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The value of mechanical cardiopulmonary resuscitation using LUCAS

A COST-EFFECTIVENESS ANALYSIS ON MECHANICAL CHEST COMPRESSIONS VS. MANUAL CHEST COMPRESSIONS IN OUT-OF-HOSPITAL CARDIAC ARRESTS IN SWEDEN

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Abstract

Introduction Economic evaluations are used in health care to help decision-makers allocate their resources. The objective of this study is to evaluate the cost-effectiveness of mechanical chest compressions compared to manual chest compressions. This is done in a Swedish setting and for out-of-hospital cardiac arrests (OHCA) using results from a large randomized controlled trial, the LINC study[1].

Methods Mechanical CPR has been seen to improve neurological outcomes determined by the Cerebral Performance Category, and these results are used in a cost estimation to evaluate the effectiveness of treatment. This study argues costs and effects as far as possible to give meaning to this measurement despite its limitations. The analysis is made with a Swedish decision-makers purchasers' perspective, as the societal perspective is considered in the discussion. A representative example was used to find the results and describes a case where 154 out-of-hospital cardiac arrest patients are annual possible treatments for 12 mechanical devices. Costs are calculated for the number of mechanical devices needed to deal with these patients along with treatment costs and additional hospital stay costs for mechanical treated patients. Effects of treatment are taken from the LINC study and a study by Phelps, Dumas, Maynard, Silver, & Rea (2013) and were translated into quality-adjusted life years (QALY). This is done with a focus group (clinical active medical doctors and nurses) that together answer a standardized instrument, EQ-5D, and in this way the paper obtain QALY-weights for each CPC-score.

Results The cost-effectiveness of mechanical CPR is presented from a short-term perspective (patients' gains in QALY during the first 6 months) as well as a longer-term perspective (patients' gain in QALY over 8 years). As time prolongs the incremental cost-effectiveness ratio results show that costs per QALY gained range from "high" 508,291 SEK (6 months) to "low" 50,508 SEK (8 years). Mechanical CPR shows to save 0.046 QALYs per OHCA patient over an 8-year period. The sensitivity analyses indicate that results do vary a lot with yearly number of treatments expected per device and the applied timeframe for effect calculation.

Conclusion The paper believes to have given a transparent overview of a representative example facing decision-makers in this area. Giving them with the possibility to look at the value of mechanical CPR in a longer timeframe and not just in the short run with survival as only outcome. It concludes that if decision-makers are willing to live with the uncertainties discussed and argued in this paper, then mechanical devices are available at low costs per QALY gained for the patients treated. This is when each device is expected to deal with 12.83 yearly out-of-hospital cardiac arrests cases.

Key words: Cardiopulmonary Resuscitation, Cerebral Performance Category, Cost-effectiveness, EQ-5D, Delphi Method, And Out-of-hospital Cardiac Arrest

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Charlie Lundgren

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[a] Physio Control is a US based company, with an office headquarters in Lund. The company's current operations include manufacturing and distributing of emergency defibrillation and automated CPR equipment.

Abbreviations

CEA	Cost-Effectiveness Analysis
CPC	Cerebral Performance Category
CPR	Cardiopulmonary Resuscitation
ICER	Incremental Cost-Effectiveness Ratio
ICU	Intensive Care Unit
LINC	LUCAS in Cardiac Arrest
OHCA	Out-of-Hospital Cardiac Arrests
ROSC	Restoration of Spontaneous Circulation
QALY	Quality-Adjusted Life Year

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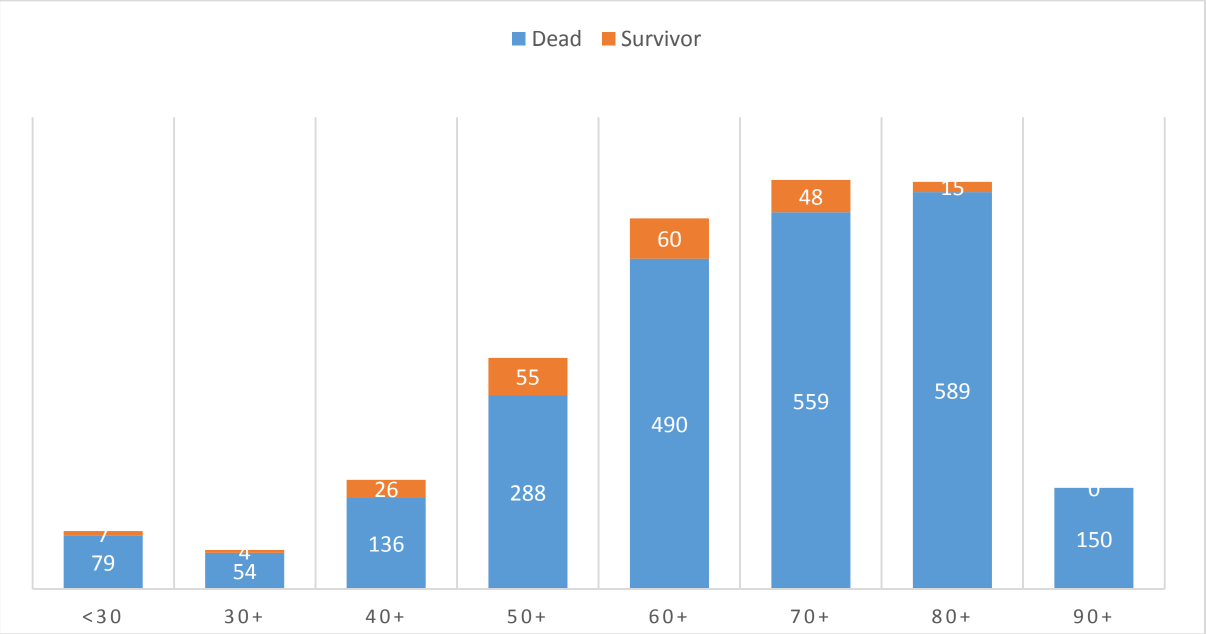
1. Introduction

1.1 Background

Economics is the science of scarcity. Health economics displays a desire to maximize the value of the budget by ensuring not just clinical effectiveness, but also the cost-effectiveness of health care provision. Since 1997, cost-effectiveness has become a key criterion in Sweden when deciding which new health care intervention that should be publicly funded. The Swedish healthcare law states that there must be a reasonable relation between costs and effects, in terms of improved health and increased quality of life[2]. Unless the cost-effectiveness also was highlighted the risk would be that very urgent illnesses were treated to such high costs that resources remaining to treat others in need were not there in time. Decision-makers and purchasers within the ambulance organization within the Swedish health care system is mainly government-funded and has the society in its perspective.

A common cause of death in the western world is cardiovascular diseases. Despite a decreasing trend over the past decades, cardiovascular diseases were still responsible for 45 percent of all deaths in Sweden in year 2012. These 34,949 persons died from cardiovascular diseases of which about 10,000 were classified as cardiac arrests. Of 5,000 cases of Out-of-Hospital Cardiac Arrests (OHCA) each year in Sweden, to date only 10 percent can be expected to survive. Figure 1 shows the number of patients with survival 6 months after cardiac arrest, by age group with data from the LUCAS In Cardiac Arrest (LINC)-study[3]. Those expected to be able to survive to 6 months after the arrest are in the age groups below 80 years old.

FIGURE 1 TREATED PERSONS IN THE LINC-STUDY, SURVIVAL AT 6 MONTHS DIVIDED PER AGE GROUP



Early and effective treatment is of vital importance to increase chances of survival[4]. Several factors are important to increase survival rates after OHCA such as; recognition of state, effective Cardiopulmonary Resuscitation (CPR), defibrillation, post-resuscitation care to achieving Return of Spontaneous Circulation (ROSC)[5]. CPR is physically demanding and variations in provision of good quality CPR according to guideline standards have been observed[6]. The effectiveness of manual CPR is largely dependent on the skill and endurance of the rescuer[7]. Success might depend on the ability to compress deep enough and not having a too long hands-off interval during the resuscitation attempt[8]. Two mechanical chest compressors, called AutoPulse and LUCAS, have been shown to improve ROSC in small studies[9] and have been developed to improve the quality of CPR.

A large randomized controlled trial, the LINC-study[10], had the objective to determine whether administering mechanical CPR combined with defibrillation compared with manual CPR, would improve survival. Results showed no change in 4-hour survival in OHCA patients between the two treatments. The LINC-study also involved an outcome of the well-known neurological outcome measure called Cerebral Performance Category (CPC) Score. This paper aims to use the results from the LINC-study as a foundation for the implementation of a cost-effectiveness analysis on mechanical CPR vs. manual CPR.

Up to this date this study is the first to exploit this reasoning. Nonetheless two ongoing studies have been identified to investigate mortality combined with QALY-calculation in England and Finland[11]. Being able to find a better way to deal with OHCA and identify cost-effective technologies for OHCA are vital for optimizing the use of healthcare spending in Sweden and elsewhere.

1.2 Purpose of the study

The purpose of this study is to evaluate the long-term incremental cost-effectiveness of mechanical CPR and simultaneous defibrillation vs. conventional manual CPR for patients with OHCA, in Sweden. This study wants to perform a cost-effectiveness analysis by evaluating CPC as an outcome measurement in a cost estimation. To demonstrate this, the study needs to calculate the value of treatment by mapping CPC-scores to corresponding EQ-5D dimensions and use these QALY-weights to describe the outcome of mechanical CPR and manual CPR during the 6 months follow up in the LINC-study. To obtain a longer perspective this paper models the expected long-term survival based on CPC -scores from the LINC-study data and other published sources.

Together these aims will provide estimates of a long-term value of alternative methods for providing good quality CPR in Sweden. They will also give insight of CPC as a measurement effect within a cost estimation.

1.3 Methods

In order to achieve the aim of this paper, a cost-effectiveness analysis was performed on results from the LINC-study. These results appeared from a trial where a mechanical device (LUCAS), with simultaneous defibrillation was being compared to conventional manual CPR, both in an OHCA environment. To get an understanding of what happens after 6 months literature searches was made using PubMed database. The only study to truly deal with long-term prognosis for different CPC-scores following OHCA was one by Phelps et al. (2013). In an American setting this paper gave additional insight for this papers' calculations. This paper extracts the survival rates from Phelps study by up to 8 years, which is the same as the economic lifetime of a LUCAS device.

This paper will use a representative example based on Skånes Universitets Sjukhus, Malmö and perform a cost-effectiveness analysis more thoroughly described in chapter 4. The costs will be based on a mechanical device called LUCAS. The effects in quality-adjusted life years (QALY) were chosen to not only consider lives saved, but also the quality of life in those years.

The decision-makers in Sweden have stated that a societal view should be applied when dealing with direct and indirect costs[12]. This however was found to be too problematic for the CPC-scale and therefore only the direct costs are included in the cost estimation and the indirect costs are discussed in chapter 6. To deal with the effects this paper estimated different QALYs for patients with different CPC-scores using the Delphi Method with a focus group of the people who assessed CPC-scores in the patients included in the LINC-study.

1.4 Outline/Disposition

From here on chapter 2 will present the subject of health economics evaluation and why it is needed and used within Swedish health care. Chapter 3 will introduce the reader to the phenomenon of sudden cardiac arrest and how its outcomes are measured. It will also introduce the possible effect difference between mechanical CPR and manual CPR. As it will expand the concept of Cerebral Performance Category-score as a measurement used to evaluate patient outcome after a cardiac arrest. This outcome will be the foundation for this papers' cost estimation. In chapter 4, the paper will explain the method and material used in this study, how the costs and effects were measured and evaluated. The results of the way of method will be presented in chapter 5 along with sensitivity analysis as results cannot be compared to previous research. These results are then discussed in chapter 6 along with covering other areas of interest in the field of the value of CPR.

2. Health economic evaluations

The purpose of this chapter is to provide the reader with knowledge of why and how a cost-effectiveness analysis (CEA) is constructed. It will also give insight into the common forms of economic evaluations and propose a way to calculate quality-adjusted life years (QALY).

2.1 Analysis Frame

Healthcare is produced through allocation with scarce resources, which requires priority setting. With the constant discussions on lack of resources within the healthcare sector, health economic evaluation has lately gained a growing influence in prioritizing decisions. But on whose conflicting objectives should we base the analysis?

There are three different perspectives when making an economic evaluation. Consistent with economic theory there is the welfarist perspective, which gives the same results as a free market would. If instead trying to optimize the resources of the health care sector budget one could use the extrawelfarist perspective by comparing costs with health gained. At last a broader societal perspective includes a wider range of consequences in costs and health effects and it is called the decision-makers perspective. The analysis in this paper has a Swedish outlook and will try to apply the perspective of the decision-maker, aiming to optimize the effects, compared to costs, for society as a whole[13].

Swedish citizen get health care based on their need and not their ability to pay. Based on economic theory one could argue that a public intervention is motivated when viewing health as a public good. However health care is a private good with externalities affecting the others in the society. An illustrative example of the positive externalities within health care, are those gains made from a vaccination program. When one citizen gets a vaccine-treatment this will lower the risk of disease for all other citizens. This example gives support to a public intervention, but does not answer the question of how much of the resources that should be put in use. New medical interventions emerge by the day. The population in Sweden is ageing, leading to a smaller health care budget. As stated above a health economic evaluation is of worth. Economic evaluation is defined by Drummond et al. (2005) as "the comparative analysis of alternative courses of action in terms of both their costs and consequences". Applicable to all economic evaluation its aim is to identify, measure and compare different interventions. Within health economics it is the costs and effects of different alternatives for prevention, diagnosis, treatment and rehabilitation of diseases that are subject to evaluation[14]. Decision-makers are not only concerned about the costs, but understandably also the result.

In order to create an understanding of the different approaches to health economic problem solving, different methods of analysis will now be discussed.

