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# SOCIOECONOMIC STATUS AND OUT-OF-HOSPITAL CARDIAC ARREST

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# SOCIOECONOMIC STATUS AND OUT-OF-HOSPITAL CARDIAC ARREST

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# THESIS FOR DOCTORAL DEGREE (Ph.D.)

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# ABSTRACT

### Background

Out-of-hospital cardiac arrest (OHCA) is a common cause of death. Around 6000 people in Sweden suffer OHCA each year and only about 10% survive. Historically, the focus of OHCA research has been on different treatments such as improved cardiopulmonary resuscitation (CPR) and early defibrillation. Less is known about how underlying risk factors such as socioeconomic status (SES) affect both the incidence and the chance of surviving an OHCA.

### Methods

The primary data source for this thesis was the Swedish Register of Cardiopulmonary Resuscitation (SRCR). Study I and Study II included consecutive cases of EMS-treated OHCAs in the Stockholm Region between the years 2006–2015 (Study I) and 2006–2017 (Study II). For these two studies the OHCAs were geocoded and linked to area-level SES data from Statistics Sweden. In Study III and Study IV SRCR OHCA data from the whole of Sweden for the years 2010–2017 were used. Data were linked to individual-level socioeconomic variables such as disposable household income and educational level from Statistics Sweden, comorbidity data from the National Patient Register and medication data from the Swedish Prescribed Drug Register.

### Specific aims and results.

The aim of **Study I** was to investigate if socioeconomic characteristics in the area of residence affect the chance of survival after out-of-hospital cardiac arrest. A total of 7431 OHCAs were included in the study. The results suggested a significant association between a higher proportion of university-educated people and 30-day survival. Compared with patients in the lowest educational quintile, the highest quintile showed an adjusted odds ratio (OR) of 1.70 (95% CI=1.15 to 2.51). No significant relationship was seen for area-level income when adjusted for education.

The aim of **Study II** was to investigate the association between area-level SES and the incidence of OHCA, and to investigate if this relationship is dependent on age. A total of 10 574 OHCAs in the Stockholm Region were included in the study. The OHCAs were distributed over 1349 areas which represented the main unit of analysis. Areas characterized by high SES showed an incidence rate ratio (IRR) of 0.56 (95% CI=0.45–0.70) among persons in the age group 0–44. The corresponding number for persons in the 45–64 age group

was 0.53 (95% CI=0.45–0.62) and it was 0.59 (0.49–0.0) among persons in the 65–74 age group. In the two oldest age groups (75–84 and 85+) there was no significant association between area-level SES and the incidence of OHCA.

The aim of **Study III** was to examine how individual-level disposable income and educational level is related to 30-day survival following an OHCA. A total of 31 489 OHCAs were included in the study. In the main model, disposable income level followed a gradient-like increase in chance of survival, with the highest estimate in the highest income quintile (OR = 1.89, 95% CI = 1.64–2.17). This relationship remained after adjusting for comorbidity resuscitation factors and initial rhythm. As regards educational level, the highest OR for 30-day survival was found among persons with four or more years of post-secondary education (OR 1.62, 95% CI=1.36–1.92).

The aim of **Study IV** was to investigate the relationship between disposable income and the chance of having a shockable initial rhythm. A total of 18 099 witnessed OHCAs were included in the study. In the low-income tercile, the proportion with shockable rhythm was 30.2%, compared with 51.4% in the high-income tercile when the EMS response time was less than five minutes. The corresponding numbers were 15.9% vs. 27.6% when the EMS response time was more than 20 minutes. In adjusted logistic regression analyses (using restricted cubic splines) the relationship between income and the probability of shockable initial rhythm followed an S-shaped curve, with a small increase in the first income tercile, a steep increase in the second tercile, that levelled out in the third income tercile. This relationship was seen regardless of potential confounders, comorbidities, cardiac-arrest characteristics and previous medication.

**Conclusions**

The current studies confirm associations between SES, incidence of OHCA, and survival following an OHCA. The results from **Study I** suggest that individuals living in areas with a higher proportion of university-educated people have a higher probability of surviving to 30 days following an OHCA. In **Study II**, areas characterized by low SES showed a higher incidence of OHCA. This relationship, however, was dependent on age, and the SES-incidence relationship disappeared among people over 75 years of age. In **Study III** both individual-level income and education were associated with the probability of 30-day survival after OHCA. In **Study IV**, income was associated with the probability of having a shockable initial rhythm. Initial rhythm may work as a mediator in the relationship between socioeconomic status and survival after OHCA.

# LIST OF SCIENTIFIC PAPERS

I. Jonsson M, Härkönen J, Ljungman P, Rawshani A, Nordberg P, Svensson L, Herlitz J, Hollenberg J.
Survival after out-of-hospital cardiac arrest is associated with area-level socioeconomic status.
*Heart* 2019;**105**:632–638

II. Jonsson M, Ljungman P, Härkönen J, van Nieuwenhuizen B, Møller S, Ringh M, Nordberg P.
Relationship between socioeconomic status and incidence of out-of-hospital cardiac arrest is dependent on age.
*J Epidemiol Community Health* 2020;**74:**726–731

III. Jonsson M, Härkönen J, Ljungman P, Nordberg P, Ringh M, Hirlekar G, Rawshani A, Herlitz J, Ljung R, Hollenberg J.
Individual-level socioeconomic status and survival after out-of-hospital cardiac arrest.
*Manuscript*

IV. Jonsson M, Ljungman P, Härkönen J, Nordberg P, Berglund E, Riva G, Ringh M, Claesson A, Forsberg S, Nord A, Hollenberg J.
Low income is associated with a lower chance of shockable initial rhythm regardless of EMS response time, bystander actions and patient characteristics.
*Manuscript*

# CONTENTS

# LIST OF ABBREVIATIONS

| | |
|---|---|
| AED | Automated External Defibrillator |
| ATC | Anatomical Therapeutic Chemical Classifications System |
| BLS | Basic Life Support |
| CCI | Charlson Comorbidity Index |
| CHD | Coronary Heart Disease |
| CI | Confidence Interval |
| CPR | Cardiopulmonary Resuscitation |
| EMS | Emergency Medical Services |
| ICD | International Classification of Diseases |
| IRR | Incidence Rate Ratio |
| LISA | Longitudinal integration database for health insurance and labour market studies |
| MAUP | Modifiable Areal Unit Problem |
| MAR | Missing at Random |
| MICE | Multiple Imputations by Chained Equations |
| NPR | National Patient Register |
| OHCA | Out-of-Hospital Cardiac Arrest |
| OR | Odds Ratio |
| PEA | Pulseless Electrical Activity |
| SCB | Statistiska Centralbyrån (Statistics Sweden) |
| SCD | Sudden Cardiac Death |
| SES | Socioeconomic Status |
| SRCR | Swedish Register of Cardiopulmonary Resuscitation |
| VF | Ventricular Fibrillation |
| VT | Ventricular Tachycardia |
| ZINB | Zero-Inflated Negative Binominal |

# 1 RATIONALE

Out-of-hospital cardiac arrest (OHCA) is a serious cardiac event that leads to death within minutes if not treated rapidly. Survival rates worldwide are low. Although there is a rich literature on differences between socioeconomic status (SES) and cardiovascular health in general, there has been a shortage of studies on SES disparities in OHCA research including high-quality individual-level socioeconomic data.

This thesis focuses on SES disparities in OHCA. The main outcomes that will be covered are the incidence of OHCA, and the chance of survival following OHCA. The fourth paper concerns how income is associated with the main predictor of survival, shockable initial rhythm.

From a societal perspective, it is important to highlight disparities in health between different groups. As health inequities can be deemed unfair,[1] the overall aim is to better understand socioeconomic differences in OHCA as a first step to minimise these differences.

# 2 BACKGROUND

## 2.1 OUT-OF-HOSPITAL CARDIAC ARREST

### 2.1.1 Definition

Out-of-hospital cardiac arrest (OHCA) has been described as "the cessation of mechanical activity as confirmed by absence of signs of circulation" (2004 Utstein guidelines;[2] explanation below). In practice, when recording cardiac arrest patients in registers, an OHCA is often reported when emergency medical services (EMS) personnel and/or a bystander attempt to resuscitate a patient (i.e. EMS-treated OHCA).

A concept related to OHCA is sudden cardiac death (SCD), which usually is defined as unexpected natural death from a cardiac cause within a short time period, generally within one hour of symptom onset.[3] As SCD is hard to define (e.g. in connection with patients found dead and symptom onset cannot be known) the concept of OHCA is more easily used.

### 2.1.2 Incidence

The incidence of out-of-hospital cardiac arrest varies worldwide. In the most recent review of OHCA incidence, crude rates per 100 000 person-years were 40.6 in Europe, 47.3 in North America, 45.9 in Asia and 51.1 in Australia.[4] In Sweden the reported incidence in the Swedish Register of Cardiopulmonary Resuscitation (SRCR) was 58/100 000 person-years in 2018.[5] Comparisons between different settings may not be too informative, as resuscitation guidelines may affect the reported incidence rates. The incidence rate is much higher among older persons compared with children and young adults.[6]

### 2.1.3 Aetiology

The aetiology of an OHCA is often difficult to know at the time of the arrest. In the previous Utstein guidelines an OHCA was to be assumed to be of cardiac origin if no other obvious cause could be found.[2] This definition was modified in the most recent guidelines to separate the causes into medical and non-medical.[7] The most common cause of OHCA is coronary heart disease (CHD), where acute coronary events such as myocardial infarction are included, followed by cardiomyopathy.[8,9] In addition to cardiac aetiologies, non-cardiac aetiologies such as pulmonary embolism and aortic dissection[9] and external causes such trauma, suicide or drowning can cause an OHCA.[10]

### 2.1.4 History of OHCA research

A famous example of a case of early successful resuscitation was published in JAMA in 1946 by Beck, Pritchard & Feil, describing a 14-year old patient who had suffered cardiac arrest after surgery.[11] Beck opened the chest and started open-chest cardiac massage. In addition to this he used an internal defibrillation advice that after two series of shocks restored the heart rhythm.

Ten years later in 1956 Zoll published a report describing a number of cases where successful external (closed chest) defibrillation had been carried out.[12] Four years later, in 1960, Kouwenhoven et al. described a new method of "closed chest" heart massage in JAMA.[13] In 1967 Pantridge and Geddes described 10 cases of successful resuscitation outside hospital in Belfast[14] and in 1970 Nagel et al.[15] argued for the use of paramedics (fire fighters) in medical emergencies such as cardiac arrest.

One place where the potential of early use of paramedics was recognized was Seattle (or King County) in the US. A programme known as "Medic One" was started in 1970. In addition to dispatch of first responders, this programme included education of the public in Bystander CPR.[16] Two years after initiation of the Medic One programme the journal Resuscitation was launched.[17] In Sweden these improvements were delayed by one decade until Stig Holmberg created the working group for cardiopulmonary resuscitation at the Swedish Society of Cardiology in 1983, to educate the public in CPR, and later creation of the Swedish Register for Cardiopulmonary Resuscitation in 1990.[18]

From the outset, the time-sensitive nature of treatment of cardiac arrest has been recognized.[12] The "chain-of-survival" concept was launched in 1991[19] and further established in cardiopulmonary resuscitation guidelines in 1992.[20] The focus of the "chain-of-survival" concept is to minimise the time from cardiac arrest to recognition, bystander CPR, defibrillation, early advanced life support and early post-resuscitation care.

The famous 'Utstein style' guidelines were published in 1991 after a symposium held at Utstein Abbey, outside Stavanger, Norway, in 1990.[21] The rationale behind the Utstein guidelines was to find a common nomenclature in resuscitation science. To date, the majority of research regarding OHCA still follows the Utstein format (although updated).

Data from the late 1990s and early 2000s showed promising results concerning prehospital defibrillation at casinos and airports by laypersons.[22,23] The main problem is that the majority of OHCAs occur at home, where no automated external defibrillators (AEDs) are available.

As a result of technological developments during the last decade, a number of applications[24,25] to dispatch laypersons to fetch an AED or perform CPR is now available, in the hope of further reducing the time to treatment.

### 2.1.5 Non-modifiable favourable factors for survival

There are a number of factors that are protective or risky as regards survival after OHCA. Some of them cannot be changed by intervention.

*Age*
As for most non-communicable diseases,[26] age is a risk factor as regards OHCA survival. Older patients generally have a lower chance of survival compared with younger patients. A high age is seldom a positive factor for any medical condition and this is true for cardiac arrest as well.[27]

*Sex*
Women have a lower chance of survival compared with men. They are usually older (resulting in more OHCAs at home and therefore more unwitnessed arrests) when they suffer their cardiac arrest, but this alone cannot explain the difference. Another factor that almost completely attenuates the difference is the proportion of cases of shockable initial rhythm.[28]

*Location*
Suffering an OHCA in a public location is associated with a higher chance of survival.[29] This is true even after adjustment for witnessed arrest, age, bystander CPR and shorter response time. The positive effect still remains difficult to understand. It is possible that factors that are hard to measure, such as times from identification to call and bystander CPR are shorter, or that the quality of bystander CPR is good.[30]

*Cardiac cause*
A cardiac aetiology (judged by EMS personnel) is generally associated with a higher chance of survival.[31] In practice the true aetiology is mostly unknown to EMS personnel and all “non-obvious” causes are classified as cardiac, in line with 2004 Utstein guidelines.[2]

*Witnessed status*
A witnessed cardiac arrest is associated with higher survival rates compared with an unwitnessed cardiac arrest.[29] The time from cardiac arrest to treatment by both bystanders and EMS is an important factor for survival and to have a witnessed cardiac arrest shortens this timespan.

*Shockable initial rhythm*

The strongest predictor of OHCA survival is to be found with a shockable rhythm (such as ventricular fibrillation (VF) and ventricular tachycardia (VT)).[32] A shockable rhythm means that the rhythm can be restored to sinus with the help of a defibrillator. It is unknown how modifiable initial rhythm is, as it is not measured near the time of arrest in most cases. Little is known of how many victims have a shockable rhythm at the time of collapse. The rates can be modified to some extent (see below).

### 2.1.6 Modifiable favourable factors for survival

There are a number of factors that are predictors of OHCA survival that can be modified by interventions.

