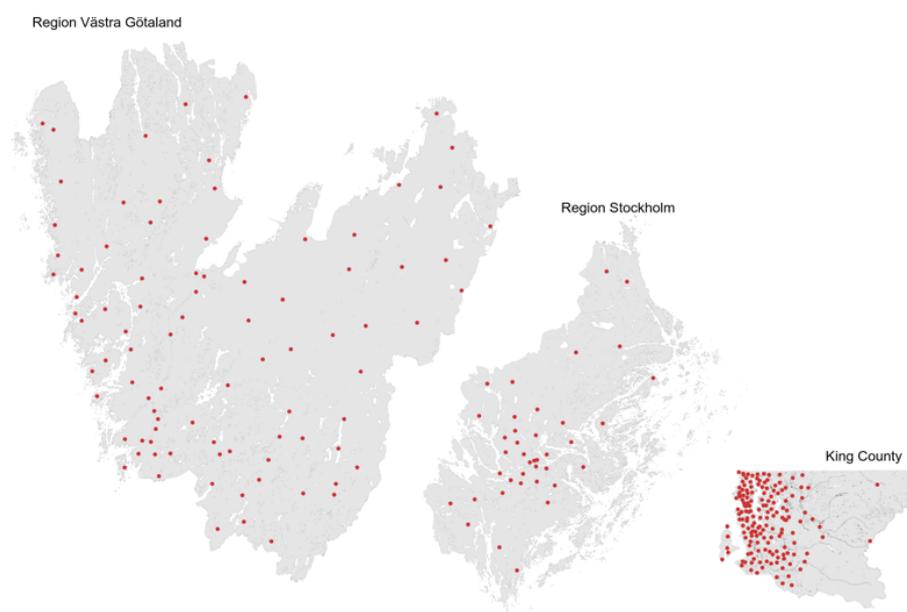


Figure 11. Density of fire stations in Region Västra Götaland (left), Region Stockholm (center) and King County, US (right).

If problems surrounding lay-responder systems could be solved, there is a great possibility that civilian volunteers could help in normal pre-hospital care and reach the victim within the first few minutes, and in the long run increase survival.

The major problem for lay-responder systems is the time it takes to pick up and bring an AED. Our studies indicate that lay responders often reach the victim before EMS and fire fighters and perform CPR, and they even attach AEDs, but to a lesser extent. A substantial proportion of the attached AEDs (40%) in Study 4 were brought to the scene through the initiatives of individual lay responders, either by being nearby in a work facility, or privately owned. Nevertheless, in the intervention group, where lay responders were aided

with a specific instruction and guidance to a public AED, the effort to try and fetch an AED was as high as in 60% of the cases.

A well-known problem is that there is a mismatch between OHCA locations and public AED placements. AEDs are mostly placed in business areas available during work hours. [91, 92, 160] During evenings and weekends the availability of AEDs drops substantially. [161] Figure 12 shows how accessibility alters over the course of a day in Stockholm. Of OHCA cases in residential areas in a Danish study, the median distance to the nearest AED was 898 meters, and only 1.2% of the cases were defibrillated by a bystander. [150] A Dutch study showed that the densities of both AEDs and lay responders in residential areas was crucial for time to defibrillation. The authors concluded that the recommended densities of AEDs and TM-responders for early defibrillation is two AEDs and more than 10 TM-responders/km². [129] The results of another Dutch study indicated that survival was related to lay-responder density. [162]