2.2 Methods of analysis for health economic evaluations

Health economic evaluations consist of four different analysis methods: a cost-minimizing analysis, cost-effectiveness analysis (CEA), cost-utility analysis and cost-benefit analysis. It should be noted that some authors do not distinguish between CEA and cost-utility analysis. Instead they are writing and treating cost-utility analysis as a special case of CEA[15]. Further on in this discussion the reader should remember that despite their names all forms of analysis has the same purpose, to determine cost-effectiveness of an intervention. All four are based on identifying and evaluating the costs. But they differ some when it comes to the measuring and assessment of the effects[16].

2.2.1 Costs and costs identification

Costs can be of different types and should in health economics be valued as the opportunity cost. Meaning the value of the effects that should have occurred if the best available alternative would have been used. The total costs of a treatment will differ depending on the perspective used, for example: patient, hospital, government or society[17]. As stated above this paper will target the decision-makers in Sweden, The Dental and Pharmaceutical Benefits Agency[18]. Meaning the aim is to use a societal perspective dealing with all related costs, both direct and indirect[19].

Related costs are those associated with the treatment. Unrelated costs are those not directly linked to the specific illness or cause. Direct costs correspond to healthcare resources that the treatment involves, for example; costs for inpatient (e.g. bed price/day* number of days) and outpatient care (ex. physician visits), nursing care, and drug costs. Indirect costs relate to mainly production losses due to sick days, reduced employment or premature death. If in advance a specific cost is unrelated and known not to affect the result, it can preferably be excluded from the analysis. Most often these are small costs with marginal impact on the cost analysis. It would also be useful to eliminate costs shared by all treatments being compared, as they leave no impact on the results. For example the indirect costs could be assumed to differ between treatments if a person is treated differently depending on their CPC-value.

Different health economic evaluations use different approaches on how to estimate the indirect costs. The human capital approach estimates productivity by using gross earnings, containing employment costs and social fees. An alternative way is the friction cost approach that estimates productivity changes depending on the time that patients need to restore initial productivity level, which will differ between different types of work[20]. However this paper will have a hard time dealing with these indirect costs, but instead debate possible improvements to the area in in chapter 6.

Once the costs are identified they have to be measured and evaluated. The estimation is not always obvious as healthcare production equipment often is used for several different treatments, therefore costs should be shared in proportion. It should also be noted that the final outcome may vary with different time aspects and one should avoid manipulating the usage of time periods that might benefit one treatment over the other[21]. When knowing what costs should be treated, the four different analysis methods can be clarified.

2.2.2 Cost-minimizing, cost-benefit, cost-effectiveness and cost-utility analysis

An overview of the four types of analysis is presented in Table 1 from Kobelt (2002). Here, one can learn that the simplest form of a health economic evaluation is a cost-minimizing analysis. While evaluating two or more alternatives this kind of analysis assumes no difference between treatments, meaning that the treatment with lowest costs is always preferred.

A cost-benefit analysis will try to price all consequences of the intervention into monetary values. This can be performed with three different approaches; human capital, revealed preferences and contingent valuation, all with different pros and cons. One example is a willingness-to-pay study, which is a basic contingent valuation method that has its difficulties in creating hypothetical situations for respondents. With this tool the author will estimate respondents' monetary beliefs, understanding that any miscommunication will cause biasness in the study results. If possible, a CEA or cost-utility analyses are more preferred when performing an economic evaluation between treatments within the health sector[22].

TABLE 1 METHODS OF ECONOMIC EVALUATION

Method of analysis	*Effect measure*
Cost-minimizing analysis	Effect is assumed to not differ between treatments.
Cost-benefit analysis	Effect is measured in monetary terms. For example through willingness to pay.
Cost-effectiveness analysis (CEA)	A specific effect measure is used. For example life years saved.
Cost-utility analysis	An effect measure that combines survival with life-quality. Often quality-adjusted life-years (QALYs)

A CEA measures effects in single one-dimensional outcomes, for example; the number of painless days, units of treated patients or in gained life-years. Cost-effectiveness models are used to assess the relative benefits of a given intervention using patient outcomes and the costs incurred in achieving those outcomes. The calculation of the additional cost per additional unit gain of benefit is known as the incremental analysis and results are presented as incremental cost-effectiveness ratio (ICER). Equation 1 is a calculation example where A and B stands for the different treatments. This allows the ratio between the difference in costs and effects between the two treatments to be calculated.

EQUATION 1 INCREMENTAL COST-EFFECTIVENESS RATIO (ICER)

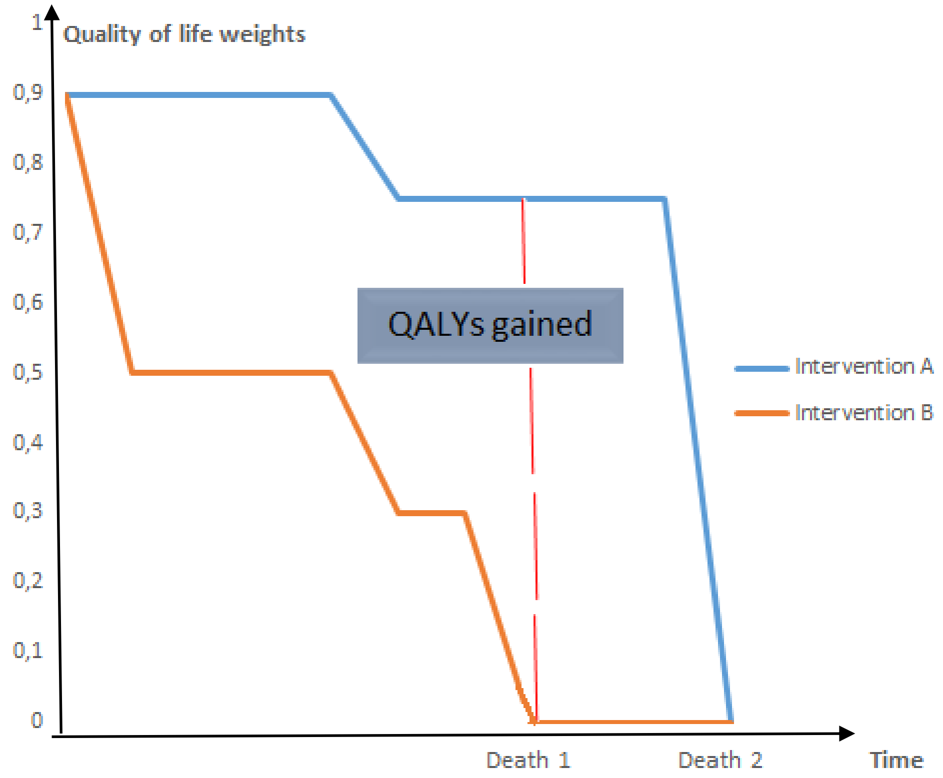
$$ICER = \frac{Cost_B - Cost_A}{Effect_B - Effect_A}$$

For example B could be the new treatment (mechanical CPR) and A could be the old treatment (manual CPR). To obtain a result on the cost-effectiveness one needs to know the costs differing between the treatments and have an effect to measure. As seen in Table 1 one could for example measure life-years saved. Cost-utility analysis is said to take CEA one-step further by combining effects into a one-dimensional outcome. This outcome is either disease-specific, such as cases detected or avoided, or more general in the form of life-years gained. Within healthcare a relevant measure of effect is the quality-adjusted life year (QALY) gained and it was also chosen as the outcome in this paper. It will be further explained in the chapter below.

2.3 Quality-adjusted life years

A QALY is a health indicator of the combined effect of surviving and the life quality of those years. To be able to estimate a QALY, the time spent during a certain health condition is weighted by a certain value ranging on a scale from 1, representing perfect health, and the number 0, representing death. It should be noted that QALYs could be less than zero when the scenario presented is considered to be worse than death. Some methodological problems has been shown to this original approach and it is a standard within the area to set the low bar to zero, therefore this paper will call this the conservative approach[23]. A way to describe a QALY calculation is to present it with a figure. Figure 2 shows sequences over time, that are associated with QALYs gained, from choosing treatment A instead of treatment B. It should be noted that the area could be split into gain in quality and the gain in quantity of life. These occur to the left and the right of the death of person 1.

FIGURE 2 QALY CALCULATION



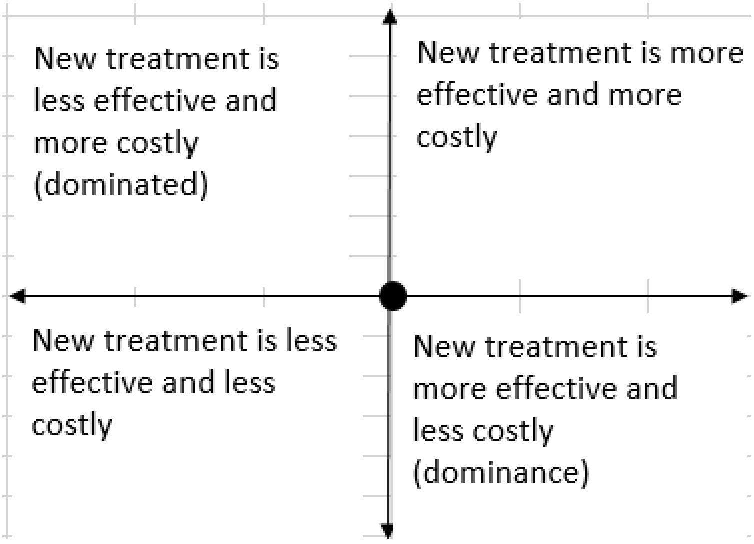
QALYs have to be calculated in some way and attempts for obtaining general guidelines, when calculating patients' preferences for different treatments, have been made. Some standardized Health Related Quality of Life- instruments are the HUI, SF-6D and EQ-5D, which is most used.

This study applies the well-known EuroQol Group (EQ-5D) survey by Dolan (1997) that describes the individuals' health state by five dimensions; Mobility, Pain/Discomfort, Self-care, Anxiety/Depression and Usual activities. For the readers' better understanding this explanation has been moved to chapter 4.4.1.

2.4 Swedish national guidelines

When results are presented in the ICER-ratio (Equation 1) the decision-makers need to make their decision regarding the new treatment. Figure 3 is called a cost-effectiveness plane and is an illustrated comparison between four possible outcomes of costs and effects. As for example mechanical CPR will be more costly than manual CPR (ending up on the north side). Then depending on whether it is less effective or more effective it will test the decision-maker. If it is more costly and less effective (northwest corner) it will be dominated by manual CPR and if it is more costly and more effective (northeast corner) it should be considered depending on its ICER-ratio. Most preferred for a new treatment is the notation of dominating another strategy, occurring when the new treatment is both more effective and cheaper.

FIGURE 3 COST-EFFECTIVENESS PLANE



By using the concept of QALYs it is possible to compare treatment of different diseases[24]. CUA and CEA identify only the best alternatives in terms of cost per QALY gained. The Swedish National board of Health and Welfare[25] has developed an assessment of costs in relation to effects presented in Table 2. This gives indications on what is cost-effective and which alternative that should be implemented when ending up in the northeast corner in Figure 3. It should be noted that these borderlines are only terms of reference and that the cost-effectiveness principle in Sweden should be applied so that the requirement for cost-effectiveness is higher for less serious medical conditions. This principle is called the needs and solidarity principle. A principle that stands above both these is the principle of human dignity standing for good health at equal terms for everyone[26].

TABLE 2 GROUPING OF COST PER QALY GAINED, DEVELOPED BY THE SWEDISH NATIONAL BOARD OF HEALTH AND WELFARE

Cost in relation to gain in health	*Cost per QALY (SEK) alternatively gained life year*
Low	< 100 000 SEK per QALY
Moderate	100 000 - 500 000 SEK per QALY
High	500 000 - 1 000 000 SEK per QALY
Very High	> 1 000 000 SEK per QALY
Not gradable	The action has no effect (there exists evidence of no effect) alternatively it cannot be evaluated.

2.5 Discounting

Discounting means a value counted backwards in time with respect to a given interest rate as a way to deal with future uncertainties. This is a problem stemming from "time preference", which refers to not all costs and benefits occurring at the same time. For example human behavior such as drinking and smoking shows that people value current pleasure higher than future possibly damaging effects. An economic example is that people hire videos for home viewing instead of waiting an extra time period to get the same "effect" for a lower price. If not applying discounting this means that health effects today would be accounted for the same way as for those gained in 10 or 15 years[27]. Berggren,

& Andersson (2001) have gathered and showed formal and informal guidelines within health economics. Guidelines agree that some form of discounting needs to be applied. It is pointed out that depending on which perspective one chooses to adopt, different outcomes are possible. When discounting health improvements it makes future populations health benefits lesser valued. Equation 2 shows how discounting is calculated and how we get the present value of future costs and effects. For example this study will use the same discount rates as The Swedish Dental and Pharmaceutical Benefits Agency recommends, namely 3 percent for both costs and effects and a sensitivity analysis ranging from 0-5 percent[28]. A common rule is to present the results both with and without discounting[29].

EQUATION 2 PRESENT VALUE CALCULATION

$$\boldsymbol{PV = \frac{FV}{(1+i)^n}}$$

Where:
PV= Present Value
FV= Future Value
i= interest
n= number of time periods

In order to provide an appropriate background of the subjects discussed in this study, we will prior to the analysis review the recent research within the field.

3. Sudden cardiac arrest and Cardiopulmonary Resuscitation

This chapter will further introduce the reader to the nature of sudden cardiac arrest and CPR and the potential advantages that mechanical CPR offers over manual CPR. This chapter also gives a brief overview of the classification and reporting in clinical findings.

