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SEVERITY, PREHOSPITAL MONITORING AND OUTCOMES

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BY
VIBE MARIA LADEN NIELSEN

DISSERTATION SUBMITTED 2023

AALBORG UNIVERSITY
DENMARK

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PhD Dissertation submitted 2023

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SUMMARY

In Denmark, every 10th ambulance dispatch is for a child. For the individual emergency medical service (EMS) professional though, it is relatively rare that he or she needs to assess and treat children compared to the many adult and elderly patients they attend. For various reasons, assessing the severity of illness or injuries in children can be more difficult than in adults, especially for healthcare professionals who do not attend to children on a daily basis. This means that EMS professionals who are expected to treat possibly life-threatening conditions in children do not have ideal preconditions for this, simply because life-threatening conditions happen so rarely. In the mid-2010s, an international movement developed to address this paradox: The concept of 'paediatric readiness' in emergency departments and ambulance services that primarily treat adults. It is a wide-ranging term and covers both the availability of paediatric-sized equipment, clinical guidelines, policies, etc. and that emergency care providers receive appropriate training in commonly occurring paediatric emergencies.

Because life-threatening emergencies are relatively rare but may progress rapidly in children, EMS professionals must make use of a systematic clinical approach at all times and in children of all ages.

The overall aim of this PhD project is twofold: *Studies I-II* investigate vital sign measurements in children attended by EMS professionals and describe the implementation of various initiatives aimed to promote a systematic clinical approach to these children. *Studies III-IV* outline the diagnostic pattern and mortality after paediatric emergency calls in Denmark.

The four studies included in this PhD dissertation were based on the following objectives:

- To investigate the severity of illness or injuries in children attended by an ambulance or helicopter in Denmark.
- To produce and implement various educational initiatives for EMS professionals aimed to promote the use of a systematic clinical approach to children with acute illness, especially infants and toddlers.
- To outline diseases and injury types in these children.
- To investigate the prevalence of pre-existing comorbidity in children attended by EMS and short-term mortality from trauma, out-of-hospital cardiac arrest and medical conditions in children with and without comorbidity, respectively.

Clinical assessment

Study I: Severity of illness or injuries reported that one in three children (28%) had either life-threatening or urgent conditions upon arrival of the ambulance. The extent of missing data on vital signs was substantial, particularly among infants and toddlers aged 2 years or younger. In collaboration with representatives of the paramedics at The North Denmark EMS, several initiatives were launched in an attempt to remedy these missing data. Among others, an instructional video demonstrated a standardised and structured approach to the examination of infants with signs of acute illness.

In a subsequent clinical observational study (*Study II: Prehospital monitoring*), we investigated if the proportion of patients with complete vital sign registration had increased following the launch of the initiatives. Complete registration included at least two values of heart rate, conscious level, oxygen saturation and respiratory rate as a proxy for a basic ABCD evaluation and reevaluation of the patient. An increase of approximately 10% was observed with larger increases among the younger age groups. The proportion of patients with complete vital sign registration was also higher compared to another Danish region with similar demography, indicating that the increases found were not just due to a temporal trend.

Diagnoses

In international literature, injuries have been the dominant cause of death from paediatric emergencies for the past decades. The nationwide epidemiological studies in this dissertation were based on data from *The Danish Clinical Quality Program – National Clinical Registries*. We listed incidences of hospital diagnoses arranged by organ system and injury types by WHO's ICD-10 classification. Estimates of short-term mortality after an emergency call were calculated using several different methods. For *Study III: Outcomes after emergency calls*, all emergency calls were included, regardless of whether an ambulance, a helicopter or another prehospital unit had been dispatched, while *Study IV: Outcomes after dispatch of HEMS* focused on the subgroup of patients for whom a helicopter had been dispatched. In comparison with other countries, the national helicopter emergency medical services (HEMS) were dispatched for more children with medical conditions compared to injuries.

After appropriate hospital diagnostics, the EMS patients were given a diagnosis, and in this cohort, diagnoses were dispersed over all 21 ICD chapters. Frequently occurring diagnoses were within the chapters *Injury, poisoning and certain other consequences of external causes*, *Diseases of the respiratory system*, *Diseases of the nervous system* and *Symptoms, signs and abnormal clinical and laboratory findings, not elsewhere classified*. A third of the injuries were to the head, and almost half of the *Symptoms and signs* were febrile convulsions. Among all children assessed by the EMS, close to 40% had previous or chronic diseases, conditions, or perinatal complications.

Mortality

The annual all-cause mortality rate was 7 per 100,000 children aged ≤15 years. As expected, short-term mortality was higher in the subgroup of children attended by HEMS (5.1% versus <1% in the total cohort of EMS patients).
Mortality estimates in *Study III* included deaths that had happened within 7 days of the emergency call. Although injuries were responsible for one out of three ambulance dispatches for children, only one in eight deaths following an emergency call could be attributed to trauma. A third of the deaths following paediatric emergencies were due to out-of-hospital cardiac arrest. In close to half of the non-survivors (42.7%), the call had been regarding medical symptoms (besides out-of-hospital cardiac arrest) or had been a problem that was unclear to the medical dispatcher.

Almost half of the non-survivors (47.5%) had no comorbidity, while a quarter of the non-survivors had chronic diseases so severe that the diagnosis implied a limited life expectancy. Both among the children *with* and *without* pre-existing comorbidity, the majority (>75%) of emergency calls for non-survivors had been made because of various medical symptoms incl. paediatric out-of-hospital cardiac arrest, and not because of trauma.

Synopsis

While mortality after paediatric emergencies is low, EMS professionals encounter children with a wide variety of symptoms and diseases and a considerable proportion of the patients have pre-existing comorbidities, some of them severe. The four studies enclosed in this dissertation emphasise the importance of training for EMS professionals and maintenance of competencies to manage and treat children with acute illnesses. Part of the educational material produced in *Study II: Prehospital monitoring* was subsequently implemented at the University College of Northern Denmark for the teaching of future paramedics from all five Danish regions. The studies also suggest that EMS professionals could benefit from education on how to tailor management of exacerbations or emergencies in children with commonly occurring comorbidities. For further research on the quality of prehospital care, subgroups of patients with specific diseases or conditions can easily be identified using this nationwide cohort with definitive hospital diagnoses. The studies also contribute to creating awareness of ‘paediatric readiness’ in the emergency health care system in Denmark. In the dissertation, specific suggestions for future paediatric research themes within prehospital medicine are provided.

SUMMARY IN DANISH

I Danmark er cirka hver 10. ambulancekørsel til et barn. For den enkelte ambulancebehandler eller paramediciner er det dog relativt sjældent at han eller hun skal vurdere og behandle børn i forhold til de mange voksne og ældre patienter, de rykker ud til. Der er mange og forskelligartede årsager til, at vurdering af alvorlighedsgraden af sygdom hos børn kan være mere udfordrende end hos voksne. Især for sundhedspersonale, der ikke til dagligt arbejder med børn. I midten af 2010'erne igangsattes en international bevægelse, som skulle angribe netop dette paradoks; at sundhedspersonale, der forventes at kunne behandle akutte og muligt livstruende tilstande hos børn, ikke har de bedste forudsætninger for dette, simpelthen fordi det sker så sjældent. Begrebet 'børneparathed' var født. Det er et vidtfavnende begreb og handler både om, at afdelinger eller beredskaber med voksne som primær patientgruppe har passende udstyr i børnestørrelser, men også om, at der regelmæssigt afsættes tid til træning i håndteringen af de mest almindeligt forekommende akutte tilstande blandt børn.

Netop fordi livstruende tilstande er sjældne, men kan udvikle sig hurtigt hos børn, må ambulancepersonale til alle tider benytte en systematisk tilgang til børn i alle aldre. Formålet med dette ph.d. projekt er derfor todelt: *Studie I-II* undersøger ambulancepersonalets målinger af vitale værdier, der optages ifm. den kliniske vurdering af børn samt beskriver initiativer til at understøtte en systematisk tilgang til denne vurdering. *Studie III-IV* skaber et overblik over diagnosemønster og dødsfald blandt børn i forbindelse med et opkald til 112.

De fire studier, som indgår i denne ph.d. afhandling, er udarbejdet med afsæt i følgende konkrete formål:

- At undersøge hvor mange af de børn, der ringes 112 om i Danmark, der har kritiske tilstande ved ambulancens eller akutlægehelikopterens ankomst.
- At udarbejde en række initiativer, som skal klæde ambulancepersonale bedre på til at vurdere alvorlighedsgraden af sygdom hos akut syge børn, i særdeleshed spædbørn og småbørn.
- At opgøre alle diagnoser og typer af skader hos disse børn.
- At afdække hvor mange børn, som havde tidligere eller kroniske sygdomme inden opkaldet til 112.
- At undersøge om dødsfald oftest sker efter ulykker, efter hjertestop eller efter akut opstået sygdom, og om dette afhænger af, om barnet havde tidligere eller kroniske sygdomme før den akutte situation opstod.

Klinisk vurdering
Studie I: Sværhedsgrad af sygdom eller skader viste, at knap et ud af tre børn, som blev tilset af en ambulance (28%), havde hastende eller direkte livstruende tilstande. Mange børn, i særdeleshed spædbørn og småbørn, fik ikke målt vitale værdier som f.eks. puls, iltmætning etc. I samråd med repræsentanter for paramedicinergruppen hos Den Præhospitale Virksomhed i Region Nordjylland udarbejdede vi en række initiativer, som skulle afhjælpe dette, blandt andet en undervisningsvideo, som demonstrerede en internationalt anerkendt systematik til undersøgelse af småbørn med akut sygdom.
Efter at disse initiativer var blevet søsat i ambulancetjenesten, overvågede vi andelen af patienter, som fik indtastet puls, bevidsthedsniveau, iltmætning og vejrtrækningsfrekvens i ambulancejournalen, som et udtryk for, at der var udført en grundlæggende helhedsvurdering af barnet (*Studie II: Præhospital monitorering*). Her observeredes en stigning i denne andel på cirka 10% sammenlignet med før initiativerne - og større stigninger sås i de yngste aldersgrupper. Andelen var også større sammenlignet med en anden dansk region med lignende demografi, hvilket tyder på, at fundene ikke blot var et udtryk for en tidsmæssig trend.

Diagnoser
I den internationale litteratur har skader i årtier været den dominerende årsag til dødsfald efter akutte tilstande hos børn. Afhandlingens landsdækkende epidemiologiske studier blev udført med afsæt i *Regionernes Kliniske Kvalitetsudviklingsprogram (RKKP)*. Vi oplistede forekomsten af forskellige hospitalsdiagnoser, ordnet efter organsystem som det kendes fra WHO's ICD-10 klassifikation. Desuden estimeredes mortaliteten efter et opkald til 112 udregnet ved brug af flere forskellige metoder. I *Studie III: Opfølgning efter 112-opkald* indgik alle opkald til 112, uanset om der blev afsendt en ambulance, akutlægehelikopter eller anden præhospital enhed. Efter indledende diagnostik på hospitalet gives patienten en diagnose, og blandt disse børn sås diagnoser inden for samtlige 21 ICD-10 kapitler. De hyppigst forekommende diagnoser var indenfor kapitlerne *Skader, forgiftninger og visse andre følger af ydre påvirkninger*, *Sygdomme i åndedrætsorganer*, *Sygdomme i nervesystemet* samt *Symptomer og abnorme fund ikke klassificeret andetsteds*. En tredjedel af skaderne var hovedskader, mens knap halvdelen i *Symptom* kapitlet var feberkramper. Blandt alle børn, der blev tilset af en ambulance eller akutlægehelikopter, havde cirka 40% haft én eller flere tidligere eller kroniske sygdomme, tilstande eller perinatale komplikationer.

Studie IV: Opfølgning efter afsendelse af en akutlægehelikopter fokuserede på den undergruppe af patienter, hvortil en akutlægehelikopter var blevet afsendt. Sammenlignet med andre lande flyver den danske akutlægehelikopter til flere børn med sygdomme set i forhold til ulykker.