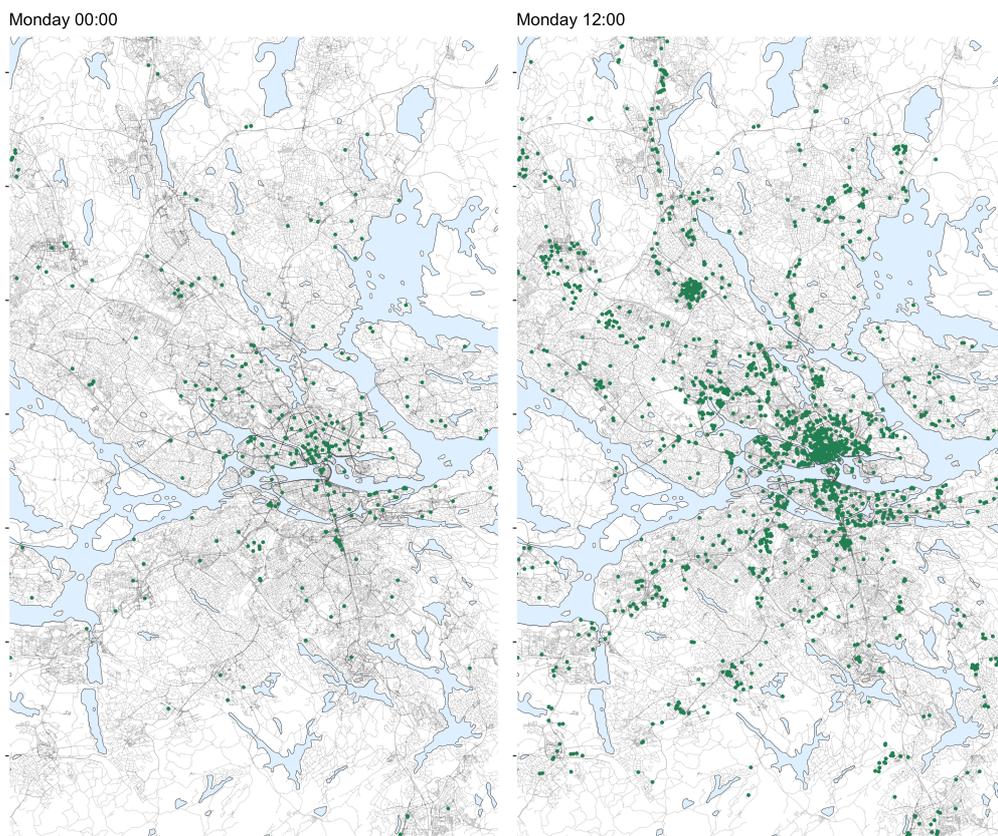


Figure 12. Map of available AEDs at 00:00 (left) and at 12:00 (right) on a Monday.

It has been considered that well-thought-out placement of AEDs in residential areas should be mandatory. [153] There, placement should be in well-known local places such as alongside local food stores or bus stations, in 24/7 open cabinets. Since AEDs are expensive, there have been worries about theft and vandalism. According to the results of a survey study addressing owners and managers in connection with public AEDs in the US, the frequency of theft and vandalism was negligible, and could be regarded as a myth. [163]

9.6 THREE IMPORTANT ORGANIZATIONAL FACTORS, FURTHER STUDIES

The presented work leads to three important organizational factors necessary to take into account when implementing and evaluating lay-responder systems.

1. Time between communication and dispatch
2. Better recruitment and adjusted configurations of located lay responders
3. Availability and density of resources

When assessing ROSC, survival and neurological data is sparse. However, current work shows promising results, at least as regards increased general bystander CPR. The problem is that some studies eventually are comparing bystander CPR or no bystander CPR as mentioned in this editorial. [164] Not until organizational factors are taken into account, with earlier dispatch and better-placed AEDs will the outcome of OHCA be improved, and not until we know what we are measuring can we compare approved outcomes.

In Study 4 the design led to substantial crossover between the intervention and control groups. From a purely observational point of view this is not bad, since the lay-responder system resulted in bystanders attaching AEDs in 29.3% of cases, and 35.3% of all cases of CPR. But to prove causality, it is not enough. Only a randomized study with a pure control arm consisting only of normal pre-hospital care could prove causality. Once a new promising concept emerges, enthusiasm and implementation can progress so rapidly that we forget to check the evidence, and once it is implemented the new concept is regarded as normal care. [165] When adding a new promising treatment to baseline care a superiority approach can be used which requires fewer study participants than if one wants to remove a never properly proven, but well established and “heavy” treatment strategy. One could argue ethically that a randomized study is only possible when a lay first-responder system is newly adopted, and really is an added intervention to an already existing pre-hospital system. Countries and areas that are implementing lay-responder

systems such as Denmark (NCT clinical trial) or Lombardy in Italy should use the opportunity to perform well-planned randomized studies with clean control arms.