3.1 Medical background

A large percentage of the people who die due to cardiac arrest die before arrival to the hospital in an Out-of-Hospital Cardiac Arrest (OHCA). For every minute that passes before help arrives, the patients' body starts getting severe damage. This is caused by the lack of oxygen to the brain and other vital organs, resulting from the cardiac arrest. The risk of death increases by ten percent for each minute that treatment has not started and death is inevitable after about fifteen minutes. The probability of surviving an OHCA increases dramatically if ventilation and circulation artificially can be kept running while awaiting ambulance arrival. There is a simple method to accomplish this, CPR, which typically involves manually pressing on the chest to keep the circulation going[30]. CPR is performed to achieve Return of Spontaneous Circulation (ROSC), which means that the heart is beating by its own again. Achieving good quality CPR is physically demanding and variations in provision of CPR according to guideline standards have been observed[31]. The effectiveness of manual CPR is largely dependent on the skill and endurance of the rescuer[32]. Success depends on the ability to compress deep enough and not having too long hands-off interval[33]. As stated in chapter 1.1, two mechanical chest compressors have been developed, named AutoPulse and LUCAS.

The two chest compression systems differ and as an example the LUCAS chest compression system is a battery-driven, piston-driven, lightweight (7.8kg), compact device designed to help improve outcomes of cardiac arrest patients and improve operations for the health care staff. LUCAS can consistently do 100 compressions per minute with a depth up to 5 cm, which is according to guidelines[34]. LUCAS can be deployed to patients within 20 seconds[35]. The Autopulse does circumferential compressions with a belt, weight 17 kg and compresses the chest with 80 compressions per minute with a depth of 20% of the chest height[36].

Mechanical chest compressors aims to save lives of cardiac arrest patients and avoid neurological damage, which is achieved by a steady supply of oxygen to the heart (achieving ROSC) in combination with simultaneous defibrillation. For those patients who do survive to arrive to the hospital, there are advanced care resources for post-resuscitation care.

The suspected causes of the cardiac arrests are presented for both the LINC-study and the Swedish Annual CPR registry in Table 3. These results imply that the LINC-study population is fairly well matched with the Swedish population as a whole. More on this in chapter 4.1.

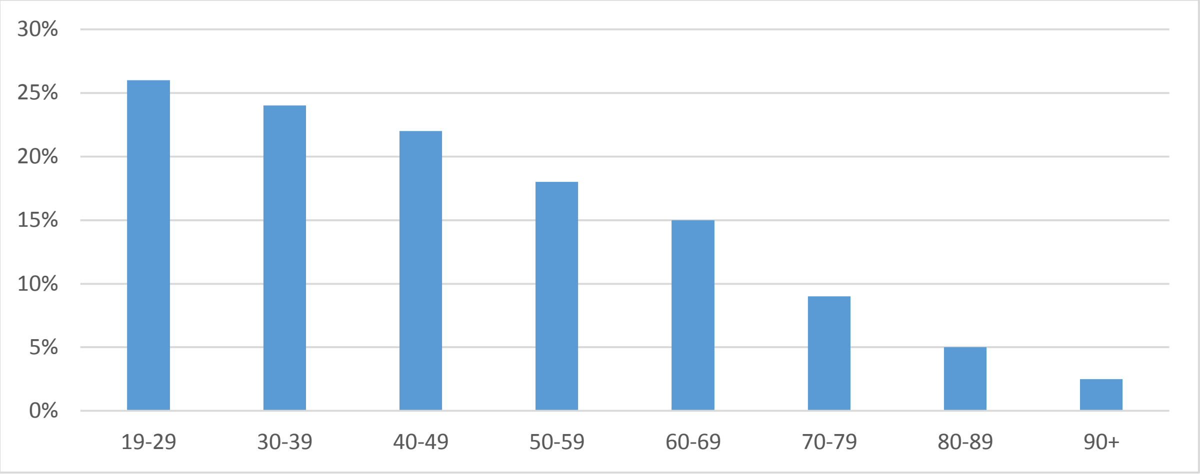
TABLE 3 SUSPECTED CAUSE OF CARDIAC ARREST

Cause of arrest	*LINC study*	*Swedish Annual CPR Registry*
Heart disease	71 %	66 %
Pulmonary disease	6 %	6 %
Respiratory arrest	5 %	2 %
Intoxication	3 %	2 %
Drowning	0 %	1 %
Other	15 %	24 %
Total	**2,329**	**62,758**

Sudden cardiac arrest can occur to anyone, but generally speaking, those who are at risk are divided into three groups. First those who are impossible to foresee as they show no diagnosis, no symptoms and have no relatives who has sustained cardiac arrest. Next the ones with symptoms such as chest pains, dizziness or unexplained fatigue. These people have perhaps not understood their symptoms as serious and the physician will have problem connecting them to a specific heart disease. Lastly the group where a diagnosis has been made and it is up to the physician to make an adequate risk-assessment on what treatment to take[37]. This indicates that the possible gains within cardiac arrest might come from other areas that are not associated with mechanical CPR.

One cannot foresee who will suffer a cardiac arrest, but it is still interesting to know that the number of cardiac arrest caused by heart disease increase by age. In Figure 4, from the Swedish national registry by Herlitz (2013) it is shown that the proportion of patients with a witness, surviving to one month, does decrease drastically by age. Giving us reasons to believe that the people who outlive a cardiac arrest are commonly younger. This means not that mechanical CPR aim to save a certain group of patients.

FIGURE 4 PERCENTAGE CHANCE OF SURVIVAL TO 1-MONTH, IN OHCA CASES WITH A WITNESS



But to what kind of life are the patients rescued to and how is this measured? The next section will deal with a measurement outcome used within the health care to determine brain capacity and future health state.

3.2 Cerebral Performance Category

A consensus statement regarding procedures for the classification and reporting of incidents and clinical findings, the so-called Utstein protocol has been published[38]. They determine in what way and by what time one should report the forecasts and results in scientific studies. The protocol recommends using the evaluation of Cerebral Performance Category-score (CPC), see (Box 1)[39]. This should be carried out at discharge from hospital and at one year after the cardiac arrest. The Swedish national registry does treasure CPC at

BOX 1 CEREBRAL PERFORMANCE CATEGORY SCALE

CPC 1 - Good cerebral performance
CPC 2 - Moderate cerebral disability
CPC 3 - Severe cerebral disability
CPC 4 - Coma or vegetative state
CPC 5 - Brain death

hospital enrollment and discharge, when following up the outcome of OHCA patients [40]. The LINC-study for example lets nurses and physicians determine the CPC-score of patients at four times through time. After discharge from intensive care unit (ICU), discharge from hospital, 1 month after ROSC and 6 months after ROSC.

CPC is used extensively due to simplicity, it is done to follow patient improvement over time, plan realistic rehabilitation operations and evaluate treatments[41]. It aims to assess domains of functioning after a cardiac arrest. For example, a CPC-score of 2 represents three domains of function: impairment (e.g. presence of hemiplegia, mental changes), level of activity performed (e.g. ability to dress independently) and level of participation (e.g. sufficient cerebral function to work part-time in a sheltered environment)[42]. However studies have shown that its validity as being directly transferable to a QALY-instrument after cardiac arrest is rather low[43].

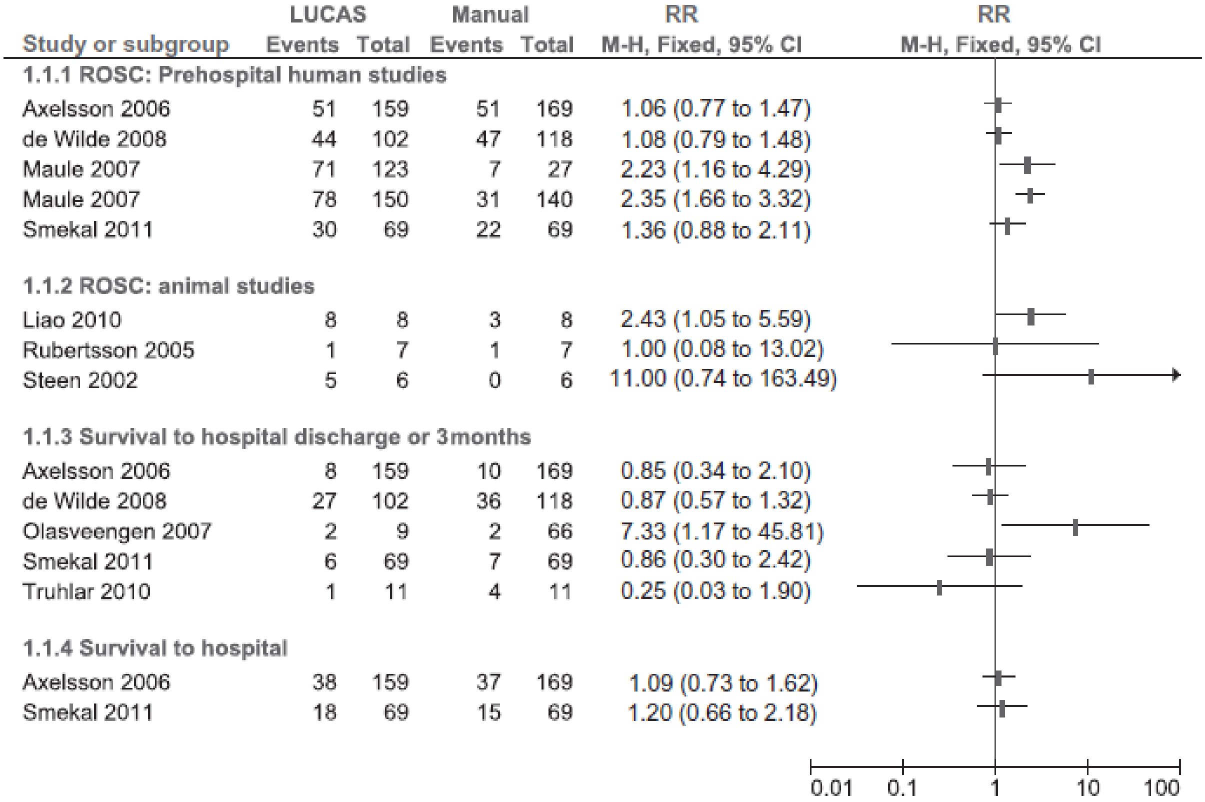
Internationally as well as in Sweden CPC serves as a gold standard, functioning as a marker for how treatment should proceed[44]. Differences in CPC-outcome have been shown by Phelps et al. (2013) to have effects on expected future life-years, this is an area this paper will exploit[45]. Phelps looks into the correlation between CPC and survival risk ratios, which is more thoroughly explained in chapter 4.1. They make that CPC at discharge from hospital is a useful tool for programmatic evaluation and research.

This chapter has informed the reader that CPC is used in clinical trials and it gives ideas to perform a numerical example, with CPC as a base for effects, on the cost-effectiveness of mechanical CPR compared to manual CPR.

3.3 Previous Research

As indicated above, mechanical CPR offers a potential advantage over manual CPR. Gates, Smith, Ong, Brace, & Perkins (2012) reviewed the literature on 322 studies comparing mechanical CPR, using the LUCAS device, with manual CPR. Table 4 from their study shows that the number of studies included in the analysis was fifteen, whereof three were on animals[46]. The meta-analysis covered studies with outcomes of survival and ROSC. Measures on ROSC were conducted in a pre-hospital setting for the human studies. Showing small but insignificant results favoring the mechanical LUCAS device. The three animal studies follow the same reasoning. Studies on survival have in common that they omitted important details of their methodology such as procedures for randomization and blinding leading to high risk of bias and their heterogeneity mean that results should be considered in caution.

Table 4 Results from a Meta-analysis by Gates et al. (2012) of mechanical CPR vs. manual CPR



Study or subgroup	LUCAS Events	LUCAS Total	Manual Events	Manual Total	RR M-H, Fixed, 95% CI
1.1.1 ROSC: Prehospital human studies					
Axelsson 2006	51	159	51	169	1.06 (0.77 to 1.47)
de Wilde 2008	44	102	47	118	1.08 (0.79 to 1.48)
Maule 2007	71	123	7	27	2.23 (1.16 to 4.29)
Maule 2007	78	150	31	140	2.35 (1.66 to 3.32)
Smekal 2011	30	69	22	69	1.36 (0.88 to 2.11)
1.1.2 ROSC: animal studies					
Liao 2010	8	8	3	8	2.43 (1.05 to 5.59)
Rubertsson 2005	1	7	1	7	1.00 (0.08 to 13.02)
Steen 2002	5	6	0	6	11.00 (0.74 to 163.49)
1.1.3 Survival to hospital discharge or 3months					
Axelsson 2006	8	159	10	169	0.85 (0.34 to 2.10)
de Wilde 2008	27	102	36	118	0.87 (0.57 to 1.32)
Olasveengen 2007	2	9	2	66	7.33 (1.17 to 45.81)
Smekal 2011	6	69	7	69	0.86 (0.30 to 2.42)
Truhlar 2010	1	11	4	11	0.25 (0.03 to 1.90)
1.1.4 Survival to hospital					
Axelsson 2006	38	159	37	169	1.09 (0.73 to 1.62)
Smekal 2011	18	69	15	69	1.20 (0.66 to 2.18)

