Influence of The Education and Training of Prehospital Medical Crews on Measures of Performance and Patient Outcomes

HANS BLOMBERG
Abstract

Prehospital care has developed dramatically the last decades with the implementation of new devices and educational concepts. Clinical decisions and treatments have moved out from the hospitals to the prehospital setting. In Sweden this has been accompanied by an increase in the level of competence, i.e. by introducing nurses in the ambulances. With some exceptions the scientific support for these changes is poor.

This thesis deals with such changes in three different subsets of prehospital care: Cardiopulmonary resuscitation (CPR), the stroke chain of survival and trauma care.

We assessed the performance of ambulance crews during CPR, using a mechanical compression device, as compared to CPR using manual compressions. There was a strikingly poor quality of compressions using the mechanical device compared to CPR with manual compressions. The result calls for caution when implementing a chest compression device in clinical practice and reinforce the importance of randomised controlled trials to evaluate new interventions. Careful attention should be given to the assurance of correct application of the device. Further implementation without evaluation of the quality of mechanical compressions in a clinical setting is discouraged.

Among patients with a prehospital suspicion of stroke we analysed the ambulance nurses’ ability to select the correct patient subset eligible for a CT scan as a preparation for potential thrombolysis. The results do not support an implementation of a bypass of the emergency department, using ambulance nurse competence to select patients eligible and suitable for a CT scan without a preceding assessment by a physician.

The association between the Prehospital Trauma Life Support (PHTLS) course and the outcome in victims of trauma was analysed in two observational studies. A study covering one county gave some support for a protective effect from PHTLS, but the estimate had a low precision. A nationwide study, covering all of Sweden, could not confirm those results. Although there was a reduction in mortality over time coinciding with the implementation of PHTLS, it did not appear to be associated with the implementation of PHTLS. Thus, we could not detect any clear beneficial impact of the PHTLS course on the outcome of trauma patients.

Keywords: ambulance, prehospital, education, CPR, stroke, trauma, outcome

Hans Blomberg, Uppsala University, Department of Surgical Sciences, Anaesthesiology and Intensive Care, Akademiska sjukhuset, SE-751 85 Uppsala, Sweden.

© Hans Blomberg 2013

ISSN 1651-6206
ISBN 978-91-554-8589-4
urn:nbn:se:uu:diva-192629 (http://urn.kb.se/resolve?urn=nbn:se:uu:diva-192629)
"As honest as possible"

Shinya Yamanaka
This thesis is based on the following papers, which are referred to in the text by their Roman numerals.

I  Poor chest compression quality with mechanical compressions in simulated cardiopulmonary resuscitation: a randomized, crossover manikin study.
   Hans Blomberg, Rolf Gedeborg, Lars Berglund, Rolf Karlsten, Jakob Johansson

II Agreement between ambulance nurses and physicians in assessing stroke patients.
   Hans Blomberg, Erik Lundström, Henrik Toss, Rolf Gedeborg, Jakob Johansson
   Submitted for publication.

III Prehospital Trauma Life Support (PHTLS) training of ambulance caregivers and the impact on survival of trauma victims.
   Jakob Johansson, Hans Blomberg, Bodil Svennblad, Lisa Wernroth, Håkan Melhus, Liisa Byberg, Karl Michaelsson, Rolf Karlsten, Rolf Gedeborg

IV Impact of Prehospital Trauma Life Support (PHTLS) training of ambulance caregivers on the outcome of traffic injury victims - a nation-wide study.
   Hans Blomberg, Bodil Svennblad, Karl Michaelsson, Liisa Byberg, Jakob Johansson, Rolf Gedeborg
   Submitted for publication.

Reprints were made with permission from the respective publishers.
Contents

Introduction...................................................................................................11

Challenges for academic emergency medicine – new devices and
concepts in prehospital care .................................................................11

Background.................................................................................................14

Prehospital emergency medical service in Sweden..........................14
Rationales for the new devices and concepts addressed in this thesis.....15
  Paper I. Mechanical chest compression devices .........................15
  Paper II. Using the ambulance nurses’ competence to decrease the
time to thrombolysis in stroke care ...................................................17
  Papers III-IV. PHTLS courses in trauma care .............................18

Aims..............................................................................................................20

Material and methods..............................................................................21

  Paper I ....................................................................................................21
    Description of the mechanical compression device LUCAS ..........21
    Study population ...............................................................21
    Study design ........................................................................21
    Definitions and statistics .........................................................22
  Paper II ................................................................................................22
    Study design and setting ........................................................22
    Study population ...............................................................22
    Inclusion ................................................................................22
    Data collection ................................................................23
    Statistics .............................................................................23
  Paper III ..........................................................................................23
    Study design ........................................................................23
    Exposure .............................................................................24
    Outcome ..............................................................................24
    Possible confounders ........................................................24
    Statistics .............................................................................24
Abbreviations

ALS  Advanced Life Support
ATLS  Advanced Trauma Life Support
CDC  Centers for Disease Control and Prevention (USA)
CDR  Cause of Death Registry (Sweden)
CI  Confidence Interval
CPR  Cardiopulmonary Resuscitation
CT  Computed Tomography
DAG  Directed Acyclic Graph
ED  Emergency Department
EMS  Emergency Medical System
EMT  Emergency Medical Technician
GCS  Glasgow Coma Scale
ICD  International Classification of Diseases
ICISS  ICD-based Injury Severity Score
IQR  Inter-Quartile Range
LUCAS  Lund University Cardiopulmonary Assist System
MEWS  Modified Early Warning Score
MCMC  Markov chain Monte Carlo
NCHS  National Center for Health Statistics (USA)
NPR  National Patient Registry (Sweden)
OR  Odds Ratio
PHTLS  Prehospital Trauma Life Support
PVC  Peripheral Venous Cannula
ROSC  Return of Spontaneous Circulation
Introduction

Challenges for academic emergency medicine – new devices and concepts in prehospital care

Prehospital healthcare has changed dramatically the last decades. Telecommunications have provided new opportunities for advanced communication between ambulances and hospitals. New devices have been implemented, such as ventilators for respiratory support, semi-automatic defibrillators, and, most recently, mechanical heart compression devices for the treatment of cardiac arrest. Implementation of the new interventions is often driven by aggressive commercial marketing and rarely is supported by strong evidence of it being beneficial for the patients.

Another prehospital reform during the last decades is that treatments, earlier performed only in the hospital, have moved out to the ambulances, with the intention of providing earlier treatment for acutely ill patients and thus lowering mortality and morbidity. This might seem to be an obvious advantage for the patient. However, with some exceptions, such as cardiopulmonary resuscitation (CPR) in cardiac arrest, thrombolysis in myocardial infarction and acute treatment of asthma, there is little scientific evidence to support this change in treatment location.

In the prehospital setting, the information available on the patient’s disease/illness, previous medical history and vital parameters is usually less robust than in the emergency department. Prehospital caregivers often conduct patient interviews and perform procedures, such as intravenous cannulation and airway management, under less than optimal conditions. These factors might influence the outcomes of the treatments given in the prehospital setting, and studies performed in-hospital might not be directly applicable to the prehospital setting. In the worst case, prehospital interventions without proven benefit for the patient, might only delay transport to hospital and thus delay adequate in-hospital treatment where more resources and higher levels of competence are available.

This movement of treatments out of the hospital, raises concerns about prehospital competence. A continuous educational programme for prehospital caregivers is one possible way to ensure the quality of care. Traditionally, ambulance organisations in Sweden have had a thorough, recurrent and mandatory educational plan in place for maintaining knowledge and skills. As part of this, the so-called concept courses, Prehospital Trauma Life Sup-
port (PHTLS)⁴ and Advanced Medical Life Support have spread and hold an important and resource-consuming position in the educational system.

Prehospital and other emergency care is surrounded by preconceptions and myths, maintained by stories in the media, of heroic interventions with advanced technical support.⁵ There is reason to believe that these myths, as well as the actual setting in which prehospital healthcare providers work, are prone to attract caregivers with certain personalities. This might result in a selection of ‘doers’ who are keen to implement new technical devices or concept courses, such as PHTLS. In general, this is probably favourable. However, a burning ambition to improve performance by implementing new devices and new courses supported by aggressive commercial marketing must be balanced by scientific evidence.

Eighteen years ago, Spaite et al. stated a warning in the Annals of Emergency Medicine:⁶

“It is likely that the relative availability of societal resources for each potential need will decrease in the future. Thus allocation will be based on the ability to objectively and convincingly prove the cost-effectiveness of a given service. Despite our beliefs and biases, EMS is enormously overfunded in relation to our current ability to scientifically justify its effectiveness. If good systems-analysis research is not developed, we predict that EMS in its current form will cease to exist because of our inability to show its value to society.” (EMS – emergency medical service)

As an example they mentioned the use of advanced airway techniques in prehospital care not being scientifically evaluated in an appropriate way when it was possible in the early 1970s and 1980s. At the time of their article (1995) the opportunity had passed, since prehospital advanced airway procedures were standard care and, therefore, it was not politically, ethically or legally possible to determine the potential impact of these procedures on patient outcomes. Thirteen years later (2008), the recommendations for prehospital airway management in prehospital care from a task force commissioned by the Scandinavian Society of Anaesthesia and Intensive Care Medicine states:⁷

“The grades of recommendations presented in this paper will be on D level [the lowest level, author’s comment] because the evidence is extrapolated and the majority of the studies have not been performed under realistic, prehospital conditions.”