Mortalitet
Den årlige mortalitetsrate var 7 per 100.000 børn i alderen til og med 15 år. Dødeligheden var som ventet højere i den undergruppe af børn, hvortil en akutlægehelikopter var blevet afsendt (5.1% versus <1% af alle de børn, der blev ringet til 112 om). Mortalitetsanalyserne i *Studie III* inkluderede dødsfald, som var sket indenfor 7 dage efter opkaldet til 112.
Selvom skader udløste hver tredje udrykning, så kunne kun ét ud af otte børnedødsfald efter et 112-opkald tilskrives en ulykke. En tredjedel af dødsfaldene var på grund af et hjertestop, der var sket udenfor hospital. Og i knap halvdelen af dødsfaldene (42.7%) havde 112-opkaldet drejet sig om forskellige symptomer på sygdom eller om et problem, som var uklart for den sundhedsprofessionelle, der besvarede opkaldet.
Knap halvdelen af alle de børn (47.5%), som ikke overlevede op til en uge efter 112-opkaldet, havde ingen forudgående sygdomme, mens en fjerdedel havde kroniske sygdomme af en sådan sværhedsgrad, at diagnosen forventeligt kunne medføre begrænset levealder. Både blandt dødsfald hos børn *med* og *uden* forudgående sygdomme havde størstedelen (>75%) af 112-opkaldene drejet sig om forskellige symptomer på sygdom eller hjertestop, og ikke om ulykker.

Afrunding
Sammenfattende sker der blandt børn i danske ambulancer og akutlægehelikoptere få dødsfald, men der ses et meget bredt symptom- og sygdomsmønster og mange patienter har en betydelig grad af komorbiditet. Disse fire studier understreger vigtigheden af, at sundhedsprofessionelle i det akutte sundhedssystem vedligeholder kompetencer til at modtage og behandle børn med akut opståede sygdomme. En del af det undervisningsmateriale, som blev udarbejdet til *Studie II*, bruges nu på University College Nordjylland, som har landsfunktion for uddannelse af paramedicinere. Studierne indikerer også, at ambulancepersonale i højere grad bør modtage undervisning i, hvordan den akutte behandling evt. skal tilpasses til børn med almindeligt forekommende komorbiditeter. Den landsdækkende kohorte med definitive hospitalsdiagnoser, der blev dannet til denne afhandling, kan med fordel benyttes til at afgrænse subgrupper af patienter med specifikke sygdomme eller tilstande til brug for fremtidig forskning i kvaliteten af præhospital behandling af disse tilstande. Afhandlingen bidrager også til at skabe opmærksomhed omkring 'børneparathed' i det akutte sundhedssystem i Danmark.

ABBREVIATIONS AND DEFINITIONS

95% CI Confidence interval, reported as [xx;xx]
ABCDE Airways – Breathing – Circulation – Disability – Exposure
ALS Advanced life support
BLS Basic life support
COVID-19 Coronavirus disease of 2019
CRS Civil Registration System
DNPR Danish National Patient Register
EMS Emergency medical services
EPALS European Paediatric Advanced Life Support
ePMR Electronic patient medical records
GCS Glasgow Coma Score
GDPR General Data Protection Regulation
HEMS Helicopter emergency medical services
HR Hazard ratio
ICD-10 *International Statistical Classification of Diseases and Related Health Problems, Tenth Revision*
ICU Intensive care unit
IQR Interquartile range
MECU Mobile emergency care unit
PEWS Paediatric early warning score
PIN Personal identification number
POHCA Paediatric out-of-hospital cardiac arrest
RKKP Regionernes Kliniske Kvalitetsudviklingsprogram (*The Danish Clinical Quality Program – National Clinical Registries*)
SpO_2 Peripheral capillary oxygen saturation
WHO World Health Organization

112: The national emergency phone number in Denmark.

Complete vital sign registration: Registration of at least two full sets of the following vital signs: respiratory rate, SpO2, heart rate and level of consciousness. Likewise, 'incomplete vital sign registration' means that less than four vital signs, or none at all, had been documented.

EMS professionals: Collective designation used for all medical professionals working in the prehospital field. Can be further specified into emergency medical technicians, paramedics, HEMS crew members and prehospital physicians.

Paediatric: Regarding children aged <16 years unless otherwise specified.

SCIENTIFIC PAPERS

I. Nielsen VML, Kløjgård T, Bruun H, Søvsø MB, Christensen EF. Progression of vital signs during ambulance transport categorised by a paediatric triage model: a population-based historical cohort study. *BMJ Open* 2020;10:e042401. doi:10.1136/bmjopen-2020-042401

II. Nielsen VML, Søvsø MB, Kløjgård TA, Skals RG, Corfield AR, Bender L, Lossius HM, Mikkelsen S, Christensen EF. Prehospital vital sign monitoring in paediatric patients: an interregional study of educational interventions. *Scand J Trauma Resusc Emerg Med* 2023 Jan 14;31(1):4.
doi: 10.1186/s13049-023-01067-z

III. Nielsen VML, Søvsø MB, Skals RG, Bender L, Corfield AR, Lossius HM, Mikkelsen S, Christensen EF. Mortality in Relation to Comorbidity Among Children Attended by Emergency Medical Services. (Manuscript submitted)

IV. Nielsen VML, Bruun NH, Søvsø MB, Kløjgård TA, Lossius HM, Bender L, Mikkelsen S, Tarpgaard M, Petersen JAK, Christensen EF. Pediatric Emergencies in Helicopter Emergency Medical Services: A National Population-Based Cohort Study From Denmark. *Ann Emerg Med* 2022 Aug;80(2):143-153.
doi: 10.1016/j.annemergmed.2022.03.024

SCIENTIFIC ABSTRACTS

VML Nielsen, MB Søvsø, T Kløjgård, NH Bruun, S Mikkelsen, HM Lossius, M Tarpgaard, JAK Petersen, EF Christensen. Paediatric Emergencies in the Danish Helicopter Emergency Medical Services [abstract]. In: *European Emergency Medical Services Congress; 2022 May 4-6; Glasgow, Scotland (UK).* Abstract no. PW3-7.

VML Nielsen, MB Søvsø, T Kløjgård, S Mikkelsen, EF Christensen. Documentation of vital signs for paediatric patients in ambulances: A cross-regional prospective observational study [abstract]. In: *European Congress of Emergency Medicine (EUSEM); 2022 Oct 16-19; Berlin, Germany.* Abstract no. OA063.

VML Nielsen, MB Søvsø, RG Skals, L Bender, AR Corfield, HM Lossius, S Mikkelsen, EF Christensen. Short-term mortality in relation to pre-existing conditions in paediatric emergency patients – A national historical cohort study [abstract]. In: *European Resuscitation Council (ERC) Congress*; *2023 Nov 2-4; Barcelona, Spain.* Abstract no. 388. *Resuscitation* 2023 Nov;192(Suppl 1):S148.
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CURRICULUM VITAE

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Vibe Maria Laden Nielsen graduated as a medical doctor from Aalborg University in 2018. She had extended the studies with an extra year dedicated to clinical research in patients with acute respiratory failure. During this work, she was introduced to the prehospital research environment and built a network of skilled colleagues. The rise of a newly established research unit, Centre for Prehospital and Emergency Research, encouraged her to stay in this field. For publication history, please refer to her ORCiD profile (no. listed above). She is also a big fan of medical simulation training, both as an instructor and as a team member, and goes by the motto

"HE WHO CONSIDERS HIMSELF AS FULLY EDUCATED, MAY IN FACT BE EDUCATED – BUT SURE IS FULL OF HIMSELF…" – PARAPHRASE FROM AN OLD CHINESE SAYING

During the years 2018-2020, she completed the first year of foundation training and was licensed to practice medicine. Accordingly, her clinical experience comes from working in the fields of emergency medicine, psychiatry, COVID-19 pandemic units and general practice, totally one and a half years. During this time, ideas originated for the work presented in this dissertation. For someone without any specialist paediatric training, it was difficult to project confidence and professionalism to caregivers when caring for the children who occasionally visit general practice and adult emergency departments (e.g. patients with conditions that need help from surgical specialities). It seemed obvious to combine this challenge with an interest in research, and as they say "the rest is history…"

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I would like to formally thank the main funder of the project, the Danish Air Ambulance. Main supervisor Dr Erika Frischknecht Christensen and collaborator Dr Søren Mikkelsen are members of the Danish Air Ambulance research committee. They were both disqualified in the decision to support the grant application for this project. The research committee had the opportunity to comment on the protocol for the entire PhD project. None of the funding bodies had any influence over neither the collection nor the interpretation of data or the reporting of the studies.

My primary supervisors, Drs Erika Frischknecht Christensen and Morten Breinholt Søvsø, deserve special thanks. They have been a great match for a supervisor team: One who takes the ideas flying high and one who makes sure they do not hover forever, but land safely every time. Erika, I never doubted your commitment to the project and always felt you had my back. And Morten, your work ethic is an inspiration to all of us at the research centre. I would also like to thank my assisting supervisor at the Paediatric Department, Dr Lars Bender, for sharing his clinical expertise and positive attitude throughout the project.

Our long-term research partner, Dr Hans Morten Lossius, was also an assisting supervisor. He gave me the opportunity to visit the Norwegian Air Ambulance Foundation, a leading research environment within prehospital medicine in Europe. I owe thanks to a number of people for making sure this visit was a convenient mix of professional discussions, pleasant company and winter swimming: Ingunn Skogstad Riddervold, Jo Røislien, Kirsti Strømmen Holm, Marius Rehn and my PhD peers at Storgata.
The Norwegian Air Ambulance Foundation is also the driving force behind the European Prehospital Research Alliance, EUPHOREA. I got to attend the 2019 meeting in Zürich to present my ideas for the project. Here we met Dr Alasdair Corfield, who is a consultant in emergency & retrieval medicine and a Professor at the University of Glasgow. So far, *Studies II: Prehospital monitoring* and *III: Outcomes after emergency calls* have been the result of our collaboration, and hopefully many more are to come.

As if a team of four competent supervisors was not enough, Søren Mikkelsen practically acted as a fifth. He is the daily manager of the physician-staffed mobile emergency care unit in Odense, Denmark, and has always provided constructive and encouraging ideas.

I am lucky to be surrounded by family and friends who supported this journey from ideas to dissertation. I am exceedingly grateful to Arne, Jytte and Grethe, as they provided unfailing support, both for me and my family. At home, Jonas, Eva and Hjalte generated energy for me to continue the journey, and it is safe to say that "this year's love, it will last." I also owe thanks to my dear friend and colleague Sofia who spurred me on whenever I was challenged.

A great thanks to all my colleagues at the Centre for Prehospital and Emergency Research. To Torben, who has an irreplaceable skill set in data management within this research field. And to Charlotte, Tim, Stine and Erik for making the everyday struggle worthwhile. And to Hans Ole, who helped me get settled in the beginning, he has been like the grandpa I forgot that I had. At Aalborg University, Tamara R. McGee and the three workbooks published by her really improved my skills in medical writing. And Søren Paaske Johnsen was a supportive opponent on my pre-defence at the end of the first year of PhD studies.

Study II: Prehospital monitoring was conducted in collaboration with the North Denmark EMS and it would not have been possible without the courteous help of paramedics Lars Borup, Jacob Kruse and Jacob Thornvig Andersen. They provided extensive feedback on the educational initiatives and insights into the daily clinical practices in the North Denmark EMS. I highly appreciate the reviews and comments made by competent clinicians: Søren Kjærgaard (consultant in paediatric anaesthesiology at Aalborg University Hospital), Martin Rostgaard-Knudsen (consultant in anaesthesiology and chief medical director of the North Denmark EMS) and Michael Dahl (consultant in anaesthesiology and daily manager of the physician-staffed mobile emergency care unit at Aalborg University Hospital). I also owe thanks to data manager Flemming Bøgh Jensen who aided data monitoring during the study period.

Without the help of all Danish EMS professionals and attending HEMS physicians, this dissertation would not have had any data. Thank you, Thomas Bøttern Christensen (data manager) and Drs Mona Tarpgaard and Jens Aage Kølsen Petersen for providing insights into the clinical work in an HEMS setting. Statistical advice was patiently given by Niels Henrik Bruun and Regitze Gyldenholm Skals from the Unit of Clinical Biostatistics at Aalborg University Hospital.