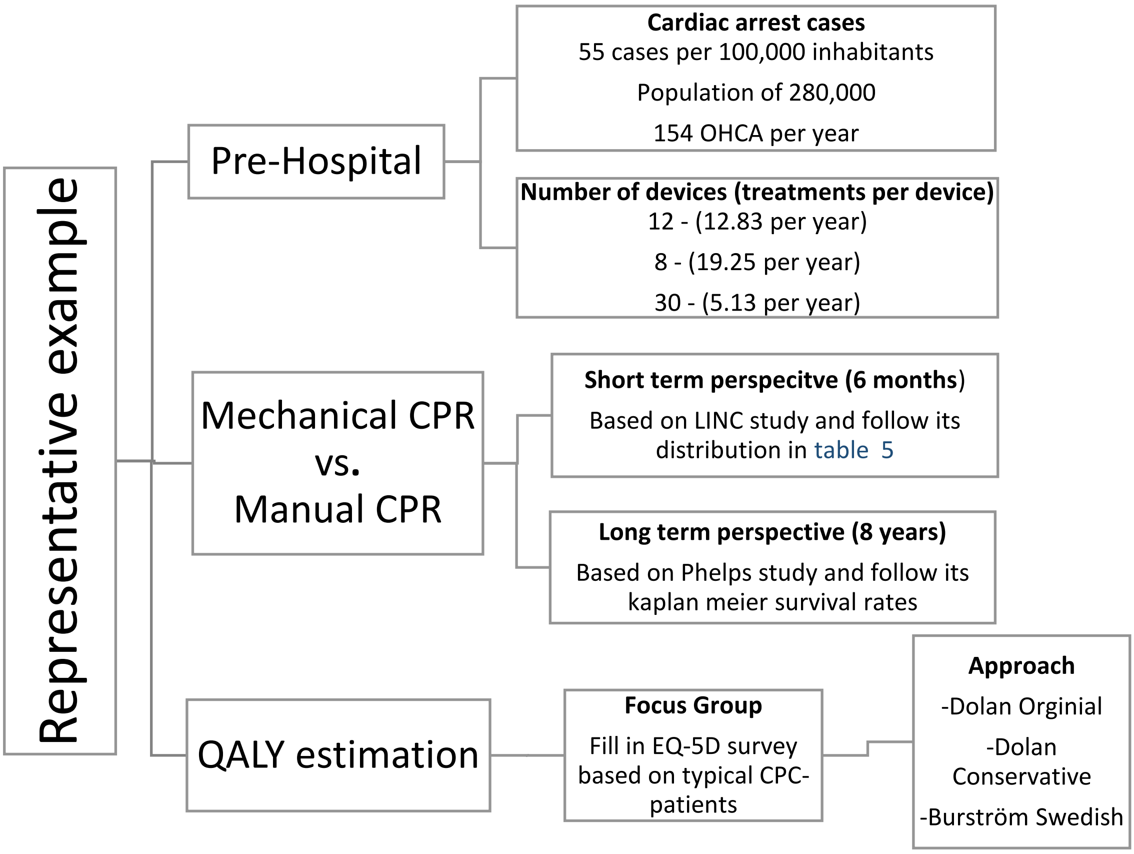
As perceived in Table 4, evidence on important clinical outcomes of treatment are inconclusive up to this date. In studies where conclusions are stronger those studies are also severely limited by methodological weakness and poor reporting. For example only one of the human studies was a small-randomized controlled trial. A Swedish before & after abstract suggested that the introduction of LUCAS was associated with a greater number of resuscitation attempts, more patients being admitted to emergency departments, and an increase in survival up to 30 days[47].

To sum up this chapter the needs to clarify results with a high-quality trial was identified. One such large-scale randomized controlled trial of LUCAS, the LINC-study, has been published after Gates et al. (2012) meta-analysis. The LINC-study is the main reason that this study focuses on LUCAS as a representation for mechanical CPR when measuring the value of mechanical CPR and simultaneous defibrillation vs. conventional manual CPR in OHCA, in Sweden.

4. Material and method

Presented in Figure 5 is a description of the study design and method used. This is included for the reader to easier follow the path that this papers' cost estimation takes. In chapter 4.1 the main material for this analysis is presented and deals with CPC-scores from mechanical CPR and manual CPR in an OHCA setting. This could be associated to the mechanical CPR vs. manual CPR branch in the figure. Chapter 4.3 takes on the costs for a LUCAS device, as a yardstick for mechanical CPR, and explains this representative example more thoroughly[b]. This is associated to the Pre-hospital branch in the figure. Lastly in chapter 4.4 the analysis uses a focus group from the LINC study to convert CPC-scores and survival to QALYs calculating the effects with different approaches to QALY weights. This is the bottom branch in the tree in Figure 5.

FIGURE 5 STUDY DESIGN OF THE REPRESENTATIVE EXAMPLE



4.1 Material

As stated, this study is based on the LINC-study: "*Mechanical Chest Compressions and Simultaneous Defibrillation vs. Conventional Cardiopulmonary Resuscitation in Out-of-Hospital Cardiac Arrest*" published by Rubertsson et al. (2013). The study was made between January 2008 and February 2013, and performed its trial at six advanced life support emergency medical services, whereof four where in Sweden, one in the Netherlands and the last one in the United Kingdom. In which all results are assumed to be applied to a Swedish scenery. The protocol has been described in detail elsewhere[48]. The LINC-study concludes no improved 4-hour survival vs. manual CPR, according to

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[b] A representative example/sample is a term used to show the typical costs or case associated to a product.

guidelines. However they also look at secondary outcomes such as neurological outcome CPC-scores, which are explained in chapter 3.2.

The LINC-study presents the number and percentage of survivors divided into CPC-scores in their two groups L-CPR (LUCAS/mechanical) and M-CPR (manual). This can be seen in Appendix C, where the reader could imagine that using mechanical CPR instead of manual CPR will make the patient end up with a lower (better) CPC-score. Tracking the darkened bars in the appendix figure sees this. When evaluating the CPC-scores of the patients at discharge from intensive care unit (ICU), there exists a significant difference at the 5 percent level between the patient groups evaluated with a CPC-score of 1. At discharge from hospital this significance remains under the lower presumption. This allows room for exploring the possibility that using mechanical CPR could be more effective in terms of achieving a CPC-score of 1 compared to manual CPR.

When conducting a CEA of a treatment one needs to decide on the appropriate timeframe. The basic rule is that the analysis should capture the relevant costs and effects that the treatment gives rise to. For chronic conditions, it is usually appropriate to apply the remainder of the patients' lives as a timeframe[49]. For cardiac arrest a long-term perspective is usually known to be 6-12 months[50]. Since the economic lifetime of a LUCAS device is 8 years this study states that this timeframe is suitable as a long-term perspective, more on this in chapter 4.3.

Therefore this paper is also based on the work by Phelps et al. (2013) who sought to determine whether CPC was associated with long-term outcome following resuscitation from OHCA. With a retrospective American cohort investigation from January 1, 2001 and December 31, 2009 they use Kaplan-Meier curves to evaluate the association between CPC and long-term survival starting at hospital discharge. The program FindGraph[c] made it possible to subtract the change per month showed in Appendix D. The graph tells us that CPC-scores, going from 1 to 4 in falling order, are of effect when determining long-term survival starting from hospital discharge, in America. Their results show that more favorable CPC was associated with better long-term prognosis. For example, at 96 months (8 years) survival was 66 % for CPC 1; 51 % for CPC 2; 31 % for CPC 3 and 17 % for CPC 4.

4.2 Method and construction of representative example

The LINC-study shows no significant effects regarding survival in patients treated with mechanical CPR. In this section the paper evaluate the way of method in the cost-effectiveness of mechanical CPR vs. manual CPR. This is done to explore if some sort of weight can be attached to the usage of mechanical CPR. As stated this paper is the first within this field. Also no studies have, up to our knowledge, evaluated the quality-of-life for patients who have undergone a mechanical treatment. Therefore this study will expand the usage of CPC as a measurement and perform a calculation example with a representative cohort as described in Figure 5.

For this calculation example the results from the LINC-study will be used to create a 154 person hypothetical population for each treatment group. This is done to form create an example of how often the device is used each year. The size of the hypothetical cohort is chosen as a typical example of number of OHCA cases in SUS, Malmö catchment area in Sweden.

According to data from Herlitz (2013) Swedish annual index, Malmö pre-hospital-region has 55 OHCA cases per 100,000 inhabitants. The Study Protocol for the LINC has been used to show that SUS, Malmö has 280,000 inhabitants and 12 LUCAS devices, as seen in Appendix B. (2.8 times 55) = 154

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[c] Program can be downloaded at: http://www.findgraph.com/

annual OHCA cases that will be possibly treated by 12 mechanical devices. This gives an average OHCA usage per mechanical device of approximately 12.83 OHCA cases per year. Meaning that each of the 12 devices will deal with 12.83 possible patients in an OHCA setting each year. Sensitivity analysis will also be made to see what happens to the cost-effectiveness if the hospital instead buys 30 devices (5.13 OHCA treatments per device/year) or 8 devices (19.25 OHCA treatments per device/year) to deal with these 154 annual OHCA cardiac arrest cases.

The reason this paper uses a representative example and not only takes the results from two groups in the LINC-study, is that those two sample populations were not equally large (LUCAS n= 1300 and manual n= 1289). Having dealt with the size of the cohorts, we can use the fact that there was a significant difference in the distribution between the CPC-scores. Also one should remember that the results in this analysis would vary if using a different survival and CPC distribution in the cohorts.

With this hypothetical population and the survival and CPC distribution from the LINC study, Table 5 shows that out of 154 mechanically OHCA patients, 18.7 (12.2 %) will survive to discharge from ICU and of the 154 manually OHCA persons, 18.0 (11.7 %) will survive to ICU discharge. In the LINC-study those numbers were 158 out of 1300 in the mechanical group and 151 out of 1289 in the manual group, which are the exact same percentages. This calculation example will not only focus on patients survival rates but also on their CPC-scores as captured in chapter 4.4.

TABLE 5 SURVIVAL RATES AND CPC DISTRIBUTION FOR THE COHORTS

	MECHANICAL CPR (N = 154)		**MANUAL CPR (N = 154)**	
SURVIVAL TO ICU DISCHARGE	**18.7**	**12.2 %**	**18.0**	**11.7 %**
WITH CPC 1	6.4	4.2 %	4.1	2.6 %
WITH CPC 2	5.2	3.4 %	5.7	3.7 %
WITH CPC 3	4.0	2.6 %	4.8	3.1 %
WITH CPC 4	3.1	2.0 %	3.5	2.2 %
SURVIVAL TO HOSPITAL DISCHARGE	**13.9**	**9.0 %**	**13.9**	**9.0 %**
WITH CPC 1	10.5	6.8 %	8.0	5.2 %
WITH CPC 2	2.3	1.5 %	3.9	2.6 %
WITH CPC 3	1.1	0.7 %	1.8	1.2 %
WITH CPC 4	0.0	-	0.1	0.1 %
1- MONTH SURVIVAL	**13.3**	**8.6 %**	**13.0**	**8.5 %**
WITH CPC 1	11.6	7.5 %	8.8	5.7 %
WITH CPC 2	1.5	1.0 %	2.4	1.6 %
WITH CPC 3	0.8	0.5 %	1.6	1.0 %
WITH CPC 4	0.0	-	0.1	0.1 %
6- MONTH SURVIVAL	**13.1**	**8.5 %**	**12.4**	**8.1 %**
WITH CPC 1	12.2	7.9 %	10.5	6.8 %
WITH CPC 2	0.8	0.5 %	1.2	0.8 %
WITH CPC 3	0.1	0.1 %	0.7	0.5 %
WITH CPC 4	0.0	-	0.0	-

4.3 Cost estimation

In the cost estimation the aim in this paper are the costs affecting the health care budget, and the cost imposed on society as a whole. Direct costs are machine costs, service costs and additional training costs, which will be explored in chapter 4.3.1. Indirect costs occur when patients end up producing less than what they did before the cardiac arrest. These costs should be included as they are of importance when measuring the value for the society and their possibilities will be explored in chapter 4.3.2.

4.3.1 Direct Costs

This analysis will take on the LUCAS device as a yardstick for mechanical CPR. The best estimated costs have been calculated from information by people at Physio Control (the owners of the LUCAS device) in Lund[51]. The sensitivity analysis will present two scenarios where costs are either higher or lower, associated with low and high usage. These two scenarios will be used both as sensitivity analysis and also to show cost differences when buying a different number of devices. For example buying 30 devices could lead to the 15 % lower prices and buying only 8 devices could lead to the 15 % higher prices.

4.3.1.1 Machine costs, including expendables and maintenance,

Most costs, except the machine costs, are shared between the two ways of treatment, these are therefore excluded from the calculation. However additional training for the paramedics are needed and it is assumed that this additional training could be attached to the regular CPR education occurring twice a year as stated in the LINC-study. Therefore it is calculated as 2 times 0.5 hours a year for each paramedic that uses the LUCAS device[52]. Data from The Study Protocol for the LINC-has been used to calculate the average, low and high usage for LUCAS, see Appendix B. For example the number of LUCAS devices that can be used on each battery charger (ranging from 1-20), the number of paramedics that will "share" each LUCAS. Lastly LUCAS is a device that does not fit all patients and is assumed to be applicable to 95 percent of patients and therefore 95 percent of treatments[53]. The economic lifetime of LUCAS stretches over 8 years and therefore the representative example will take on this timeframe for the cost estimation. Together these assumptions give rise to the total costs per LUCAS device per year for an 8-year period. The costs are 23,942 SEK per device and year ranging from 19,905-31,037 SEK in the two sensitivity scenarios. When applying the 3 percent discounting the costs are 22,867 SEK (19,038-29,492SEK) each year for the 8-year period. All costs are in 2013 years prices and presented at its full in Appendix M.

4.3.1.2 Variable costs

In addition to the machine costs there are the treatment costs in form of disposable suction cups that will be added on with 285 SEK per treatment. A sole cost that is beyond of the machine and that differ between mechanical and manual CPR are the added hospital stay costs. These are calculated as depending on the severity of the neurological damage and based on data from LINC-shown in Table 5 in chapter 4.2. The reason they cost more is that there are more survivors to ICU discharge in the group who had been treated mechanically. Surviving patients stay a various amount of time at the different hospital services. Data from both ICU discharge and discharge from hospital were available to complete this partitioning. In Appendix F, the time in days from ROSC to ICU- and Hospital discharge is displayed to tell that most patients stay equally long until being released from the ICU. Note that patients with a CPC-score of 4 are in coma and could be removed earlier. The cost per day is derived from the cost per minute at the ICU recovery area. Data from Regionvårdsnämnden (2013) shows different costs depending on which ICU department patients stay at, see Appendix N. It is assumed that the only thing differing between the typical CPC persons is the time spent at the recovery room and it is equally likely that patients stay at the two different ICU departments. Thereby the cost per day at ICU is calculated to an average of 18,000SEK (15,840-20,160 SEK). With this assumption the cost at ICU per average patient is 10,300SEK for a LUCAS treated person and 9,761SEK for a manually treated person. Remember that less than 12 percent has survived to ICU discharge and these are the ones included in the calculation.