Another example of poor scientific support for already implemented procedures is spinal immobilisation, which is one of the corner stones of the PHTLS concept. According to the 2010 guidelines from the American Heart Association:⁸

“It is still not clear whether and how often secondary spinal cord injury occurs and whether the methods that have been rec-
ommended for spinal stabilization or movement restriction are effective.”

There are even indications of possible harmful effects from reduced pulmonary function as a result of using spinal immobilisation with straps\(^9\) and of increased intracranial pressure induced by cervical collars.\(^{10}\)

The above reasoning, taken as a whole, raises some questions about competence and the introduction of new concepts and devices in the prehospital setting. Are the competences and skills sufficient to implement the new devices? Are we using the full potential of the prehospital crews’ competence? Do the so-called concept courses have measurable benefits for the patient?

This thesis deals with the above questions in three subsets of prehospital care – CPR, the stroke chain of survival and trauma care.
Prehospital emergency medical service in Sweden

Sweden, with a population of about 9 million, is divided in 21 administrative regions (counties). Each county in Sweden is responsible for medical health care including prehospital emergency medical services.

During the major part of the 20th century there was no regulation establishing responsibility for the transportation of patients in Sweden. In 1963 firemen (45%), taxi drivers (35%), janitors at hospitals (15%) and volunteers (5%) performed the service. Gradually the county councils have taken on the responsibility for prehospital care, and by the end of the century the responsibility for prehospital care was incorporated into the counties ordinary health care system. However, in some counties the ambulance service is still operated by private ambulance companies or local fire departments on an entrepreneur basis.

During the last part of the 20th century, the prehospital staff consisted mainly of emergency medical technician (EMT) equivalents (ambulanssjukvårdare in Swedish), with only a few nurses working in the prehospital setting. All staff members were authorised to deliver pharmaceuticals according to a protocol established by the medical director. This was an exception from the general legislation in Swedish health care, which demanded nursing competence for the delivery of pharmaceuticals. Since the late 1980s there has been a constant raise in educational level, as more nurses entered prehospital care. By the end of the century, 25% of all ambulance staff in Sweden had a nursing education. Still though, the EMTs were allowed to deliver pharmaceuticals to patients.

In 2005 the National Board of Health and Welfare removed this exception allowing EMTs to handle pharmaceuticals. As a result, all ambulances today are staffed with at least one nurse. They provide medical treatment based on condition-specific algorithms and are supervised by a medical director. In general, the staff perform Advanced Life Support (ALS) in emergency situations, with the exception of tracheal intubation, drainage of pleura and inotropic infusions. Some regions diverge from this, allowing tracheal intubation in cases of cardiac arrest. The employment of specialised nurses (mainly prehospital care, anaesthesia and intensive care) is increasing and some organisations demand this competence. Also, some organisations have
differentiated delegations for specialised and non-specialised nurses (e.g. pharmacologically assisted intubation for nurses specialised in anaesthesia).

Some of the larger cities use an emergency car staffed with a physician as a support for the ambulance fleet. Helicopters are used in some counties/regions. Their assignments differ, some having mainly a commitment to inter-hospital transportation, while others are used primarily as a prehospital resource. Still, road ambulances with nursing competencies handle the overwhelming majority of prehospital emergencies in Sweden.

Rationales for the new devices and concepts addressed in this thesis

Paper I. Mechanical chest compression devices

Annually in Europe, it is estimated that approximately 275 000 cardiac arrests are treated by emergency medical services, with a 10.7% survival to hospital discharge. A similar survival proportion of 8.4% is reported for the United States. Survival to one month after cardiac arrest in Sweden was 9.8% in 2009, according to the national registry of prehospital cardiac arrests. The differences in survival rate seen between developed countries are difficult to explain, since most countries follow the same guidelines in principal. Differences in co-morbidity, genetics, health care systems, geography and population densities are possible explanations, but differences in definitions and registration of cardiac arrest between organisations and countries might be a more likely explanation.

Efforts to improve survival rates during the 1990s primarily targeted early defibrillation with the introduction of semi-automatic defibrillators. The survival rate has also increased during the last decades, but not to the extent expected. The scientific community has, therefore, shifted its focus, exploring other fields in the CPR algorithm, such as the quality of compressions.

The importance of the correct performance of compressions has been demonstrated in both animal and human studies. Clinical studies have shown that both increased compression depth and a reduction in the time without compressions (no-flow time) are associated with an increased likelihood of successful defibrillation. Consequently, there has been a shift also in the clinical guidelines, stressing the importance of the quality of chest compressions, including a lowering of the no-flow time, during CPR. Despite this, both in-hospital and out-of-hospital studies have indicated sub-optimal chest compressions and undesirably long no-flow times. This knowledge concerning the importance of correct compressions is the basis for the re-invention and development of several mechanical compression devices now available on the market.
The idea of mechanical chest compressions is not new. Pike et al.\textsuperscript{30}, in 1908, described a method of ‘extra-thoracic massage’ used in a dog model. In 1961, Harkins and Bramson\textsuperscript{31} reported on an electro-pneumatic machine that used compressed gas to drive a spring-loaded piston applied to the patient’s sternum. In 1963 Safar et al.\textsuperscript{32} evaluated the ‘Beck-Rand external cardiac compression machine’, a battery powered, portable device weighing 32 kg. They concluded that the time spent transporting, applying and adjusting the machine precluded its use at the start of resuscitation. Also they believed that it would be valuable only in cases where there was a need for prolonged resuscitation, and that possibly it could be used by ambulance personnel. The ‘Thumper’ was developed during the 1960s and was recommended for hospital and prehospital use.\textsuperscript{33} Different models of the ‘Thumper’ have been on the market since then, some with automatic ventilation included. Today the Thumper\textsuperscript{®} 1007CC is the model available on the market.

Improvements in design – creating portable and easy to handle devices together with an increasing knowledge of the importance of good quality compressions – have renewed the idea of mechanical chest compressions. Today, two devices dominate the world market – LUCAS\textsuperscript{®} (Lund University Cardiopulmonary Assist System, Jolife AB, Lund, Sweden) and Auto-pulse\textsuperscript{®} (ZOLL Medical Corporation). Intuitively, these devices have obvious advantages. They enable the crew to be seated with their safety belts fastened while performing CPR during transport (as opposed to the situation when performing manual compressions) and increase their ability to perform other important interventions as a result of an alleviated workload.\textsuperscript{34} The devices also provide consistent compression rates and allow defibrillation during ongoing chest compressions. Some studies suggest improved CPR using the devices in special settings, such as in the catheter laboratory and during flights.\textsuperscript{35-37} Nevertheless, there is today limited evidence to support a prehospital use from clinical outcome studies.\textsuperscript{1,38-39}

The introduction and use of mechanical chest compression devices during the last decade is a typical example of how the invention, development, marketing and implementation of a new device in prehospital care are ahead of scientific evidence to support the use of these devices in clinical practice. A recent Cochrane analysis concluded there is no evidence to recommend mechanical chest compression devices in clinical practice.\textsuperscript{39}

Many of the newer devices, designed specifically for use in the prehospital environment, are easy to handle, light and portable. Several reports have also demonstrated the feasibility of using mechanical chest compression devices in the prehospital setting.\textsuperscript{40-41} However, to date, the largest randomised controlled trial has indicated a possibility of harm, and therefore, caution is advised until more data is available.\textsuperscript{42}

Documented feasibility is not always enough to ensure the optimal use of a device in clinical practice. Studies of new devices, drugs and protocols in CPR are often performed in well-defined settings during predefined periods
of time, and with a selected and dedicated staff given specific training. This may explain why the subsequent evaluation of actual performance and outcomes, after implementation in routine clinical practice, can yield conflicting results.\textsuperscript{43} In the case of mechanical compression devices, there are few studies on the quality of performance when these are used in routine clinical practice and on how the introduction of a new device influences other interventions (e.g. ventilation and time to defibrillation) during CPR.\textsuperscript{44}

A new device, with documented feasibility for clinical use, and animal studies supporting an improved outcome, might still not perform well in routine clinical practice. With this in mind we studied ambulance crews, who had a mechanical chest compression device implemented in regular clinical practice (Paper I). Our main interests were compression quality and the possible deterioration of other interventions during CPR.