*Bystander CPR*

Bystander CPR (e.g. CPR by a layperson before EMS arrival) is a stable predictor of OHCA survival and have been so for a long time.[33,34] Bystander CPR can be provided with 30 compression and 2 rescue breath or by chest compression only. CPR provides an artificial circulation that have several positive effects on survival. CPR leads to an increase in coronary perfusion pressure[35] (CPP) that on its own is associated with increased chance of return of spontaneous circulation (ROSC).[36] The increased perfusion pressure is also associated with successful defibrillation[37] and studies have found that CPR prolongs the period with shockable rhythm[38,39] (for example see Figure 1). Another positive effect of CPR is that the CPP is correlated to the cerebral perfusion pressure (provides oxygen to the brain), which lowers the risk of brain damage.

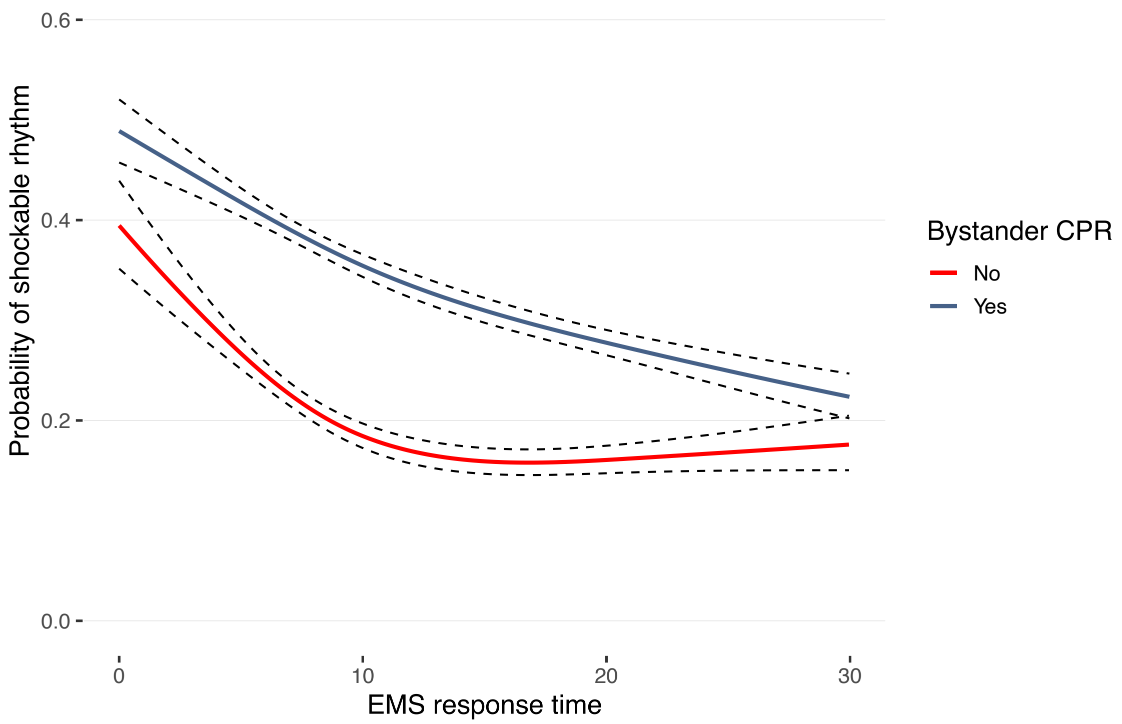


**Figure 1.** The blue line represents cases with bystander CPR, the red line cases with no CPR. The Y axis is the probability of being found in shockable rhythm. Bystander-witnessed cases in Sweden, 2010–2017. Bivariate model.

Bystander CPR rates can be modified in numerous ways. A traditional approach is to educate a large group of people such as school children.[40] Another more recent approach is to dispatch laypersons with knowledge in CPR to cardiac arrests.[25,41]

*EMS response time*

The response time of the EMS is a strong predictor of OHCA survival.[29,42] Response time is used as a proxy measure for the time of cardiac arrest to the time of professional treatment. The EMS response time can be modified by increasing the number of ambulances or first-responder units such as fire-fighters and police. One of the most successful EMS systems regarding response time is found in King County, Seattle, which has a high number of fire stations, resulting in very short basic life support (BLS) response times[43] (Figure 2).

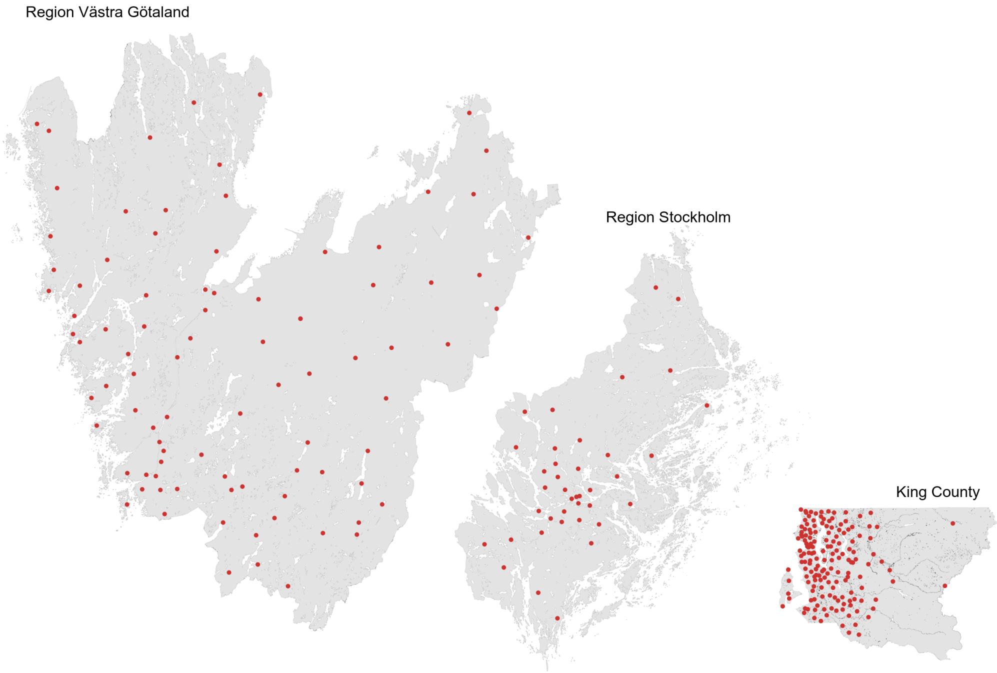


**Figure 2.** Fire stations in Västra Götaland Region, Stockholm Region, and in King County, Seattle.

*Early defibrillation*

Related to initial rhythm, bystander CPR and response time is early defibrillation. Defibrillation is the most effective treatment when the patient has a shockable initial rhythm. A defibrillator delivers a strong electrical shock to the heart with the purpose of ending the current rhythm (arrhythmias such as VF or VT). The heart can then establish a normal rhythm.[44] There are numerous ways to increase the number of patients defibrillated before EMS arrival. One way is to place AEDs in locations with a higher probability of OHCA occurrence, such as airports and sport facilities. Another way to reduce the time to defibrillation is to dispatch first responders, such as in King County, US (Figure 2) or to dispatch laypersons to fetch an AED.

## 2.2 SOCIOECONOMIC STATUS

### 2.2.1 Definition

There is no universally accepted definition of socioeconomic status. Socioeconomic status is a multidimensional concept that categorises individuals or groups into relative positions in a society.

### 2.2.2 Measures of socioeconomic status

As SES is a multidimensional concept, it can be measured in various ways. Three commonly used measures are income, education and occupation. These three measures are sometimes used interchangeably but measure different aspects of SES.[45]

*Income*

Income is the measure that best reflects material resources.[46] Material resources can affect health in various ways. In the most direct way income can be used to purchase food and housing. Further income gives the opportunity to purchase both healthier food and better housing. An indirect effect of a good income and related housing is that one can afford to live in an area with a better environment and lower crime rates etc. In settings where healthcare is not universal, income can be used to purchase health insurance. In an absolute sense a low income may make it difficult to make ends meet. This could result in a stressful situation with adverse health effects.

In addition to material resources, income can also have a symbolic value that could affect a person's status.[47] A person's rank/status in society could influence health both positively and negatively. Data on primates and other animals have shown that animals with low rank have higher levels of stress.[48,49]

One problem with income as a measure of socioeconomic status is the risk of reverse causation. If a person becomes ill, they tend to earn less money. The correlation seen between income and health can therefore be dictated by health rather than income. Another problem is that income can vary over time. A person's income during a single year may be a poor measurement of material resources.

*Education*

Education has several positive health effects. One way it affects health is simply as a confounder to both income and occupation. One direct pathway between education and health offered by Mirovsky & Ross is that education increases feelings of being in control over one's life[50]. This control, in addition to knowledge, makes it easier to embrace behaviours that promote health, such as exercise, and also the abandonment of bad habits such as smoking[51] and excess drinking.[52] Education can be measured in several ways, such as years of schooling, or in categories such as primary, secondary and tertiary. One great advantage of education as a measure is stability over time. After young adulthood one's educational level is generally stable. One advantage of this is that most people have not developed chronic health problems at a young age, and therefore education does not suffer from reverse causation to the same extent.

*Occupation*

The workplace can affect the health of a person in various ways. Some occupations involving the use of heavy machinery may lead to serious injuries. The demand-control model originally developed by Karasek[53] was further developed into the demand-control-support model.[54] The basic idea is that if you have an occupation with high demand and low support you will be in a high strain (stressful) situation that will have adverse health effects. Occupation can also be a marker of status in the same way as income. As the majority of cardiac-arrest patients are above retirement age, occupation may not be the best measure in cardiac-arrest research.

These three measures of socioeconomic status (income, education and occupation) are all related to each other, generally in the sense that education affects occupation, which in turn affects income. Previous research suggests that they may be related to different diseases in different ways.[55]

### 2.2.3 Levels of socioeconomic status

Socioeconomic status can be measured at different levels. The two most common levels are at an area level and at an individual level.

SES measured at an area level is in some cases the easiest way to assess it. If you have information about the patient's area of living you can simply add the area-level data (e.g. income and proportion with university education). Area-level measures can work both as a proxy of individual-level SES and as a measure of area effects. Area effects such as environmental factors and crime can in turn have their own adverse effects on health outcomes. If area-level measures are used as a proxy for individual-level data, the size of the area may play a significant role. If municipality is used as "area" the heterogeneity within that area is likely to be much larger than in small neighbourhoods. According to the "Modifiable

Areal Unit Problem" (MAUP) larger areas tend to produce stronger correlations compared with smaller ones,[56] but may on the other hand suffer from confounding bias.[57]

Using area-level measure can also lead to false conclusions, so called ecological fallacies.[58] An ecological fallacy occurs when we falsely assume that a relationship seen using aggregated data is true on an individual level.

Individual-level measurements do not suffer from the risk of ecological fallacies, but they have the disadvantage that area effects cannot be measured. A person with high income and a high educational level may still suffer adverse health effects if he or she lives in an area with high levels of crime and air pollution, for example.

## 2.3 PREVIOUS RESEARCH ON THE SES–OHCA RELATIONSHIP

This thesis covers two aspects of the SES–OHCA relationship. First, previous studies covering socioeconomic differences in connection with OHCA survival will be presented, followed by studies covering SES and incidence of OHCA. There are a number of studies focusing on SES and differences in bystander CPR rate. This aspect will not be covered in this thesis.

### 2.3.1 Socioeconomic status and survival after OHCA

The number of studies on the relationship between SES and survival after OHCA has increased in recent years. During the early to mid-1990s a couple of studies focusing on socioeconomic differences in survival emerged from the US. One study by Hallstrom et al.[59] included 356 patients with ventricular fibrillation in King County, US. In multivariate analysis there were 183 patients and the authors found a significant positive trend in relation to increasing home tax value.

Feero et al.[60] published data from Oregon in 1995. They compared low- and high-income communities and did not find any significant differences in survival to hospital discharge. This may, however, have been due to the limited sample size (n=67). Another study, from 1998 and conducted in Michigan, US, also did not reveal any statistically significant association with area-level household income.[61] Again, this might have been a result of limited sample size (n=1317). Galea et al. studied SES and race differences among 3891 patients in New York City in 2002–2003 and found no significant results as regards area-level household income.[62] Vaillancourt et al.[63] studied OHCAs in Ontario, Canada, and found a reverse relationship with a higher level of property value. The study included 3600 cases that occurred in "single-residential dwellings", excluding more than 50% of the OHCAs. Another study, from Toronto, Canada, including 9485 patients, revealed no association between area-level deprivation and survival to hospital discharge.[64]

A study from King County, US, including 1789 OHCA patients showed a significant association with tax-assessed home value (similar to the results presented by Hallstrom et al., 1993, above) but not for area-level household income.[65]

Other studies outside North America have shown different results. Two studies from South Korea with large sample sizes revealed significant associations between area-level deprivation and survival after OHCA.[66,67] From Taipei, Taiwan, Chiang et al.[68] found a significant crude association when looking at low- and high-SES areas, but they did not conduct any multivariate analyses. A recent study from Singapore[69], including 8900 patients, where the main focus was to study ethnic differences, did not show any significant effect of socioeconomic status.

Three studies distinguish themselves from the rest, as individual-level data was used. One could perhaps argue that property-tax values could be regarded as individual-level data, but may be a poor measure in some areas (especially in newly gentrified areas). The first study was conducted in Denmark and included children and adolescents (under the age of 21).[70] The investigators found no significant associations after adjustment, probably because of limited sample size (n=459). The other study, by Wells et al., involved the SES–OHCA survival relationship in 1380 VF patients in King County, and a significant association was found as regards education, but not occupation.[71] A Danish nation-wide study by Møller et al.[72] studied patients admitted to hospital after successful resuscitation and found a significant association between household income and 30 day survival.

To summarise, results concerning the relationship between SES and survival after OHCA are conflicting. The lack of relationship seen in some studies may in some cases be due to insufficient power. Another explanation is that different measures may yield different results, and the relationship may not be universal, but dependent on setting.