Appendix F shows that almost all of the patients that at ICU discharge were valued a CPC-score of 4 have later either improved or more probable died. Since only calculating the costs of those alive this means that there is a small sample standing (0.4%). This analysis is assuming that a patient with a CPC-score of 4 stays the same amount of days at the hospital as a person with a CPC-score of 3 (30.13 days). After awakening from the ICU, patients are moved to several different areas in the hospital, such as the cardiovascular-, neurology-, internal medicine- and possibly the geriatric department (if the patient is aged)[54]. Since location of patients is not based on the CPC-score, the average daily costs of all four departments created a daily cost for each patient of 3,266SEK (2,505-4,046SEK). With this assumption the cost at the hospital after ICU discharge per average patient is 4,756SEK for a LUCAS treated person and 4,989SEK for a manually treated person. Together with the costs per suction cup these two form the variable costs per patient using the LUCAS device.

4.3.1.3 Presentation of direct costs

The representative example has 12 devices; each depreciated over 8 years and which will be used on 95 percent of 154 assumed cardiac arrest cases. Table 6 presents the 2013 future value discounted costs in SEK, depending on the number of devices, showing a base-case result of 2,281,601SEK (1,913,953-2,917,583SEK). These will late on be depreciated over 8 years. The variable costs are calculated from 146.3 treatments (95% of 154 cardiac arrest cases) times the difference in costs per average patient in the two groups. The table also shows that the number of devices bought in to deal with 154 annual cases do drive costs and will therefor affect ICER results in the analysis.

TABLE 6 TOTAL DIRECT COSTS, IN SEK

	15 % Higher and Low usage	*Best Estimate*	*15 % Lower and High usage*
Cost per year for LUCAS	29,492	22,867	19,037
Suction cup costs	41,695	41,695	41,695
Added Hospital costs	44,630	44,630	44,630
Total costs 8 devices	1,973,830	1,549,842	1,304,743
Total costs 12 devices	2,917,583	2,281,601	1,913,952
Total costs 30 devices	7,164,468	5,574,513	4,655,391

4.3.2 Indirect Costs

When dealing with the indirect costs of different CPC-values one needs to find out where the patients end up after the cardiac arrest and if there are any differences between the CPC groups. This paper lacks information about long-term health care costs for survivors or placement depending on CPC-score. A sole study to deal after cardiac arrest patients placement by Rittenberger et al. (2011) was found not to be applicable to this papers' population. Their American population consisted of half in- hospital cardiac arrests and other half OHCA survivors. Using Kendall's tau correlation they find a poor relationship (0.23) and reason around that CPC is heavily weighted toward mental functioning. However their study had a population where 73 percent of the patients had been graded a CPC-score of 3 and only 1 percent had a CPC-score of 2. This data does not nearly match the Swedish index and it is questioned if their results really could be applied to this study. The Swedish National Registry of Cardiac Arrest 2013[55] shows that around 83 percent has a CPC-score of 1 and 5 percent has a CPC-score of 3 in the in-hospital cardiac arrest survivors at discharge from hospital in Sweden. Further on CPC has been criticized as poorly defined being a subjective measurement[56]. Rittenberger et al. (2011) state that when they were in doubt the focus group would always choose the worst outcome, possibly having problems separating CPC group 2 from 3. Also half of their population was in-hospital cardiac arrest survivors whom probably already had some problems that might affect the result.

In the LINC-study the mean age of the patients included was 69.1 years old, proposing that most patients were retired at the time of the cardiac arrest. In a study of Swedish cardiac arrest survivors from Gothenburg by Graves et al. (1997) the median age was 67 years old (mean= 64 years) and 74 percent had retired before their arrest. This indicates that possible benefits to society of patients returning to work are of less importance. As a calculation of production loss depending on CPC-score is very difficult it also brings even more uncertainty into the calculation, whereby it is not included in this analysis. Decision-makers do preferably want the societal view in Sweden, but as it the indirect costs comes with large uncertainties it is in this paper only debated in chapter 6. This paper will instead in chapter 4.4.2 assume that QALYs alone deal with these differences.

4.4 Effects

This study's major contribution and difficulty is the measuring of effect. Using the material in Appendix C the LINC scores speaks of a small significant difference on the number of patients that survive to ICU discharge. This gives the idea that a greater difference exists and by performing an illustrative example this study hopes to show just this. In the coming chapters the study will use the material in chapter 4.1 to link CPC-scores to QALYs using EQ-5D survey and a focus group.

4.4.1 EQ-5D and the DELPHI method

The literature gives no direct translation from CPC-scores to a quality of life measure. Instead this study turns to a small focus group of five experts in assessing CPC-scores on cardiac arrest patient[d]. The Delphi method[e] is then used to create a link from CPC to QALYs using a quality of life instrument (EQ-5D). It is known that these are two separate instruments used for measuring health on different levels and the goal is to find where they overlap and estimate a probable response of how the patients, with different CPC-scores, would answer the EQ-5D survey. In Appendix G the reader can explore the five dimensions of the EQ-5D survey and the possible response options and there on compare it to the CPC description in Appendix A.

C.-C. Hsu & Sandford (2007) and others have questioned this spur to let experts assess "objective" evaluations of the quality of life for patients surviving a cardiac arrest. Yet CPC is a measurement used within health care and despite its limitations this study aims to withdraw the effects as far as possible. Another possibility would be to let patients judge their own quality of life at these states, but this is hard to achieve in the retrospective setting of this paper. It should also be noted that EQ-5D in itself is a tool for measuring quality of life and it has been observed that the quality of life is affected by patients' own expectations. Methodological problems remains even when patients themselves answer the survey[57]. This study will however assume that the focus group will together form the response of a typical person and on average therefore is correct enough to allow implementing the results to the cost-effectiveness analysis on an average treated patient.

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[d] These experts are the people who assessed CPC-scores of the patients in the LINC-study

[e] For a more thorough insight to the Delphi-method see "The Delphi Technique:

Making Sense Of Consensus" by C.-C. Hsu & Sandford (2007)

The experts were asked to individually fill in a standard EQ-5D survey on behalf of four typical persons each with a separate CPC-score. They had the possibility to not just comment or mark that all patients with a specific CPC-score would answer the same way, but also what share of patients they believed would answer in a particular way. An example of the survey, in the question of the patient mobility, can be seen in Appendix H.

When the individual surveys were completed, the information were gathered and summed up with included comments to subsequently be handed out with the possibility for the experts to revise their results. In this way it is believed to seek out information that may generate a consensus on the part of the focus group and correlate informed judgments on this topic. The main results from the focus group are showed in Appendix I. These are used to the calculation of specific QALY-weights for the typical CPC-patients.

Since no individual data for the patients were available for patients a major assumption was needed for the next step. Independence was assumed, when translating the results into QALY-weights, between the five dimensions in an EQ-5D survey. This means that a person that has difficulties in one dimension will not affect nor be more likely to have problems in another dimension. For example a person that is “confined to bed” (level 3 mobility) will not be more likely to have problems in their usual activities than a person that has “no problems walking about” (level 1 mobility). This is done to be able to calculate the incidence of a constant or any level 3 dimension for the typical “average” CPC-person of each score. For example Appendix I show that according to the focus group a CPC-1 person will 70.8 percent of times have some sort of disability problem, disrupting the 11111 state of full health. This typical CPC-1 person will also 20.6 percent of times suffer any level 3 condition, most likely stemming from level 3 anxiety or depression. These results could be compared to a typical CPC-4 person that with these calculations will for certain (100 percent) be affected by both the constant and N^3. This is even though none of the level 3 dimensions alone reaches 100 percent.

EQ-5D was chosen as a result of its simplicity. The limited contact with the experts implies that the author has not affected the experts in any improper way. The assumption leads to no variation among the patients in each CPC group. Making these results meaningless for improvement efforts within the area, but should still be able to function in fulfilling its task in the estimation of costs and benefits in this analysis[58]. The following section will further describe how these translations from CPC-scores to EQ-5D gives rise to the QALY-weights.

4.4.2 Health utilities

Each health condition is associated to a certain QALY-weight that was estimated during a British population-study by Dolan (1997). He used the time trade-off method where he asked the respondents if they would consider to live on in some amount of years in their current health state (for example, frequent migraines) or to live fewer years at full health. Assuming a scenario with 10 years of migraines, the respondent may be indifferent between this health state and a lifetime of 7 years at full health. This would mean that each year with the health state frequent migraines is associated to a QALY of 0.7. The time trade-off method gives a cardinal value that follows under an assumption that choices are made without any risks. Practical issues in the time trade-off method is the choice of lifetime and the impact it has on the results. Another available technique is the Standard Gamble method that lets patients choose between two alternatives varying the probabilities in one of them. The last utility valuation method is the visual analogue scale, which is a rating scale based on psychometric theory. It lets the respondent point out the QALY weight on a scale where the best and worst possible health states are already attached.

Dolan (1997) shows how the deteriorating health gives worsening quality of life values compared to a person of full health. According to Drummond et al. (2005) studies have shown that measurements of preferences are similar regardless of demographic factors such as nationality, gender and income. Therefore the weights can be used to estimate life quality on a Swedish patient population as well. In later years Burström et al. (2013) has performed a Swedish experience-based value set for EQ-5D health states, using a general population health survey data-set. The Swedish weights will be used as a sensitivity analysis for this analysis as they are drawn in a Swedish setting. The reason they do not subject under the base-case is that they were created by respondents judging their own health state and does not include hypothetical conditions. This could limit their applicability on a CPC-population, where CPC 4 patients in a coma would be excluded.

For a full coefficient-list and QALY-weights see Appendix J. This paper will apply Dolan (1997) original approach and not the conservative that limits the QALY-weight to a score between 0-1. It has been argued that the vegetative state, associated to a CPC 4 patient is worse than death[59]. Also since the study does not exploit the indirect costs a negative QALY-weight will account for some of this shortage.

4.4.3 Calculation of EQ-5D results

When knowing what coefficients and which to use it is possible to calculate the QALY-weigh for the different conditions. For example in Dolan (1997) every theoretical condition is referred to by a sequence of digits, where 11111 is the state of full health with a score of 1. The calculation of each of the 243 possible conditions starts from the value 1 and subtracts from the score with every deviation. Except for the dimensions a constant is subtracted if any dimension reaches level 2 or 3, and if any level 3 is reached another harsher constant is added as well. In Appendix K the reader can explore a calculation example of the state 11223, which is asserted to a QALY-weight of 0.255 in Dolan (1997). Using the results from the focus group in Appendix I, it is possible to calculate different QALY scores for the typical CPC-patient’s condition. Data from Burström & Rehnberg (2006) showed in a large study, using Dolans’ conservative approach, that an QALY estimated for an average 65-69 year old person in Sweden is 0.81. This mean value ranges from 0.71-0.86 depending on which age group is observed. This is used to compare to the results obtained from this study where a CPC-1 patient is referred to a QALY-weight of 0.77, CPC-2 patient; 0.62; CPC-3 patient -0.08; and CPC-4 patient -0.36. This result strengthen the fact that commonly a CPC score of 1, 2 is considered a good outcome and 3, 4 is considered a bad outcome. For a full list of approaches and their QALY-weights see Appendix L.

4.4.4 Short-term perspective

With QALY-weights obtained it is possible to calculate an estimated effect for the hypothetical cohorts estimated from the LINC-study. The study starts with the same 6-month perspective as the LINC-study and attaches the QALY-weights to the number of days spent in each CPC-state instead of using survival as an outcome. This allows us to calculate the estimated QALYs saved per day for the entire cohort. This is depending on if the distribution between CPC-scores follow the results of mechanical CPR or manual CPR. The short-term effects for the 154 treated cohort shows that 4.58 QALYs will be saved following the CPC distribution of mechanical CPR and 3.84 QALYs, following the CPC distribution of manual CPR. This means that with a time horizon of only the first 6 months after the cardiac arrest the cohort is saving 0.74 QALYs if using mechanical CPR instead of manual CPR. This means that on average each of the 154 possible treatments would save 0.005 QALYs with this timeframe. The reader should remember that these results would differ if the analysis used another distribution than the one taken from the LINC study.

4.4.5 Long-term perspective

Dramatic changes of CPC between 3 and 12 months after a cardiac arrest are uncommon. Kajaste, & Kaste (1993) show that 23 percent of patients have a minor improvement and only 8 percent appeared to have worsened in this time period. Drysdale, Grubb, Fox, & O'Caroll (2000) looks at memory impairment at 8 months after the cardiac arrest and detects no signs of improvement during a three-year follow-up period. In chapter 4.1 we show that Phelps et al. (2013) study will be used to link together with data from the LINC-study. In this way we provide the effects up to 8 years (96 months). With this base this paper assumes that CPC-values are consistent from 6 months and forward. The only thing altering after that is an increased chance of death depending on what CPC-score the patients had at 6 months. This is applied because no information of patients after 6 months was available.

In Table 7, this paper investigates the linking of the results from Phelps and the LINC-study. This created a problem as the LINC-study only had one survivor that was evaluated as a CPC-4 person, meaning it is a small sample for long-term outcome. Overall the table shows that people survive at a higher degree in the LINC-study and one has to reason around this. It is known that in the LINC-study the average amount of days a person stays at the hospital until discharge after a cardiac arrest is 21.67 days with a median of 17 days. That same number for Phelps study was not available, but indications show that a typical patient in America is in for around 7-10 days[60]. This might also be the reason for the higher death rates shown during the first 6 months in Phelps study. The reason that patients stay a shorter time in an American hospital might be that they get paid per care event and not per hospital day. Also the US patients without health insurances does not have guaranteed healthcare that stretches past the acute care.