Paper II. Using the ambulance nurses’ competence to decrease the time to thrombolysis in stroke care

Stroke is a devastating disease with high mortality and causes serious disability.\textsuperscript{45-47} Annually, 22 million patients suffer a stroke, with 4 million of these living in high income countries.\textsuperscript{48-49} Each year, strokes cause over 4 million deaths – the second most common single cause of death.\textsuperscript{45} In Sweden, a stroke is the third most common cause of death and the most common cause of neurological disability.\textsuperscript{50} Ninety percent of the cerebral vascular insults are caused by ischemic stroke, where urgent treatment with a recombinant tissue plasminogen activator (thrombolysis) is an efficient and cost effective treatment.\textsuperscript{51-55} Although the evidence for thrombolysis is strong, its implementation is low.\textsuperscript{56} One of the major barriers is the delay in the stroke chain of survival.\textsuperscript{55,57}

The main delay is patient delay, but hospital delay can often be substantial too.\textsuperscript{58-59} Likely explanations for hospital delay are the multiple handovers with oral reports, multiple examinations and long waiting times for physicians and in-hospital transportation.\textsuperscript{58}

The evolution of prehospital care has involved also the treatment of ischemic stroke. Pre-admission notification by the EMS system has been shown to cut some of the delays before a CT scan and potential thrombolysis.\textsuperscript{60-62} In Sweden today it is common practice to use the ambulance nurses’ competence to diagnose the suspicion of a stroke using stroke identification tools\textsuperscript{63} and to prepare for hospital arrival by alerting the emergency department (ED). The prehospital identification of a stroke by EMT and paramedics using stroke identification tools has a high accuracy.\textsuperscript{64}

With the above knowledge, transporting patients suspected of having a stroke directly to the CT scanner, bypassing the ED, could be time saving and thereby beneficial for the patient. A complete foundation for a treatment
decision, including the result of a CT scan, would then be available for the physician at first assessment. Repeated assessments and reports would be minimised with a potential shortening of the time to thrombolysis. Crucial in such a shortcut is the selection of the correct patients. Adding a triaging tool for severity scoring and phone consultation with a physician are used in some Swedish organisations to ensure accuracy in this selection. The scientific support for the safety and efficiency of these procedures is poor, and the level of support needed for the ambulance nurses to perform a correct selection is unknown. By comparing the judgments made by ambulance nurses and those of the physicians assessing stroke patients, we evaluated whether the ambulance nurses’ own knowledge base, combined with a stroke identification tool, was enough for correct patient selection in a potential implementation of this shortcut (Paper II).

Papers III-IV. PHTLS courses in trauma care

Trauma is the leading cause of death among persons below 60 years of age. It is a well established belief that optimal treatment in the early phase following trauma has a major impact on mortality. Therefore, over the years, raising the educational level of prehospital caregivers and implementing specific educational programmes that target trauma care have been two widely adopted strategies for improving the outcome for trauma victims. This strategy has high face validity, but the strength of the scientific evidence is poor.

Today, a substantial proportion of ambulance crews include an ALS-trained member. There are studies on conditions other than trauma indicating that ALS training and higher educational levels among ambulance crews improves outcomes. However, there is little support for such an association in trauma care. One often quoted study in favour of PHTLS is from Trinidad and Tobago which shows an increase in survival after the implementation of PHTLS. However, a major concern with this study is the use of four year old historical controls and not being able to account for an improvement in survival over time from other causes. Also the study was performed in a low-income country, with low basic prehospital care competence. Therefore, it is difficult to apply the results to middle and high income countries. Other studies have shown a decline in survival in specific subgroups after implementation of ALS programmes. A recent Cochrane analysis concluded that, to date, there is no scientific evidence supporting the benefit of ALS-programmes to the patients in respect of mortality or morbidity. The courses are, though, generally appreciated and studies have shown that health care providers feel more secure and comfortable in emergency trauma situations and know better how to handle and treat trauma patients.
PHTLS has been recognised as one of the leading educational programmes for prehospital emergency trauma care. Since its introduction in the 1980s, nearly half a million prehospital caregivers in over 50 countries have taken this course.\textsuperscript{4} The core component is a 16-hour course with a mixture of lectures and interactive skill stations. In summary, it teaches a structured assessment, including examination and treatment of life threatening symptoms in the trauma patient. Regional faculties run the courses. A national faculty is responsible for compliance to the course material and reports each course to the National Association of Emergency Medical Technicians. The course material consists of a student book, an instructor manual and a PowerPoint presentation for each lecture. The book is revised every fourth year, and a Swedish translation is added as a supplement to the book. The average official price per student, including course material, is USD 1000. In Sweden, the employer usually pays the salary and any accommodation needed during the course. Every fourth year a one day refresher course is recommended.

Despite the widespread implementation of PHTLS, there is scant scientific evidence for any beneficial effects on trauma outcomes.\textsuperscript{75,78} Substantial effort and money are put into this training programme and there is an obvious need to evaluate the potential benefits for patients.

Therefore, we conducted two epidemiological studies analysing the possible association between PHTLS education and mortality in subsets of trauma patients (Papers III and IV).
Aims

In **Paper I** the objective was to assess performance of ambulance crews during CPR, using a mechanical compression device, as compared to CPR using manual compressions. The ambulance crews had use of a mechanical chest compression device embedded in their routine clinical practice.

In **Paper II** the aim was to evaluate the level of agreement between ambulance nurses’ and emergency physicians’ judgments of patients with a pre-hospital suspicion of stroke and/or a lowered level of consciousness. Two major judgments were evaluated: (1) the need for a CT scan and (2) the need for interventions and/or increased monitoring before the CT scan.

In **Paper III** the intent was to investigate the association between the PHTLS training of ambulance crew members and the outcomes among all types of injured patients. The outcomes studied were mortality and return to work.

In **Paper IV** the objective was to investigate the association between the PHTLS training of ambulance crew members and patient outcomes for victims of motor vehicle traffic crashes. The outcomes studied were mortality and return to work.
Material and methods

Paper I

Description of the mechanical compression device LUCAS

LUCAS is a battery driven chest compression device. A piston with a suction cup delivers compressions with depths of 4 to 5 cm at a frequency of 100/min. In between every 30\textsuperscript{th} compression there is a three-second pause allowing ventilation. The piston is adjusted vertically and horizontally to a correct position on the patient before being turned on. To avoid sliding, a stabilisation strap is wrapped around the shoulders of the patient.

Study population

In order to use a study population unbiased by the investigators and as representative as possible of ambulance organisations using the LUCAS device in ordinary clinical practice, we choose an ambulance organisation which:

- was not connected to the investigators’ own organisation,
- had a mechanical compression device as part of the standard treatment for cardiac arrest and was incorporated in regular practice,
- used the mechanical compression device as a pure replacement for manual compressions,
- was not involved in any studies concerning CPR.

The LUCAS device had been used for eight months. The organisation had two different protocols for CPR – one for LUCAS-CPR used in ambulances equipped with the mechanical device and one for manual CPR in the other ambulances. From 160 employees, 48 were randomly selected for the study, creating 24 crews with at least one nurse in each crew.

Study design

Each crew served as their own control in a randomised cross-over design, performing two 10-minute full CPR scenarios according to their ordinary CPR-protocol; one scenario with the aid of LUCAS (LUCAS-CPR) and an identical scenario, but with manual compressions (manual CPR) only. The scenario to be performed first was randomly determined. A computerised
manikin, visual observations and video recording were used to collect the data. The ECG simulator was set to show refractory ventricular fibrillation throughout the experiment.

Definitions and statistics

Compression depths greater than or equal to 3.8 cm were considered adequate. No-flow time was defined as intervals of more than 1.5 second without compressions. The no-flow fraction was defined as the no-flow time during a specified interval divided by the total time of this interval. Treatment groups were compared using the Wilcoxon matched pairs signed rank test and potential carry-over effects were examined.

Paper II

Study design and setting

This non-interventional study of agreement between patient assessments was performed from October 2008 to June 2009 at the University Hospital of Uppsala. In 2008 the hospital’s catchment area for patients having experienced a stroke had a population of 268 000 inhabitants.

Study population

**Prehospital staff:** Nine ambulances, of which six were operational around the clock, served the area. A stroke algorithm, including a stroke assessment instrument (face-arm-speech-test, time window, level of consciousness, blood glucose, seizures and anticoagulation therapy) is followed when a stroke is suspected. When the ambulance nurse, with the guidance of the stroke algorithm, identifies a patient eligible for potential thrombolysis, the prehospital protocol includes inserting a peripheral venous cannula (PVC), stabilising vital parameters and alerting the ED.

**Physicians at the emergency department:** The ED was staffed with two physicians dedicated to medical disorders – one senior physician, specialising in internal medicine or emergency medicine and one resident physician with two to five years’ experience.

Inclusion

Patients where the ambulance nurse either suspected a stroke, diagnosed a lowered level of consciousness (Glasgow Coma Scale [GCS] 3–14), or both were included. The study did not include patients with trauma or cardiac
arrest, those under 18 or those assessed by a physician before arriving at the hospital.

Data collection
The ambulance nurse recorded inclusion criteria (stroke symptoms, lowered level of consciousness, or both), patient age, GCS, and ED arrival time on a paper questionnaire. Immediately before arriving at the ED, the nurse responded to the two main study questions:
1) Did the patient need a CT scan?
2) Did the patient need interventions and/or an increased degree of monitoring before the CT scan?

If the ambulance nurse considered that the patient was in need of preceding interventions, they selected one or more of the following categories: airway management, insertion of PVC, fluid resuscitation, medication, an increased degree of monitoring, or other.

After they arrived at the ED, all study patients were assessed by a physician who answered study questions identical to those posed to the ambulance nurse. The physician was not informed about the answers from the ambulance nurse. If a resident physician was handling the case, they consulted the senior physician before answering the study questionnaire.

Vital parameters included in the Modified Early Warning Score (MEWS) were collected from the ambulance and hospital records and used as an indicator of any change in illness severity between the ambulance nurses’ and the physicians’ examinations.