**Table 1.** Summary table of studies on SES and survival after OHCA.

| | Location | Level of SES | Patients | Relationship |
|---|---|---|---|---|
| Hallstrom et al., 1993 | King County, US | Semi-individual | 183 | + |
| Feero et al., 1995 | Oregon, US | Area | 67 | NS |
| Sayegh et al., 1998 | Michigan, US | Area | 1317 | NS |
| Clarke et al., 2005 | King County, US | Semi-individual | 1789 | + |
| Galea et al., 2007 | New York, US | Area | 3891 | NS |
| Vaillancourt et al., 2008 | Ontario, CA | Semi-individual | 3600 | - |
| Ahn et al., 2011 | Seoul, South Korea | Area | 34 227 | + |
| Chiang et al., 2014 | Taipei, Taiwan | Area | 3573 | + |
| Rajan et al., 2015 | Denmark | Individual | 459 | NS |
| Buick et al., 2016 | Toronto, CA | Area | 9485 | NS |
| Wells et al., 2016 | King County, US | Individual | 1380 | + |
| Lee et al., 2018 | Seoul, South Korea | Area | 120 365 | + |
| Rakun et al., 2019 | Singapore | Area | 8900 | NS |
| Møller et al, 2020 | Denmark | Individual | 6,105 | + |

### 2.3.2 SES and incidence of OHCA

There are several studies on the relationship between socioeconomic disparities and OHCA incidence. Among the studies from North America that have concerned this relationship, Feero et al.[60] found a significant difference in OHCA incidence between low- and high-income areas after adjustment for age and sex. Reinier et al.[73] studied OHCA incidence in Oregon and found crude differences in incidence rates in all area-level SES measures (income, poverty, home value and education). A more extensive study by Reinier et al. including data from seven metropolitan areas in North America revealed a significant association between area-level household income and incidence of OHCA.[74] In both studies by Reinier et al. the relationship was stronger among persons under the age of 65 years.

Another approach to study SES differences is to look at areas with a high incidence rate of OHCA and see if they distinguish themselves from other areas. Studies using this approach generally show that high-incidence areas are characterised by low SES.[75–77]

Studies outside North America have shown similar results. Folke et al.[78] aimed to identify high-risk areas in Copenhagen city centre (population 600 000), using a 100 × 100 meter grid and they found that both low levels of education and low levels of income were associated with the incidence of OHCA. Castra et al.[79] carried out a Bayesian analysis of OHCA incidence in municipalities around Paris, France, and found that high-incidence areas had lower levels of education and higher levels of poverty. Ahn et al.[66] found a higher incidence of OHCA in areas with high levels of deprivation in South Korea, as did Dicker et al. in New Zealand.[80]

Other studies have shown conflicting results. Straney et al.[81] found a lower incidence with higher SES (using an index), while higher-level education was associated with higher OHCA incidence. Rakun et al.[69] found no association between socioeconomic disadvantage and incidence of OHCA in Singapore.

As with studies on survival, the published literature on SES–OHCA incidence has yielded different results. However, the vast majority of studies have shown significant associations between socioeconomic variables and the incidence of OHCA.

**Table 2.** Summary table of studies on SES–incidence of OHCA.

| | Location | Area | Relationship |
|---|---|---|---|
| Feero et al., 1995 | Oregon, US | Census | + |
| Reinier et al., 2006 | Oregon, US | Census | + |
| Reinier et al., 2011 | US, Canada | Census | + |
| Ahn et al., 2011 | Seoul, South Korea | Districts | + |
| Sasson et al., 2012 | Ohio, US | Census | + |
| Semple et al., 2013 | Ohio, US | Census | + |
| Raun et al., 2013 | Houston, Texas | Census | + |
| Folke et al., 2010 | City of Copenhagen, Denmark | 100 × 100 meter squares | + |
| Castra et al. 2016 | Suburban Paris, France | Municipalities | + |
| Straney et al., 2016 | Victoria, Australia | Local government areas | +/- |
| Rakun et al., 2019 | Singapore | Zip codes | NS |
| Dicker et al., 2019 | New Zealand | Census | + |

### 2.3.3 Socioeconomic status and adjustment for VF/VT

Among the studies that have concerned the relationship between SES and survival after OHCA it is not uncommon to adjust for initial rhythm. Some investigators have not used any adjustment when measuring survival.[60,68,72] Several others have presented multiple models with and without VF/VT as a covariate.[62,65,70] In many studies VF/VT has been used as an adjustment variable,[61,63,64] while two studies have included only patients with VF/VT as initial rhythm.[59,71]

A shockable initial rhythm may work as an intermediate variable on the presumed causal pathway between socioeconomic status and OHCA survival. This potential problem has been highlighted by Blom et al.,[28] who found that sex differences in OHCA survival are, to a large part, explained by differences in initial rhythm. Adjustment for initial rhythm could therefore lead to so-called overadjustment bias,[82] meaning that we underestimate the true socioeconomic disparities in relation to survival. A better understanding of the relationship between SES and initial rhythm may increase our understanding of the mechanisms behind the SES–survival relationship.

**Table 3.** Summary table of studies on SES–OHCA survival, and VF/VT adjustment

| | Location | Level of SES | Adjustment for VF/VT in multivariable models |
|---|---|---|---|
| Hallstrom, 1993 | King County, US | Semi-individual | Only VF patients |
| Feero, 1995 | Oregon, US | Area | - |
| Sayegh, 1998 | Michigan, US | Area | Yes |
| Clarke, 2005 | King County, US | Semi-individual | Both |
| Galea, 2007 | New York, US | Area | Both |
| Vaillancourt, 2008 | Ontario, CA | Semi-individual | Yes |
| Ahn, 2011 | Seoul, South Korea | Area | Both |
| Chiang, 2014 | Taipei, Taiwan | Area | - |
| Rajan, 2015 | Denmark | Individual | Both |
| Buick, 2016 | Toronto, CA | Area | Yes |
| Wells, 2016 | King County, US | Individual | Only VF patients |
| Lee, 2018 | Seoul, South Korea | Area | No, only age and sex |
| Rakun, 2019 | Singapore | Area | Both |
| Møller et al, 2020 | Denmark | Individual | No, only age and sex |

# 3 AIMS

The general aim of the thesis was to study socioeconomic differences in relation to OHCA.

The specific aims for the studies were the following:

## 3.1 STUDY I

To study the probability of 30-day survival after OHCA in relation to area-level SES measured by income and the proportion of university-educated cases. We also investigated if there were any sex differences in this relationship.

## 3.2 STUDY II

To determine if areas characterised by lower SES show a higher incidence of OHCA, and, if so, if this relationship is dependent on age.

## 3.3 STUDY III

To investigate whether individual-level SES, measured by educational level and disposable income, are associated with 30-day survival after OHCA.

## 3.4 STUDY IV

To investigate how income is related to the probability of having a shockable initial rhythm.

# 4 DATA AND METHODS

## 4.1 DATA SOURCES

### 4.1.1 Swedish Register for Cardiopulmonary Resuscitation

The common denominator for all studies in this thesis is the Swedish Register of Cardiopulmonary Resuscitation (SRCR).[83] The SRCR was established in the beginning of the 1990s in Gothenburg and during the first years it covered Gothenburg and surrounding areas. However, coverage has increased over time and since 2010 all EMS agencies in Sweden report to the register. The register is operated by Registercentrum Västra Götalandsregionen with support from the Swedish Association of Local Authorities and Regions. From the beginning of the 1990s to the late 2000s EMS agencies sent in paper copies to the register. During 2007 to 2009 the register gradually moved to online registration and since 2010 all regions in Sweden have reported online. The register follows the Utstein template[2] and demographic factors such as age and sex, along with factors surrounding the OHCA such as location, witnessed status, aetiology and initial rhythm are registered. Focus is on different treatments such as bystander CPR, CPR by first responder, defibrillation before EMS, response time, as well as different treatments provided by EMS.

### 4.1.2 The LISA database (Statistics Sweden)

The LISA (Longitudinal integration database for health insurance and labour market studies) database[84] includes data for all persons living in Sweden. The database receives data from a number of registers and contains information concerning a large number of socioeconomic variables. Data ordered from the LISA database were education (highest level of completed education), family disposable household income, individual disposable household income and occupation. The LISA database was used for Study IV.

### 4.1.3 The National Patient Register (National Board of Health and Welfare)

The National Patient Register (NPR) contains data on all cases of in- and out-patient care in Sweden.[85] The register was created in the mid-1960s and from 1987 is complete for all inpatient care in Sweden. Since 2001, all cases of out-patient care have been included as well. Data requested from the NPR were international classification of diseases (ICD)-10 codes five years before the OHCA. Data from the NPR were used for Studies III and IV.

#### 4.1.4 Cause of Death Register (National Board of Health and Welfare)

The Cause of Death Register[86] contains ICD-10 codes of the underlying cause of death in all cases in Sweden, in a similar manner as in the NPR. This data was requested for Studies III and IV.

#### 4.1.5 The Swedish Prescribed Drug Register (National Board of Health and Welfare)

The Swedish Prescribed Drug Register contains data on prescribed medications. Data is available as Anatomical Therapeutic Chemical Classifications System (ATC) codes. Prescribed medications in various categories were ordered to cover up to five years prior to the cardiac arrest.

### 4.2 STUDY DESIGN

#### 4.2.1 Study I: Area-level SES and survival after OHCA

The first study is an observational cohort study including OHCA patients that resided in the Stockholm Region during a 10-year period (2006–2015). An individual's SES was assessed by using the home address of the patient, which was later linked to area-level data from Statistics Sweden (SCB). The grid prespecified by SCB contained areas that were 250 × 250 meters in urban areas and 1000 × 1000 meters in rural areas (Figure 3). This is because SCB is not allowed to publish data if the source population contains less than five persons. Data were downloaded from the GET service maintained by the Swedish University of Agricultural Sciences (https://zeus.slu.se).

If the patient's home address was located within a grid the median disposable household income and the percentage of university-educated people within the area were used as measures of SES. The income and education variables were converted into five groups based on quintiles.

Patients with missing ID, EMS-witnessed cases and cases where no SES information was attainable were excluded from the study. The main outcome of the study was 30-day survival.

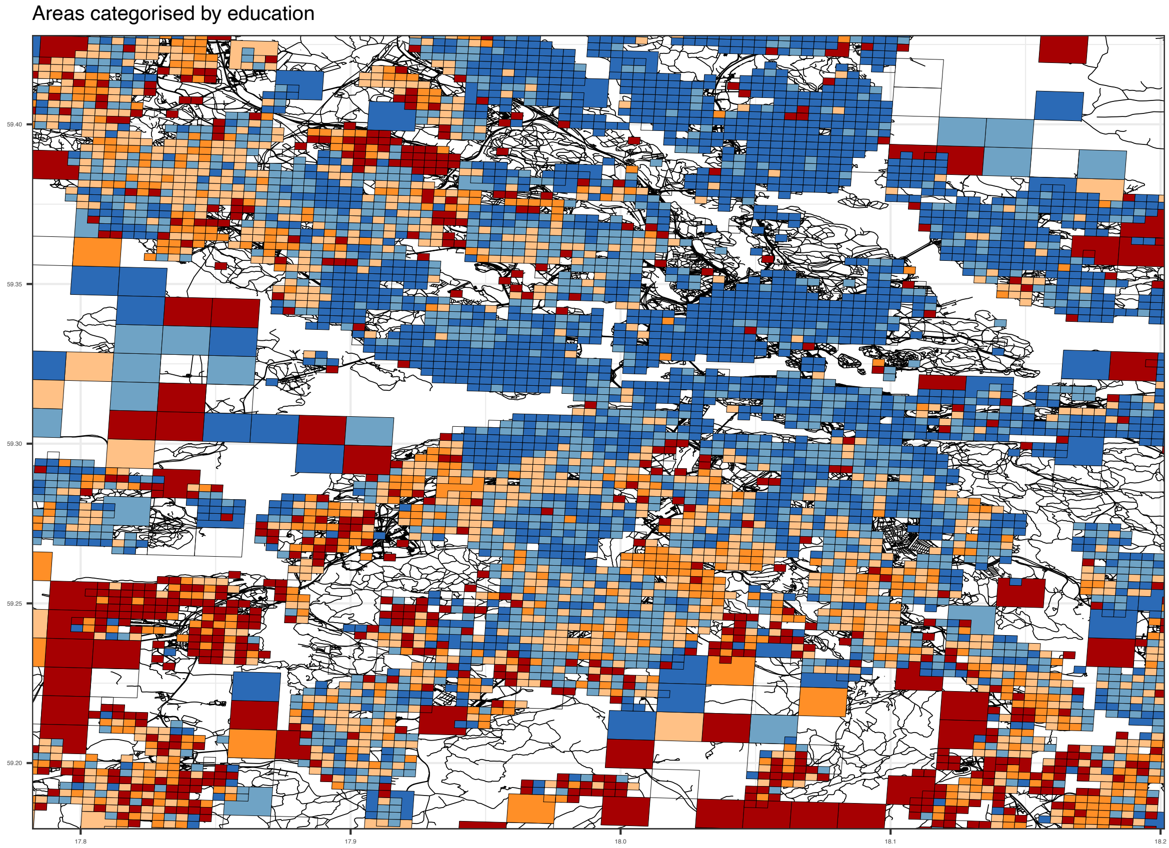


**Figure 3.** Example of areas used in Study 1. Blue = high proportion of university-educated people.

### 4.2.2 Study II: Socioeconomic status and incidence of OHCA in relation to age

The second study in this thesis concerned the incidence of OHCA in relation to SES. We used an ecological approach, so the units of comparison were not patients but the areas themselves. The study included all base units (basområden) in the Stockholm Region (Figure 4). Patients with missing ID and those residing outside the Stockholm Region were excluded, as they were not part of the denominator in the incidence calculations. To categorise the areas by SES an index was constructed by using quintiles of both family income (from earnings) and the proportion of people with university education. Incidence rates per 100 000 person-years were calculated for all patients and by age groups (0–44, 45–64, 65–74, 75–84 and 85+).