Table 7 Relationship between LINC-study and Phelps study

		Discharge form hospital		**At 6 months**	
		Number of persons	Survivor	Number of persons	Survivor
Phelps	CPC1	606	100 %	572	94 %
	CPC2	227	100 %	190	84 %
	CPC3	97	100 %	70	72 %
	CPC4	50	100 %	17	34 %
LINC	CPC1	149	100 %	146	98 %
	CPC2	49	100 %	49	100 %
	CPC3	21	100 %	17	81 %
	CPC4	1	100 %	1	100 %

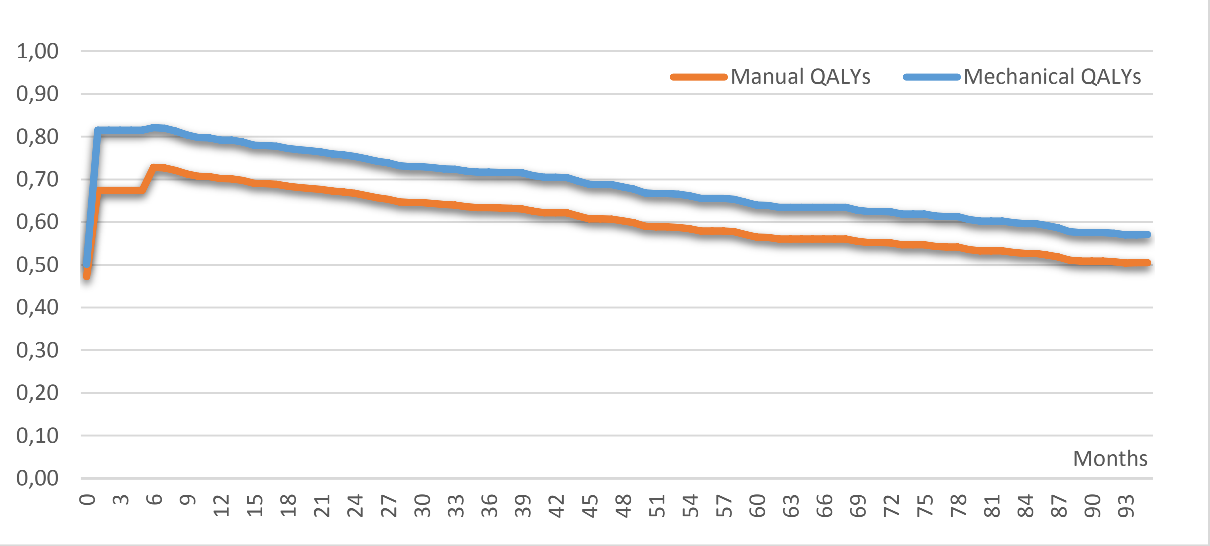
Since the relationship of survivors seems weak we will use the results from the LINC-study all the way up to 6 months. From this point the CPC-distribution will remain the same and start using the survival rates from Phelps at 6 months instead of hospital discharge. A new Kaplan-Meier survival rates starting at 6 months was created in Excel and can be seen in

Appendix E. When comparing the two survival graphs in the appendix, one can see that some of the former clear relationship between survival and CPC-score has been lost. However, after 6 months people with a CPC of 1 or 2 is still dying in a slower pace than those with a CPC of 3 or 4. This result strengthen the fact that commonly a CPC-score of 1, 2 is considered a good outcome and 3, 4 is considered a bad outcome.

4.4.6 Presentation of effects

Figure 6 shows the QALYs saved for the cohorts in each month, based on the short-term and the long-term calculations. The space between the two lines is the gained QALYs for mechanical CPR compared to manual CPR. The graph shows non-discounted effects. The first 6 months has been calculated so that the QALYs gained during ICU stay, hospital stay and up to one month occurs in month 1. The gained effects made during month two to six has been divided by five and that is why they are linear at this point in time. The graph also indicates that effects do keep adding up when looking at a longer time horizon. This might be of value for decision-makers that not only look at survival, but also instead want the analysis with a longer time horizon.

FIGURE 6 SAVED QALYS PER MONTH, PER COHORT



As the aggregated effects do get larger with time, the uncertainty in the result is also increasing. The 8 year discounted effects of being treated with mechanical CPR gives 7.14 (5.96-6.94) QALYs gained for the 154 person cohort. This implies that for each treated OHCA patient on average 0.046 (0.039-0.045) QALYs will be saved during this timeframe, remembering that only approx. 13 treated patients per group survived up to 6 months. The numbers in the brackets are calculated with the Swedish and conservative approach.

This is the first calculation of its kind and it shows that the largest gains in QALYs saved per month for mechanical CPR is being made during the period from 1-6 months after ROSC. This is mainly because more patients in the treated cohort are alive during this time.

5. Results

In this chapter, the base-case analysis results for a short-term (6 months) and long-term (8 years) along with sensitivity scenarios will be presented. The costs will be presented from a health care budget perspective.

5.1 Base-case analysis

The result is presented in terms of direct cost only. The cost estimation for the representative example of a pre-hospital area with 154 cardiac arrest cases a year and 8 LUCAS devices shows the following results in Table 8, in SEK (2013). The results should be viewed as additional costs for the mechanical device. The table refers to the hospital stay costs as an extra cost for mechanical CPR compared to manual CPR, inferring that manual CPR is not free of charge.

With the assumptions explained in chapter 4 the results indicate that in a short-term (6 months) mechanical CPR is associated with 508,291 SEK per QALY gained. In Table 2 this is referred to as a "high" cost per QALY gained. The vague thresholds created for the cost-effectiveness principle say that these costs need to fall below 500,000 SEK per QALY gained to be considered as moderate costs. When stretching the timeframe up to 8 years after the cardiac arrest, the result of the analysis shows that the cost is 50,508 SEK per QALY gained, indicating a "low" cost. The costs differ between the two columns because in the long-term the costs are discounted at 3 percent.

The reason the results differ so much between the two time horizons are that the costs for treating patients with a mechanical device are the same no matter how long after treatment the decision-maker believes to stretch his timeframe. If for example one would only look at survival at a certain point then there would be no difference in effects and you could take on the cost-minimizing analysis. Then mechanical CPR would be far more expensive than manual CPR and we could conclude that mechanical CPR is dominated by manual CPR. When instead extracting the time horizon to 6-months and using CPC-scores to calculate QALYs, the effects come at a "high" ICER cost. In this paper we have also extracted the effects beyond the typical 6 months or 1 year to the same period as an economic lifetime of the mechanical device. In this way the decision-maker can see effects further down the line from the costs they invested in the mechanical devices. This implies that the money invested is more cost-effective than what could be believed from viewing only survival as an outcome.

TABLE 8 COST-EFFECTIVENESS FOR MECHANICAL CPR VS. MANUAL CPR IN A OHCA SETTING (2013 SEK)

	Short-term (6 months)		Long-term (8 years)	
	Costs	QALYs	Costs	QALYs
Mechanical	373,626	4.58	360,736	59.90
Machine	287,300		274,409	
Treatment	41,696		41,696	
Extra Hospital stay	44,631		44,631	
Manual		3.84		52.76
Difference	373,626	0.74	360,736	7.14
ICER, SEK	508,291		50,508	

5.2 Sensitivity Scenarios

The results of the base-case analysis are based on the assumptions that have been accounted for in the previous chapter 4. Different sensitivity scenarios were performed to test the impact on the main result. In Table 9 the sensitivity analysis of one variable at a time is presented. Revealing that the driving factors in result stems from the time horizon of the effects and the number of devices needed to treat the cohort. Other scenarios checked are which QALY-calculation approach to use, which discounting percentages or if we want to change the costs at ICU and hospital stay. The thesis aims at applying a Swedish setting and by using the Burström weights we obtain a higher ICER cost for mechanical CPR. This is based on the knowledge that over the 8-year discounted period the mechanical device saves 5.963 QALYs compared to saving 7.142 using Dolans calculations. One possible way to implement these Swedish weights with more ease would be to assume the same quality of life for a person with CPC-score of 4 and one with a score of 3. In this case we could use the Swedish weights, even though they are not created to include hypothetical conditions (CPC-score of 4). Keeping the same QALY-approach throughout the analysis timeline is more practical and serves easier for translating the results to other non-Swedish populations.

Using a 5 percent discounting rate to both costs and effects adds 2,471 SEK to the cost per gained QALY. If disregarding discounting we can subtract 2,789 SEK. If we had used the newer QALY-weights with a Swedish approach, then effects between the two treatment groups would be smaller than presented. The cost per gained QALY would be 9,985 SEK higher and even more when looking with a short-term time horizon.

TABLE 9 UNIVARIATE SENSITIVITY ANALYSIS

Parameter	Total benefit	Total Annual Costs (SEK)	ICER (SEK)
Baseline	7.142	360,736	50,508
Discount rate			
0 percent	7.830	373,626	47,719
5 percent	6.744	357,298	52,979
Number of devices			
8 devices (19.25 treatments/device)	7.142	269,266	37,701
30 devices (5.13 treatments/device)	7.142	772,350	108,141
Machine costs			
-15 percent & high usage	7.142	314,780	44,074
+15 percent & low usage	7.142	440,233	61,639
Time horizon			
5 years	5.010	360,736	72,006
1 year	1.287	373,626	290,402
6 months	0.735	373,626	508,291

QALY-calculation			
Conservative approach	6.937	360,736	52,000
Swedish approach	5.963	360,736	60,493
Hospital stay			
Cost per day 2,502	7.142	368,739	51,629
Cost per day 4,046	7.142	352,574	49,366
Added cost per ICU stay 15,840	7.142	351,276	49,184
Added cost per ICU stay 20,160	7.142	370,195	51,833

Some multivariate sensitivity analysis should also be of value for the decision-maker. If for example believing that the pre-hospital region do not take on 12.83 treatments per year, they are here presented with cases where more or less devices are supplied for the annual OHCA cases. If believing that each device can be expected to deal with as many as 19.25 treatments per year they might buy 8 devices at 15 % higher costs. This would lead to a cost per QALY gained of 45,122 SEK in the 8 year timeframe and 455,225 SEK per QALY gained with a 6 months' timeframe. If the decision-maker instead believes that each device will be applied to fewer treatments each year (5.13) they will in the case of this representative example buy 30 devices and we could also assume 15 % lower costs. This would lead to a cost per QALY gained of 92,054 SEK in the 8-year timeframe and 929,807 SEK per QALY gained with a 6 months' timeframe, varying plenty from baseline results.

The baseline results stems from a case where a region has 128 OHCA cases and 12 mechanical devices. The numbers of devices are based on Appendix B that shows for example that Uppsala had 50 OHCA cases and 10 devices, meaning 5.00 treatments per device. The decision-maker for Uppsala would then be better of looking at the cost per QALY gained for the case of 30 devices per 154 OHCA cases (5.13 treatments per device) than the baseline results (12.83 treatments per device).

6. Discussion

The purpose of this paper has been to perform a cost-effectiveness analysis to explore the cost-effectiveness of mechanical CPR compared to manual CPR. This is a current topic as a recent large randomized controlled trial has been published in the LINC-study. Studies have shown that there does not exist any change in survival between treatments. This paper has with the help of the neurological outcomes in the LINC-study tried to show that some difference in quality-adjusted life years are there to be exploited. It should be remembered that given another survival distribution results from the calculations would be altered.

This paper presented a typical representative example of SUS, Malmö pre-hospital region where 12 devices deals with 154 OHCA cases. The results in this paper hope to help the decision-maker when evaluating whether to purchase mechanical devices for treatment of OHCA patients. The paper hope to show that survival is not the only effect-measurement available and that the benefits of mechanical CPR add up with a longer timeframe. The main result with an 8-year timeframe for effects, indicate that when comparing mechanical CPR to manual CPR the costs per QALY gained are considered as “low”, according to The Swedish National board of Health and Welfare. If instead only applying the 6-months results from the LINC-study the costs per QALY gained are “high" according to. The results indicate that both the number of treatments per device and year and the timeframe used to measure effects do drive the costs and effect a great deal. Implying that decision-maker need to perceive the number of possible treatments the devices when thinking about buying mechanical devices.

This study does display that CPC-scores are not an optimal outcome measurement and have its share of critique. However this study does fully explore the CPC-scale and tries to withdraw all information available to give meaning to the results. Much of this analysis builds on the assumption that the focus group is able to derive the CPC-score into possible EQ-5D answers. The Delphi method is used by the Swedish national board of health and welfare (Socialstyrelsen) as to make consensus in difficult decisions within health care guidelines. Possible weakness to the method could be that the experts did not put enough time and effort into the survey. Also a consensus among expert does not necessarily mean it is the correct prediction. Also these are predictions the experts are assessing and those almost always come with uncertainty. Another limitation is the assumption of independence among the different dimensions in EQ-5D. Otherwise the calculation of the constant and N^3 would not be possible at an aggregated level. In chapter 4.4.1 we talk about added levels to the dimension but not added dimensions in the Health Related Quality of Life-instrument. The last limitation is that we cannot for natural reasons differ between survivors and non-survivors in terms of extra hospital stay costs. We do instead calculate the cost per average OHCA patient depending on if they were treated with mechanical CPR or manual CPR.

The results in this paper also suffer from not obtaining any CPC varying costs to society for the patients after their hospital stay. Decision-makers should regard the effects of these limitations when setting priorities. In this paragraph we discuss the usage of mechanical CPR in a societal view. Mechanical CPR could possibly effect in more ways than those that have been explored in this analysis. Several studies identify that usage of seatbelt will halve the risk of injury or death at a possible crash during transport[61]. Slattery & Silver (2009) acknowledge the possible strategies for mitigating the risks by for example improving ambulance safety standards or freeing up providers’ hands by the availability of e.g. mechanical CPR devices. If assuming that mechanical CPR lets the paramedics be seated in the back during emergency calls L. Becker (2003) demonstrated that compared to being unrestrained the passengers were less likely to suffer from fatal-, severe- and moderate- injuries. This indicate to the possibility of mechanical CPR having even lower costs per

QALY gained for the society and it makes rise for a CEA study of mechanical CPRs during emergency ambulance ride.