Vibe Maria Laden Nielsen, 2023

TABLE OF CONTENTS

1 INTRODUCTION

Children fall ill regularly. Yet life-threatening conditions are infrequent,[1–4] and some visits to the paediatric emergency department are related to non-urgent medical problems that do not require hospital care.[5,6]

Injuries are the leading cause of death among children in high-income countries, especially traumatic brain injuries.[7–13] Consequently, studies on trauma care and transport modes have dominated the research conducted in the paediatric patient population in prehospital settings.[14–21] Advances in trauma care organisation have led to decreased trauma-related mortality in children.[7,12,13,22] However, according to the Centers for Disease Control and Prevention, all-cause mortality rate in children aged 1-19 years increased by almost 20% in the US between 2019 and 2021 and the increase predated the Coronavirus disease of 2019 (COVID-19) pandemic.[23] In the same period, the number of transport-related injury deaths decreased.[23]

The US Children's Safety Initiative identified several "educational priorities for EMS professionals: paediatric airway management, responder anxiety when working with children and general paediatric skills".[24] Parents' confidence in EMS professionals increases with involvement, communication and a calm focused approach to observation and use of equipment.[25] The individual EMS professional relatively rarely encounters children, especially children with serious illnesses, as the majority of EMS patients are from the adult and elderly population. Identifying a child with serious illness can be challenging for non-paediatric healthcare professionals for a variety of reasons. Firstly, incidences of serious illnesses and injuries are lower than in the general population. Secondly, both aetiology and normal ranges for vital signs differ from adults' and vary with age. And clinical deterioration can occur more abruptly in children than in adults, e.g. a low blood pressure or a low heart rate may be a sign of impending cardiac arrest.[26] Finally, there is the added stress of communicating with both patient and caregivers simultaneously. All these factors contribute to the challenge of identifying the few children at risk of serious illness among the many other children with non-urgent illnesses.

In Denmark, only a tenth of the EMS patients are children and commonly, the cause of the emergency call is not obvious to the medical.[27,28] Counting since 2010, just under 300 children aged ≤15 years have died per year in Denmark.[29] But how many of those deaths were attributable to emergencies? The number of calls to the Danish national emergency number regarding patients aged ≤15 years gradually increased during the last half of the 2010s.[30] However, the number of traffic-related accidents involving children slightly decreased in the concurrent period.[31] The increasing number of calls regarding children most likely results from other causes than traffic-related accidents.

1.1 PAEDIATRIC READINESS IN EMERGENCY CARE SETTINGS

Assessing a patient's acuity level without any paraclinical testing is a challenge to both EMS professionals and other emergency care providers, and some studies relate this to inadequate training related to clinical judgement and treatment of children.[6,24,32–36]

This challenge has led to the emergence of 'paediatric readiness', which means that competencies, guidelines, policies and properly sized equipment as well as commonly used medications are in place for the performance of high-quality emergency care for children in general emergency care settings.[37,38] Quantification of paediatric readiness has had international attention in the previous years. Evidence is building to support that increased paediatric readiness scores in non-paediatric emergency care facilities reduce mortality.[20,39–42]

The term 'paediatric readiness' also includes administration and coordination of care, e.g. competency evaluations of medical staff, patient safety initiatives, quality improvement policies and specific procedures for involving families in cases of death, suspected child maltreatment or other special circumstances. In the context of the work reported in this dissertation, however, we focus on the part of the term that includes clinician tools, e.g. triage systems tailored to children, cognitive aids, calculation rules, drug dose regimens, etc.

1.2 PAEDIATRIC EARLY WARNING SCORES

Early identification of children at risk of critical illness may prevent deterioration via the initiation of clinical interventions while a serious condition is still reversible. Paediatric early warning scores (PEWS) were developed for early recognition of critical illness. They are conditioned on the fact that deviating vital signs often precede an adverse outcome such as intensive care admission or death.[2,3,36,43–45]

Multicentre studies have confirmed paediatric scoring systems' ability to predict admission to an intensive care unit in children both in and outside of hospital.[2,3,43,46] The infrequency of ICU admittance and death in the paediatric population challenges the attainment of hard evidence for a clinical benefit from the use of early warning scores. A US multicentre randomised controlled trial reported a significant decrease in the occurrence of predefined clinical deterioration events at hospitals using PEWS compared to hospitals with usual care.[3,36] Another randomised trial conducted at several paediatric departments in Denmark included 16,000 children and compared two different PEWS without detecting any difference in unplanned transfers to a higher level of care, possibly due to the rarely occurring outcome.[47]

Triage systems, early warning scores and track and trigger systems are all designed to aid the identification of patients at risk of clinical deterioration, however differences do exist. Early warning scores are mainly used at hospitals and emergency departments for admitted patients to identify an unfavourable development in the patient's clinical condition (the afferent part). Yet the mere calculation of an early warning score is pointless if it is not followed by appropriate actions. In track and trigger systems, a certain sum of points triggers a fixed response (the efferent part).

With the relatively short prehospital transport times in Denmark, an EMS triage system is mainly meant to aid the decision on which hospital to convey the patient, and to 'flag' children for whom senior competencies should be called to the paediatric emergency room ahead of arrival.

The point of these systems is not to ignore or overrule the single practitioner's clinical assessment skills but to support his or her concern for the patient. Some scoring systems even include 'treatment provider concern' in line with vital signs.[48]

Specific vital sign measurements give a predefined number of points, and the early warning score is the sum of those points. In children, deviating vital signs are defined according to age, and normal ranges vary markedly between infants, toddlers, school children and adolescents.[49] Consequently, normal ranges are very difficult to memorise for EMS professionals, for whom the majority of patients are adults. Prehospital scoring systems must prevent failure to recognise severe illness or injuries leading to delayed or missed alarm of receiving ED personnel. Advantages of using a paediatric scoring system in the prehospital setting include:

1) Systematic collection of all vital signs. This minimises the risk of missing subtle changes from the time of ambulance arrival to arrival at hospital.

2) Stratification of ranges that are perceived as 'normal' according to child age. This supersedes rote learning.

3) A common professional and objective terminology to improve the situational awareness of the receiving team in the hospital, and if appropriate, the call for senior clinician involvement before the patient arrives at the hospital.

All clinical scoring systems balance sensitivity and specificity.[50] In prehospital medicine, diagnostic uncertainty is an inevitable element. Above all, the goal of a prehospital scoring system is a high sensitivity so the chance of missing a child with a serious condition is minimal.[44] Naturally, some level of overtriage will be present in a general paediatric EMS population. Early warning scores have poor sensitivity for hospital admission though,[51] which make them unsuitable as decision tools for non-conveyance situations.

A wide variety of paediatric early warning scores are used internationally, all with different parameters weighing differently. However certain vital signs (SpO_2, heart and respiratory rates) are widely used with respect to their impact on adverse outcomes.[50,52,53]

Using PEWS (Scotland), a score comprised of eight parameters, sensitivity for predicting a combined outcome of admission to a paediatric intensive care unit within 48 hours or 30-day mortality ranges from 0.88 to 0.96 for low PEWS scores (1-2).[2] Even a single deviating vital sign may be predictive of an adverse outcome in children.[36,54,55] Towards developing a 'quick PEWS' using fewer and readily available vital signs in the prehospital setting, AUROCs for that combined outcome were tested and found to be similar to that of the full PEWS (range 0.55 to 0.76 dependent on the combination of vital signs in 'quick PEWS' versus 0.71 for the full PEWS (Scotland)). And specificity was not heavily compromised (0.63 to 0.83 in 'quick PEWS' versus 0.78 in the full PEWS (Scotland)).[2,53]

Different scoring systems are used in Danish hospitals. With the implementation of a national prehospital electronic patient medical record (ePMR) system, the Danish Regions' Paediatric Triage Model was embedded in this system (Figure 1.1). The model was constructed in cooperation with both prehospital and paediatrician representatives from all five health regions. The triage score is displayed by colours: green for 'not urgent', yellow for 'less urgent', orange for 'urgent' and red for 'life-threatening' emergencies.[56] No escalation protocol is embedded in this model. It is a resource intended to aid a systematic and focused approach to observation of paediatric patients in the prehospital setting.

Paediatric Triage Model

Triage level	1 Life-threatening	2 Urgent	3 Less urgent	4 Not urgent
A	Airway obstruction	Partial airway obstruction	Partial airway obstruction only at physical activity	No airway obstruction
B	SpO_2 < 85% without O_2 SpO_2 < 90% with O_2 Respiratory rate red	SpO_2 85-92% without O_2 SpO_2 90-96% with O_2 Respiratory rate orange	SpO_2 93-94% without O_2 SpO_2 ≥ 97% with O_2 Respiratory rate yellow	SpO_2 ≥ 95% without O_2 Respiratory rate green
C	Heart rate red Capillary refill time > 4 sec*	Heart rate orange Capillary refill time 4 sec*	Heart rate yellow Capillary refill time 3 sec*	Heart rate green Capillary refill time ≤ 2 sec*
D	Unconscious GCS ≤ 8	Altered level of consciousness or irritability GCS 9-13	Awake or can be awakened but fussy GCS 14	Awake or can be awakened and alert GCS 15
E	Temp < 35	Temp > 41 In children < 3 mos.: temp < 36 or ≥ 38.5	Children 3 mos. – 3 years: temp ≥ 38.5 and fussy	

* central capillary refill time, if peripheral not ≤ 2 sec

Respiratory rate

Child age	1	2	3	4	3	2	1
0-2 mo.	<10	10-19	20-29	30-60	61-80	81-90	>90
3-11 mo.	<10	10-19	20-29	30-60	61-70	71-80	>80
1-2 years	<10	10-14	15-19	20-30	31-40	41-50	>50
3-7 years	<10	10-12	13-15	16-24	25-30	31-35	>35
≥ 8 years	<8	8-9	10-11	12-25	26-30	31-35	>35

Heart rate

Child age	1	2	3	4	3	2	1
0-2 mo.	<50	50-69	70-89	90-180	181-205	206-230	>230
3-11 mo.	<40	40-59	60-79	80-160	161-190	191-230	>230
1-2 years	<40	40-58	59-74	75-130	131-165	166-200	>200
3-7 years	<40	40-54	55-69	70-110	111-125	126-165	>165
≥ 8 years	<40	40-44	45-49	50-110	111-120	121-140	>140

Figure 1.1. *The Danish Regions' Paediatric Triage Model is used in all Danish EMS (Danish Regions, 2012). Reprint from supplemental material to Paper I (Appendix A).*[36]

1.3 RATIONALE AND CONCEPTUALISATION OF THE STUDIES

Because life-threatening conditions are rare but may progress rapidly in children, EMS professionals must be prepared at all times to use a systematic approach for assessing children of all ages. The paediatric EMS population is diverse which makes finding the children at risk of clinical deterioration a bit like looking for a polar bear in a snowstorm. Initially, we asked ourselves:

How do EMS professionals identify children at risk of clinical deterioration among the many other children with non-urgent illnesses or minor injuries in our EMS?

The obvious answer would be to use the Paediatric Triage Model described above. Originally, we aimed to investigate the effectiveness of the triage model in a stepped wedge randomised trial in both Danish and Scottish services. The planning of this trial started in late 2019, only the planning effectively came to a halt in early 2020. Due to the onset and progression of COVID-19, we could not include patients from the UK. Power calculations showed that the patient volume in Denmark would be too small to detect any clinically meaningful differences in 'hard clinical endpoints' such as ICU admittance or death. In paediatric emergency medicine, hospital admission may be an appropriate solution to an emergency even if the clinical condition is stable. Therefore, we considered hospital admission to be unsuitable as an outcome measure of effectiveness.