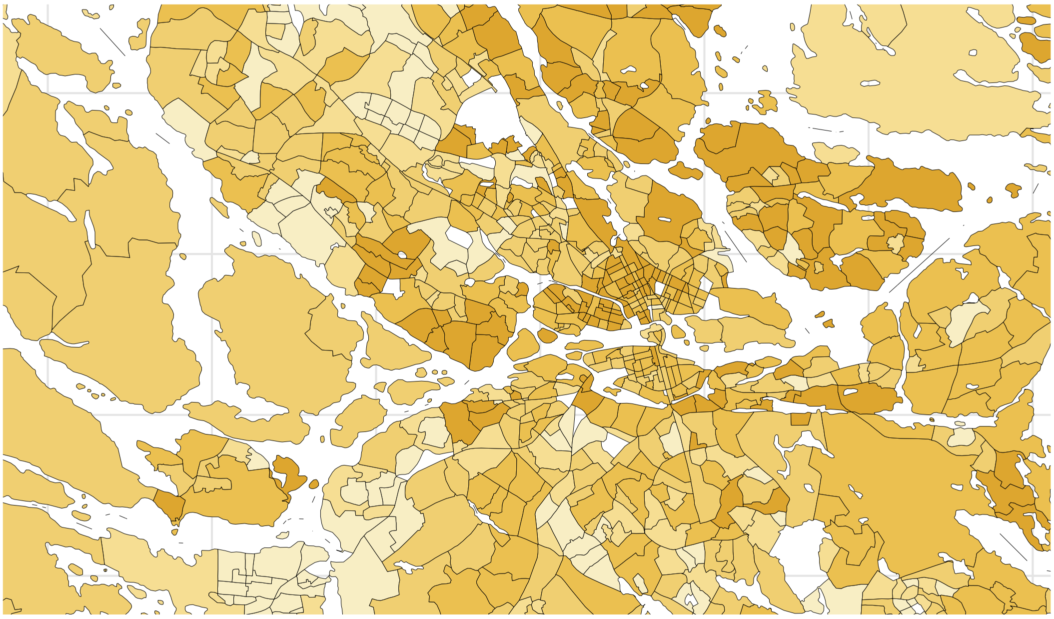

**Figure 4**. Map of base units in the Stockholm region used in Study II. Darker colour = higher SES.

### 4.2.3 Study III: Individual-level socioeconomic status and survival after OHCA

The third paper in this thesis concerns an observational cohort study covering all OHCAs reported to the SRCR in Sweden between the years 2010 and 2017. Socioeconomic data were collected from Statistics Sweden and comorbidity data from the NPR. Patients with unknown identity or residents outside Sweden were excluded because of the impossibility to link them to national registers. The main outcome was survival to 30 days. The two main exposures were the highest level of completed education, divided into five groups, and disposable family household income. The socioeconomic variables obtained concerned the year before the OHCA, as education status is recorded as that at the 31$^{st}$ of December each year. As income is likely to be heavily reduced after an OHCA, income data collected also concerned the year before the OHCA.

### 4.2.4 Study IV: Low income is associated with a lower chance of shockable initial rhythm regardless of EMS response time, and other patient characteristics

In Study IV we utilized the data from Study III. In addition to SES and comorbidity data, pharmaceutical data was collected from the Swedish Pharmaceutical Register. The outcome of Study IV was shockable initial rhythm, defined as ventricular fibrillation and ventricular tachycardia. To obtain more reliable information on timestamps all unwitnessed cases were excluded, as the EMS response time does not represent time from OHCA to treatment. EMS-witnessed cases were also excluded.

## 4.3 STATISTICAL CONSIDERATIONS

In addition to study design there are some statistical considerations that need to be addressed. Regarding selection of patients, one common denominator for all studies using OHCA data is that EMS-witnessed cases are excluded from the analyses. The reason for this is mainly statistical. Cases witnessed by EMS are not those with data on bystander CPR. One way to handle this is to set bystander CPR to either 0 or 1, but none of the alternatives are appealing, as CPR by EMS is of course better than no CPR, and is likely to be better than bystander CPR. Another factor to consider is the response time. Response time in OHCA research is mainly a measure of time from OHCA to the time of EMS treatment. In EMS-witnessed cases this time can be relatively long, but the true time should be zero, as they are at the scene when OHCA occurs. One could handle this by recoding the response time to zero. This is not appealing, as it will affect the validity of the response time variable for all cases if 10 to 15% of all cases have a response time of zero.

Baseline variables are presented as counts and proportions, and continuous variables as medians with inter-quartile range (IQR). This is a result of the notorious lack of normally distributed variables in OHCA research.

The statistical software used in the studies were R statistical software version 3.4.3 (Paper I), version 3.5.2 (Paper II), version 3.6.0 (Paper III) and version 4.0.0 (Paper IV).

### 4.3.1 Study I

In Study I, baseline characteristics are presented as counts and proportions. Continuous variables are presented as medians with quartile 1 (Q1) and quartile 3 (Q3). To test differences in baseline variables $X^2$ tests for trend were used and for continuous variables Jonckheere–Terpstra tests for trend were used.

Further statistical considerations included handling missing data by means of multiple imputations by chained equations (MICE).[87] The total amount of missing variables used in the multivariate analyses was around 7%. Fifteen datasets were imputed and the results were calculated by means of logistic regression adjusted for age, sex, emergency medical services response time, witnessed status, initial rhythm, aetiology, location, year of cardiac arrest and population density. Logistic regression was conducted using all 15 datasets and the results were pooled using Rubin' rules. "Missing" was assumed to be missing at random (MAR).[88]

### 4.3.2 Study II

In Study II no comparisons between baseline variables were made, as the numbers are for the total population. To analyse incidence rate ratios (IRRs) a zero-inflated negative binomial (ZINB) model was used. The choice of analytic method was a result of the fact that one of the assumptions in the original Poisson model was that the mean of counts and variance should be the same. If the variance is larger than the mean of counts then the model is overdispersed. In Study II there were signs of overdispersion. In addition to the overdispersion there were signs of excess zeros, which means that there were too many observations (areas) with no cardiac arrests. In this case this is related to areas that are very sparsely populated. The ZINB model uses a two-step approach. The first is to see if an area is likely to have any OHCAs, while the other step is to test the effect of the exposure of interest after the zero-cases are removed. To test which model would be most suitable, the ZINB model was tested by using Vuong's non-nested hypothesis test[89] against a Poisson model, a zero-inflated Poisson model and a negative binomial model. The test suggested that ZINB had the best fit. Areas with very high incidence were handled by removing observations according to the 1.5 IQR rule (or Tukey's fences)[90].

The SES index created was created due to some problems with multicollinearity between the income and education variables, and also due to some signs of a Simpson's paradox, meaning that the relationship between exposure and outcome in the whole sample was different compared to when stratified in subgroups.

### 4.3.3 Study III

In Study III we used data from both the NPR and Statistics Sweden. Income (disposable family household income) was categorised into quintiles, while education was categorised into the following categories: primary, secondary, post-secondary less than three years, post-secondary three years and post-secondary four years or more. Data were analysed using multivariate logistic regression. Before that, missing data were imputed using multiple imputations (10 datasets). The results were pooled using Rubin's rules. The analytical approach was to create five regression models with increasing numbers of covariates. Model 1 (the primary model in the education analysis) was adjusted for age, sex, year of OHCA, retirement status and civil status. In model 2 we added the Charlson Comorbidity Index (CCI), in model 3, which was considered the primary model for income (as all potential confounders were included), we added educational level/income. Model 4 included further resuscitation variables such as witnessed status, bystander CPR, public location and cardiac aetiology. The fifth and last model also included initial rhythm.

### 4.3.4 Study IV

Study IV involved the same data as in Study III, with the addition of pharmaceutical data from the Swedish Pharmaceutical Register, which is maintained by the National Board of Health and Welfare. The data were analysed by using logistic regression with restricted cubic splines (RCSs). Cubic splines were used to see if the relationship between income and shockable initial rhythm was non-linear. To aid interpretation, income was also categorised into terciles.

## 4.4 ETHICAL CONSIDERATIONS

An ethical problem in cardiac-arrest research is the question of whether or not it is acceptable to conduct research without informed consent (which of course is impossible). This does not apply in register-based research, as no further harm (interventions) can be inflicted on the patients. This does not mean that register-based research is without ethical considerations. Although survivors of OHCA may have given consent to be included in a register, they may not have given any consent to have their data linked to that in other registers with information on health and socioeconomic factors. The risk for the patients included in the studies is therefore that sensitive information is leaked. To minimise the risk of this integrity breach, information that could reveal identity are removed when the data are collected from Statistics Sweden and the National Board of Health and Welfare.

All studies were approved by the regional ethics board in Stockholm (Dnr: 2017/716-31 and 2018/495-32).

# 5 RESULTS

## 5.1 STUDY 1: AREA-LEVEL SES AND SURVIVAL AFTER OHCA

After exclusion of cases with missing ID or living outside Stockholm (n=1011), EMS-witnessed cases (n=1301) and cases with missing data on SES variables (n=48), the analytical sample consisted of 7431 patients.

There was a crude relationship between both area-level education and area-level income, and survival after OHCA. The relationship was present at day one, day 30 and after one year (Figure 5).

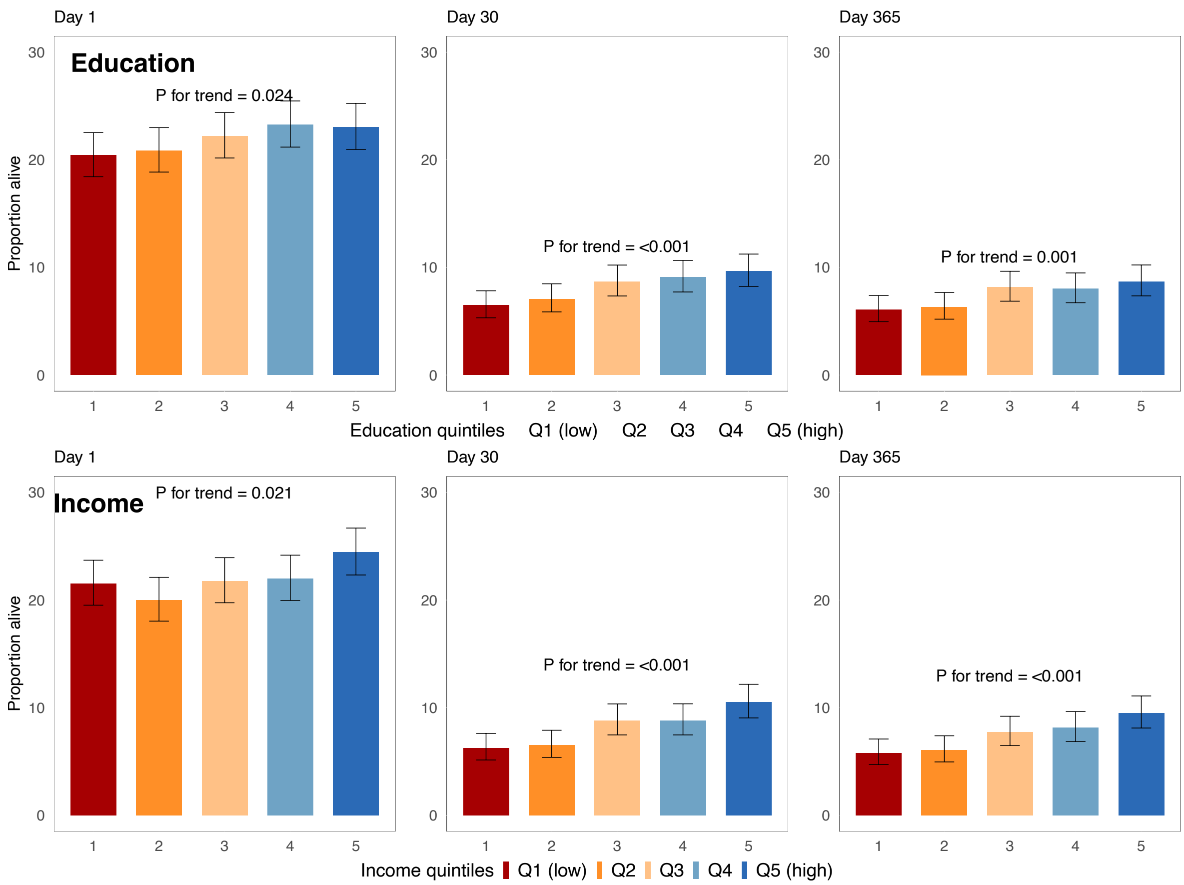


**Figure 5.** Crude relationship between area-level education and area-level income, and 1-day, 30-day and 365-day survival.

In the models including only one SES measure there was a clear gradient with an increasing chance of survival with an increasing proportion of university-educated people. The odds ratio (OR) for survival in the highest education group was 1.93 (95% CI = 1.41–2.64). For income the results were similar, with a corresponding OR for survival of 1.88 (95% CI = 1.36–2.59).

After inclusion of the other SES measures (income/education) in the model the results for education were attenuated but still statistically significant. The OR in the highest income group was 1.70 (95% CI = 1.15–2.51). For income the trend was further attenuated and none of the figures were any longer statistically significant. The highest OR was found in the highest income quintile (1.31, 95% CI = 0.87–1.98). For details see Table 4.