I hope that part of the research I do will bring knowledge into this field and amend the techniques for dispatch of laypersons. The emergence of CPR in 1960 took a long time to reach the high level of bystander CPR seen in Sweden today. [166] The development of the defibrillator from a 120 kg bulky open-chest apparatus to a smart, safe and simple survival kit that does not need pre-understanding to use, took 60 years. The creation of the EMS in the 60s and resuscitation with defibrillators out in the field was finally legitimate as late as at the end of the 80s in Sweden. No more than 20 years have passed since the emergence of AEDs, 10 years since the launch of smartphones, and a few years since widespread access to inbuilt/assisted GPS in smartphones, and newly launched precision upgrades.

[167]

10 CONCLUSIONS

The app is safe and efficient, but there is still a need to locate accessible AEDs in the most suitable places. Dispatch of lay responders should also be at an earlier stage, in parallel with the EMS.

Study 1: A smartphone application can be used to recruit CPR-trained lay volunteers to go to OHCA for CPR and to bring AEDs. Further improvements are needed to shorten the time to attachment of an AED and defibrillation before EMS arrival.

Study 2: We found that the estimated traveling speed of a responder was 2.3 m/s (or 5.14 mph) among all volunteers, and 1.8 m/s or 4.03 mph in areas with high population density. Lay responders who run directly to start CPR show shorter response times compared with those who run to fetch and bring an AED first.

Study 3: Dispatched laypersons responding to a smartphone alert to a suspected OHCA rate the experience as energetic and mostly positive. No harm to any lay responder was seen. The responding groups had low scores as regards posttraumatic stress, and a high level of general wellbeing at follow-up.

Study 4: Smartphone dispatch of lay responders to public AEDs did not increase the rate of AED attachment before arrival of the EMS or professional first responders, compared with dispatch to perform CPR. If dispatched lay responders arrived prior to the EMS, the likelihood of bystander AED use and CPR was increased.

11 SAMMANFATTNING PÅ SVENSKA

Bakgrund och syfte

Hjärtstopp utanför sjukhus är ett stort folkhälsoproblem som drabbar runt 300 000 européer varje år. Om behandling inte påbörjas inom de första minuterna så är chansen till överlevnad låg. En viktig faktor för överlevnad är tiden från larm till påbörjad behandling i form av hjärt-lungräddning (HLR) och defibrillering. För att minska tiden till behandling så har olika strategier använts såsom utplacering av hjärtstartare i samhället och utlarmning av räddningstjänst och poliser.

Syftet med denna avhandling är att studera effekten av en tredje extraresurs, frivilliga lekmän utlarmade av larmcentralen. Syftet med **studie 1** var att utvärdera den tekniska funktionen och prestandan för ett urlarmningssystem för frivilliga volontärer under en "run-in" fas. Syftet med **studie 2** var att studera hastigheten och responstiden för de utlarmade volontärerna. I **studie 3** var syftet att mäta positiva och negativa emotionella reaktioner, välmående, och posttraumatiskt stressyndrom bland de utlarmade volontärerna. I **studie 4** var syftet att studera om livräddare instruerade till att hämta en hjärtstartare, med hjälp av en smartphoneapplikation, kunde öka andelen fall där hjärtstartare var uppkopplad av lekmän innan ankomst av ambulans, räddningstjänst och polis.

Metod och resultat

I **studie 1** användes data från smartphoneapplikationen som länkades samman med data från Sveriges hjärtlungräddningsregister. Under 6 månader 2016 så aktiverades systemet 685 gånger. I 224 av dessa fall påbörjade ambulansen behandling. Efter exkludering av fall som var bevittnade av ambulans (n=11) samt fall där ingen svarat på enkäten (n=15) så återstod 198 fall i analysen. Resultaten visade att utlarmade volontärer tog sig fram till platsen i 116 fall (58%) och hann före ambulans i 51 gånger (26%). I 17 fall (9%) kopplades en hjärtstartare upp och i 4 fall defibrillerades patienten (2%). Den Euklidiska mediandistansen (fågelvägen) var 560 meter (IQR=332-860) för volontärerna som blev instruerade att göra HLR och 1280 meter (IQR=748-1776) för volontärerna som blev instruerade att hämta en hjärtstartare.