Rather than testing the effectiveness, we decided to uncover the proportion of patients with deviating vital signs and the progression of those.[36] In *Study I: Severity of illness or injuries*, we discovered a noticeable amount of missing data on vital signs in paediatric patients, which was not unique to our service.[53,57–60]

In *Study II: Prehospital monitoring*, we conducted various educational initiatives with the overall intention of creating awareness of 'paediatric readiness' in our regional EMS. Standardised educational efforts aimed to neutralise the diverse skill sets that EMS professionals have in this area. The initiatives focused primarily on clinical assessment of children aged 2 years or younger, as vital sign registration was particularly deficient in this age group.[36,53,56,57] It was not straightforward how to formally evaluate these efforts though. It was important that the project was not just a matter of registration for the paper's sake. A 'blind' focus on vital signs could generate many 'false positives', i.e. the triage system would 'flag' many patients who were not at risk of clinical deterioration.[61] Nonetheless, in an adult EMS population, an association between incomplete vital sign registration and increased mortality risk had been reported.[62]

We decided that the primary outcome in *Study II* would be the registration of two sets of vital signs to detect any changes during EMS care time. As death is a rare event among paediatric emergency patients, we had to apply another clinically meaningful outcome to consider whether an improved registration practice had had any clinical impact. In *Study II*, we investigated if the implemented educational initiatives were associated with increased vital sign registration (primary aim) *and* if more patients had experienced a clinical improvement measured by changes in vital signs (secondary aim). We supposed that the mandatory recording of vital signs would contribute to a basic evaluation in more paediatric EMS patients, especially in infants and toddlers. The primary outcome was compared both before and after the educational initiatives and by different regional services (intervention region versus reference region).

Consequently, the dissertation is sectioned in two: *Studies I-II* regard clinical assessment of the severity of illness or injuries in paediatric EMS patients, whereas *Studies III-IV* have an epidemiological approach for studying clinical outcomes.

Advances in trauma care organisation and prehospital management have led to decreased trauma-related mortality in children.[7,12,13,22,38] The newly observed increase in all-cause mortality among US children stresses the importance of conducting epidemiological studies on mortality from paediatric emergencies.[38]

For EMS professionals, patient care ends with the handover of the patient to the receiving emergency department personnel without systematic follow-up. In the South Denmark Region, reasons for calling have previously been explored, and 44% of emergency calls regarding children were categorised as either 'sick child', 'unclear problem' or 'ordered mission'.[28] In the nationwide epidemiological *Studies III-IV*, we outlined hospital diagnoses and follow-up outcomes for all types of emergencies, not exclusively trauma or cardiac arrest. Initially, this outline was meant as the opening study for the dissertation, however COVID-19 delayed the provision of data from the average 1.5 to 11 months.

We explored the prevalence of comorbidity in the EMS paediatric population, both because pre-existing comorbidity could influence mortality after paediatric emergencies, and because EMS professionals may need further guidance when encountering children with chronic diseases that require specialised care.

Helicopter emergency medical services (HEMS) are dispatched for specific situations or to limited geographical areas (e.g. offshore islands), and they are a safe mode of transport for critically ill children.[15,17,18,63,64] In previous studies of paediatric patients for whom HEMS had been dispatched, characterisations have been limited to 'major/minor trauma' or 'non-trauma' or described by preliminary diagnoses, dispatch criteria, chief complaints, clinical signs or specific accident types.[65–72] In *Study IV: Outcomes after dispatch of HEMS*, clinical outcomes for this subgroup were presented separately so that a comparison of outcomes to other HEMS systems was possible. *Study IV* is the first one to add final hospital diagnoses and follow-up on clinical outcomes after *all* dispatches of a European single-nation HEMS.

2 OBJECTIVES

The overall aim is twofold: *Studies I-II* investigate vital sign measurements in children attended by EMS professionals and describe the implementation of various initiatives aimed at promoting a systematic clinical approach to these children. *Studies III-IV* outline the diagnostic pattern and mortality after paediatric emergency calls in Denmark.

The work reported in this dissertation pursues two of Aalborg University's strategic missions outlined in the *Framework Programme for Research and Innovation in Europe*: Conducting research within the health data science discipline to promote the health and wellbeing of children and young people.

2.1 STUDY I: SEVERITY OF ILLNESS OR INJURIES

- To classify the severity of illness or injuries in children attended by ambulances using patients' first observed vital signs according to a paediatric triage model.
- To examine the progression of patients' clinical condition during ambulance transport categorised according to this model.[36]

2.2 STUDY II: PREHOSPITAL MONITORING

- To evaluate if educational initiatives for EMS professionals were associated with an increase in vital sign registration.
- To investigate if patient factors or specific situations were associated with complete vital sign registration.[56]

2.3 STUDY III: OUTCOMES AFTER EMERGENCY CALLS

- To outline the diagnostic pattern and prevalence of pre-existing comorbidity among all paediatric patients for whom an emergency call had been made, followed by a visit to any hospital in Denmark.
- To investigate short-term mortality from trauma, out-of-hospital cardiac arrest and medical conditions after emergency calls in both children with and without pre-existing comorbidity.[38,73]

2.4 STUDY IV: OUTCOMES AFTER DISPATCH OF HEMS

- To report clinical outcomes in paediatric patients for whom a physician-staffed HEMS had been dispatched and the level of severity of illness or injuries assessed by severity score at the scene, performance of advanced prehospital procedures, in-hospital intensive care needs and mortality.[64]

3 METHODS

3.1 SETTING

The five Danish EMS serve 5,806,081 inhabitants in mixed rural, semi-rural and urban areas (42,962 km^2). Children aged ≤15 years comprised 18% of the background population of 5.7m Danes per 1 January 2016.[74] As in the other Scandinavian countries, the Danish healthcare system is tax-supported. Healthcare services are organised within five separate regions who are each responsible for operating district general hospitals, university hospitals and EMS. 24-hour operative out-of-hospital primary care services or medical helplines exist in all five regions, although they are organised in different ways. Access to emergency care is free of charge for both citizens and noncitizens, however an emergency department visit requires a referral if the patient does not arrive via ambulance or helicopter.

Studies I: Severity of illness or injuries and *II: Prehospital monitoring* were conducted only in the North Denmark Region and in the North and South Denmark regions, respectively. The North Denmark EMS covers a mixed urban–rural area of 7,933 km^2. In April 2022, the regional health services itself took on the operation of all ambulances and their staff from a private operator, Falck.

The South Denmark EMS cover an area of 12,262 km^2. Although the South Denmark Region is larger than the North Denmark Region both geographically and in terms of population, the regions have a similar demographic structure where children aged <18 years make up 19.7% (240,577/1,222,967) and 19.1% (112,514/589,837) of the inhabitants, respectively (2020Q3).[56,75] The North and South Denmark Regions have similar EMS systems and standard care, as described in the following.

All prehospital units use the same electronic medical records system. It is integrated into the hospitals' electronic medical records systems so that real-time data are visible to the receiving personnel at one of the 21 Danish emergency departments.[38]

3.1.1 DISPATCH CENTRES

Each region operates an emergency medical dispatch centre. The North Denmark regional dispatch centre answers 30 emergency calls per 1,000 inhabitants <18 years per year. The health professionals at the centre manage the dispatch of

EMS units according to the level of urgency (A to E, A being the most urgent), with help from a criteria-based dispatch support tool, the *Danish Index for Emergency Care*.[76,77] The dispatcher starts by identifying if the patient is in cardiac arrest and needs dispatcher-assisted cardiopulmonary resuscitation. If not, they ask clarifying questions formulated in the index and choose the most appropriate criterion and urgency level. These determine which type(s) of EMS unit(s) should be dispatched in the particular situation.[77] Dispatch criteria are not equal to diagnoses, they describe symptoms, e.g. 'Allergic reaction', 'Fever', 'Headache' or specific situations, e.g. 'Traffic accident' or 'Poisoning in children'. Selected criteria for dispatches with urgency level A translated to English appear as online supplemental material to Paper IV (Appendix D).[64]

3.1.2 GROUND EMERGENCY MEDICAL SERVICES

Calls to the national emergency number (112) that are related to health emergencies are forwarded from the police to a regional emergency medical dispatch centre. Several prehospital responses exist: Lay-person first responders, ambulances, rapid response vehicles manned by paramedics and mobile emergency care units (MECUs) or helicopters staffed with an experienced physician specialised in anaesthesiology and intensive care medicine. Generally, a physician-staffed MECU is engaged in about 20–25% of ambulance dispatches in both the North and South Denmark regions.

Emergency medical technicians and paramedics are trained in paediatric advanced life support before recruitment into the services. In-service training for maintaining these skills that existed before our studies commenced has been described in detail in Paper II (Appendix B).[56] In daily clinical practice, a free mobile application, 'Akut Barn', is used at each EMS professional's discretion (current version 2.1, Rigshospitalet (2022) [Mobile app]).

3.1.3 HELICOPTER EMERGENCY MEDICAL SERVICES

The nationwide HEMS is dispatched for roughly 1-2% of emergency calls (Figure 1.2). The services are described in detail in Paper IV (Appendix D).[64] Since the introduction of the national HEMS in 2014, all helicopter transports in Denmark have an entry in the database *Hemsfile*.

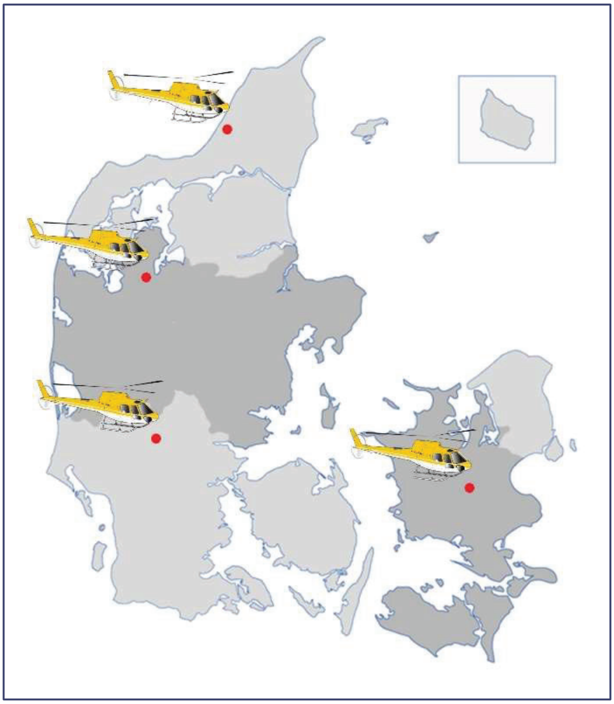


Figure 1.2. *The four HEMS bases are strategically located to ensure access to emergency care all over Denmark.*

3.2 STUDY OUTLINE

The papers of *Studies I: Severity of illness or injuries, II: Prehospital monitoring* and *IV: Outcomes after dispatch of HEMS* are enclosed in appendices A, B and D, while the submitted manuscript for *Study III: Outcomes after emergency calls* is enclosed in Appendix C. All of the studies consecutively included paediatric patients for whom an emergency call had been made and at least one prehospital unit had been dispatched, regardless of whether the patient was brought to a hospital.

For all studies, age groups matched the Danish Regions' Paediatric Triage Model: 'newborns' (0–2 months), 'infants' (3–11 months), 'toddlers' (1–2 years), 'preschool and school children' (3–7 years) and 'adolescents' (8–15 years). For *Studies I* and *II*, patients aged 16-17 were included in 'adolescents' as well. Patients without a valid personal identification number (PIN) could not be identified as children of a certain age and were therefore not eligible for the studies. Data were pseudo-anonymised before analysis.

STUDY	**DESIGN**	**POPULATION**	***N***
I	Regional population-based cohort study (2006–2018)	Children aged <18 years attended by the North Denmark EMS Exclusion criteria: No valid PIN	25,039
II	Prospective quasi-experimental[78] study with interrupted time-series design in the North Denmark and South Denmark regions (2019-2021)	Children aged <18 years attended by the North Denmark EMS (educational intervention) or South Denmark EMS (reference) Exclusion criteria: Scenarios where EMS professionals would not perform a formal ABCDE evaluation of the patient*	23,136
III	Nationwide population-based cohort study (2016-2021)	Children aged ≤15 years for whom an emergency call to 112 had been made in Denmark Exclusion criteria: Interfacility transfer, no valid PIN	121,230
IV	Nationwide population-based cohort study (2014-2018)	Children aged ≤15 years attended by the national physician-staffed HEMS Exclusion criteria: Interfacility transfer, no valid PIN	651

Table 3.1. *Study designs and populations. In all of the studies, a unique patient could have had more than one event during the study period.*

**Calls classified as urgency level D, 'patient needed transport in a supine position, no treatment needs', or level E, 'other mode of transport, e.g. taxi, or guidance to other acute* *care options'; interfacility transfers; duration of the mission was less than 30 seconds; no patient was found at the scene; helicopter EMS was the first unit at the scene (as they had a different ePMR system); the patient was declared dead at the scene according to the prehospital ePMR or the patient had received basic life support.*[56]

3.3 ETHICS AND AUTHORISATIONS

As Denmark is a member of the European Union, the study complies with the General Data Protection Regulation (GDPR). Accordingly, the study has been registered in the North Denmark Region, who permitted the collection and storage of data according to GDPR standards (IDs 2018-152, 2018-168, F2022-151). The GDPR is supplemented by the *Danish Act on Research Ethics Review of Health Research Projects*.[1] The act reads that registry-based studies without any patient encounters do not require approval from an ethics committee, as long as the individual patient cannot be identified. The management at Aalborg University Hospital and the Danish Patient Safety Authority waived the need for individual patient consent to access ePMRs (record numbers 3-3013-2707/1, 3-3013-1675/3 plus amendments 31-1521-14 and 2022-011290).