**Table 4.** Results of the multiple adjusted logistic regression analyses. Reprinted with permission from the BMJ publishing group.

| | Model 1 | Model 2 | Model 3 |
|---|---|---|---|
| | OR (95% CI) | OR (95% CI) | OR (95% CI) |
| Education Q1 | 1.0 (<0.001)* | | 1.0 (0.003)* |
| Education Q2 | 1.27 (0.92 to 1.75) | | 1.24 (0.90 to 1.72) |
| Education Q3 | 1.65 (1.21 to 2.24) | | 1.53 (1.10 to 2.14) |
| Education Q4 | 1.76 (1.30 to 2.40) | | 1.61 (1.13 to 2.28) |
| Education Q5 | 1.93 (1.41 to 2.64) | | 1.70 (1.15 to 2.51) |
| Income Q1 | | 1.0 (<0.001)* | 1.0 (0.388)* |
| Income Q2 | | 1.34 (0.96 to 1.87) | 1.18 (0.83 to 1.66) |
| Income Q3 | | 1.56 (1.14 to 2.14) | 1.23 (0.87 to 1.75) |
| Income Q4 | | 1.49 (1.08 to 2.05) | 1.12 (0.77 to 1.63) |
| Income Q5 | | 1.88 (1.36 to 2.59) | 1.31 (0.87 to 1.98) |
| Female sex | 1.23 (0.99 to 1.53) | 1.23 (0.99 to 1.53) | 1.23 (0.99 to 1.54) |
| Age | 0.97 (0.96 to 0.98) | 0.97 (0.97 to 0.98) | 0.97 (0.96 to 0.97) |
| At home | 0.45 (0.37 to 0.54) | 0.45 (0.37 to 0.54) | 0.45 (0.37 to 0.54) |
| Response time (per min) | 0.97 (0.96 to 0.99) | 0.97 (0.96 to 0.99) | 0.97 (0.96 to 0.99) |
| VF/VT | 9.29 (7.42 to 11.62) | 9.2 (7.36 to 11.51) | 9.3 (7.43 to 11.64) |
| Witnessed OHCA | 2.83 (2.20 to 3.65) | 2.8 (2.17 to 3.62) | 2.83 (2.19 to 3.65) |
| Non-cardiac aetiology | 1.31 (0.96 to 1.80) | 1.31 (0.95 to 1.79) | 1.31 (0.96 to 1.8) |
| Bystander CPR | 1.39 (1.10 to 1.76) | 1.37 (1.09 to 1.74) | 1.39 (1.10 to 1.76) |
| Year of OHCA | 1.10 (1.07 to 1.14) | 1.1 (1.06 to 1.14) | 1.1 (1.07 to 1.14) |
| Population density (Q1) | 1.0 | 1.0 | 1.0 |
| Population density (Q2) | 0.97 (0.75 to 1.26) | 1.04 (0.79 to 1.35) | 0.99 (0.76 to 1.3) |
| Population density (Q3) | 1.04 (0.79 to 1.36) | 1.18 (0.88 to 1.58) | 1.09 (0.81 to 1.46) |
| Population density (Q4) | 0.84 (0.64 to 1.10) | 1.02 (0.77 to 1.34) | 0.9 (0.67 to 1.21) |

*p for trend.

In the sex-stratified analysis, the crude differences for men followed a pattern similar to that for all patients, with a more distinct trend as regards education vs. income. In the mutually adjusted model (adjusted for covariates and income) there was a significant trend between increasing education and the chance of 30-day survival. The OR in the highest education group was 1.69 (95% CI = 1.06–2.70).

For women the results were somewhat different. First of all, the overall survival rates were lower. In contrast to men, income followed a clearer trend compared with education. In the mutually adjusted analysis there was a positive trend as regards education, but the results were not statistically significant and the confidence intervals were very imprecise.

## 5.2 STUDY II: AREA-LEVEL SES AND INCIDENCE OF OHCA IN RELATION TO AGE

In Study II the number of base-unit areas was 1418. After removal of areas with missing SES information (n = 69), 1349 areas remained. After removal of outliers by using the 1.5 IQR rule and removal of excess zeros, the remaining areas included in the analyses ranged between 1215 and 1276.

When adjusted for the proportion of inhabitants with a foreign background, the incidence of OHCA followed a clear gradient with a decreasing incidence in areas of high socioeconomic status. When stratified by age-group the association was seen in age-groups 0–44, 45–64 and 65–74. After that the relationship diminished. In the age-group 75–84 there was a very weak trend towards a lower incidence and in the 85+ group the relationship was completely absent (Figure 6).

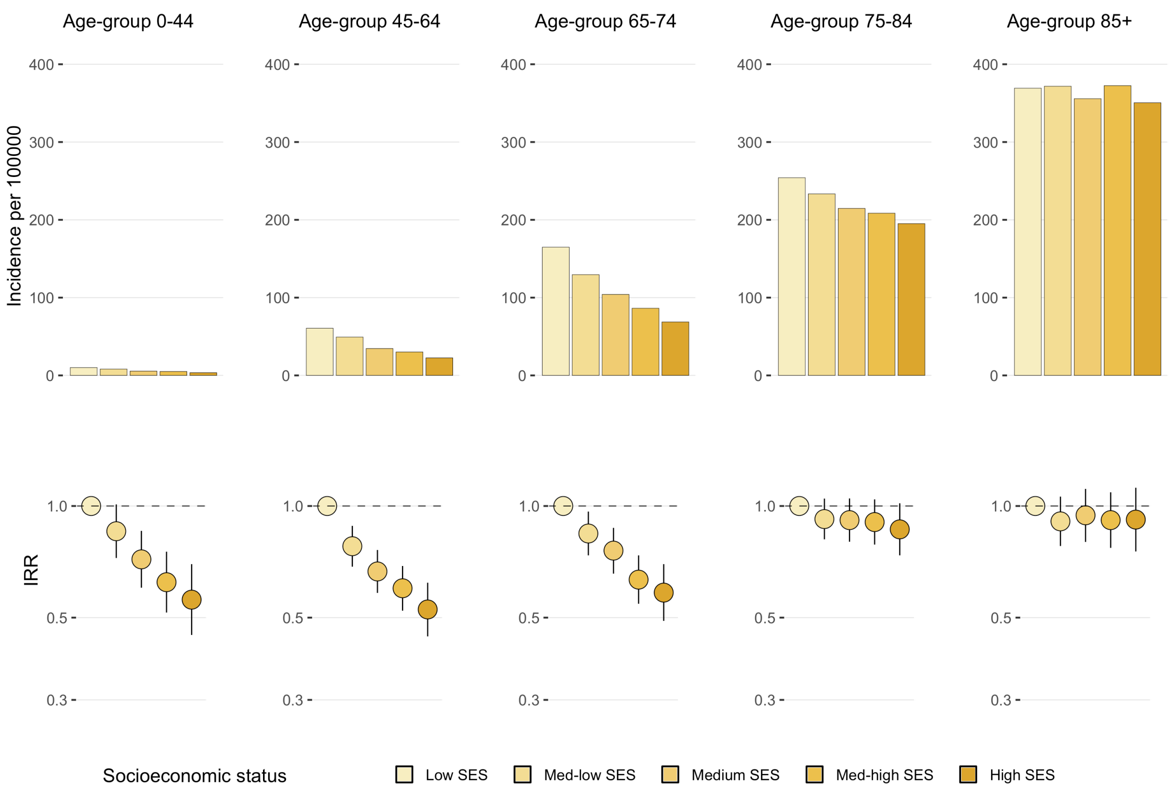


**Figure 6.** Adjusted IRRs of OHCA by SES in different age groups. Reprinted with permission from the BMJ publishing group.

In sex-stratified analyses, a similar pattern was seen. The incidence among men in the age-group 0–44 was very low but still followed a socioeconomic gradient with a higher incidence in the low-SES groups. With increasing age, the overall incidence increased and there was a clear socioeconomic gradient up the age of 74. After that the trend became weaker and among persons over 85 years of age there was no clear trend. For women the results were similar with the exception that the overall incidence was much lower in all age-groups. The SES gradient was clear up to the age of 74, then weakening and almost not apparent among the oldest group (85+).

In Figure 7 the total incidence proportion per age-group is shown. By far the largest part of the population was found in the age-group 0–44 (60% of the population). The proportion of the total population decreased rapidly in the higher age-groups and only 2% were over 85 years old. The proportion of cases of OHCA followed a different pattern. Ten per cent of the OHCAs were in the 0–44 group, while the 45–64, 65–74, and 75–84 age-groups represented around 23–24% each and 19% of all OHCAs were in the oldest group.

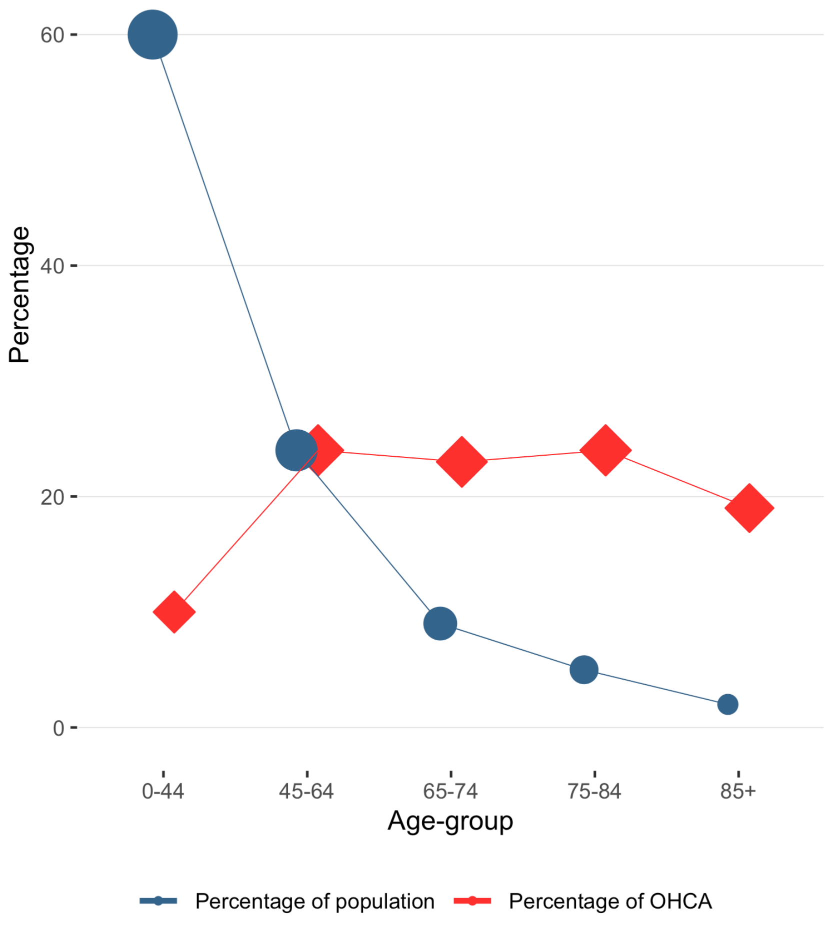


**Figure 7.** Proportion of the population and OHCA in each age group. Reprinted with permission from BMJ publishing group.

## 5.3 STUDY III: INDIVIDUAL-LEVEL SOCIOECONOMIC STATUS AND SURVIVAL AFTER OHCA

The third study included all patients in Sweden between 2010 and 2017 (n = 40 687). Patients under the age of 25 (n = 2050), EMS-witnessed cases (n = 6083), cases of missing outcome (n = 321) and missing SES information (n = 1396) were excluded from the study. The analytical sample consisted of 30 837 patients.

The first model, including age, sex, year of OHCA, retirement and civil status, showed a clear gradient with a higher chance of survival with increasing income. The OR for survival in the highest income quintile was 1.92 (95% CI = 1.68–2.20). When the CCI was added to model the results became slightly stronger. In the primary model (Model 3) the OR for 30-day survival was 1.89 (95% CI = 1.65–2.17) in the highest quintile vs. the lowest. In Model 4, where the resuscitation variables were added, the OR was 1.66 (95% CI = 1.43–1.92). In the last model (Model 5), where initial rhythm was added, the income–survival association was further attenuated and the OR for 30-day survival was 1.42 (95% CI = 1.21–1.66). For details see Figure 8.

| Income | OR | 95% CI | P-value |
|---|---|---|---|
| Model 1: adjusted for sex, age, year, retirement and civil status, | | | |
| Q1 | 1·00 | | |
| Q2 | 1·08 | (0·93-1·25) | 0·319 |
| Q3 | 1·25 | (1·08-1·44) | 0·002 |
| Q4 | 1·51 | (1·32-1·74) | 0·000 |
| Q5 | 1·92 | (1·68-2·20) | 0·000 |
| Model 2: model 1 + Charlson comorbidity index | | | |
| Q1 | 1·00 | | |
| Q2 | 1·09 | (0·94-1·26) | 0·279 |
| Q3 | 1·28 | (1·11-1·48) | 0·001 |
| Q4 | 1·56 | (1·36-1·79) | 0·000 |
| Q5 | 2·00 | (1·74-2·29) | 0·000 |
| **Model 3: model 2 + Education** | | | |
| Q1 | 1·00 | | |
| Q2 | 1·09 | (0·94-1·27) | 0·245 |
| Q3 | 1·26 | (1·09-1·46) | 0·002 |
| Q4 | 1·52 | (1·32-1·75) | 0·000 |
| Q5 | 1·89 | (1·65-2·17) | 0·000 |
| Model 4: model 3 + Resuscitation variables | | | |
| Q1 | 1·00 | | |
| Q2 | 1·04 | (0·89-1·22) | 0·641 |
| Q3 | 1·19 | (1·02-1·39) | 0·024 |
| Q4 | 1·45 | (1·25-1·68) | 0·000 |
| Q5 | 1·66 | (1·43-1·92) | 0·000 |
| Model 5: model 4 + Initial rhythm | | | |
| Q1 | 1·00 | | |
| Q2 | 0·96 | (0·81-1·13) | 0·602 |
| Q3 | 1·08 | (0·92-1·27) | 0·324 |
| Q4 | 1·26 | (1·07-1·47) | 0·004 |
| Q5 | 1·42 | (1·21-1·66) | 0·000 |