Statistics
Cohen’s kappa was used to estimate the level of agreement between the ambulance nurses and the ED physicians when assessing patients. As a complementary analysis, sensitivity, specificity and likelihood ratios were calculated, assuming the physicians’ judgments as the gold standard.

Paper III
Study design
This observational cohort study was performed in Uppsala County, which, in 2004, had a population of 302,500 inhabitants. We identified all trauma patients handled by the ambulance organisation from 1998 through 2004 using the Swedish National Patient Registry (NPR), the Cause of Death Registry (CDR) and prehospital electronic patient records. Patients discharged alive on the same date as their hospital admission and patients
without a valid personal identification number were excluded. Information on the use of social insurance benefits was collected from The Swedish Social Insurance Agency.

Exposure
The date for completed PHTLS training for each individual ambulance staff member was obtained from the national faculty of PHTLS. This information was linked to each injury event. If at least one crew member had completed the course the patient was considered exposed to a PHTLS-trained ambulance crew.

Outcome
The composite outcome of either prehospital or hospital death was used as the primary outcome measure. Additionally we also analysed return to work as an outcome measure.

Possible confounders
Injury severity using the international classification of diseases (ICD)-based injury severity score (ICISS), injury region, causes of injury, basic educational level (nurse/EMT) and work experience of the crewmembers, years of study and patient’s age and sex were considered as potential confounders and included in the multivariable models.

Statistics
Multivariable logistic regression analysis was used to model the composite outcome of prehospital or hospital death. The multivariable logistic regression model was also used to calculate the predicted mortality for each injury event. The difference in mean predicted mortality between the PHTLS group and the non-PHTLS group was used as an estimate of the absolute risk reduction. A Kaplan-Meier plot and Cox proportional hazards regression was used to assess the time to return to work.

Paper IV
Source design
This semi-individual study with ecological exposure (information on group level) covered all of Sweden. The first PHTLS course in Sweden was held in 1998 and was followed by gradual implementation through 2004 in some,
but not all, regions. This staggered implementation allowed control of variations in outcome over time and other differences in regional systems and hospital care.

Prehospital emergency medical service system

The proportion of registered nurses employed varied between regions and increased during the study period from less than 25% in 1998 to about 50% by the end of the study. There were no major changes in the standard of prehospital trauma care or equipment used during the study period, and no major differences between regions. A fraction of the nurses (20% in 2003) were specialised in anaesthesia, and some of them were authorised to perform intubation on unresponsive patients. A PHTLS certification did not change the authorisation to use any equipment or perform any specific intervention.

Study population

Data on all patients in Sweden admitted to hospital or dead prehospital, with injury as the principal discharge diagnosis during the years 1998 to 2004, were extracted from the Swedish NPR and CDR. Prehospital injury deaths were identified as autopsied injury deaths not associated with a hospital admission using information from the CDR. A complete person-based linkage of the datasets was done based on the unique personal identification number.

Motor vehicle traffic crashes were selected using the causes of injury matrix, developed by the National Center for Health Statistics (NCHS) – Centers for Disease Control and Prevention (CDC). Cases where information on the region or the cause of injury was missing were excluded. When patients had recurrent injury events, violating the assumption of independent events, only the first occurrence during the study period was included in the analysis. Information on the use of social insurance benefits was collected from The Swedish Social Insurance Agency.

Because of the dichotomisation of exposure (see below) and a low PHTLS implementation during the period 1998 to 2000 (Figure 1), these years contributed no exposed cases. We therefore restricted the study population to 28,041 motor vehicle traffic injuries during the period 2001 to 2004.

Exposure

The date for each PHTLS course and the region where each participant was employed was taken from the records of the Swedish national faculty for PHTLS.
Figure 1. The regional implementation of PHTLS in Sweden from 1998 to 2004. The legend shows the exposure varying from zero to one point five. Exposure is defined as the region-specific number of staff certified in PHTLS at each time point, divided by the estimated number of employees in each region in 2003.

For each region of the country, the degree of implementation was estimated by the ratio of the number of staff certified in PHTLS in that region to the total number of employees in the ambulance service in that region. For each injury event, the exposure to PHTLS was then determined by matching the date and region of the injury to a date- and region-specific proportion of ambulance personnel having completed the PHTLS course. This continuous variable was considered to reflect the degree of regional PHTLS implementation. With the information on individual exposure available from study III and using the receiver operating characteristic (ROC) curve and the Youden index to determine an optimal cut-off level, we derived a binary exposure variable for PHTLS (yes/no).

Outcomes

Four outcomes and subsets of patients were analysed:

- prehospital mortality, defined as all injury deaths without a hospital admission,
- 30-day mortality, defined as death within 30 days from the date of hospital admission,
- time to death among patients admitted to hospital alive, defined as the time from the date of hospital admission to the date of death,
- time to the return to work of survivors following hospital discharge, limited to patients working before the injury, having at least one day of sick leave and surviving at least one year after discharge from hospital.

The follow-up was at least one year following the injury event.
Possible confounders

By drawing a directed acyclic graph (DAG)\textsuperscript{94} and including information from study III, the resulting minimally sufficient adjustment set for estimating the total effect of PHTLS on mortality consisted of:

- calendar year – to account for a possible period effect (such as changes in trauma care over time during the study period),
- region – to account for possible differences in trauma care between regions,
- receiving hospital for an outcome other than prehospital mortality – to account for possible differences in trauma care between hospitals.

We also estimated multivariable models with covariates generally considered to be potential confounders in a trauma study. These models included age, gender, injury severity, role of the injured victim and co-morbidity. Injury severity was measured with the ICISS.\textsuperscript{83-85} The victim’s role in the motor vehicle traffic injury was classified according to the matrix developed by the NCHS – CDC.\textsuperscript{87} Co-morbidity was classified using the Charlson index calculated from hospital discharge diagnoses for the five years preceding each injury event.\textsuperscript{95-96}

Statistics

A Bayesian approach with Markov chain Monte Carlo (MCMC) methods was used to estimate odds ratios for binary outcomes. The health care region was modelled as a random effect to account for regional differences other than PHTLS training. In order to further handle potential differences in the quality of hospital care, the receiving hospital was included as a random effect in a multi-level hierarchical model of 30-day mortality. Only patients admitted to hospital alive were eligible for this model. The 2.5th and 97.5th percentiles defined the 95% credibility interval with the interpretation that, with the given prior and observed data, the parameter is within the interval with a probability of 0.95.

Time to death and time to return to work were described using Kaplan-Meier curves. Cox proportional hazards regression was used to model time to event data. Survival time was calculated from the hospital admission date to the date of death or the end of the study follow-up on 31 December 2005. When return to work was analysed, the end of the study follow-up was one year after injury.

Models of prehospital mortality and 30-day mortality were also estimated for the continuous exposure variable and on a sub-group with more severe injuries as determined by ICISS $\leq 0.940$. 


Results

Paper I

Inclusion

Three of the 24 ambulance crews were excluded, leaving 21 crews (42 individuals) completing the study. The median employment time in prehospital care was 137 months (inter-quartile range (IQR), 71–230 months). The median time since the last training session in CPR was 3 weeks for both manual (IQR, 2–24 weeks) and mechanical compressions (IQR, 1–9 weeks). The number of training sessions performed with manual compressions was 11 (IQR, 7–20), and with mechanical compressions, 3 (IQR, 2–4).

Primary endpoints

The study revealed no substantial difference in the time to first defibrillation or the no-flow time prior to first defibrillation (Table 1). There was no difference in the no-flow fraction, either prior to first defibrillation or for the whole scenario.

Table 1. Time to first defibrillation and no-flow time.

<table>
<thead>
<tr>
<th></th>
<th>LUCAS-CPR</th>
<th>Manual CPR</th>
<th>Mean difference</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Time to first defibrillation</td>
<td>182</td>
<td>178</td>
<td>4</td>
<td>-12 to 21</td>
</tr>
<tr>
<td>(seconds)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No-flow time until first</td>
<td>79</td>
<td>73</td>
<td>6</td>
<td>0 to 12</td>
</tr>
<tr>
<td>defibrillation (seconds)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No-flow time for the</td>
<td>181</td>
<td>200</td>
<td>-20</td>
<td>– 36 to 1</td>
</tr>
<tr>
<td>whole scenario (seconds)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Presented as the mean difference between LUCAS-CPR and manual CPR times, 95% confidence interval (CI) for the difference.

Compression quality

There were differences in the compression quality when using LUCAS as compared to manual compressions. For the whole scenario, the number of adequate compressions using manual CPR was 78% higher in relation to LUCAS-CPR. Analysing adequate compressions as a fraction of the total number of chest compressions in order to minimise the influence of the
higher compression rate during manual CPR gave similar results. For the whole scenario the mean fraction of adequate compressions was 88% with manual CPR, and 58% with LUCAS-CPR (Figure 2).