Study II: Prehospital monitoring did have patient encounters, however no interventions were introduced on patient level. The North Denmark Region Ethics Committee reviewed the study and granted an exemption from formal ethics approval on 11 March 2020. The patients who were eligible for *Study II* and their caregivers would likely be in a state of either physical or mental stress at the time of inclusion. Combined with the potential urgency of the medical condition, this caused us to apply for a waiver of informed consent from each individual patient to access their ePMRs in *Study II* as well. Consequently, permission to collect, store and publish outcome data from ePMRs according to the GDPR and the Danish Health Care Act was granted by The North Denmark Region delegated by the Danish National Health Authorities (IDs 2020–100 and 2020–027132 and supplement 2022-011291).

3.4 DATA SOURCES AND DATA MANAGEMENT

In Denmark, there is a unique setup for prehospital research because data from all ambulance transports are collected in the same way in all of the five regions. HEMS is a national service, which means that patient data can be provided on a

[1] *These legal restrictions apply to the availability of all data, which means that none of the data sets have been made publicly available.*

national level, whereas ground EMS are regional services. From 2006 onwards, EMS professionals in the North Denmark Region have routinely filled prehospital ePMRs. In 2015, all Danish ground-level units started using prehospital ePMRs from the same provider (*amPHI™* by *Judex A/S*, Aalborg, Denmark). Raw data sets are a mix of data regarding the emergency call, dispatch of prehospital units and patient medical records, and linkage between systems is necessary for the creation of rational, clinically meaningful incidents. The creation of a common data management strategy and terminology («*EMS Patientforløb*») enabled us to do valid prehospital research across regions.[79] We refer to previous works for the definite time stamps and variables linking each EMS unit to a specific event and patient medical record.[79,80] We collected data back to the first calendar year, 2016, from which nationwide data with identical records became available. Time stamps and locations of dispatched units were collected from a separate logistics system (*EVA 2000* and from 2016 onwards *Logis CAD* (*Logis Solutions*, Naerum, Denmark)).

Prehospital data were linked with national registers using 10-digit PINs. In Denmark, the unique civil PIN is called a CPR (Central Person Register) number. To avoid confusing the abbreviation CPR with cardiopulmonary resuscitation, the number is referred to as a PIN throughout the dissertation. Details of the linkage process can be found in Appendices C-D, Methods sections.

3.4.1 PREHOSPITAL ELECTRONIC PATIENT MEDICAL RECORDS

The prehospital ePMR is displayed on a specially designed tablet that EMS professionals carry with them to the patient's side. Ground units in the North Denmark EMS are equipped with LIFEPAK® 15 monitors (©*Physio-Control, Inc.*, WA 98052, USA) or ZOLL® X Series® monitors (*ZOLL Medical Corporation*, MA 01824, USA) (replaced during December 2020). Details of the monitor functions are described in Paper II (Appendix B).[56]

For *Studies I: Severity of illness or injuries* and *II: Prehospital monitoring* that were conducted in a regional setting, data were retrieved from prehospital ePMRs. For *Study III: Outcomes after emergency calls*, we acquired a supplemental data set containing ePMRs to accommodate possible selection bias due to missing PINs. This is discussed in detail in section 3.8.3.

3.4.2 THE DANISH CLINICAL QUALITY PROGRAM – NATIONAL CLINICAL REGISTRIES

All five regions are obliged to transfer both logistics and patient data to *The Danish Clinical Quality Program – National Clinical Registries*. In 2016, The Danish Quality Database for Emergency Medical Services was approved under this programme. In the first years, only logistics data and a few variables regarding cardiac arrest were available. From 2020 onwards, more quality indicators regarding patient care were added. The quality indicators are revised successively. For this dissertation, the database was used to define the study population, as it contains all calls to the national emergency number, 112, and for data management purposes. Details of this database have previously been described.[80] Each of the five Danish regions may choose to evaluate specific quality indicators within their own prehospital services.

3.4.3 HEALTH REGISTRIES UNDER THE DANISH HEALTH DATA AUTHORITY

Outcomes were retrieved from The Danish National Patient Register (DNPR),[81] which contains nationwide health administrative data, and The Danish Civil Registration System (CRS).[82] The DNPR includes all hospital encounters, whether they are acute, elective or outpatient activities. The encounters are separated at department level, and consequently, intensive care unit stays are present in the register. Each encounter has a diagnosis within the *International Statistical Classification of Diseases and Related Health Problems, Tenth Revision* (ICD-10) attached. Data were linked to the DNPR using PINs and the timestamp of the first ambulance that had arrived at a hospital.

The CRS Register contains a PIN for all residents in Denmark and holds information on migration and vital status. Both the DNPR and CRS registries are centralised under The Danish Health Data Authority, who is responsible for pseudonymisation, updates and regular data quality control procedures. Data management and analysis were performed by remote desktop access through a secure virtual private network tunnel at the Danish Health Data Authority.[38]

3.4.4 HEMSFILE

Danish Air Ambulance agreed to disclose data from the national *Hemsfile* database. Details on the collection, completeness and quality of this database have previously been described.[83]

3.5 STUDY SIZES

For *Studies I, III* and *IV*, no sample size calculations were performed due to their population-based designs. For *Study II: Prehospital monitoring*, the sample size was calculated using a formula for comparing proportions in two independent study populations with a dichotomous primary endpoint. We chose a target that was a minimum 10% increase from the pre- to the post-intervention period as a target lower than that would not be clinically relevant (details can be found in the Methods section in Paper II, Appendix B).[56]

3.6 STUDY-SPECIFIC VARIABLES

3.6.1 STUDY I: SEVERITY OF ILLNESS OR INJURIES

First observed vital signs (heart rate, Glasgow Coma Score, respiratory rate, oxygen saturation), categorised according to the Danish Regions' Paediatric Triage Model (Figure 1.1). Normal ranges are displayed in green, while the colours yellow, orange and red refers to ascending triage level. Oxygen saturation was observed with consideration of supplemental oxygen treatment (binary with options 'atmospheric air' or 'oxygen' regardless of the flow by either nasal catheter, reservoir mask, Hudson mask, nebuliser, continuous positive airway pressure or tracheal intubation).[36] Outcome variables are reported in section 3.7.

3.6.2 STUDY II: PREHOSPITAL MONITORING

The same vital sign ranges as presented for *Study I* above. Outcome variables are reported in section 3.7.

3.6.3 STUDY III: OUTCOMES AFTER EMERGENCY CALLS

In this study, we reported reasons for calling, hospital diagnoses and short-term mortality after all emergency calls regarding children in Denmark.
For investigation of the association between reasons for calling and death within 7 days, dispatch criteria were grouped, and in the following, reasons for calling are designated as indicated in the *Danish Index for Emergency Care*.[76,77]

- ‘Trauma’ if dispatch criteria were

  Large scale accident
  Fire or electrical injury
  Drowning
  Diving accident
  Traffic accident
  Accidents (not traffic-related)
  Minor wounds – fractures – injuries
  Violence – abuse

- ‘Paediatric out-of-hospital cardiac arrest (POHCA)’ if dispatch criteria were

  Unconscious child (before puberty)
  Unconscious adult (after puberty)
  Plus the patient had received cardiopulmonary resuscitation from either a bystander or from healthcare professionals outside of a hospital according to current reporting standards.[38,84,85]

- ‘Suspected death’ (dispatch criterion 25)

- ‘Medical symptoms’ if dispatch criteria were

  Any of the remaining criteria in the *Danish Index for Emergency Care*[76] (e.g. allergic reaction, fever, poisoning, headache, seizure, abdominal pain, back pain, breathing difficulties, etc.)
  or
  Unconscious child (before puberty)
  Unconscious adult (after puberty)
  Without receiving cardiopulmonary resuscitation.

- ‘Missing dispatch criteria’[38]

This association was stratified by comorbidity subgroups.[38] Comorbidity was classified using diagnoses from both inpatient *and* outpatient hospital visits *and* visits to private practitioners in all medical specialities from five years preceding each patient’s emergency call.

We downloaded a list of all ICD-10 codes via the tools provided by The Danish Health Data Authority[86] and manually reviewed the complete list. Each ICD-10 code was put into one of three categories: ‘Comorbidity’, ‘Severe chronic comorbidity’ or ‘None’. The categorisation was done based on previous literature[87,88] and orpha.net (an international portal for rare diseases) and

customised to present-day Danish settings. The complete list can be forwarded upon request to the authors of Paper III (Appendix C).[38]
Then we crosschecked the list with diagnoses from five years preceding the emergency call for each patient. Accordingly, all patients were categorised into one of the three subgroups: 'Comorbidity', 'Severe chronic comorbidity' or 'None'.

The 'Comorbidity' group included both previous diseases, conditions or perinatal complications, with exceptions being recovered infections and previous injuries without any sequelae. The 'Comorbidity' group also included chronic diseases. Examples were diabetes and other endocrine and metabolic diseases, psychiatric disorders, previous organ transplant, epilepsy, asthma and gastrointestinal or urogenital diseases. In Denmark, children with those conditions would ordinarily be referred to either a paediatric department or a private practitioner for definite diagnostics and planning of treatment to be followed up by their general practitioner. For example, a child with a differential diagnosis of diabetes should be referred to a paediatric department for further diagnostics, planning of treatment, patient education, self-monitoring, check-ups for growth and detection of possible complications.

The 'Severe chronic comorbidity' group included diseases or conditions with potentially considerably reduced lifespan. Examples of conditions in the 'Severe chronic comorbidity' group were advanced congenital cardiovascular malformations, cerebral palsy, tetraplegia, certain types of cancer and rare metabolic disorders.[38]

If patients had had no visits at all to a hospital or a private practitioner in the five years preceding the emergency call, they were categorised in the subgroup 'None'.[38]

3.6.4 STUDY IV: OUTCOMES AFTER DISPATCH OF HEMS

An eight-level National Advisory Committee for Aeronautics (NACA) severity score is assessed on scene by the attending HEMS physician and ranges from no injury or disease (score of 0) to lethal injury or disease (score of 7).[64,89]
The performance of advanced prehospital procedures was collected from predefined variables in the *Hemsfile* database.

3.7 STUDY-SPECIFIC OUTCOMES

3.7.1 STUDY I: SEVERITY OF ILLNESS OR INJURIES

Patients progressing to a triage score with a lower level of urgency during ambulance transport. This outcome measure was described in detail in Paper I (Appendix A):[36]

"To calculate a triage score, the patient must have had at least one vital sign documented. The first triage scores were based on the first entry of each vital sign, while the last triage scores were based on the last entry of each vital sign. If a vital sign had only *one* value documented during the entire transport, this value was only included in the first triage score and the last value would be 'missing'. To prevent unreliable scores due to missing data, the last triage score was also deemed 'missing', if a single first vital sign was yellow, orange or red *and* the last value of that same vital sign was a missing value." Without this clause, a missing value could have influenced the outcome.