Jones & Lee (2005) indicated through a questionnaire in Hong Kong that back pain in ambulance officers could be linked to CPR as it is often undertaken in compromised positions. There are, however, no reports of any relationship between CPR and the prevalence of back pain in ambulance officers. Still this is an area worth exploring for future studies that want to compare the utility gains for mechanical CPR.

Blomqvist, Mattson, & Hellström-Hyson (2012) performed a small qualitative study at pre-hospital CPR where they examined how a mechanical CPR system has affected paramedics working environment. Opinions on mechanical CPR impact were unanimously positive as it lowered stress, increased safety during transport and provided better contact with patients. They also emphasized the usage of mechanical CPR as a tool only and that the skill of regular manual CPR still needs to be applied on patients that do not fit and in case the mechanical device abruptly stops working.

Axelsson (2008) shares the experiences from mechanical CPR at OHCA, in the Gothenburg area. The report strengthens the former reports but also speaks of some deviations during the study period. Experiences such as a blister on the body from the suction cup sliding, complaints about that the equipment being too big and heavy to be included in the standard equipment. They spoke of the occurrence of rib fractures on patients, which is a phenomenon that has been better documented in a book by Smekal (2013). His studies have shown that any rib fracture is 14-15 percent more likely to appear from mechanical CPR than from manual CPR. These effects, from using mechanical CPR compared to manual CPR, are likely to affect the QALY gained negatively among survivors.

Possible future research could be following up OHCA patients with a longer timeframe to see where they end up after their discharge from hospital. This research would hopefully divide results by both age groups and CPC-scores. Other possibilities are also to use a more exploring measurement than the CPC-scale and maybe let patients themselves answer a Health Related Quality of Life-instruments as soon as they are able.

7. Conclusion

This thesis aims at giving a value for decision-makers when comparing mechanical CPR vs. manual CPR in OHCA, in Sweden. It includes a mapping of CPC-scores to QALY-weights and calculates a short- and long-term utility for mechanical CPR. This study believes to have given a transparent overview of a representative example facing decision-makers. Leaving them with the possibility to look at the value of mechanical CPR over a longer period and not just in the short run and with survival as the only outcome. The study concludes that if decision-makers are willing to live with uncertainties discussed and argued in this paper, then mechanical devices are available at “low” costs per QALY gained for the patients treated timeframe. On top of this, the author believes that mechanical device should be viewed as a tool to be more valuable the longer it is expected to function. The study states that this 8-year timeframe is a suitable time-horizon for decision-makers to calculate the effects as this is the economic lifetime for a LUCAS device and that surviving patients are expected to live on after a cardiac arrest even though an OHCA population has a mean age in the older 60s.

When looking at patient utilities in the QALY-weights obtained from CPC-scores. The paper concludes that recent research in the area is correct to divide neurological outcomes in good (CPC 1,2) and bad (CPC 3,4) outcomes instead of using the whole scale. The QALY-weights obtained from results by the focus group should not be used in medical evaluation but could still work as an indicator of economic results. Future research should look to see where patients end up based on the CPC-scores, to be able to more accurately evaluate long-term costs and effects of mechanical CPR and manual CPR. This study does however believe to have done the best with the research available.

Appendix

A. Cerebral Performance Category Scale
B. The Study Protocol for the LINC
C. LINC CPC-scores
D. Kaplan-Meier estimates: Survival with start at discharge from hospital
E. Kaplan-Meier estimates: Survival with start at 6 months
F. Time in days from ROSC to ICU/Hospital discharge
G. Dimensions in EQ-5D
H. Example of EQ-5D survey
I. Results from Focus-group
J. Dolan and Burström Coefficients
K. Calculation example of state 11223
L. QALY-weights
M. Cost table
N. Costs for hospital stay

Appendix A

Cerebral Performance Category Scale[62]

- CPC 1 - Good cerebral performance: conscious, alert, able to work, might have mild neurologic or psychological deficit.
- CPC 2 - Moderate cerebral disability: conscious, sufficient cerebral function for independent activities of daily life. Able to work in sheltered environment.
- CPC 3 - Severe cerebral disability: conscious, dependent on others for daily support because of impaired brain function. Ranges from ambulatory state to severe dementia or paralysis.
- CPC 4 - Coma or vegetative state: any degree of coma without the presence of all brain death criteria. Unawareness, even if appears awake (vegetative state) without interaction with environment; may have spontaneous eye opening and sleep/awake cycles. Cerebral unresponsiveness.
- CPC 5 - Brain death: apnea, areflexia, EEG silence, etc

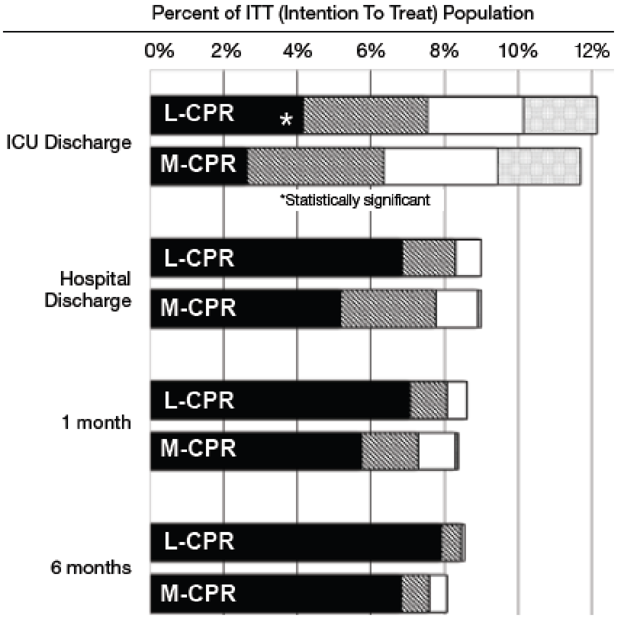
Appendix B

The Study Protocol for the LINC[63]

City	Nr. Hospitals	Nr. Paramedics	Treatments / year	Nr. Lucas	Treatments / LUCAS	Paramedics / LUCAS
Uppsala	1	85	50	10	5.00	8.50
Gävle	1	106	55	9	6.11	11.78
Västerås	1	55	55	8	6.88	6.88
Malmö	1	150	140	12	11.67	12.50
Dorset	2	100	135	26	5.19	3.85
Utrecht	8	275	225	50	4.50	5.50
Average	**2.33**	**128.50**	**110**	**19.17**	**5.74**	**6.70**

Appendix C

LINC CPC-scores[64]



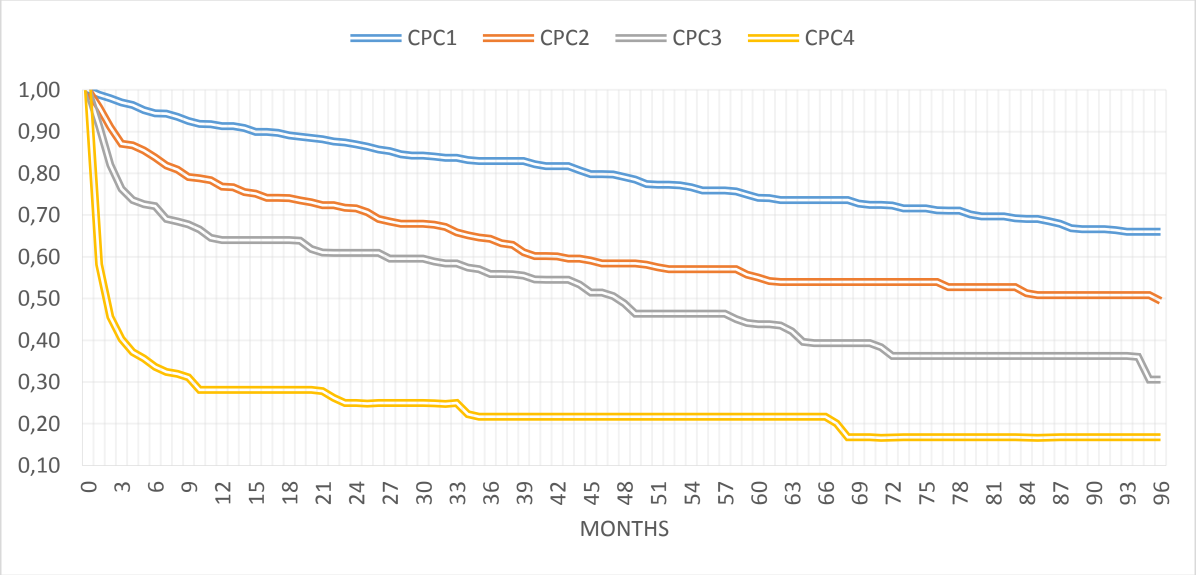
n (%)

CPC 1 ■	CPC 2 ▨	CPC 3 ☐	CPC 4 ░	p
54 (4.2%)	44 (3.4%)	34 (2.6%)	26 (2.0%)	0.04
34 (2.6%)	48 (3.7%)	40 (3.1%)	29 (2.2%)	
89 (6.8%)	19 (1.5%)	9 (0.7%)	0 (0%)	0.08
67 (5.2%)	33 (2.6%)	15 (1.2%)	1 (0.1%)	
92 (7.1%)	13 (1.0%)	7 (0.5%)	0 (0%)	0.17
74 (5.7%)	20 (1.6%)	13 (1.0%)	1 (0.1%)	
103 (7.9%)	7 (0.5%)	1 (0.1%)	0 (0%)	0.29
88 (6.8%)	10 (0.8%)	6 (0.5%)	0 (0%)	

The p-value presented to the far right is the probability of obtaining the observed sample results (or a more extreme result) when the null hypothesis (LUCAS saving more people to a CPC specific CPC-score) is actually true. The significance level is traditionally set to 5 or 1 percent, but could with lower presumption against the hypothesis be moved to a 10 percent level.

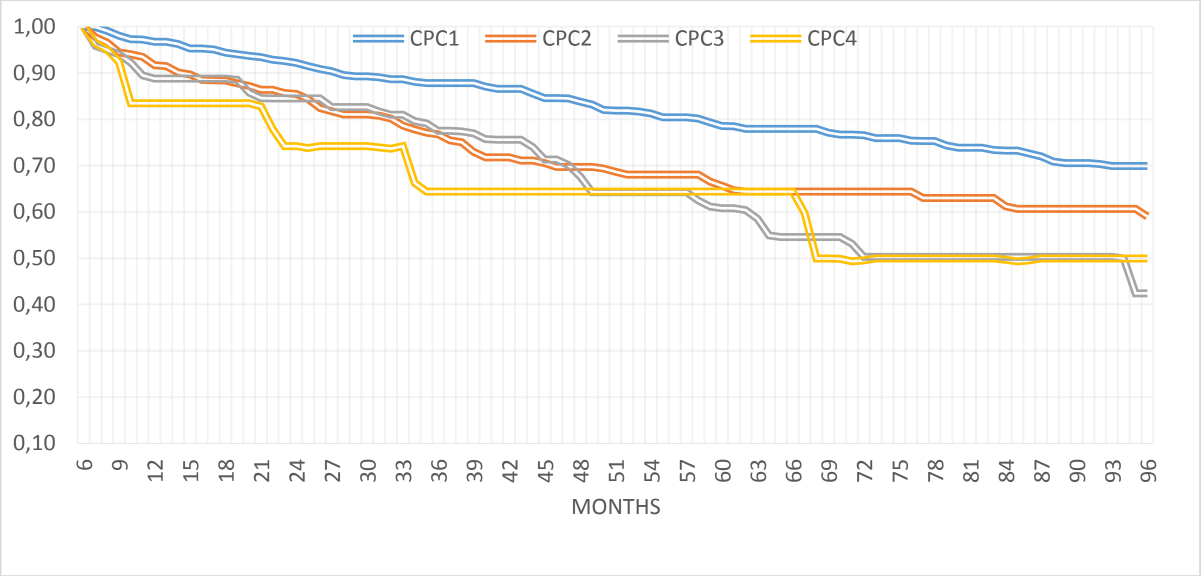
Appendix D

Kaplan-Meier estimates: Survival with start at discharge from hospital



Appendix E

Kaplan-Meier estimates: Survival with start at 6 months



Appendix F

Time in days from ROSC to ICU/Hospital discharge[65]

CPC at ICU discharge	N (%)	Median (Q1-Q3)	Range	Mean (SD)
CPC 1	87 (28.2 %)	4.0 (1-7)	0-30	5.18 (5.5)
CPC 2	92 (29.9 %)	4.0 (2-7)	0-27	5.14 (4.9)
CPC 3	74 (24.0 %)	4.0 (1-7)	0-25	5.15 (5.4)
CPC 4	55 (17.9 %)	1.0 (0-3)	0-14	2.42 (3.4)
Total	308 (100 %)	3.0 (1-6)	0-30	4.67 (5.1)
CPC at Hospital discharge				
CPC 1	155 (66.8 %)	17.0 (11-28)	0-106	20.37 (14.1)
CPC 2	52 (22.4 %)	17.5 (11-31)	0-61	21.77 (14.7)
CPC 3	24 (10.3 %)	25.5 (12-47)	0-84	30.13 (22.7)
CPC 4	1 (0.4 %)	14.0 (14-14)	14-14	14.00 ()
Total	232 (100 %)	17.0 (11-29)	0-106	21.6715.5)

Appendix G

Dimensions in EQ-5D[66]

Mobility

1. No problems walking about
2. Some problems walking about
3. Confined to bed

Self-Care

1. No problems with self-care
2. Some problems washing or dressing self
3. Unable to wash or dress self

Usual Activities (e.g. work, study, housework, family or leisure activities)