![Figure 2. Panel A shows the fraction of adequate compressions until the first defibrillation. Panel B shows the fraction of adequate compressions during the whole scenario of 10 minutes. Each line connects one crew’s results in LUCAS-CPR and manual CPR. Box-and-whisker plots for LUCAS-CPR and manual CPR respectively. Boxes represent the IQR, • is the median, whiskers representing maximum and minimum values (values more than three inter-quartile distances away from the median are considered outliers and are marked with dots).](image)

**The use of the stabilisation strap and correction of mal-position**

In LUCAS-CPR only 12 out of the 21 ambulance crews (57%) applied the stabilisation strap on the LUCAS device. The median time from the first mechanical compression to the application of the strap was 249 seconds. Correction of a mal-position of the LUCAS was done by five ambulance crews (24%), as verified by video review. The median time from the first inadequate compression to the correction was 241 seconds. In one case the correction was insufficient, i.e. it did not lead to adequate compressions after the correction.

**Performance of mechanical compressions in relation to educational level and professional experience**

The fraction of adequate mechanical compressions did not differ depending on the level of education of the crews. The results did not indicate any substantial correlations between the fraction of adequate mechanical compressions and any of the following factors: number of training sessions using LUCAS-CPR completed, number of LUCAS-CPRs performed in clinical
practice, time since last training session using LUCAS-CPR or time since last LUCAS-CPR performed in clinical practice.

Paper II
Inclusion
A total of 230 patients fulfilled the inclusion criteria. Thirty cases were excluded leaving 200 cases to analyse – 146 with typical stroke symptoms with or without a lowered level of consciousness and 54 with a lowered level of consciousness without typical stroke symptoms. The median time interval between the assessment by an ambulance nurse and that carried out by a physician was 30 minutes (IQR 10 to 83), and this was similar for all inclusion categories.

Assessment of the need for a CT scan
The agreement regarding the need for a CT scan was low: $\kappa = 0.22$ (95% CI: 0.06 to 0.37). The ability of ambulance nurses to correctly select patients in need of a CT scan had a sensitivity of 84% (95% CI: 77 to 89) and a specificity of 37% (95% CI: 23 to 53). The likelihood ratios indicated a low contributable effect by the ambulance nurse’s judgment. An analysis restricted to patients with stroke symptoms showed an even lower agreement, while there was a tendency towards higher agreement with decreasing patient age. Table 2 displays cross-tabulated figures.

<table>
<thead>
<tr>
<th>Table 2. Cross tables showing the ambulance nurses’ and physicians’ judgments of whether or not a patient needed a CT scan.</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>a. All cases</strong></td>
</tr>
<tr>
<td><strong>Ambulance nurse</strong></td>
</tr>
<tr>
<td>Yes</td>
</tr>
<tr>
<td>No</td>
</tr>
<tr>
<td><strong>Total</strong></td>
</tr>
</tbody>
</table>

Stroke symptoms include all symptoms, other than lowered level of consciousness, giving rise to a suspicion of a stroke.
Assessment of the need of interventions before a CT scan

When the ambulance nurses assessed whether the patient was in need of interventions or increased monitoring before the CT scan, the agreement was also low, \( \kappa = 0.32 \) (95% CI: 0.18 to 0.47). The ambulance nurses’ ability to select correctly patients needing interventions before a CT scan had a sensitivity of 33%. In 18% (36/200) of cases the ambulance nurses considered further interventions before a CT scan unnecessary, while the ED physicians deemed interventions necessary (Table 3). Analysis restricted to patients with stroke symptoms or cases with no difference in MEWS between the two assessments (90 cases) did not have any major effect on the results. There was a positive correlation between higher MEWS and a higher proportion of patients considered to be in need of interventions before the CT scan, both for the ambulance nurses and the physicians. There was a tendency towards a higher level of agreement when a shorter time had elapsed between the two examinations.

Table 3. Cross tables showing ambulance nurses’ and physicians’ judgments of whether or not a patient needed interventions or increased monitoring before a CT scan.

<table>
<thead>
<tr>
<th></th>
<th>a. All cases</th>
<th>b. Stroke symptoms</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Ambulance nurse</td>
<td>Physician</td>
</tr>
<tr>
<td>Yes</td>
<td>18</td>
<td>9</td>
</tr>
<tr>
<td>No</td>
<td>36</td>
<td>137</td>
</tr>
<tr>
<td>Total</td>
<td>54</td>
<td>146</td>
</tr>
</tbody>
</table>

Stroke symptoms include all symptoms, other than lowered level of consciousness, giving rise to a suspicion of a stroke.

Interventions

The most frequently proposed intervention was the insertion of a PVC, regardless of agreement or disagreement in the assessment. Disregarding cases where insertion of a PVC was proposed by either an ambulance nurse or a physician (36 cases) lowered the level of agreement to \( \kappa = 0.20 \) (95% CI: 0.00 to 0.40).
Paper III

Study population and exposure

During the 7-year study period, EMSs responded to 2830 injury events with complete data for the analyses (Figure 3).

5235 severe injuries (hospitalized > 1 day or dead) with documented participation of EMS

- 483 without a valid personal identification number in EMS record

Information on educational level among ambulance personnel added

- 1129 with incomplete information to determine crew PHTLS certification status

3623 severe injuries (hospitalized > 1 day or dead) with documented participation of EMS and information on ambulance crew’s PHTLS certification status

- 793 without complete information on both crew members’ identity and PHTLS certification status and covariates

2830 incident injuries (hospitalized > 1 day or dead) with documented participation of EMS and information on identity and PHTLS certification status for both members of the ambulance crew and all covariates in the multivariable model

Figure 3. Flow diagram for selection of the study population. EMS—Emergency medical service.

The proportion of injury events handled by ambulance crew members with PHTLS training increased over time (Figure 4).
Ambulance crews in the PHTLS group had more years of employment in ambulance services as compared to the non-PHTLS group. Otherwise there were no major differences in patient characteristics, response time, on-scene time or transport time between the two groups.

Relative and absolute mortality risk
The mortality was 4.7% (36/763) without PHTLS training and 4.5% (94/2067) with PHTLS training. The unadjusted, odds ratio (OR) for mortality was 0.96 (95% CI, 0.66-1.44). The adjusted OR was 0.71 (95% CI, 0.41-1.25), indicating a 29% reduction in mortality for cases handled by an ambulance crew where at least one member had PHTLS training. The corresponding predicted absolute risk reduction was 0.2%. A P-value function is presented to illustrate the size and precision of the estimate (Figure 5).
Figure 5. The P-value as a function of possible estimations of the odds ratio.

Sub-group analyses
Restricting the study population by excluding injuries caused by falls strengthened the estimated protective effect of PHTLS to OR = 0.54, but with poor precision (95% CI, 0.13-2.41).

There was a stronger protective association with mortality with a short interval since PHTLS training compared to those with longer intervals, and also if both ambulance crew members had had PHTLS training compared to only one crew member being trained in PHTLS. Both results, though, show poor precision in the estimate.

Return to work (not published)
In the sub-group where return to work could be evaluated (n = 322), approximately 80% had returned to work within one year. Adjusted for potential confounders, the PHTLS group appeared to have a higher rate for return to work within one year, but the precision of this estimate was poor (hazard ratio, 1.2; 95% CI, 0.81-1.7).
Characteristics of excluded patients
There were no major differences when characteristics among the excluded cases were compared to the study population.

Paper IV
Study population
In total, 28,041 cases were analysed. There was a male dominance (67%) and the median age was 32 year (IQR, 20 to 51 year). The majority of patients had minor injuries (65%) and 86% were occupants or driver of a motor vehicle. In the cohort, 10,378 cases were exposed to PHTLS and 17,663 were unexposed. The distribution of age, gender, injury severity (ICISS) and the victim’s role in the accident were similar in the exposed and unexposed groups.

Prehospital death and 30-day mortality
The majority of deaths (77%) during the first 30 days occurred before admission to hospital. While prehospital mortality decreased over time, in-hospital mortality appeared to be fairly stable over time (Figure 6). The prehospital mortality in the PHTLS group was 4.9% (505/10,378) compared to 5.0% (890/17,663) for subjects not exposed to PHTLS (no-PHTLS group).

![Figure 6. The mortality among victims in motor traffic crashes in Sweden from 1998 to 2004. The in-hospital and 30-day mortality are among patients admitted to hospital alive.](image)
The unadjusted odds ratio (OR) for prehospital death in the PHTLS group compared to the no-PHTLS group was 0.96 (95% credibility interval, 0.86 to 1.08). Adjusted for year, region, age, gender, injury severity, role of victim and co-morbidity the OR was 1.11 (95% credibility interval, 0.88 to 1.38) (Figure 7).

The 30-day mortality among patients admitted to hospital alive in the PHTLS group was 1.4% (138/10 378) compared to 1.7% (227/17 663) in the no-PHTLS group. The unadjusted OR (prehospital deaths included) was 0.94 (95% credibility interval, 0.85 to 1.03). Excluding prehospital deaths and adjusting for all confounders, including region and hospital in a hierarchical model, the OR was 0.80 (95% credibility interval, 0.53 to 1.17) (Figure 7).

Restricting the study population, by excluding minor injuries (ICISS > 0.94), provided similar estimates as the main analysis (Figure 7). Models using general estimating equations with independent structure provided similar estimates as the MCMC analysis (data not shown). Results from models including PHTLS exposure as a continuous variable are shown in Figure 8.