I studie 2 användes koordinater från smartphoneapplikationen för att studera volontärernas rörelser. Under 7 månader inkluderades 1406 misstänkta hjärtstopp. Bland dessa misstänkta hjärtstopp larmades 9058 volontärer ut varav 2176 tog sig fram till platsen för det misstänkta hjärtstoppet (studiepopulationen). Medianhastigheten var 2.3 meter/sekund (IQR=1.4-4.0) för alla larm, medianresponstiden var 6.2 minuter och mediandistansen var 956 meter (IQR=480-1661). I de mest tätbefolkade områdena så var medianhastigheten 1.8 meter/sekund jämfört med 3.1 meter/sekund i glesbefolkade områden.

Studie 3 inkluderade 886 oexponerade och 1389 exponerade volontärer. Volontärerna delades in i 3 grupper; oexponerade (unexp), exponerad 1 (Exp-1) (de som försökte men misslyckades att nå platsen innan ambulans), och exponerad 2 (Exp-2) (de som antingen hann före ambulans eller de som hjälpte till med HLR/hjärtstartare). Med hjälp av Swedish Core Affect Scales (SCAS) två dimensioner valens och aktivering sågs att exponerade volontärer rapporterade högre grad av aktivering (Exp-1 = 7.5, Exp-2=7.6) jämfört med de oexponerade (7.0) ($p < 0.001$). Exponerade volontärer rapporterade en lägre grad av valens (Exp-1 = 6.3, Exp-2=6.3) jämför med de oexponerade (6.8) ($p < 0.001$). PCL-6 (PTSD) poäng var högre bland oexponerade (10.4) jämfört med exponerade volontärer (Exp-1= 8.8, Exp-2: 9.2) ($p=0.007$). Inga signifikanta skillnader kunde ses i WHO's välmåendeindex (Un-Exp: 77.7; Exp-1: 77.8; Exp-2: 78.2) ($p=0.963$).

I studie 4 randomiserades misstänkta hjärtstopp till antingen intervention där majoriteten av volontärerna (4 av 5) blev instruerade att hämta närmaste hjärtstartare, eller till kontrollgruppen där alla blev instruerade att ta sig direkt till hjärtstoppet för att påbörja HLR. Data från smartphoneapplikationen kopplades ihop med data från svenska hjärt-lungräddningsregistret. Under den 13 månader lång studieperioden randomiserades 2553 misstänkta hjärtstopp. Av dessa så behandlades 815 (32%) av ambulans. I interventionsgruppen kopplades en hjärtstartare upp i 13.2% av fallen jämfört med 9.4% i kontrollgruppen ($p=0.087$). Bland alla inkluderade fall (både intervention och kontrollgrupp) så stod utlarmade volontärer för 29.3% av uppkopplade hjärtstartare samt 35.3% av all bystander HLR.

Slutsatser

Slutsatsen från run-in studien (**studie 1**) var att det är genomförbart att larma ut frivilliga volontärer till misstänkta hjärtstopp, men för att få ner tiden till defibrillering så måste fortsatta förbättringar av systemet göras. Resultaten från **studie 2** visade att volontärer transporterar sig snabbare än tidigare använda estimat och att hastigheten är beroende på befolkningstäthet. Denna information kan användas både i simuleringsstudier och som konfiguration i liknande smartphoneapplikationer. **Studie 3** visade att frivilliga volontärer rankade upplevelsen av att bli utlarmade som hög-energisk och mestadels positiv. Ingen indikation sågs för att de tog skada då de rapporterade höga poäng på välmående och låg grad av posttraumatisk stress vid tiden för uppföljning. Slutsatsen från **studie 4** var att instruktionen att hämta närmaste hjärtstartare inte ökade andelen uppkopplade hjärtstartare innan ambulans, räddningstjänst och polisens ankomst jämfört med de fall där instruktionen var att påbörja HLR. Om volontärer anlände före ambulans, räddningstjänst och polis ökade sannolikheten för hjärtstartaruppkoppling och HLR.

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