1. No problems with performing usual activities
2. Some problems with performing usual activities
3. Unable to perform usual activities

Pain/Discomfort

1. No pain or discomfort
2. Moderate pain or discomfort
3. Extreme pain or discomfort

Anxiety/Depression

1. Not anxious or depressed
2. Moderately anxious or depressed
3. Extremely anxious or depressed

Appendix H

Example of EQ-5D survey

What is the probability that an average person with a value of 2 on CPC scale answers:

- No problems walking about ___________%
- Some problems walking about ___________%
- Confined to bed ___________%

Additional Comments: ____

Appendix I

Results from Focus-group

Dimension	*CPC 1*	*CPC 2*	*CPC 3*	*CPC 4*
Mobility level 1	91.0 %	64.0 %	18.0 %	0.0 %
Mobility level 2	9.0 %	34.0 %	38.0 %	2.0 %
Mobility level 3	0.0 %	2.0 %	44.0 %	98.0 %
Self-care level 1	94.0 %	74.0 %	6.0 %	1.0 %
Self-care level 2	6.0 %	26.0 %	32.0 %	4.0 %
Self-care level 3	0.0 %	0.0 %	62.0 %	95.0 %
Usual-activity level 1	93.0 %	76.0 %	3.0 %	1.0 %
Usual-activity level 2	7.0 %	21.0 %	10.0 %	1.0 %
Usual-activity level 3	0.0 %	3.0 %	87.0 %	98.0 %
Pain/Discomfort level 1	72.0 %	61.0 %	35.7 %	34.0 %
Pain/Discomfort level 2	26.0 %	28.0 %	30.7 %	24.0 %
Pain/Discomfort level 3	2.0 %	11.0 %	33.7 %	42.0 %
Anxiety/Depression level 1	51.0 %	45.0 %	16.0 %	2.5 %
Anxiety/Depression level 2	30.0 %	34.0 %	30.0 %	13.8 %
Anxiety/Depression level 3	19.0 %	21.0 %	54.0 %	83.8 %
Constant	**70.8 %**	**90.1 %**	**100.0 %**	**100.0 %**
N^3	**20.6 %**	**33.2 %**	**99.2 %**	**100.0 %**

N^3 = if any dimension has a level 3 score

Appendix J

Dolan and Burström Coefficients[67]

	Dolan (1997)	Burström *et al.* (2013)
Dependent Variable	1-TTO	TTO
Intercept	0.081	0.969
Mobility		
Level 2	0.069	-0.067
Level 3	0.314	-0.125
Self-care		
Level 2	0.104	
Level 3	0.214	
Level 2 or 3		-0.028
Usual Activities		
Level 2	0.036	-0.101
Level 3	0.094	-0.136
Pain/Discomfort		
Level 2	0.123	-0.035
Level 3	0.386	-0.090
Anxiety/Depression		
Level 2	0.071	-0.055
Level 3	0.236	-0.208
N3^	0.269	-0.043

N^3 = If any dimension has a level 3 score

Appendix K

Calculation example of state 11223

Full health	***1.000***
Constant term (for any dysfunctional state)	-0.081
Mobility: level 1	0.000
Self-care: level 1	0.000
Usual activities: level 2	-0.036
Pain or discomfort: level 2	-0.123
Anxiety or depression: level 3	-0.236
Level 3 occurs within at least one dimension	-0.269
Therefore, the estimated value for 11223 =	0.255

N^3 = If any dimension has a level 3 score

Appendix L

QALY-weights

Approach to calculation	*CPC 1*	*CPC 2*	*CPC 3*	*CPC 4*
Dolan Conservative	0.77	0.62	0.00	0.00
Dolan Original	0.77	0.62	-0.08	-0.36
Swedish Weights	0.88	0.81	0.52	0.41

Appendix M

Cost table

	15 % Higher and Low usage	Best Estimate	15 % Lower and High usage
Machine cost	108 100 kr	94 000 kr	79 900 kr
Machine life years	8	8	8
Machine costs per year	**13 513 kr**	**11 750 kr**	**9 988 kr**
Power supply	3 450 kr	3 000 kr	2 550 kr
Power supply life years	8	8	8
Total power supply costs per year	**431 kr**	**375 kr**	**319 kr**
Battery charger	8 855 kr	7 700 kr	6 545 kr
Battery charger life years	8	8	8
Number of LUCAS per Battery charger	*20,00*	*12,00*	*8*
Total battery charger costs per LUCAS per year	**55 kr**	**80 kr**	**102 kr**
Average Battery cost (no discount)	6 900 kr	6 000 kr	5 100 kr
Average Battery cost (8 years) discounted 3%	6 331 kr	5 505 kr	4 679 kr
Average Battery cost (8 years) discounted 5%	6 003 kr	5 220 kr	4 437 kr
Battery life years	3	3	3
Number of batteries needed	*3*	*2*	*2*
Total battery costs per year (no discounting)	**6 900 kr**	**4 000 kr**	**3 400 kr**
Total battery costs per year (discounted 5% 3%)	**6 331 kr**	**3 670 kr**	**3 120 kr**
Total battery costs per year (discounted 5% 5%)	**6 003 kr**	**3 480 kr**	**2 958 kr**
Service cost per year (no discounting)	**6 900 kr**	**6 000 kr**	**5 100 kr**
Service cost per year (8 years) discounted 3%	**6 236 kr**	**5 423 kr**	**4 609 kr**
Service cost per year (8 years) discounted 5%	**5 853 kr**	**5 090 kr**	**4 326 kr**
Average Training costs for 1 paramedic 1h a year (no discount)	259 kr	259 kr	259 kr
Average Training costs for 1 paramedic 1h a year (8 years) discounted 3%	234 kr	234 kr	234 kr
Average Training costs for 1 paramedic 1h a year (8 years) discounted 5%	220 kr	220 kr	220 kr
Number of parademics on each LUCAS	*12,50*	*6,70*	*3,85*
Training costs per year (1 year/no discount)	**3 238 kr**	**1 736 kr**	**996 kr**
Training costs per year (discounted 3%)	**2 926 kr**	**1 569 kr**	**900 kr**
Training costs per year (discounted 5%)	**2 746 kr**	**1 473 kr**	**845 kr**
Total cost for LUCAS per year (no discounting)	**31 037 kr**	**23 942 kr**	**19 905 kr**
Total cost for LUCAS per year (discounted 3%)	**29 492 kr**	**22 867 kr**	**19 038 kr**
Total cost for LUCAS per year (discounted 5%)	**28 985 kr**	**22 581 kr**	**18 821 kr**
Suction Cup price per treatment	285 kr	285 kr	285 kr
Number of OHCA-treatments for LUCAS per year	*146,3*	*146,3*	*146,3*
Total Suction Cup costs per year	**41 696 kr**	**41 696 kr**	**41 696 kr**
Extra Hospital Costs per OHCA patient	305 kr	305 kr	305 kr
Number of OHCA-treatments for LUCAS per year	*146,3*	*146,3*	*146,3*
Total Hospital costs per year for cohort	**44 631 kr**	**44 631 kr**	**44 631 kr**
Total 8 years cost for 30 LUCAS devices (no discounting)	1 017 424 kr	804 575 kr	683 466 kr
Total 8 years cost for 30 LUCAS devices (discounted 3%)	971 094 kr	772 350 kr	657 460 kr
Total 8 years cost for 30 LUCAS devices (discounted 5%)	955 867 kr	763 756 kr	650 954 kr
Total 8 years cost for 8 LUCAS devices (no discounting)	334 619 kr	277 859 kr	245 564 kr
Total 8 years cost for 8 LUCAS devices (discounted 3%)	322 264 kr	269 266 kr	238 629 kr
Total 8 years cost for 8 LUCAS devices (discounted 5%)	318 204 kr	266 974 kr	236 894 kr
Total 8 years cost for 12 LUCAS devices (no discounting)	458 765 kr	373 626 kr	325 182 kr
Total 8 years cost for 12 LUCAS devices (discounted 3%)	440 233 kr	360 736 kr	314 780 kr
Total 8 years cost for 12 LUCAS devices (discounted 5%)	434 143 kr	357 298 kr	312 177 kr

Appendix N

Costs for hospital stay

Department		*Daily costs*
Cardiovascular		**2,983 SEK**
	Hospital days, normal fee	2,983 SEK
Neurology and rehabilitation medicine		**3,535 SEK**
	Hospital days, normal fee	3,584 SEK
	Nursing day	3,520 SEK
	Hospital days, normal fee**, inpal pa**t	3,500 SEK
Internal medicine		**2,505 SEK**
	Hospital days, normal fee	2,502 SEK
Geriatric		**4,046 SEK**
	Nursing day	4,021 SEK
	Hospital days, normal fee**, inpal pat**	4,071 SEK
Average cost per day		**3,266 SEK**
Cost per day (ICU)		**18,000 SEK**
	Popmin	15,840 SEK
	Vårdmin	20,160 SEK

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[1] (Rubertsson et al., 2013)

[2] ("Nationella riktlinjer för hjärtsjukvård -Bilaga 3 till beslutsstödsdokument – Metod," 2008)

[3] (Rubertsson et al., 2013)

[4] (Herlitz, 2013; "Socialstyrelsen.se," 2014).

[5] (Eftestøl, Sunde, & Steen, 2002;105(9); Paradis, Martin, Rivers, & al., 1990;263(8); Sato, Weill, Sun, & al., 1997;25(5); Steen, Liao, Pierre, Paskevicius, & Sjöberg, 2002;55(3))

[6] (Herlitz, 2013; Nolan, Deakin, Soar, Böttiger, & Smith, 2005)

[7] (Rubertsson, Grenvik, Zemgulis, & Wiklund, 1995;23(12))

[8] (Olasweengen, Wik, & Steen, 2008;76(2); Wik et al., 2005)

[9] (Westfall, Krantz, Mullin, & Kaufman, 2013; 41(7))

[10] (Rubertsson et al., 2013)

[11] (Perkins, Woollard, Cooke, Deakin, & al., 2010; Tenhunen et al., 2014)

[12] ("Läkemedelsförmånsnämndens allmäna råd," 2003)

[13] (Drummond, Sculpher, Torrance, O'Brien, & Stoddart, 2005)

[14] (Jönsson, 1999)

[15] (Drummond et al., 2005)

[16] (Drummond et al., 2005)

[17] (Drummond et al., 2005)

[18] TLV, is a central government agency whose remit is to determine whether a pharmaceutical product or dental care procedure shall be subsidized by the state. We also contribute to quality service and accessibility of pharmacies.

[19] ("Läkemedelsförmånsnämndens allmäna råd," 2003)

[20] (Drummond et al., 2005)

[21] (Drummond et al., 2005)

[22] (Drummond et al., 2005)

[23] (Bernfort, 2012)

[24] (Drummond et al., 2005)

[25] ("Nationella riktlinjer för hjärtsjukvård -Bilaga 3 till beslutsstödsdokument – Metod," 2008)

[26] ("Nationella riktlinjer för hjärtsjukvård -Bilaga 3 till beslutsstödsdokument – Metod," 2008)

[27] (Torgerson & Raftery, 1999)

[28] ("Läkemedelsförmånsnämndens allmäna råd," 2003)

[29] (Kobelt, 2002)

[30] (Herlitz, 2013; "Plötslig hjärtdöd, en temaskrift från Hjärt-Lungfonden, 2006," 2006)

[31] (Eftestøl et al., 2002;105(9); Paradis et al., 1990;263(8); Sato et al., 1997;25(5); Steen et al., 2002;55(3)) (Herlitz, 2013; Nolan et al., 2005)

[32] (Rubertsson et al., 1995;23(12))

[33] (Olasweengen et al., 2008;76(2); Wik et al., 2005)

[34] (Association, 2010)

[35] (Steen, Liao, Pierre, Paskevicius, & Sjöberg, 2003;58(2))

[36] (Corporation)

[37] (Herlitz, 2013; "Plötslig hjärtdöd, en temaskrift från Hjärt-Lungfonden, 2006," 2006)

[38] (Cummins RO et al., 1991)

[39] (Jennett B & M, 1975)

[40] (Herlitz, 2013)

[41] (Andersson et al., 2011)

[42] (L. B. Becker, Aufderheide, & al., 2011)

[43] (J. W. Hsu, Madsen, & Callaham, 1996; Rittenberger, Raina, Holm, Joo Kim, & Callaway, 2011;82; Stiell et al., 2009;53)

[44] ("HLR.nu," 2012)

[45] (Engdahl, Bång, Lindqvist, & Herlitz, 2003; Graves et al., 1997)

[46] The paper present one more animal study not included in the table.

[47] (Olsson & Steen, 2008)

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[48] (Rubertsson et al., 2013;21:5)
[49] (Bernfort, 2009)
[50] (Cummins RO et al., 1991)
[51] (Arnwald, Lindroth, & von Schenck, 2014)
[52] (Ekonomifakta, 2014; SCB, 2014)
[53] (Rubertsson et al., 2013)
[54] (Smekal, 2014)
[55] (Herlitz, 2013) p. 57
[56] (J. W. Hsu et al., 1996)
[57] (Carr & Higginson, 2001)
[58] (Ranstam, Robertsson, W-Dahl, Löfvendahl, & Lidgren, 2011)
[59] (Patrick, Starks, Cain, Uhlmann, & Pearlman, 1994)
[60] (Mayo, 2014; O'Riordan, 2010; Villegas, 2014)
[61] (L. Becker, 2003; Petzäll, 2008; Slattery & Silver, 2009)
[62] (L. B. Becker et al., 2011;124)
[63] (Rubertsson et al., 2013;21:5)
[64] (Rubertsson et al., 2013)
[65] (Rubertsson et al., 2013)
[66] (Dolan, 1997)
[67] (K Burström et al., 2013; Dolan, 1997)

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