*Figure 7 and 8. (next pages)* Prehospital and 30-day mortality including exposure to PHTLS as a dichotomised variable (Fig 7) and a continuous variable (Fig 8). Region included as random effects, assuming observations within a region more correlated than observations between regions. Hierarchical (region and hospital) modelling of the association between PHTLS training and 30-day mortality among patients surviving to hospital admission. OR, odds ratio.
### Figure 7

<table>
<thead>
<tr>
<th>Population</th>
<th>Adjusted for</th>
<th>OR (95% credibility interval)</th>
</tr>
</thead>
<tbody>
<tr>
<td>All (n=26,041)</td>
<td>-</td>
<td>0.96 (0.85 to 1.08)</td>
</tr>
<tr>
<td>Injury severity &gt; minor (n=9,685)</td>
<td>-</td>
<td>1.10 (0.98 to 1.24)</td>
</tr>
<tr>
<td>All (n=28,041)</td>
<td>Region</td>
<td>0.93 (0.81 to 1.06)</td>
</tr>
<tr>
<td>Injury severity &gt; minor (n=9,685)</td>
<td>Region</td>
<td>0.90 (0.77 to 1.04)</td>
</tr>
<tr>
<td>All (n=28,041)</td>
<td>Region and year</td>
<td>1.07 (0.92 to 1.23)</td>
</tr>
<tr>
<td>Injury severity &gt; minor (n=9,685)</td>
<td>Region and year</td>
<td>1.04 (0.87 to 1.21)</td>
</tr>
<tr>
<td>All (n=28,041)</td>
<td>Year</td>
<td>1.08 (0.95 to 1.22)</td>
</tr>
<tr>
<td>Injury severity &gt; minor (n=9,685)</td>
<td>Year</td>
<td>1.06 (0.92 to 1.20)</td>
</tr>
<tr>
<td>All (n=28,041)</td>
<td>Year, region, age, gender, injury severity, role of victim and co-morbidity</td>
<td>1.11 (0.88 to 1.36)</td>
</tr>
<tr>
<td>Injury severity &gt; minor (n=9,685)</td>
<td>Year, region, age, gender, injury severity, role of victim and co-morbidity</td>
<td>1.11 (0.87 to 1.37)</td>
</tr>
<tr>
<td>All (n=26,463)</td>
<td>-</td>
<td>0.94 (0.85 to 1.03)</td>
</tr>
<tr>
<td>Injury severity &gt; minor (n=8,210)</td>
<td>-</td>
<td>0.92 (0.83 to 1.03)</td>
</tr>
<tr>
<td>All (n=28,041)</td>
<td>Year and region</td>
<td>1.01 (0.89 to 1.14)</td>
</tr>
<tr>
<td>Injury severity &gt; minor (n=9,685)</td>
<td>Year and region</td>
<td>0.99 (0.85 to 1.14)</td>
</tr>
<tr>
<td>All (n=28,041)</td>
<td>Year, region, age, gender, injury severity, role of victim and co-morbidity</td>
<td>1.02 (0.83 to 1.23)</td>
</tr>
<tr>
<td>Injury severity &gt; minor (n=9,685)</td>
<td>Year, region, age, gender, injury severity, role of victim and co-morbidity</td>
<td>1.02 (0.82 to 1.24)</td>
</tr>
</tbody>
</table>

A. Prehospital mortality

B. 30-day mortality

Survivors to hospital

Prehospital deaths included

Log. OR, 95% credibility interval
<table>
<thead>
<tr>
<th>Population</th>
<th>Adjusted for</th>
<th>OR (95% credibility interval)</th>
</tr>
</thead>
<tbody>
<tr>
<td>All (n=28 041)</td>
<td>Year and region</td>
<td>1.24 (0.98 to 1.55)</td>
</tr>
<tr>
<td>Injury severity &gt; minor (n=9 685)</td>
<td>Year and region</td>
<td>1.32 (0.92 to 1.96)</td>
</tr>
<tr>
<td>All (n=28 041)</td>
<td>Year, region, age, gender, injury severity, role of victim and co-morbidity</td>
<td>1.54 (1.07 to 2.13)</td>
</tr>
<tr>
<td>Injury severity &gt; minor (n=9 685)</td>
<td>Year, region, age, gender, injury severity, role of victim and co-morbidity</td>
<td>1.53 (1.09 to 2.16)</td>
</tr>
<tr>
<td>All (n=28 041)</td>
<td>Year and region</td>
<td>1.11 (0.91 to 1.35)</td>
</tr>
<tr>
<td>Injury severity &gt; minor (n=9 685)</td>
<td>Year and region</td>
<td>1.13 (0.90 to 1.40)</td>
</tr>
<tr>
<td>All (n=28 041)</td>
<td>Year, region, age, gender, injury severity, role of victim and co-morbidity</td>
<td>1.23 (0.92 to 1.63)</td>
</tr>
<tr>
<td>Injury severity &gt; minor (n=9 685)</td>
<td>Year, region, age, gender, injury severity, role of victim and co-morbidity</td>
<td>1.31 (1.04 to 1.79)</td>
</tr>
<tr>
<td>All (n=26 463)</td>
<td>Region and hospital</td>
<td>0.95 (0.62 to 1.36)</td>
</tr>
<tr>
<td>Injury severity &gt; minor (n=8 210)</td>
<td>Region and hospital</td>
<td>0.97 (0.65 to 1.41)</td>
</tr>
<tr>
<td>All (n=26 463)</td>
<td>Region, hospital and year</td>
<td>0.89 (0.54 to 1.38)</td>
</tr>
<tr>
<td>Injury severity &gt; minor (n=8 210)</td>
<td>Region, hospital and year</td>
<td>0.88 (0.53 to 1.37)</td>
</tr>
<tr>
<td>All (n=26 463)</td>
<td>Region, hospital, year, age, gender, injury severity, role of victim and co-morbidity</td>
<td>0.85 (0.45 to 1.48)</td>
</tr>
<tr>
<td>Injury severity &gt; minor (n=8 210)</td>
<td>Region, hospital, year, age, gender, injury severity, role of victim and co-morbidity</td>
<td>0.92 (0.47 to 1.67)</td>
</tr>
</tbody>
</table>

Figure 8.
Time to death

The median follow-up was 2.8 years after hospital admission. Among patients admitted to hospital alive, the unadjusted hazard ratio (HR) for PHTLS was 1.03 (95% CI, 0.91 to 1.18). Adjustment for calendar year and region (as frailty components) resulted in a HR of 1.07 (95% CI, 0.92 to 1.23). Further adjustment for age, sex, injury severity, role of victim, and co-morbidity did not indicate any association with PHTLS (HR 0.99; 95% CI, 0.85 to 1.14). Adjustment for hospital instead of region as a frailty factor resulted in a similar estimate (HR 1.02; 95% CI, 0.86 to 1.21).

Return to work

Return to work was assessed among 6061 patients surviving at least one year after hospital discharge and having at least one day of sick leave. Approximately 70% had returned to work within one year from the time of the injury. There was no association between PHTLS and the time from hospital admission until a return to full work when adjusted for age, sex, injury severity, role of the victim, year of injury, and region (adjusted HR = 0.98 (95% CI, 0.92 to 1.05). Adjusting for the receiving hospital instead of the region as a frailty variable resulted in an identical estimate.
Methodological and statistical considerations

This thesis includes four papers, covering three topics, with the common denominator being prehospital education and competence. In the four different papers we used four different methodological approaches demanding different methodological considerations and analytical tools. Since interpretation of causal inference is highly dependent on an understanding of the methodology and statistical tools used, I will shortly discuss the pros and cons of the design of the individual studies.

The experimental study (Paper I)

Study I was an experimental, randomised, crossover design study on a manikin in an experimental setting. The study cohort was relatively small, representing an average ambulance organisation in Sweden. The distribution of gender, age and education corroborated the representativeness. The experimental approach has high validity. The randomisation process reduced the effects of both measured and unmeasured confounding. The crossover design, each subject being its own control, removed the effects of inter-individual differences. The selection of a study population as representative as possible of the target population (ambulance staff in general) was crucial for the possibility of generalising the results. In this sense, this study has a high validity, i.e. it is likely that our results are representative for ambulance staff in Sweden treating a manikin. Nevertheless, the manikin setup implies caution in generalising the results to the clinical situation, even though circumstances other than the manikin, such as equipment and patient scenario, modelled reality as closely as possible. Thus, generalisation to the clinical setting is likely to be the weakest point in this study.

The observational agreement study (Paper II)

Study II was an observational study, where the judgment of ambulance nurses was compared to that of physicians. No actual intervention took place, i.e. no patients actually bypassed the ER. Although the gathering of information might have influenced the medical staff, this study was closer to clinical practice than an experimental study. Some known plausible confounders
were measured and discussed in relation to the results. However, without randomisation, potential unknown confounding could not be controlled for. Statistically, there were two different approaches in analysing this study:

1) analysing the agreement between the judgments made by the ambulance nurse and the physician, without grading whether one judgment was more valid than the other (Cohen’s kappa)\textsuperscript{80}

2) setting the physician’s judgment as the gold standard and consequently evaluating the ambulance nurse’s judgment in comparison with this gold standard (sensitivity, specificity and likelihood ratios).\textsuperscript{81,98}

The former method is frequently used in evaluating agreements between two (or more) subjects, taking into account the possibility of agreement just by chance. However, the Cohen’s kappa (0-1) is a number without an obvious interpretation. Although there have been attempts to facilitate a meaningful interpretation with predefined and named categories, it is still difficult to have an intuitive understanding. The latter method is more robust in its presentation. Sensitivity and specificity have a more intuitive meaning. Collapsing sensitivity and specificity into a single measure, the likelihood ratio, gives an estimate of how much the ambulance nurse’s judgment added to the decisions compared to a priori information. These measures are more easily understood and a generalisation to what would really happen to patients assuming implementation of the concept is fairly straightforward. However, setting the physician’s judgment as the gold standard is not an obviously correct assumption. Not knowing the exact premises on which the physicians made their decisions and not having the outcome for each patient is a weakness of the study.