3.7.2 STUDY II: PREHOSPITAL MONITORING

The study had the overall goal of improving EMS professionals' abilities to assess children via a number of educational initiatives, e.g. teaching a standardised approach and recommended doses of commonly used medications. The initiatives focused primarily on clinical assessment of children aged 2 years or younger, as we had learned from *Study I: Severity of illness or injuries* that vital sign registration was particularly deficient in this age group.[56]

Educational initiatives
The first initiative launched was an instructional video demonstrating the ABCDE approach by use of a 1-year-old manikin, based on the European Resuscitation Council's Guidelines on paediatric advanced life support principles (2015 edition[90] updated by the 2021 edition[91] with written consent from the council).[56] The video was mandatory for all North Denmark EMS professionals and for newly recruited staff, but optional for physicians. The management team sent out reminders to staff who had not yet signed for watching the video. Further details on the roll-out of the initiatives are accounted for in Paper II (Appendix B).[56]

Primary outcome measure
The primary outcome was the registration of *two* sets to detect any changes in the following vital signs: respiratory rate, peripheral capillary oxygen saturation (SpO_2), heart rate and level of consciousness, hereafter designated 'complete

vital sign registration'. We assessed the primary outcome by using monthly aggregated data and split the total study period into 15 months before the educational initiatives commenced, the 'pre-intervention period' (July 2019 to September 2020), and 15 months after the educational initiatives commenced, the 'post-intervention period' (October 2020 to December 2021).[56] South Denmark EMS served as a reference region due to the similarities described earlier (section 3.1).

Secondary outcome measures
A secondary outcome measure was the proportion of patients, whose triage score progressed to a less urgent level during ambulance transport. Triage scores were calculated from the first and last sets of vital signs obtained by the EMS professionals using the methodology described for *Study I* in section 3.7.1. This outcome was calculated for patients from the North Denmark Region only to compare pre- and post-intervention periods. Lastly, we investigated associations between various patient factors or specific situations and the outcome of complete vital sign registration.

3.7.3 STUDY III: OUTCOMES AFTER EMERGENCY CALLS

Primary hospital diagnosis was the first diagnosis assigned by a physician after appropriate diagnostic tests at the receiving hospital, regardless of sequential admissions at different departments or different facilities during that hospital stay. The ICD-10 classification system is used in Denmark.[92] If a diagnosis from chapters XVIII (*Symptoms, signs and abnormal clinical and laboratory findings, not elsewhere classified*) or XXI (*Factors influencing health status and contact with health services*) was given, it was replaced by the successive organ-specific or cause-specific diagnosis during that hospital stay, if any.[64]

Short-term mortality was explored after 1, 7 and 30 days from the time of the emergency call. Patients were lost to follow-up and therefore excluded if they had no current address in Denmark, PIN was annulled, patient disappeared or travelled abroad as indicated in the CRS Register.[38]

3.7.4 STUDY IV: OUTCOMES AFTER DISPATCH OF HEMS

Primary hospital diagnoses and short-term mortality were assessed as described above for *Study III* (section 3.7.3) with the addition of in-hospital intensive observation and/or care needs.

3.8 STATISTICAL ANALYSES

For all studies, statistical analyses were performed with Stata/MP versions 15.1 and 17.0 (*StataCorp LLC*, TX 77845, USA). No data were imputed.

Before the study-specific analyses, a few repeatedly used epidemiological principles will be explained. The *US Centers for Disease Control and Prevention* defines incidence proportion (IP) as a measure of the probability of developing a disease or condition during a specified follow-up period.

$$Incidence\ proportion = \frac{New\ cases\ of\ a\ disease\ in\ the\ study\ period}{Initial\ study\ population\ at\ risk}$$

Incidence may also be reported as a rate, i.e. new cases of a disease in a population over time, with the sum of years each person has been at risk (person-years).[93] In this dissertation, incidence rates (IR) will be expressed as x.x per 100,000 persons per year.

$$Incidence\ rate = \frac{New\ cases\ of\ a\ disease}{Person - years}$$

When a comparison is needed between groups with and without a certain exposure, ratios between the incidence proportions can be calculated.

$$Relative\ risk = \frac{IP\ in\ the\ exposed\ group}{IP\ in\ the\ unexposed\ group}$$

In survival analysis, the hazard rate is the probability with which death occurred in a certain period of time. A hazard ratio (HR) is the ratio of hazard rates between an exposed group and a predefined reference group within that period.[93]

3.8.1 STUDY I: SEVERITY OF ILLNESS OR INJURIES

Vital signs were grouped as described in section 3.6.1 and presented by frequency. The proportion of patients having at least one abnormal vital sign at first observation was calculated for each age group and tested in a univariate binomial regression using the 'newborn' category as reference.[36]

Post hoc Cox regressions for death within 30 days from the emergency call were performed with complete vital sign registration as exposure (binary and discrete, respectively). We excluded patients who were regarded as having died before the EMS had arrived at the scene (death date was equal to date of emergency call *and* the patient had not received any resuscitative efforts).

The extent of missing data was considerable and unevenly distributed across age groups. Data were probably not missing at random,[94] though we did not investigate this systematically. To check this potential source of bias, we did investigate whether EMS professionals tended to omit vital sign registration only in patients with 'non-urgent' conditions. We compared the distribution of acuity levels assigned by the emergency department nurse upon arrival at hospital in patients with complete and incomplete vital sign registration. Details can be found in Paper I (Appendix A).[36]

3.8.2 STUDY II: PREHOSPITAL MONITORING

The primary outcome, two full sets of vital signs, was presented graphically as proportions according to pre- and post-intervention periods in each region.

The graphic illustration was supported by a binomial regression model, and a detailed description of this model and its adjustments can be found in Paper II (Appendix B).[56] Patient factor associations with complete vital sign registration were presented by relative risks and risk differences compared to the relevant reference group for each factor.[56]

Sensitivity analyses

Sensitivity analyses of the primary outcome were performed with first-time events for each unique patient.[56]

3.8.3 STUDY III: OUTCOMES AFTER EMERGENCY CALLS

For survival analysis, patients were considered at risk from the date of emergency call until either death or the end of follow-up (January 2022). All-cause mortality estimates were calculated using last-time events only by modified Poisson regression with robust variance estimation.[38,95] We analysed time to death using the Kaplan Meier failure function and decided on a 7-day limit for forward survival analysis.

In a Cox proportional hazards model with time since inclusion as time scale, we estimated 7-day mortality between the reasons for calling (described in section 3.6.3), stratified by comorbidity subgroup. Assumptions of proportional hazards were assessed visually by log-minus-log plots and using Schoenfeld residuals. Hazard rate ratios were reported as crude and adjusted for sex (dichotomous, no missing data) and age (categorical, no missing data) with 'Trauma' as reference.[38]

Sensitivity analyses
Independent censoring was explored (available in supplements to Paper III, Appendix C).[38] Including all events in survival analysis may introduce bias, as the time between the first an subsequent emergency calls would be 'immortal time'. Therefore, we performed survival analysis using last-time events only and then performed sensitivity analyses using first-time events only and all events, respectively. In addition, we acquired a supplemental data set including both the ePMRs for patients *with* and *without* valid PINs and estimated mortality from those by crosschecking selected variables.

3.8.4 STUDY IV: OUTCOMES AFTER DISPATCH OF HEMS

The NACA score was dichotomised for analysis: 0 to 3 denoted 'noncritical emergencies' and 4 to 7 denoted 'critical emergencies' according to previous literature.[64,72,74,96] The outcome 'intensive care needs' was presented with a Kaplan-Meier plot (a detailed description can be read in Paper IV, Appendix D).[64] All patients with a valid PIN were followed for 30 days and only discontinued in case of death.

Sensitivity analyses
Not all patients had a valid PIN, and sensitivity analyses were performed to assess if this exclusion criteria had induced selection bias. Risk differences were calculated for NACA scores and performance of advanced prehospital procedures among patients with or without valid PINs. Mortality was also calculated using a predefined variable in the *Hemsfile* database, 'Mission outcome', that denoted if the patient was alive at the end of the mission.[64]

4 RESULTS

4.1 STUDY I: SEVERITY OF ILLNESS OR INJURIES

Deviating vital signs
Exact figures of each of the four vital signs are presented according to age groups in Tables 1-4 in Paper I (Appendix A).[36]

Upon arrival at the scene, 10.3% of the patients had 'life-threatening' conditions, while 17.7% had 'urgent' conditions, 25.1% had 'less urgent' conditions and 44.9% had 'non-urgent' conditions (missing data in 1,673/25,039). There was little variation between age groups as depicted in Figure 4.1. The figure also illustrates changes from first to last triage scores according to age group.

Missing data
For all of the four vital signs, the proportion of missing data decreased with ascending age group. We investigated if vital signs tended to be missing in non-urgent patients, however we did not find a systematic pattern to back this. The proportion of patients with a 'non-urgent' acuity level (assessed by the emergency department nurse) was similar among patients with incomplete and complete prehospital vital sign registration ('not urgent' in 41% versus 46%) (χ^2 (3, n=239) = 5.1, p=0.166).[36]

Progression of triage score to a lower level of urgency
Patients needed at least one vital sign documented to calculate a triage score. Close to all patients (93.3%) had data for a first triage score and 84.8% (21,230) had data for both first and last triage scores. The four vital signs for the triage scores were all documented concurrently (median (IQR) 6 (2–13) minutes in the first set and 4 (0–13) minutes in the last set of vital signs).[36]

We calculated the proportion of patients progressing to a triage score with a lower level of urgency during transport as an indicator of improvement in clinical condition. This outcome varied with age: 146/354 (41.2%) for newborns, 440/986 (44.6%) for infants, 1278/3212 (39.8%) for toddlers, 967/2814 (34.4%) for preschool and school children and 4029/13 864 (29.1%) for adolescents (p<0.001).[36]

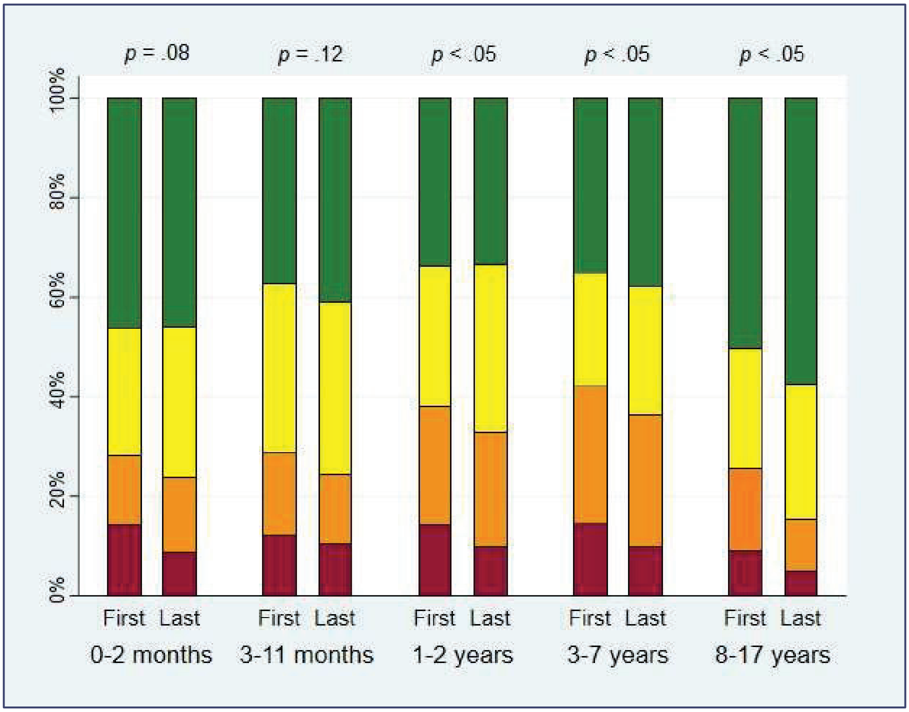


Figure 4.1. *Distribution of first and last triage scores according to age group. Red: life-threatening; orange: urgent; yellow: less urgent; green: not urgent. Non-missing: 21,230/25,039. Reprint from Paper I (Appendix A).*[36]

Post hoc analyses on vital sign registration and outcome

Patients with incomplete registration (<4 vital signs) had a crude HR for 30-day mortality of 3.3 [1.8;6.3] compared to patients with all 4 vital signs (SpO_2, GCS, respiratory and heart rates) registered. Adjusted HR for age, sex and performance of cardiopulmonary resuscitation was 2.9 [1.5;5.6].

The association between vital sign registration and 30-day mortality was also explored with vital signs as a discrete exposure variable (4 vital signs as reference). We found that having 0 vital signs registered had a crude HR of 3.7 [1.6;8.9], 1 vital sign had a crude HR of 2.8 [1.1;7.1], 2 vital signs had a crude HR of 4.6 [2.2;10.0] and 3 vital signs had a crude HR of 2.9 [1.3;6.6]. Adjusting for age and sex had marginal influences on HRs, however adjusting for cardiopulmonary resuscitation meant that the association between having only *one* vital sign registered and 30-day mortality was no longer statistically significant.