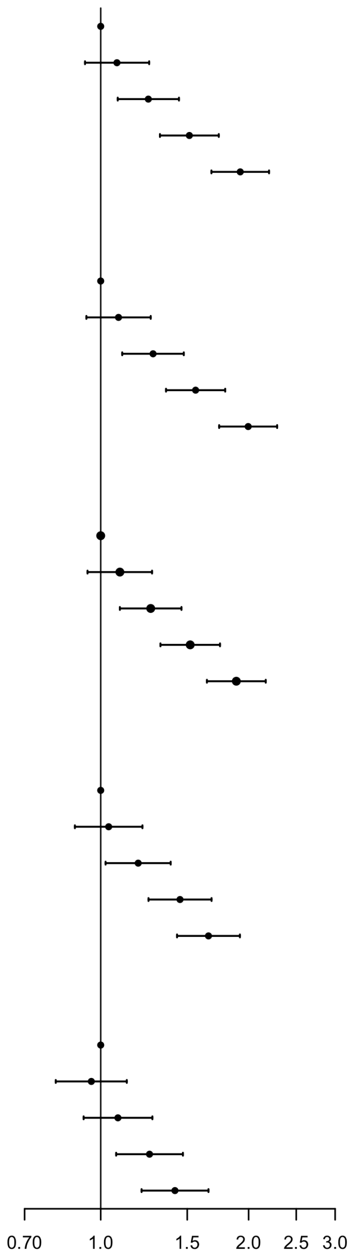


**Figure 8**. Forest plot of 30-day survival by income quintiles.

In Figure 9 the results for education are shown. In the primary model (Model 1) there was a significant association with any kind of post-secondary education. The highest OR was found among those with four or more years of post-secondary education (OR=1.62, 95% CI = 1.36–1.91). When the CCI score was added (Model 2) the results were similar to those in Model 1. When income was added to the model the results were slightly attenuated but still statistically significant. In Models 4 and 5, where resuscitation variables and initial rhythms were added, the association between educational level and 30-day survival was further attenuated and no longer significant in all groups.

| Education | OR | 95% CI | P-value |
|---|---|---|---|
| **Model 1: adjusted for sex, age, year, retirement and civil status,** | | | |
| Primary | 1·00 | | |
| Secondary | 1·03 | (0·94-1·13) | 0·523 |
| Post-secondary ≤2y | 1·43 | (1·24-1·65) | 0·000 |
| Post-secondary 3y | 1·42 | (1·19-1·69) | 0·000 |
| Post-secondary ≥4y | 1·61 | (1·36-1·91) | 0·000 |
| Model 2: model 1 + Charlson comorbidity index | | | |
| Primary | 1·00 | | |
| Secondary | 1·03 | (0·94-1·13) | 0·469 |
| Post-secondary ≤2y | 1·46 | (1·27-1·68) | 0·000 |
| Post-secondary 3y | 1·45 | (1·21-1·73) | 0·000 |
| Post-secondary ≥4y | 1·63 | (1·37-1·93) | 0·000 |
| Model 3: model 2 + Income | | | |
| Primary | 1·00 | | |
| Secondary | 0·99 | (0·90-1·08) | 0·804 |
| Post-secondary ≤2y | 1·33 | (1·16-1·54) | 0·000 |
| Post-secondary 3y | 1·30 | (1·09-1·55) | 0·004 |
| Post-secondary ≥4y | 1·41 | (1·18-1·67) | 0·000 |
| Model 4: model 3 + Resusitation variables | | | |
| Primary | 1·00 | | |
| Secondary | 0·98 | (0·89-1·08) | 0·732 |
| Post-secondary ≤2y | 1·28 | (1·10-1·49) | 0·002 |
| Post-secondary 3y | 1·20 | (0·99-1·45) | 0·068 |
| Post-secondary ≥4y | 1·25 | (1·04-1·51) | 0·018 |
| Model 5: model 4 + Initial rhythm | | | |
| Primary | 1·00 | | |
| Secondary | 0·97 | (0·88-1·08) | 0·576 |
| Post-secondary ≤2y | 1·26 | (1·07-1·49) | 0·005 |
| Post-secondary 3y | 1·17 | (0·96-1·44) | 0·125 |
| Post-secondary ≥4y | 1·21 | (0·99-1·48) | 0·066 |

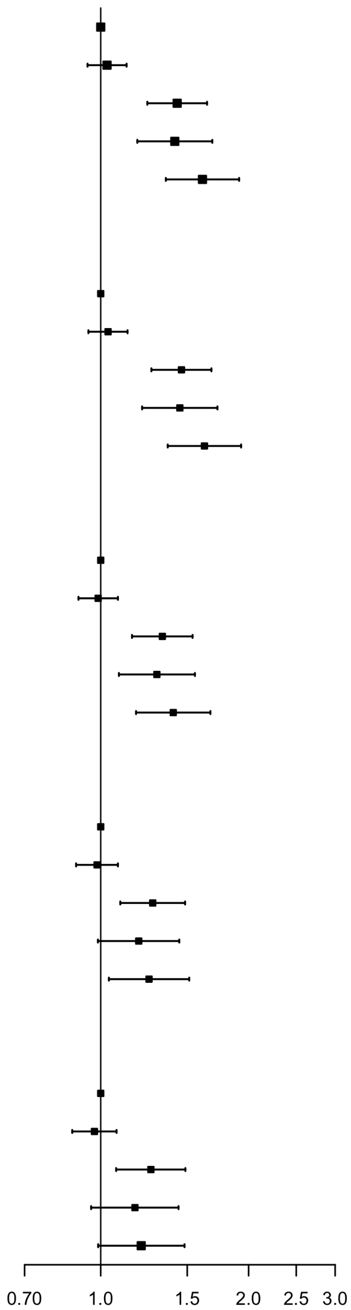


**Figure 9**. Forest plot of 30-day survival by educational categories.

For men (Figure 10A) the relationship between educational level and 30-day survival was non-linear. All post-secondary educational groups were associated with significantly higher adjusted ORs for survival compared with primary education only. Income followed a more stepwise increasing pattern, with the lowest adjusted OR among those in the first income quintile and the highest adjusted OR among those in the fifth income quintile (OR = 1.91, 95% CI = 1.35–1.97).

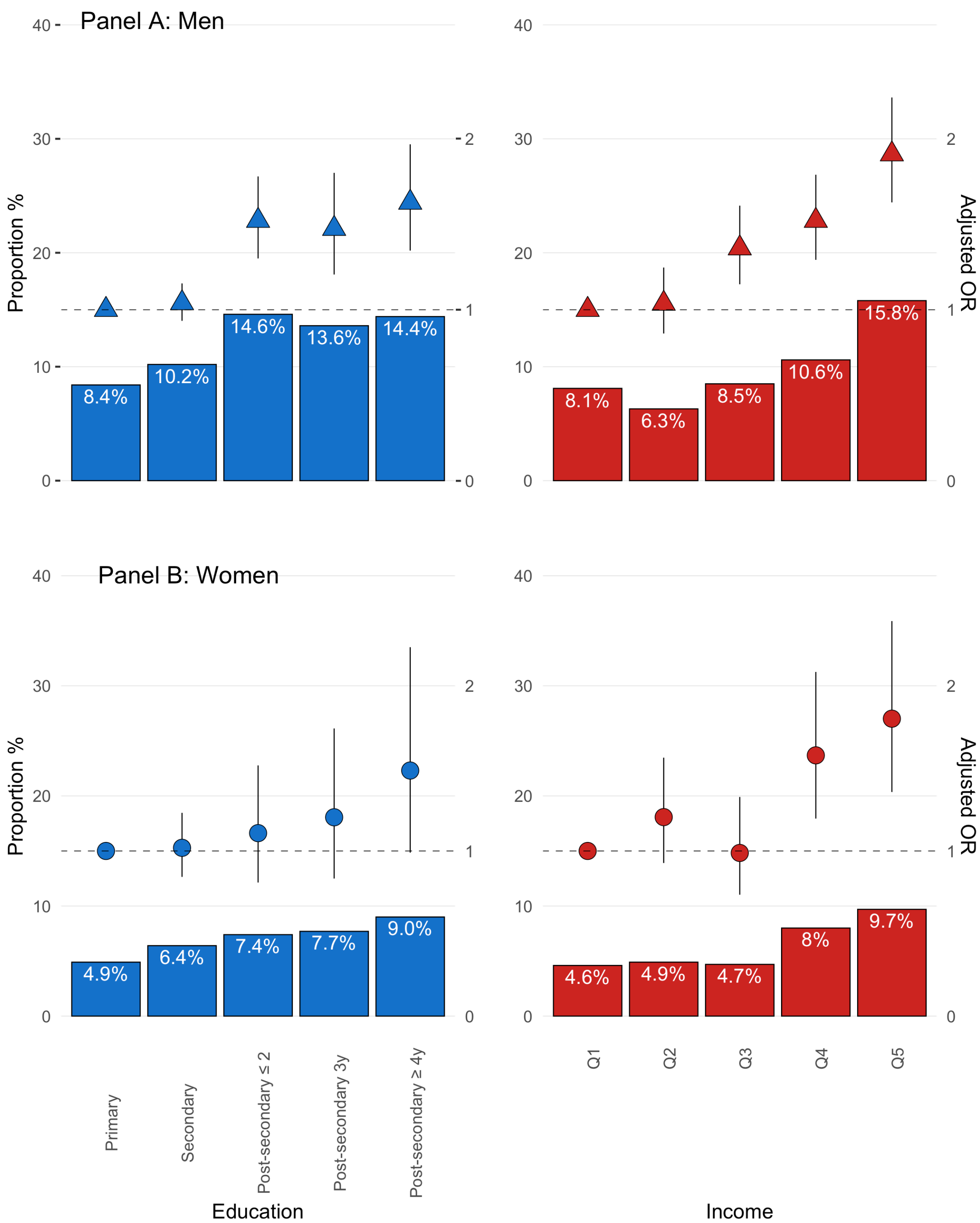


**Figure 10.** Crude proportion of 30-day survival and adjusted OR for men (panel A) and women (Panel B).

Among women (Figure 10B) the relationship between educational level and income followed a different, more curve-linear pattern, with a higher chance of survival in the higher educational groups. These differences, however, were not statistically significant. The highest adjusted OR was found among women with four or more years of post-secondary education (OR = 1.48, 95% CI = 0.99–2.23). The relationship between income and 30-day survival for women followed what appeared to be a linear trend (with the exception of the third income quintile, where no relationship could be seen). The adjusted OR for survival was 1.80 (95% CI = 1.36–2.39) in the highest income quintile.

In sensitivity analysis income was measured as a continuous variable with restricted cubic splines. The results showed an increasing probability of 30-day survival with increasing income in all models. In Model 5, where initial rhythm was added to the model, the results were strongly attenuated.

## 5.4 STUDY IV: LOW INCOME IS ASSOCIATED WITH A LOWER CHANCE OF SHOCKABLE INITIAL RHYTHM REGARDLESS OF EMS RESPONSE TIME, AND OTHER PATIENT CHARACTERISTICS

In the fourth and last study we used the same data as in Study III, with the addition that unwitnessed cases were excluded. The final analytical sample consisted of 18 099 witnessed OHCAs.

As seen in Figure 11A there was a higher proportion of cases of shockable initial rhythm in the third income tercile (blue) compared with both the second (grey) and first terciles (red). The crude proportion of cases with shockable initial rhythm in the third (highest) income tercile was 51.4% when the response time was less than five minutes, and 27.6% when the response time was more than 20 minutes. The corresponding proportions among the first (low income) tercile were 30.2% and 15.9%.

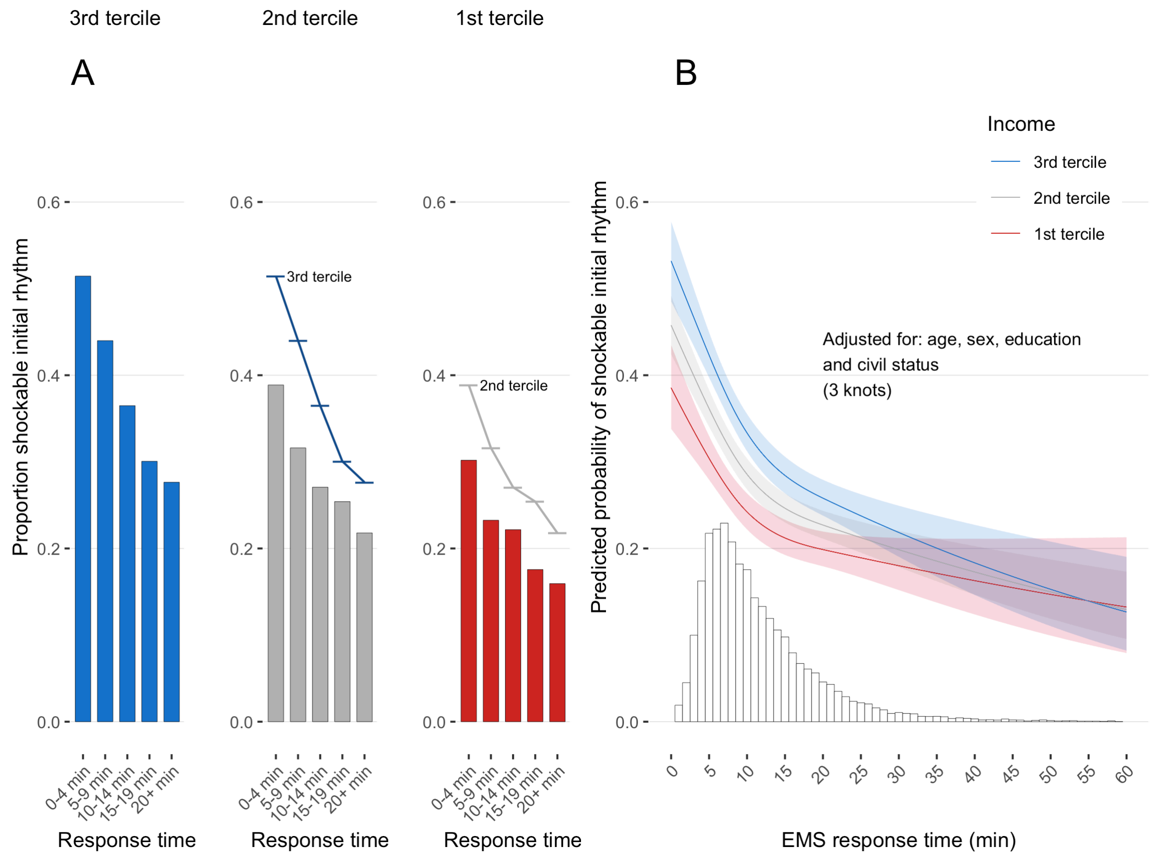


**Figure 11.** A. Crude proportions of shockable initial rhythm by income tercile. B. Probability of shockable initial rhythm by income terciles. Adjusted for age, sex, education and civil status.

In Figure 11B the association between EMS response time and the probability of having a shockable initial rhythm is shown. As can be seen, the probability is high (~40–50%) during the first few minutes. With longer EMS response times the probability of shockable initial rhythm decreases rapidly to around 15 minutes, where the decrease flattens out. The curves follow the same pattern for all income groups but the high income tercile starts with a higher probability.