The epidemiological study on an individual level (Paper III)

In study III we used an individual level epidemiological study design, i.e. we had individual information on exposure, outcome and possible known confounders in each analysed case. By careful selection and control of plausible confounders the problem of confounding in such an observational design could be reduced. Given the observational nature, without a randomisation process, unknown confounding could not be controlled for.

The relatively high number of excluded patients, because of missing information, was a drawback, but the profiles of the excluded patients did not differ substantially from those not excluded. An association between outcome and exclusion is possible, i.e. more severely injured patients requiring more medical attention raises the risk of incomplete medical charts. However, the association between exposure and exclusion is unlikely, making the exclusion a non-differential exclusion. Likewise it is not plausible that the missing information regarding the crew’s competence and PHTLS status was associated with the outcome.
Nevertheless, the random error was undesirably large, creating an insecurity in the estimate. The main reason for this was the overall low incidence of the outcome event, death.

The epidemiological study on an semi-individual level (Paper IV)

In study IV we had individual information on the outcome and plausible confounders, but the exposure data was only available at a group (regional) level. This group or ecologic exposure data implied a semi-individual study.97

Disregarding all other aspects in judging the study’s credibility, the semi-individual study design has a higher degree of validity for etiologic inference compared to truly ecologic studies, but less validity than an individual study design.97 A semi-individual study contrasts the ecologic design in some important aspects of interpretation and resembles more an individual study design. The effect of covariates is more unpredictable in ecologic studies as compared to semi-individual studies. In ecologic studies, any covariate can confound the outcome, even if it is not a risk factor and a priori statements about the potential effect of confounders are not feasible.99 Direction in bias resulting from non-differential misclassification is unpredictable in ecologic studies,100 while misclassification bias is generally conservative in semi-individual studies.97 Furthermore, bias because of the within group variation of unknown covariates is reduced with an increasing number of groups in semi-individual studies, while an increasing number of groups in ecologic studies does not completely resolve that problem.100-101

In this semi-individual study covering all of Sweden, with a staggered gradual implementation of PHTLS over several regions and individual level data of outcome and covariates, the study characteristics resemble an individual level more than an ecologic study design. Still, as in study III, the observational nature prevents the control of unknown or unmeasured confounding.

A Bayesian approach was used in the statistical analyses of binary mortality outcomes. This allowed for the handling of correlated data within hospitals and regions using hierarchical random effects models, thereby controlling for systematic differences in hospital care and regional healthcare systems effects. The Bayesian approach also provides credibility intervals as a measure of the precision of the estimates. Credibility intervals have the additional advantage of having a more intuitive interpretation than ordinary CIs.
Discussion

Paper I

Interpretation of the results
The results obtained concerning the primary endpoints are important in that they indicate a possibility to implement mechanical chest compression devices in CPR, without jeopardising other factors known to be of major importance for survival. It is of the utmost importance though, that our results are confirmed by studies performed in a true clinical setting.

The strikingly poor quality of compressions with the mechanical device raises concern, since the device is already in regular use in several ambulance organisations worldwide. If our results holds true also in the clinical setting, patients might not be getting the best possible treatment during CPR when mechanical devices are used.

We did not observe any obvious correlation between education and skill training versus performance in this study. Nevertheless, the quality of educational programmes and instructor competence are important aspects to consider.\textsuperscript{102-103}

Strengths and limitations
As mentioned earlier, the ability to generalise our results to the clinical setting is a crucial step in the interpretation of the result of this study. There could be several reasons for the poor quality obtained. Some reasons might be due to the fact that the study was performed as an experimental setup. Other reasons might in fact reflect the performance in the clinical setting.

The crossover design together with the representative study population having implemented the new device in regular practice, contribute to the strengths of this study.

The artificial, unnaturally optimal simulator setting with minimal distractions may not reflect the performance of CPR in the clinical setting. The crossover design and the setting being identical in all performances, make it unlikely that this would influence the possibility to extrapolate the results into clinical practice. The simulation setting might also influence the incentive of the ambulance crew. However, the quality of manual compressions and the performance of key interventions were comparable to previous stud-
ies from clinical settings, indicating adequate overall performance from the crews studied.27,104

A manikin is not a human being. This is probably the major limitation in extrapolating the results to clinical practice. Compared to a human, the manikin is lighter and its surface differs from human skin. This might influence how the device behaves and sliding could possibly be different on the manikin than on humans. Nevertheless, sliding is a known phenomenon also during clinical use of the LUCAS device. The application of the stabilisation strap is supposed to inhibit sliding and it is emphasised in the training programme for the device.34 An initial mal-positioning of the device or failure to apply the stabilisation strap, combined with failure to observe and correct the position when sliding of the device does occur, are unlikely to be entirely caused by the manikin setup. There is little reason to believe that the above mentioned failures are not a reflection of the staffs’ ordinary behaviour also in clinical practice.

Results from a multicenter study using another mechanical compression device (Autopulse) revealed a substantial variability in CPR performance with the mechanical device, despite a standardised educational programme.105 These results corroborate those of the present study.

Summary

The device in our study certainly delivers chest compressions with a constant depth. However, given incorrect initial placement or sliding, it does not necessarily generate an adequate compression depth at the intended location. If the poor compression quality found in this study also reflects performance in the clinical setting, this might cause sub-optimal CPR and partly explain the failure of the mechanical devices to improve the outcome in clinical trials.

Paper II

Interpretation of the results

This study investigated one possible way to shorten the time to thrombolysis in stroke patients, by taking advantage of the already existing competence of ambulance nurses in prehospital settings. From this aspect, the poor results were discouraging. The nurses had a low sensitivity for selecting the same patients as the physicians and the kappa values for agreement were below 0.5 in all analyses, including sub-groups.
Assessment of the need for a CT scan
The poor results observed in this study were somewhat surprising and in contrast to the high levels of accuracy reported in other studies using stroke identification instruments in prehospital settings. For more than a decade, the ambulance service participating in this study has been involved in the stroke chain of survival through a comprehensive programme that includes a stroke identification instrument. Although prehospital instruments for diagnosing a stroke have a high degree of accuracy, they do not contain explicit instructions for assessing whether or not a CT scan is required.

Assessment of the need of interventions before a CT scan
The poor level of agreement and low sensitivity regarding the assessment of interventions and monitoring before a CT scan also fail to support the transition of decisions from physicians to ambulance nurses. There is, however, possible room for improving the basis on which the nurses judge the patients’ need for interventions. Pre-METTS© is a triaging tool adapted for prehospital use and has been reported as valid in assessing prehospital trauma. The correlation in our study between higher MEWS and the proportions of patients in need of interventions or monitoring before a CT scan, as judged by both ambulance nurses and physicians, supports the idea that a triage tool could be supportive in this type of prehospital decision making.

Strengths and limitations
Fluctuations in symptoms and changes in the patients’ conditions over time could explain the disagreement between the ambulance nurses’ and the physicians’ assessments. When the time between the two examinations was less than 20 minute there was a tendency towards higher agreement on the assessed need for interventions. However, there was no apparent relation between the difference in MEWS between the two examinations and the degree of agreement.

The MEWS parameters used in our study were retrospectively collected from patient records. Other studies show substantial variability in inter-rater agreement in grading a patient’s level of consciousness, one of the items in MEWS. This could question the use of MEWS as the sole indicator of disease severity in patients. Indeed, there might be other time-dependent indicators of a patient’s condition that are not captured by MEWS.

As mentioned above the assumption that the physician’s judgment is the gold standard is debatable. The accuracy of a physician’s diagnosis of stroke varies widely, and some studies show as high or even higher accuracy when paramedics diagnose patients in the prehospital phase using stroke identification tools. In designing this study, we tried to optimise
the physician assessments by requiring the participation of a senior physician. Still, not being able to correlate these decisions with patient outcomes is a weakness of this study.

Summary
There is poor agreement between ambulance nurses and ED physicians in assessing suspected stroke patients’ need for a CT scan and for interventions and monitoring before a CT scan. Additional tools to support prehospital decision making appear to be required before suspected stroke patients can be taken directly to a CT scanner by the ambulance team, bypassing the ED.

Papers III and IV
Interpretation of the results

Study III
There was a relative risk reduction of 29% in mortality by the implementation of PHTLS. This estimate, however, had low precision. The absolute risk reduction was low. Time to return to work among patients working before the injury and alive at hospital discharge was shorter for patients exposed to PHTLS, but this result also had low precision.

Study IV
In this nation-wide population-based study of motor vehicle traffic injuries a reduction in prehospital mortality coincided with the gradual implementation of PHTLS training of ambulance personnel over the study period. However, this reduction in prehospital mortality over time did not appear to be associated with regional implementation of PHTLS. There was no association between PHTLS and survival time or time to return to work.