These post hoc analyses indicate that missing registration of vital signs was associated with mortality in this study population.

Summary

Just under a third of the children had either life-threatening or urgent conditions with little variation among age groups. A large amount of missing data impeded the results, especially among newborns, infants and toddlers. Overall, a third of the patients had triage scores that progressed to a lower level of urgency during ambulance transport and concurrent care.

4.2 STUDY II: PREHOSPITAL MONITORING

In the intervention region, practically all EMS professionals completed the video learning (98.7%).

Changes over time

The primary outcome of complete vital sign registration increased in the intervention region from the pre- to the post-intervention period *and* compared to the reference region with large variations between age groups (Figure 4.2).[56] For children of all ages, the proportion of patients with complete vital sign registration was 40.5% [38.9;42.0] in the intervention region and 23.7% [22.7;24.6] in the reference region in the post-intervention period.[56]

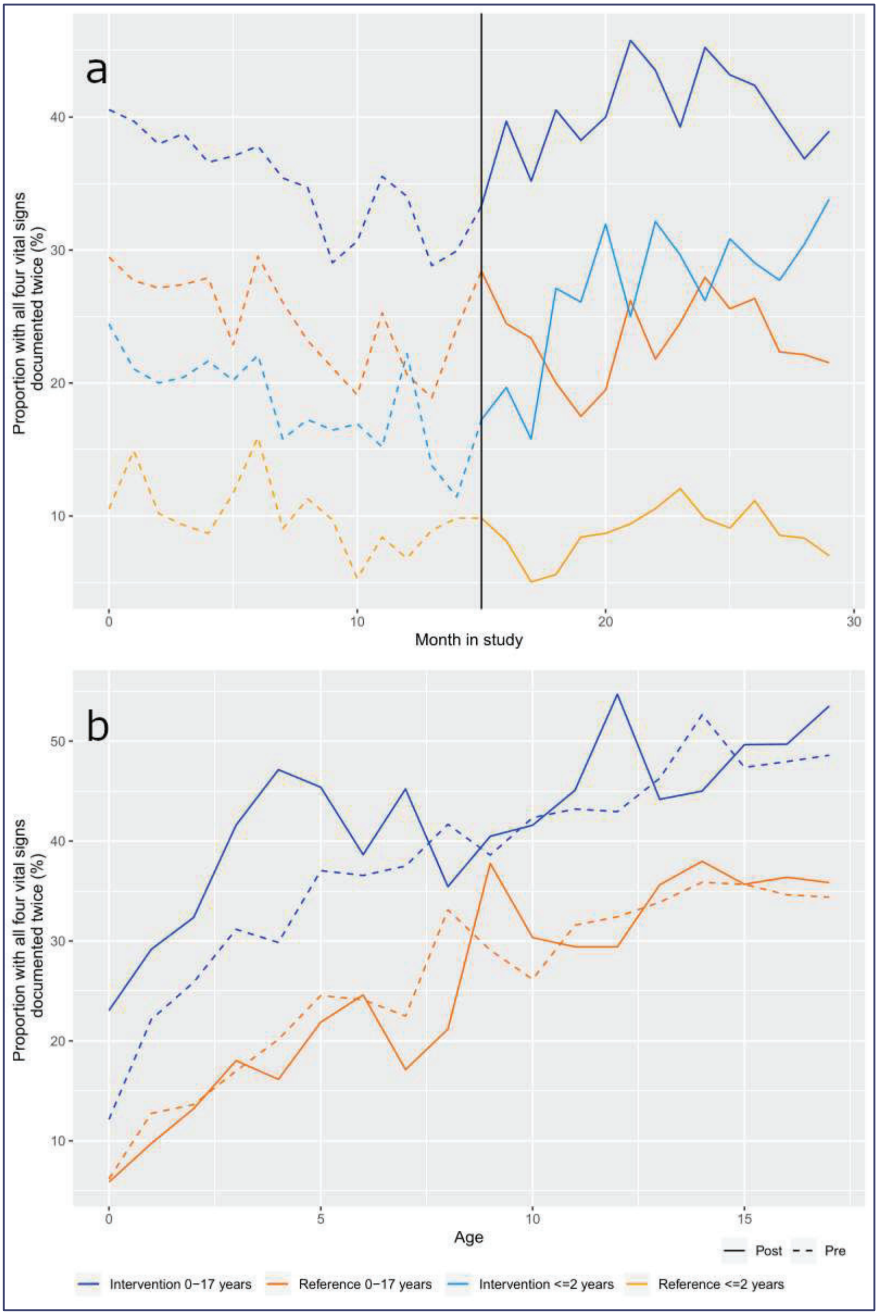


Figure 4.2. *Complete vital sign registration by time (a) and by age (b). The vertical line represents the cut-off date from the pre- to the post-intervention period.*
Full population: N=23,136. Age ≤2 years: n=7,335. Reprint from Paper II (Appendix B).[56]

Changes per age group in each region

From the pre- to the post-intervention period, the primary outcome increased in the intervention region from 18.8% to 27.4% [5.3;12.0] among patients aged ≤2 years, from 33.5% to 43.7% [4.9;15.5] among patients aged 3–7 years, and there was an insignificant increase among patients aged ≥8 years (from 46.4% to 47.9% [-1.7;4.7]).

In the reference region *without* the specific educational initiatives, proportions were steady for all age groups throughout the entire study period: from 10.2% to 9.0% [-2.9;0.4] among patients aged ≤2 years, from 20.9% to 19.1% [-5.0;1.4] among patients aged 3–7 years and from 33.7% to 34.5% [-1.3;2.8] among patients aged ≥8 years.[56]

Sensitivity analyses

Sensitivity analyses of the primary outcome with first-time events only produced similar unadjusted results (n=18,008).[56] Adjustment for COVID-19 incidence peaks and treat-and-release situations did not change our results notably (relative risks and absolute differences, both crude and adjusted, are displayed in Table 2 in Paper II (Appendix B)).[56]

Progression of triage score to a lower level of urgency

The secondary outcome measure, progression of triage score to a lower level of urgency as an indication of clinical improvement, also increased from 24.9% [23.6;26.3] to 29.3% [27.9;30.8] in the intervention region during the study period. All changes in triage scores can be found in Additional file 2 to Paper II (Appendix B).[56]

Factors associated with complete vital sign registration

The youngest patients were less likely to have had complete vital sign registration, even in the post-intervention period. Among infants and toddlers aged ≤2 years, 15.1% had *no* vital signs recorded, while single entries of heart rate and SpO_2 had the highest proportions of missing data. Both improved from the pre- to the post-intervention period though (35.5% to 28.5% for heart rate and 40.0% to 31.1% for SpO_2).

All of the remaining investigated patient factors are presented in Table 3 in Paper II (Appendix B).[56] Having a 'non-urgent' (green) first triage score *did* decrease the probability of complete vital sign registration compared to the patients with 'urgent' scores (RR 0.8 [0.7;.09]). Still, more than a third of the patients with incomplete vital sign registration (36.8% [34.7;38.8]) had 'urgent' (i.e. yellow, orange or red) scores in the post-intervention period.[56]

Summary

The educational initiatives for EMS professionals were associated with an increase in the extent of vital sign registration in patients aged 7 years or younger, both when comparing the primary outcome by time relative to the initiatives and by regional service level.[56]

4.3 HOSPITAL DIAGNOSES AFTER EMERGENCY CALLS (STUDIES III AND IV)

Nearly sixty percent of all emergency calls regarding patients aged ≤15 years were assessed as urgency level A and led to an EMS dispatch with lights and sirens. The incidence rate of paediatric out-of-hospital cardiac arrest (POHCA) was 3.5 per 100,000 children aged ≤15 years per year.

At the hospital, primary diagnoses were dispersed over almost all ICD-10 chapters with injuries, 'symptoms and signs', respiratory diseases and diseases of the nervous system being the dominant chapters among dispatches with lights and sirens, although with variations within age groups (Figure 4.3).

A complete outline of all diagnosis chapters is visible in the Supplement.

Chapter *XIX: Injury, poisoning and certain other consequences of external causes* was the main chapter that contained the most patients (38.0%). Head injuries were the most frequent injury type across all age groups (9,362/28,144 = 33.3%). Within the *Symptoms and signs* chapter, *R56.0;Febrile convulsions* were dominant (11,521/24,595 = 46.8%).[38] Most of the hospitalised patients (80.3%) had hospital stays of less than 24 hours.

Among all patients, more than half had no pre-existing comorbidity, whereas almost 40% did have previous or chronic diseases, conditions, or perinatal complications. A small group of children (<4%) had severe chronic diseases or conditions with potentially considerably reduced lifespan.[38] Only a few in the entire EMS cohort (900/76,956 = 1.2%) had not had any in-patient or out-patient hospital visits or visits to any private practitioner in any medical speciality in the five years preceding the emergency call.

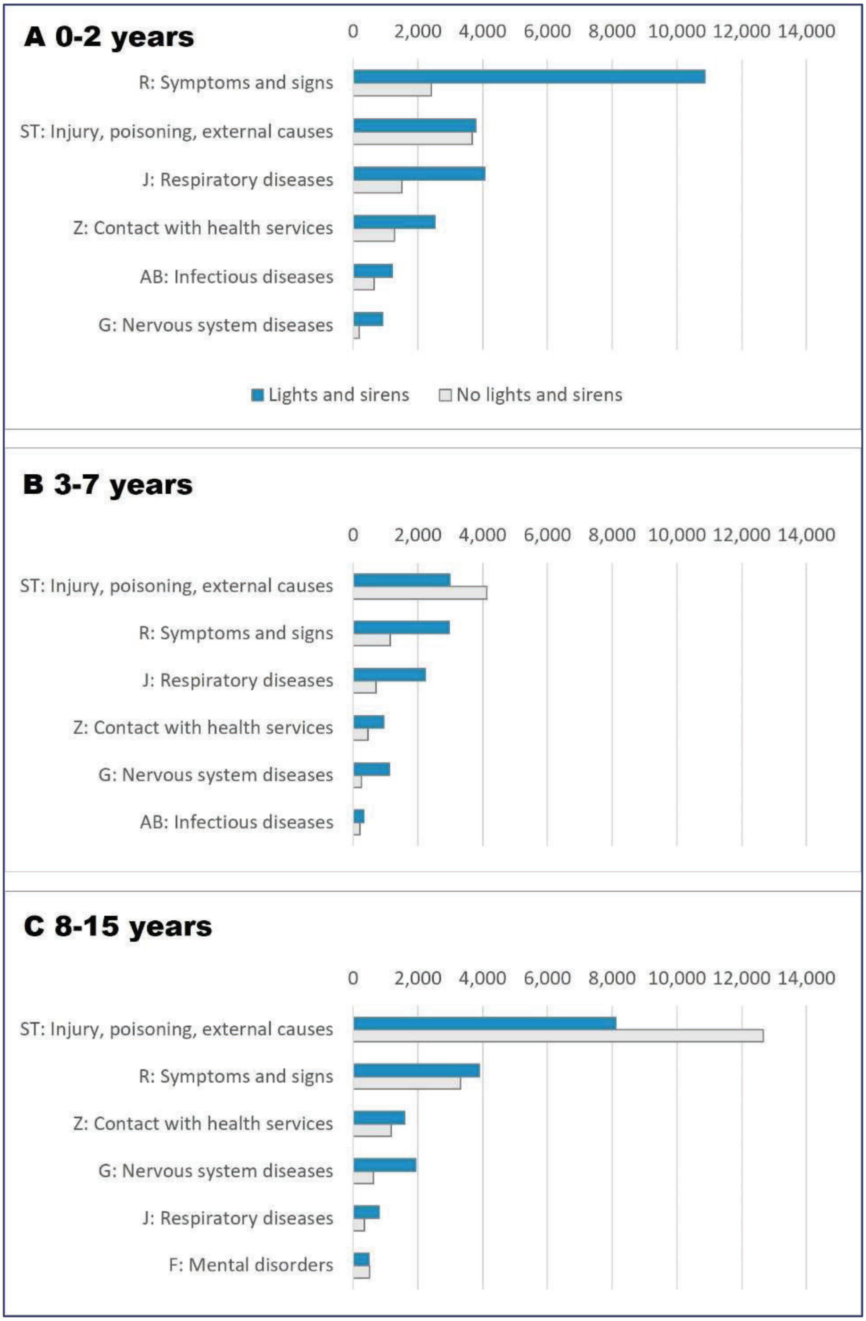


Figure 4.3. *The six most frequent chapters of primary hospital diagnoses, listed according to the use of lights and sirens and stratified by age group (panel A-C). Letters refer to ICD-10 chapters. A complete outline of all chapters is visible in the Supplement.*

For the subgroup of patients attended by HEMS, the diagnostic pattern was similar, except that HEMS was more frequently dispatched for burn victims, drowning victims and patients with diseases of the circulatory system.[64] Among the patients attended by HEMS, half of them had a hospital diagnosis within the ICD-10 *Injury* chapter, which includes injuries (32.2%), burns (11.2%), foreign body airway obstruction, drowning, poisoning, and other types of injuries.[64] Of the organ-specific ICD-10 chapters, respiratory, neurological and cardiac diseases were the most frequent along with infections (Figure 4.4).