Figure 12 shows the association between income (as a continuous variable) and the probability of shockable initial rhythm. When adjusted for age, sex, education and civil status (Model 1) there was an increase in probability up to the end of the first tercile. In the second tercile a steep increase in probability of shockable initial rhythm was seen and in the third tercile there was an initial increase that levelled out among those with an income greater than 400 000 SEK.

In Model 2, where EMS response time was added to the model, the curve follows a very similar pattern as for Model 1. In Model 3, where comorbidities and previous medications were added, the curve still has a similar pattern but is slightly attenuated. In the fourth model, where OHCA characteristics (bystander CPR, aetiology and location) were added, the curve is further attenuated but the relationship remains, with a higher probability of shockable initial rhythm among OHCA patients with high income.

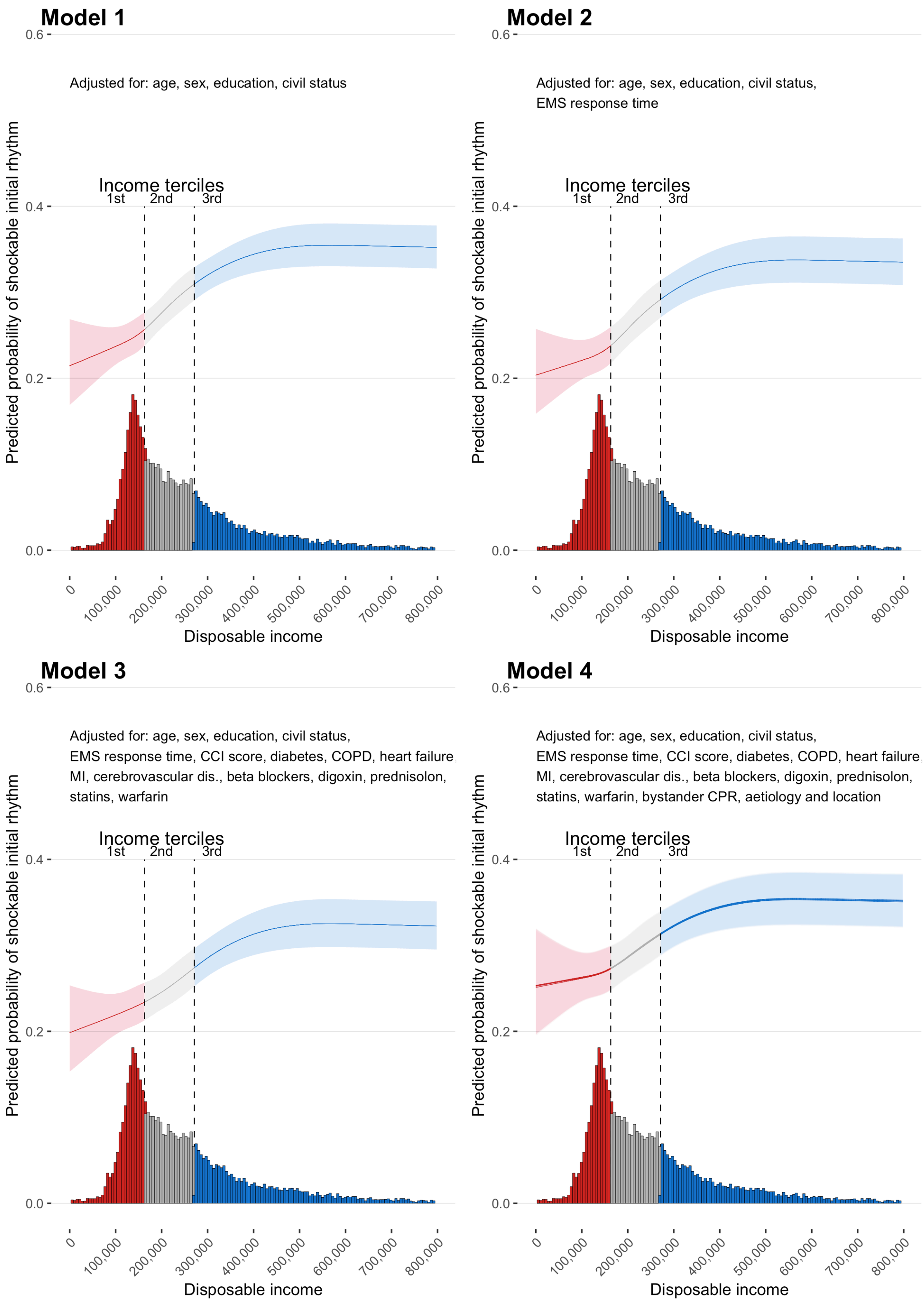


**Figure 12.** Income and the probability of initial shockable rhythm. Each curve represents of each of the 10 imputed datasets.

# 6 DISCUSSION

OHCA is one of the major causes of death in the western world with a rapid increase of incidence in older age groups.[6] The main purpose of this thesis was to investigate how socioeconomic status affects the incidence and the chance of survival following an OHCA. In addition, the role of income on the probability of shockable initial rhythm, one of the strongest predictors of survival, was studied.

This thesis, along with many other studies concerning socioeconomic factors, follows the tradition of focusing on health inequities. Whitehead and Dahlgren[1] have differentiated between inequities and inequalities by saying that the former are "*Systematic, socially produced* (and therefore modifiable) and *unfair"* (page 2). This is in contrast to other health inequalities such as more cardiovascular disease among the elderly compared with children.

As socioeconomic differences in OHCA incidence and survival can be deemed to be unfair, it is of importance to measure and understand why these differences have occurred. The goal of social inequity research should always be to minimise these differences.

## 6.1 PROBLEMS WITH REGISTER-BASED RESEARCH

The main problem with register-based observational research is that causality cannot be assumed. Factors that may disturb causal inference (i.e. confounders) can, however, be accounted for. The SRCR is a national quality register that has been around for almost 30 years and since 2010 all ambulance organizations in Sweden report to the register. When studying potential risk factors such as SES and comorbidity it is not possible to conduct experiments and therefore we are left with different forms of observational studies.

Among the problems associated with using registers perhaps the most serious is that the patients not included may differ from those who are. In relation to SES one could imagine that persons from lower SES groups may not be included to the same extent as persons from high SES groups, or vice versa. The results from Study II do not suggest that persons with low SES would be underreported in Swedish registers, as the incidence was higher in low SES areas.

The quality of the different variables in the SRCR varies. Some variables such as response time, whether or not bystander CPR was performed, and location, are of higher quality compared with educational level of the bystander, type of CPR, and aetiology of the OHCA. Most of the variables used as potential confounders in this thesis are of the more certain type, in order to keep misclassification bias to a minimum.

In addition to SRCR data, register data from Statistics Sweden and the NPR were used. The quality of data from Statistics Sweden is generally high[91] as it is for most diagnoses in the NPR.[92] The quality of the "add-on" data from these registers can therefore be assumed to be high. What the registers do not include is information on the quality of SES measures. The positive effect of education may depend on which school the person went to, and so on. The same could be said for comorbidity data. Two persons with the same diagnosis (e.g. diabetes) may be at different levels of severity of illness. These differences are hard to capture in registers.

## 6.2 ARE THE EXPOSURE VARIABLES RELIABLE MEASURES OF SES?

Two important exposure variables were used in this thesis: income and education. In Studies I and II area-level measurements were used. The numbers were calculated among the persons living in each area and the data were delivered by Statistics Sweden. The exposure variables in Studies I and II cannot directly be translated to individual level, as the measures are aggregated.

In Studies III and IV one could argue that a comorbidity index loses some of the specificity of multiple diagnosis codes. One of the arguments against summary scores in research is that even if the weights were correct when they were derived from the original population they are probably not correct in a new population. One solution to this is to reweight the codes, as suggested by Schneeweiss and Maclure[93] and Ghali et al.[94] The results of a more recent study, by Austin et al.,[95] however, suggest that if the data used to calculate the score is of high quality, then summary scores can be used as substitutes of individual variables, regardless of whether or not the original weightings were set a long time ago.

The socioeconomic measures used in Studies III and IV were the highest level of completed education, and disposable household income. Income, in these studies, may suffer from measurement error, as we only used income for the year prior to the cardiac arrest. It has been suggested that income may be a better predictor of health compared with other SES measurements,[96,97] although the relationship could suffer from reversed causation[45] (i.e. poor health leads to lower income, and not the other way around). It has also been argued that household measurements of income may not be as good for women, as to a larger extent they stay at home (at least in a American context).[98] However, using individual income may be even less accurate, as a homemaker in a wealthy home could have access to a significant amount of money. Education, on the other hand, does not suffer from reversed causality to the same extent as income and is generally stable after a person's young adulthood. The value of education as an SES measure, however, may differ between the sexes, as women generally tend to have lower economic returns on education compared with men.[98]

## 6.3 IS THERE A RELATIONSHIP BETWEEN AREA-LEVEL SES AND SURVIVAL AFTER OHCA?

The results from Study I suggest that area-level SES affects the probability of survival after OHCA. They suggest that both income and education predict survival on their own, but education seemed more robust when the two factors were mutually adjusted. Our results are in line with those of some other studies in which area-level measurements of SES have been used. While the results of the smallest studies have failed to reach significance due to limited sample size,[60,61] they are at odds among mid-size studies, where some have found significant associations[65,68] while others have not.[62,64,69] The largest studies have all revealed significant associations.[66,67] Studies that have involved the use of household measurements (i.e. tax-assessed home value) have revealed some kind of association, either positive[59,65] or negative.[99] It is possible that the type of SES measurement may affect the results in various ways.

The setting where the studies are conducted may play a role. While some studies in the US have revealed significant associations,[59,65] Canadian studies have shown either no relationship or a reversed relationship.[64,99] The area with the highest number of "positive" findings is Asia, where three out of four studies have revealed significant associations between SES variables and survival after OHCA.[66–69]

One neglected factor that may be of importance is the level of aggregation when measuring area-level SES. If the area is large in size, heterogeneity among the individuals living there is likely to be larger. This could in turn lead to less precise measurements and therefore a higher risk of confounding. Most investigators do not report the number of areas where they have measured SES variables and therefore it is hard to evaluate the quality of the measurement. In Study I we looked at the number of areas (squares) in the Stockholm region where there are more than 16 000 areas, which can be compared to the work of Ahn[66] and Lee[67], who used districts in South Korea (n = 250), which is likely to have resulted in a less precise measurement of SES.

## 6.4 DO AREAS WITH LOW SES SHOW A HIGHER INCIDENCE OF OHCA?

The results of Study II would suggest that areas characterised by low SES have a higher incidence of OHCA compared with areas with high SES. This, with very few exceptions, is in line with previously published literature. Regardless of whether the authors have aimed to measure the incidence in low-SES areas,[66,73,74] or to investigate what constitutes an area with a high incidence of OHCA,[76,77] the results show that low SES seems to be related to a higher incidence OHCA. In two studies from North America Reinier et al.[73,74] found a stronger relationship between SES and incidence of OHCA among persons under the age of 65.

In Study II the same pattern was seen as in a study by Reinier et al. The relationship was strong among patients under the age of 74 but had almost disappeared completely in the older age-groups. One explanation for this offered by Reinier et al.[74] is that persons over the age of 65 are eligible for Medicare in the US. This is an unlikely explanation, as Sweden has a universal healthcare system. Another explanation for this may be the “age-as-leveller” hypothesis,[100] which suggests that biological factors are of increasing importance the older we get. Factors such as SES are of minor importance among the elderly. A related explanation is survivorship bias, i.e. the sickest low-SES persons may have already died, leaving the healthiest individuals alive, while the sickest high-SES persons are still alive.

## 6.5 IS THERE A RELATIONSHIP BETWEEN INDIVIDUAL-LEVEL SES AND SURVIVAL AFTER OHCA?

In the third study we aimed to investigate the role of individual-level SES and survival after OHCA. There are a very limited number of studies that have involved the use of individual-level SES measurements in OHCA research. Wells et al. studied patients with VF as initial rhythm in King County, US, and found clear relationships between the level of education and admission to hospital, being discharged alive and discharged to home, while no clear relationship was seen as regards occupational status.

These results are somewhat different from the results in Study III, where income seemed to be a stronger predictor than education, at least when all patients were included. The differences in survival in relation to socioeconomic variables were seen among both men and women.

A national study from Denmark that included children and adolescents up to the age of 21 did not show any significant differences in survival by different SES measures after covariate adjustment.[70] This was, however, probably due to the limited sample size. It is hard to compare the results with those we found in Study III, as all patients under the age of 25 were excluded. Individual-level measures may be misleading in some cases where persons have not finished university and incomes are relatively low. Another Danish study found a relationship between household income and 30-day survival among patients admitted to hospital.

The results from Study III suggest that there is a relationship between both income and education in relation to survival after OHCA. Compared with previously published investigations, Study III involved a large national sample of OHCA cases, including all rhythms and age-groups.

## 6.6 SHOULD RESULTS BE ADJUSTED FOR INITIAL RHYTHM?

The results from both Studies III and IV suggested that initial rhythm may play an important role in explaining SES differences in relation to survival after OHCA. Study III, in particular, showed that addition of initial rhythm into the model weakened the association between income and survival. This kind of adjustment is likely to be “over-adjustment” if the aim is to study overall SES differences in relation to survival after OHCA. As it is impossible for the measured initial rhythm to affect a person’s income, it should not be considered to be a confounder in the classical sense.

A more likely scenario is that income affects both a person’s chance of surviving an OHCA, and the chance of having a shockable initial rhythm. Therefore, initial rhythm could be on the casual path from income to survival and should be considered to be a mediator. The results from Study IV suggest that persons with a lower income have a lower proportion of shockable initial rhythms, regardless of age, sex and EMS-response time. This in turn would also suggest that initial rhythm may be on the causal path between SES and survival after OHCA.