The combined results of study III and IV
The results of studies III and IV are apparently contradicting. However, there are some methodological differences between the studies that need to be considered.

The overall aim for both studies III and IV was to evaluate the potential effect that the implementation of PHTLS has for the outcome for trauma patients. However, the detailed aims differ between the two studies. Study III analysed trauma in a cohort of injured patients in general, including a large population with low-energy traumas, such as hip fractures as a result of falls. Study IV analysed a cohort of victims of motor vehicle traffic crashes, with mainly high-energy trauma. This difference in the selection of the study
population is reflected in the distribution of injury severity, with the more critically and severely injured being in study IV. Also the age distribution differs, with the older patients being in study III, presumably with an accompanying higher co-morbidity, although this was not measured in study III. Patients with a high level of co-morbidity could possibly be more resistant to treatments focused on traumatic injuries. Thus, if there is a protective effect from PHTLS, one would possibly have expected a stronger association in study IV, where the population is more severely injured and has a lower degree of co-morbidity than those in study III.

Also the mortality outcome measurements differed between the two studies. In study III we measured the composite outcome of prehospital and hospital mortality, while in study IV we measured prehospital mortality and 30-day mortality separately. In study IV the majority of deaths occurred before hospital admission, while in study III the majority of deaths occurred in hospital. What measures to use in trauma outcome studies is debatable. One could speculate that prehospital mortality is an imprecise outcome measure in trauma. The closer a death occurs to the time of injury, the more likely it might be that the trauma mechanism in itself is the overwhelming predictor of death, while treatments given are of less importance. It could be that the injuries are so severe that the patient dies in spite of any treatment efforts. In that sense, hospital mortality and 30-day mortality might be a more sensitive measure to capture a potential effect of PHTLS. Indeed, in study IV there was a tendency towards a protective effect by PHTLS in 30-day mortality among survivors admitted to hospital. In study III, where the overall result indicated a protective effect by PHTLS, the majority of deaths occurred in hospital.

The low precision seen in some of our results are, to a large extent, the consequence of the low overall mortality. In study IV this is the likely explanation as to why the precision deteriorates when the analysis is restricted to patients admitted to hospital alive. The majority of deaths were prehospital, with comparably few in-hospital deaths.

Strengths and limitations

Although the two studies differ in their methodological approach, both studies are observational studies, thus limiting the ability for causal inference. In both studies we had individual information on all confounders and outcomes. In study III we also had information on exposure at the individual level, while in study IV the exposure was an ecologic measure at the regional/group level. Thus, in study III we analysed in each case, if the patient outcome was associated with the PHTLS status of the ambulance crew in that same case. In study IV we analysed if the outcome in each case was associated with the regional implementation of PHTLS, and the actual crew
competence in each case was not known. Study IV should not be given an interpretation on the individual level, but instead inform on the potential impact at the population level. Using the opportunity of a staggered regional implementation of PHTLS in a nation-wide cohort provided an opportunity to avoid the use of historical control subjects, and increased the credibility of the results.

The implementation of PHTLS might create a Hawthorne-like effect not only on individuals, but also on the organisation as a whole. Thus, a general focus on trauma might raise the overall performance in trauma care not only of PHTLS certified individuals, but also of uncertified staff in the same organisation. It is conceivable that the actual knowledge content of the PHTLS course could be gained in other ways and through other types of education and training. Not having detailed information on the actual competence or knowledge level of the ambulance crew nor the actual decisions made or interventions performed in each case, is a limitation of both study III and IV. Whether it is the certified or the uncertified staff who are most likely affected by a possible Hawthorne-like effect, will determine the direction of this potential bias. However, in comparing the results of the two studies it is likely that the effect is similar in both cases.

The ability to generalise our results to other settings should be considered, since the PHTLS course has been implemented worldwide. The PHTLS course is highly standardised with supervision from national faculties. However, the basic educational level of prehospital crews varies between different settings and this could hamper the ability to generalise the results to other settings, such as paramedic or EMT-based systems.

Summary

The results of study III provide some support of an association between the implementation of PHTLS and lowered mortality, although the precision of the estimated associations was low. The results from study IV could not confirm the results from study III. Even though a reduction of prehospital mortality was observed over time in study IV, it did not appear to be associated with regional implementation of PHTLS. We could not detect any clear beneficial impact of the PHTLS course on the outcomes of trauma patients.
Conclusions

The use of mechanical chest compression devices needs further evaluation before implementation in regular clinical practice. The results from study I call for caution when implementing a chest compression device in clinical practice and reinforce the importance of randomised controlled trials. Careful attention should be given to the assurance of correct application of the device. Further implementation without evaluation of the quality of mechanical compressions in a clinical setting is discouraged.

Our results in Paper II could not support an implementation of a shortcut in the stroke chain of survival using ambulance nurse competence supported by a stroke identification tool to bypass the ED. Indeed, there is a need to shorten the time to thrombolysis in patients suffering an ischemic stroke, and the knowledge gained in this study could possibly be used for designing further attempts to fulfil this need.

The implementation of the PHTLS concept does not appear to lower mortality. The possible protective effect observed in study III could not be confirmed in study IV. Taken together, in spite of a comprehensive analytical approach, the results do not provide evidence of any obvious beneficial effect of PHTLS implementation. Observational studies, however, remain limited in their ability to evaluate the effects of interventions and a modest effect on mortality cannot be ruled out.
Future perspective

The LUCAS device is an example of a commercially successful industrial design. Nevertheless, our results indicate a potential for further development. The auditory, real-time feedback used in automated external defibrillators could possibly be applied to mechanical compression devices as well.\textsuperscript{118} The outline of the education and skill training to be competent to use mechanical devices needs to incorporate an evaluation of the performance of key components to assure compliance. Another interesting question is how to maintain the skill and knowledge of ambulance staff over time. A reduction in incentive and enthusiasm over time is likely and needs to be addressed.

It is not clear how the competence of ambulance nurses should best be used. In a continuing effort to increase efficiency and improve prehospital care, it is likely that the transfer of advanced treatments and decisions from physicians to nurses will continue. In order to maintain patient safety during such a process it is crucial that such changes in clinical practice are subjected to scientific evaluation.

Concept courses in trauma care have received high acceptance and have been rapidly implemented despite a lack of scientific support of their effectiveness. The reason might be that they filled a gap in the ordinary educational system. All concept courses in trauma care use the pneumonic ABCD (Airway, Breathing, Circulation, Disability) as a structure for assessment and prioritising treatments. This core principle has now spread to the university teaching of physicians and nurses and there is good reason to believe that the next generation of prehospital care providers might be well acquainted with the core concept of PHTLS from their basic education. This could possibly diminish the future need for PHTLS and similar courses. Irrespective of the educational context, there is a clear need for scientific evaluation of the usefulness of specific educational programmes and their actual effects on patient outcomes.

The statement made eighteen years ago by Spaite et al.\textsuperscript{6}, concerning the importance of objectively and convincingly proving the cost effectiveness of a given service, is still valid for the future development of prehospital care. There is an obvious need for well-designed studies targeting specifically the prehospital setting. The prehospital development should follow the same principles as health care in general – robust scientific evidence should precede clinical implementation.
Acknowledgements

This work was carried out at the department of Anesthesiology and Intensive care, Uppsala University Hospital. I would like to thank the executives at the University and Hospital departments for given support and time.

I am more than grateful to the team that guided me through this learning adventure:

Rolf Gedeborg, my supervisor and scientific guide, with more knowledge in scientific research than anyone else I know*. Your total support and never ending patience in listening, explaining, teaching and teaching again has sorted out the magic of science and taught me the value of short sentences.

Jakob Johansson, my co-supervisor and coach. With an aura of energy and support, imaginary deadlines and the ability to push without pushing, you dragged me in, squeezed me through and forced me out.

Karl Michaelsson, my co-supervisor tranquilizing my epidemiological worries by teaching epidemiology and the principle of simplicity: “you do not need to know it all”

I also want to send my gratitude to:
Per Andersson - Head of the Ambulance Service, Jessica Colldén Benneck - Educational Nurse, and all others at the Ambulance Service, for all support and putting up with me being distracted during the last months.

And to all others, who contributed in different ways:
Erik Lundström, Per Blomqvist, Rolf Karlsten, Liisa Byberg, Henrik Toss, Bodil Svennblad, Lars Berglund, Lisa Wernroth, Håkan Melhus, Steven Butler, Isabel Andersson, Torsten Gordh, Emma Pontén and

my mother Ulla and my brother Anders for just being there and my late father Lars for having been there.

And finally my Family: Stina, Simon, Nils and Hedvig for truly advanced life support.
* p<0.05, no thesis without a p (Bätt översatt: Ingen avhandling utan att kissa)
References


67. Lerner EB, Moscati RM. The golden hour: scientific fact or medical "urban legend"? *Acad Emerg Med* 2001;8:758-760.


A doctoral dissertation from the Faculty of Medicine, Uppsala University, is usually a summary of a number of papers. A few copies of the complete dissertation are kept at major Swedish research libraries, while the summary alone is distributed internationally through the series Digital Comprehensive Summaries of Uppsala Dissertations from the Faculty of Medicine.