## 6.7 IS INCOME MORE IMPORTANT THAN EDUCATION?

The results from Studies I and III give conflicting answers to the question of which factor is of most importance as regards survival after an OHCA. In Study I education (measured at area-level) was a more robust predictor compared with income. In Study III the opposite was true. Study III revealed that income had a more robust relationship with survival compared with education. However, there may be different mechanisms that explain area-level and individual-level associations. The positive effect of area-level education may be due to more community engagement, which may not be captured using individual-level data. One should, however, be careful in dismissing the effect of education. When not adjusted for income, any form of post-secondary education was associated with a higher chance of survival. Education can be seen as a way to achieve a higher income, and therefore the mutually adjusted analysis could be regarded as over-adjustment.

On a theoretical basis education has been linked to what Mirovsky and Ross[50] called "learned effectiveness". This can be taken to mean that a person with higher education can perceive that they have control in changing health-negative types of behaviour (such as smoking and excess alcohol consumption), and they can also pick up good health habits such as exercise and healthy diets. Educated people may also be more efficient agents when they need healthcare resources, and therefore receive better care compared with people without higher education.

Income, on the other hand, is more related to material resources.[46] The gradient between income and health tends to follow a stepwise pattern, with better health in each higher income group. The lack of income is not only a problem among the poorest. A higher income can provide various health-protecting factors such as availability of healthy food and better access to general practitioners/healthcare. A higher income provides the opportunity to live in an area without a number of environmental stressors such as crime and noise/air pollution.

Another way material resources can have adverse effects on health is described in Wilkinson's theory of relative deprivation.[101] The theory suggests that a person with a low income (relative to his or her peers) can experience feelings of inferiority. This results in a stressful situation which may lead to chronic stress (so-called allostatic load). Both epidemiological[101,102] data and data on primates[48] give some support to this theory.

## 6.8 WHY DO PATIENTS WITH LOW INCOME HAVE A LOWER RATE OF SHOCKABLE INITIAL RHYTHM?

One can only speculate about the reasons why persons with low income have lower rates of ventricular fibrillation. One biological explanation may be a relationship between SES and increased oxidative stress, and the "energy-starved heart". If this hypothesis is true, the relationship between low SES and rates of shockable rhythm could be explained by the fact that low SES is associated with higher levels of oxidative stress.[103,104] Oxidative stress, via damage to mitochondrial DNA, can result in impaired mitochondrial function.[105,106] Impaired mitochondria produce lower amounts of adenosine triphosphate (ATP), which is the main source of energy for myocardial muscle-cell contraction. Previous data from autopsies have shown that ATP levels are 25–30% lower among heart-failure patients.[107] This ATP deficiency could explain the lower rates of shockable initial rhythm. Previous studies on dogs have shown a depletion of ATP with a longer duration of ventricular fibrillation, which is expected, as it is an energy-expensive state.[108] If low-SES individuals have a lower ATP supply at the onset of the cardiac arrest, a lower rate of shockable initial rhythm is to be expected.

Another somewhat related mechanism could be what is called biological ageing. A lower income could lead to a state of chronic stress that affects cell ageing.[109] Cell ageing can be measured using telomeres, which are DNA proteins at the ends of chromosomes.[110] A shorter telomere length suggests a more advanced ageing process. Previous studies have shown a relationship between socioeconomic factors and shorter telomere length,[111,112] as well as for telomere length and cardiovascular health.[110] This could be taken to mean that people from lower SES groups have an accelerated ageing process. Persons from a low-SES group would therefore have a lower incidence of shockable rhythm as a result of the same mechanism that results in a lower proportion of VF/VT among older persons.

Another possible explanation for the lower incidence of shockable initial rhythm could be higher rates of smoking among low-SES individuals. Smoking behaviour is socially patterned, with higher rates among persons in a low socioeconomic position.[113] Although there are a limited number of studies on how cigarette smoke is associated with shockable rhythm, a study on dogs from 1972 suggested that tobacco smoke resulted in a lower ventricular-fibrillation threshold.[114]

Another possibility that should not be excluded is that the association could be a result of residual confounding. This could involve timestamps that are not measured (at least not in a satisfactory way) or recorded in the registers, such as time from collapse to call, or time from call to initiation of CPR. Also, registers cannot provide quantitative information on the quality of CPR, which is likely to affect the chance of having both a shockable rhythm and survival.

## 6.9 CAN SES DIFFERENCES BE REMOVED?

The differences in both incidence of and survival after OHCA between different SES groups seen in this thesis suggest that interventions should be carried out to reduce these inequalities. In epidemiology it is common to refer to intervention as either upstream or downstream. The idea is that upstream intervention has a more preventive approach, while downstream interventions treat something that has already happened. To exemplify this one could regard a smoking ban as an upstream intervention, while smoking cessation represents a downstream intervention.[115] It is generally regarded as more efficient to prevent disease (ban smoking) than to treat those already sick (smoking cessation).

To create interventions that reduce socioeconomic disparities in connection with any health condition is no easy task. One upstream intervention to reduce differences in both the incidence of, and survival after an OHCA, would be to reduce social and economic disparities overall in society. Such changes are possible to implement, but strong political support is needed. Current trends in the US[116] and the majority of OECD countries[117] suggest that the opposite is happening, with increasing income inequalities. Previous research has shown that even though individual health behaviour plays a role in the SES–health relationship it accounts for only a minor part of the overall relationship.[118,119] If serious attempts are to be made to reduce what may be the root cause, major policy changes will be needed. The results of the studies included in this thesis suggest that there are relatively large differences in a setting with universal healthcare coverage. A study from Oregon, US, showed that the incidence of OHCA was reduced after extension of health insurance among people between the ages of 45–64.[120]

Further downstream solutions may be more realistic, or at least less expensive to implement. One such solution may be to aim CPR training programmes to areas of lower socioeconomic status. Data from the US have shown that both the proportion of persons educated in CPR[121] and AED usage[122] differed along with socioeconomic factors. Another factor that could help reduce the survival differences in OHCA could be to distribute AEDs in socioeconomically weaker areas. Previous research from South Korea has shown that more affluent areas have a higher density of available AEDs.[123] Studies from Denmark have shown that AED availability is crucial for successful AED usage.[124] One problem is that AEDs seldom are located where cardiac arrests commonly occur (at home). Fredman et al. have reported results from Stockholm suggesting a mismatch between OHCA occurrence and location of AEDs.[125]

New technologies such as the use of mobile phones to dispatch laypersons to suspected OHCAs,[25,41] together with distribution of AEDs with 24/7 availability, could help reduce socioeconomic differences in survival after OHCA. For this to be realized there is a need to involve people from lower-SES groups as volunteers in such services.

Another way to "treat" SES differences in cardiovascular health was offered by Tawakol et al.[126] They suggested treating the effects of stress by using drugs that reduce arterial inflammation or inhibit the release of pro-inflammatory cells. Even if this would theoretically work, such a solution would be both expensive and impractical.

## 6.10 FUTURE RESEARCH

The relationship between socioeconomic factors and OHCA, and health in general, is most probably not direct. Instead, there are likely to be multiple intermediate factors on the causal pathway. In other words, the 1s and 0s in your bank account do not affect your health; instead, economic security may decrease your stress levels and in the end result in better health.

A potential intervention to reduce SES differences in survival may be to distribute AEDs and educate the people in low SES areas in AED usage and bystander CPR. The results from study IV does however raise some problems regarding AEDs. If low SES individuals have a lower chance of shockable initial rhythm at the time of collapse, the increase of AEDs may not be of much use. Therefor the aim of further research should exclude potential residual confounding – such as the time intervals between collapse and call/CPR initiation, the time interval between EMS arrival at the scene and start of treatment and other unmeasured factors such as the quality of CPR provided. These questions need answers before a cost-effective intervention can be implemented.

There are a number of questions that are not answered in this thesis. One of them is if survival follows the same “age-as-leveller” pattern as for incidence. If so, further information is needed regarding both primary and secondary prevention. The interaction between SES status and comorbidity has not been studied in the field of OHCA research. The effect of previous comorbidities may be different in different SES groups.

On a much smaller level, future studies should also be carried out to investigate the roles of cell factors such as telomere length and ATP production in OHCA. This may lead to different preventive strategies and also fill some blanks in the SES–OHCA relationship.

# 7 CONCLUSIONS

To summarise the results presented in this thesis, I have found that socioeconomic factors influence both the incidence of and 30-day survival after OHCA.

*Study I*

Area-level education is associated with 30-day survival after an OHCA. Area-level income does not independently influence 30-day survival.

*Study II*

Areas characterised by high SES have a lower incidence of OHCA compared with areas characterised by low SES. This relationship is highly dependent on age and disappears after the age of 75.

*Study III*

Individual-level SES is associated with 30-day survival after OHCA. Higher income, among men and women, and education among men were associated with improved 30-day survival after OHCA.

*Study IV*

Low income is associated with a lower probability of shockable initial rhythm. This relationship is not explained by potential confounders, and previous comorbidities/medications. Initial rhythm may work as a mediator in the relationship between SES and survival after OHCA.

# 8 SAMMANFATTNING PÅ SVENSKA

**Bakgrund**

Varje år drabbas ca 6000 personer av plötsligt hjärtstopp utanför sjukhus. Av dessa överlever endast ca 10 %. Historiskt sett har fokus inom hjärtstoppsforskningen varit på behandlingar som kan öka överlevnaden vid plötsligt hjärtstopp. Exempel på sådana behandlingar är hjärtlungräddning (HLR) och tidig defibrillering och helautomatiska hjärtstartare. Hur bakomliggande faktorer såsom socioekonomisk status påverkar incidens av, och överlevnad efter plötsligt hjärtstopp är studerat in mindre utsträckning.

**Metoder**

Grunden till denna avhandling är det Svenska Registret för hjärt-lungräddning (HLR-registret). I **studie I** och **studie II** inkluderades ambulansbehandlade hjärtstopp i Region Stockholm mellan åren 2006 till 2015 (studie I) och åren 2006 till 2017 (studie II). I de två första studierna geokodades hjärtstoppen för att kopplas ihop med områdesdata från Statistiska Centralbyrån (SCB). I **studie III** och **studie IV** används data from HLR-registret mellan åren 2010 och 2017. Hjärtstoppsdata kopplades ihop med socioekonomiska data, såsom disponibel hushållsinkomst och utbildningsnivå från SCB. Utöver detta kopplades data även ihop med data rörande tidigare sjukdomar (komorbiditet) från nationella patientregistret samt läkemedelsdata från läkemedelsregistret.

**Specifika syften och resultat**

Syftet med **studie I** var att undersöka ifall om socioekonomiska faktorer i bostadsområdet påverkar chansen att överleva ett plötsligt hjärtstopp. Studien inkluderade 7431 hjärtstopp i region Stockholm. Resultaten visade att personer boende i områden med högre andel universitetsutbildade hade en högre 30-dagarsöverlevnad jämfört med personer boendes i områden med lägre andel universitetsutbildade. Det justerade oddskvoten var 1.70 (95% CI=1.15 to 2.51). Efter justering av för utbildningsnivå kunde inget signifikant samband ses för områdets inkomstnivå.

Syftet med **studie II** var att studera ett områdes socioekonomiska status (SES) är associerat med incidensen av plötsligt hjärtstopp utanför sjukhus. Utöver detta studeras om sambandet är beroende på ålder. Studien inkluderade 10 574 hjärtstopp i region Stockholm. Hjärtstoppen fördelade sig på 1349 områden vilket var den primära analysenheten. Områden med hög SES hade en lägre incidens (IRR= 0.63, 95% CI=0.56-0.71) jämfört med områden som karaktäriserades av låg SES. Detta samband var beroende på ålder, bland befolkningen i åldern 0–44 år, motsvarade IRR var 0.56 (95% CI=0.45-0.70), motsvarande för 45–64 var IRR 0.53 (95% CI=0.45-0.62) och 0.59 (95% CI=0.49-0.70) för personer i åldersgruppen 65–74. Bland personer över 75 år (75–84 och 85+) sågs inte längre något samband mellan SES och incidens av hjärtstopp.

I **studie III** var syftet att studera om sambandet mellan socioekonomiska faktorer (disponibel inkomst och utbildning) på individuell nivå påverkar chansen till 30-dagars överlevnad. Studien inkluderade 31 489 hjärtstopp. I den primära modellen för inkomst sågs en ökande chans för överlevnad med ökad inkomst. Det högsta estimatet fans i den högsta inkomstkvintilen (OR=1.89, 95% CI=1.64-2.17). I den primära modellen för utbildning sågs ett signifikant samband mellan alla typer av eftergymnasial utbildning och 30-dagars överlevnad. Det högsta estimatet fanns bland de med fyra eller fler år av eftergymnasial utbildning (OR 1.62, 95% CI=1.36-1.92).

I **studie IV** studerades sambandet mellan disponibel inkomst och frekvensen av defibrillerbar första rytm. 18 099 hjärtstopp inkluderades i studien. Resultaten visade att den lägsta inkomst-tertilen hade 30.2% defibrillerbar rytm jämfört med 51.4% bland den högsta inkomst-tertilen då ambulansens framkörningstid var mindre än 5 minuter. Motsvarande siffror för långa framkörningstider (mer än 20 min) var 15.9% och 27.6%. I de logistiska regressionsanalyserna sågs ett s-format samband med en svag ökning i den lägsta inkomst-tertilen, en kraftig ökning i den mittersta samt en ökning som avtar i den högsta inkomst-tertilen.

**Slutsats**

Artiklarna i denna avhandling bekräftar att det finns en samband mellan socioekonomisk status, incidens av, och överlevnad efter plötsligt hjärtstopp utanför sjukhus. **Studie I** visade att personer boendes i områden med en hög andel högskoleutbildade har en högre sannolikhet att överleva i 30-dagar efter ett plötsligt hjärtstopp. **Studie II** fann att ett områdes socioekonomiska karaktäristik är associerat med incidens av hjärtstopp. Detta samband är dock beroende av ålder då inget signifikant samband fanns bland personer över 75 år. Resultaten från **studie III** visade att både individuell inkomst och utbildning är associerat med chansen till 30-dagars överlevnad efter plötsligt hjärtstopp utanför sjukhus. **Studie IV** fann att inkomst är associerat med defibrillerbar första rytm. Initial rytm kan vara en intermediär faktor i sambandet mellan socioekonomisk status och överlevnad efter hjärtstopp.

# 9 ACKNOWLEDGEMENTS

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