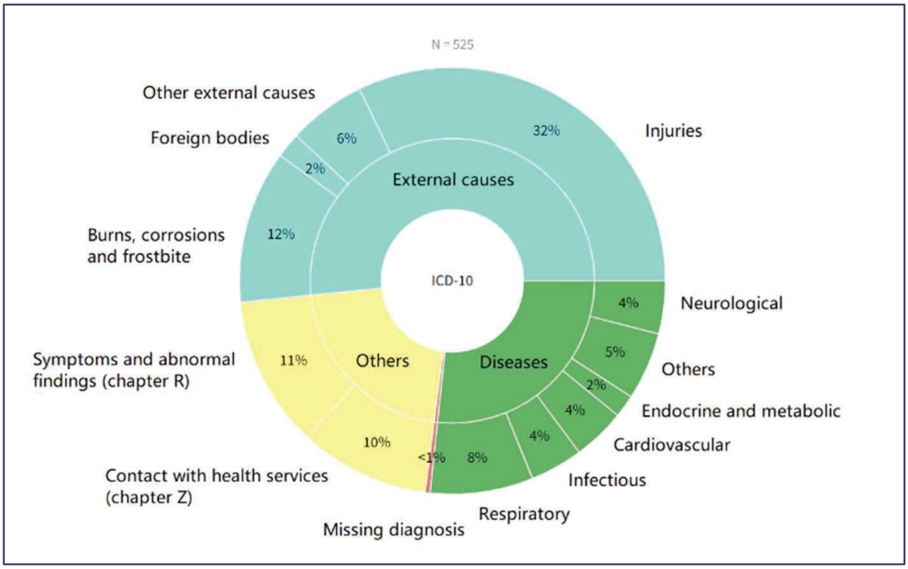


Figure 4.4. *Hospital diagnoses for the subgroup of children attended by HEMS, N=525.*

4.4 MORTALITY AFTER EMERGENCY CALLS (STUDY III)

Survival analysis included all patients, regardless of hospital contact, and counted 76,956 unique patients.[38]

Short-term mortality

The annual incidence rate of all-cause mortality was 7.0 per 100,000 children aged ≤15 years using last-time events only (428 deaths, population at risk: 1,023,297).[73] Similar mortality was found when using first-time events only and all events, respectively (Table 4.1).[38]

Reasons for emergency call were investigated among deceased patients. Among the children who did not survive 7 days after the emergency call, the call had regarded trauma (32/255 (12.5%)), POHCA (93/255 (36.5%)), medical symptoms or a problem that was unclear to the medical dispatcher (109/255 (42.7%)) or suspected death (15/255 (5.9%)) (missing data in 6/255 (2.4%)) (p<0.001).[38] In the group of deceased children without any comorbidity, unconsciousness (not due to trauma or cardiac arrest) was the most frequent 'medical' dispatch criterion.

Of all the 255 patients who died within 7 days from the emergency call, 77 (30.2%) had died *before* the EMS had arrived, and only 12 of these were due to trauma. As dispatch criteria are not meant to be used as 'diagnostic criteria', we also manually reviewed the last diagnosis preceding death in each of these 255 patients. 13.7% (35/255) had a last diagnosis within the main ICD-10 chapter *Injury, poisoning and certain other consequences of external causes*.[73] The remaining patients' last diagnoses can be found in Table 4.2.[38]

ORIGINAL DATA SET					
		First-time missions	Last-time missions	All missions	All missions (mission level†)
1-day	N	76,956	76,956	99,281	101,094
	Deaths (no.)	175	206	223	273
	Risk (%)	0.23	0.27	0.22	0.27
	95% CI	0.20;0.26	0.23;0.31	0.20;0.26	0.24;0.30
7-day	Deaths (no.)	218	255	276	NA
	Risk (%)	0.28	0.33	0.28	
	95% CI	0.25;0.32	0.29;0.37	0.25;0.31	
30-day	Deaths (no.)	231	282	318	NA
	Risk (%)	0.30	0.37	0.32	
	95% CI	0.26;0.34	0.33;0.41	0.29;0.36	

Table 4.1. *Mortality estimates from Poisson regression on individual patient level versus mission level. Reprint from Paper III (Appendix C).*[38]

†*Data retrieved from prehospital ePMRs contained both patients* with *and* without *valid personal identification numbers. From these records we identified prehospital deaths (comparable to 1-day mortality) by the following definition: either 'declared dead on scene' or a Glasgow Coma Score of 3* plus *any cardiopulmonary resuscitation, cf. the Danish Cardiac Arrest Registry.*[85]

No. (%)		**P value**‡
ICD-10 Chapter		
Sudden cardiac death (*I46.1*)	40 (15.7)	
Injury, poisoning, and other external causes (ST)	35 (13.7)	
Cardiac arrest (*I46.0/9*)	34 (13.3)	
Congenital disease or perinatal complication (PQ)	30 (11.8)	
Contact with health services (Z)	19 (7.5)	
Other ill-defined and unspecified causes of mortality (*R99*)	17 (6.7)	<.001
Missing data	17 (6.7)	
Nervous system diseases (G)	16 (6.3)	
Infection (AB)	15 (5.9)	
Cancer (CD)	15 (5.9)	
Respiratory disease or respiratory failure (J)	9 (3.5)	
Other disease, condition, or complication§	8 (3.1)	

§Other diseases, conditions, or complications that could not be added to any of the groups above.
‡Calculated by χ^2 test.

Table 4.2. *Last ICD-10 diagnosis assigned by a physician in patients who died within 7 days of the emergency call, n=255. Reprint from supplemental material to Paper III (Appendix C).*[38]

Mortality in relation to age

Newborns (0-2 months) and infants (3-11 months) had an increased risk of death compared to the oldest age group (crude HRs: newborns 4.9 [3.4;7.1], infants 2.5 [1.7;3.6]). There were insignificant differences in mortality among toddlers or 'preschool and school children' compared to the oldest age group, respectively (crude HRs: toddlers 0.8 [0.5;1.1], 'preschool and school children' 1.1 [0.8;1.6]).

We found that 41% of the non-survivors aged less than 12 months were considered to be dead on arrival of the EMS. When excluding these 77 patients, age <1 year was still associated with an increased risk of death within 7 days (crude HRs: newborns 5.4 [3.5;8.3], infants 2.4 [1.5;3.6]). Sex-adjusted HRs were similar.

Mortality in relation to comorbidity

Figure 4.5 displays the distribution of reasons for emergency call within the three comorbidity subgroups (numerical data are supplied in Paper III, Appendix C).[38]

Nearly half of the non-survivors (47.5%) had no comorbidity, and 97/121 = 80.2% [95% CI, 71.9-86.9] of those had had emergency calls regarding various medical symptoms incl. POHCA (corresponding figure excl. POHCA and 'suspected deaths' was 30.6%).

A quarter of the non-survivors (25.1%) had had either previous or chronic diseases without a marked alteration of life expectancy, and 54/64 = 84.4% [73.1-92.2] of those had had emergency calls regarding various medical symptoms incl. POHCA (corresponding figure excl. POHCA and 'suspected deaths' was 53.1%).[38]

Frequent diseases and conditions in the 'Comorbidity' group were: Asthma (3.7% of the entire EMS cohort, *N*=76,956), epilepsy (2.9%), prematurity/immaturity (2.8%), neonatal jaundice (1.7%), diabetes (0.8%) and cardiovascular diseases (1.1%)(ICD-10 codes *I00-I99* excl. **I27.8A;Eisenmenger syndrome*, **I42.5;Other restrictive cardiomyopathy*, **I46.1;Sudden cardiac death*, *I49.1-4;Extrasystoles*).

Children in the 'Comorbidity' group had had a median (IQR) of 16 (9-31) prior encounters with a hospital or specialised practitioners in the five years preceding their last emergency call, while the number of encounters for children with 'Severe chronic comorbidity' was 88 (45-164).[38]

Frequent diseases and conditions in the 'Severe chronic comorbidity' group were: Cerebral palsy/hemiplegia/paraplegia/tetraplegia (0.8%), advanced congenital cardiovascular malformations (0.3%)(selected *Q2* codes + the exceptions marked with * above) and malignant neoplasms (0.2%).

While 27.5% (70/255) of the non-survivors had prior 'Severe chronic comorbidity', only 2.0% (1,545/76,701) in the survivor group had had prior severe chronic comorbidity.

The hazard ratio for patients with calls regarding medical symptoms was not significantly different from the reference group, i.e. patients with calls regarding trauma, in either of the comorbidity subgroups (Figure 4.6).

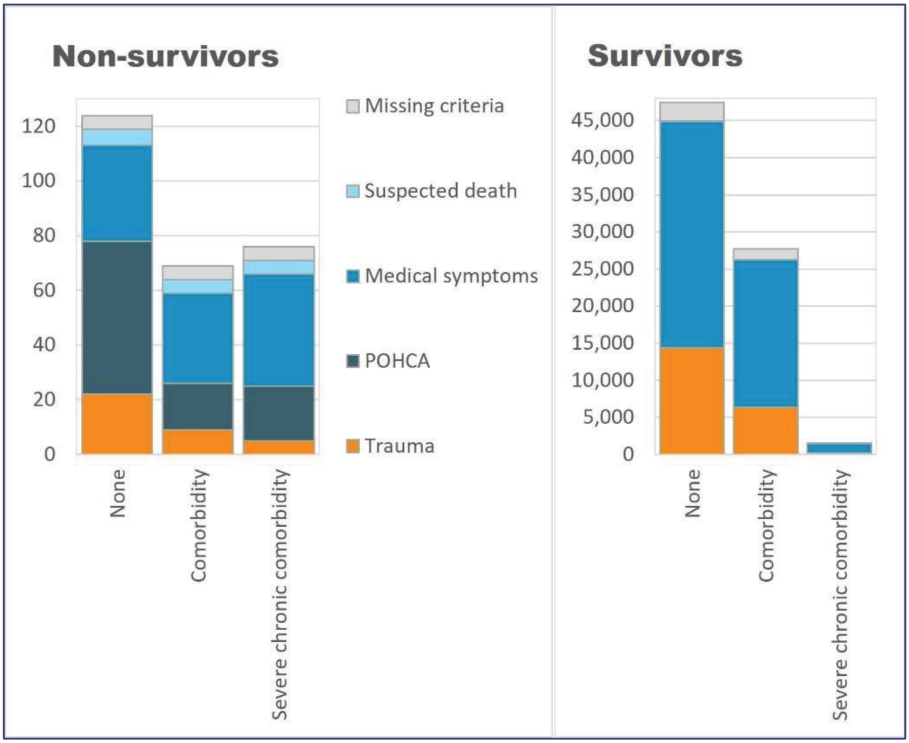


Figure 4.5. *Reasons for calling the national emergency number, 112, in Denmark, stratified by comorbidity subgroup: 'None' (n=47,563), 'Comorbidity' (n=27,778) and 'Severe chronic comorbidity' (n=1,615). Survivors and non-survivors refer to death within 7 days of the last emergency call. Reprint from Paper III (Appendix C).*[38] *Frequency data can also be found in table format there.*

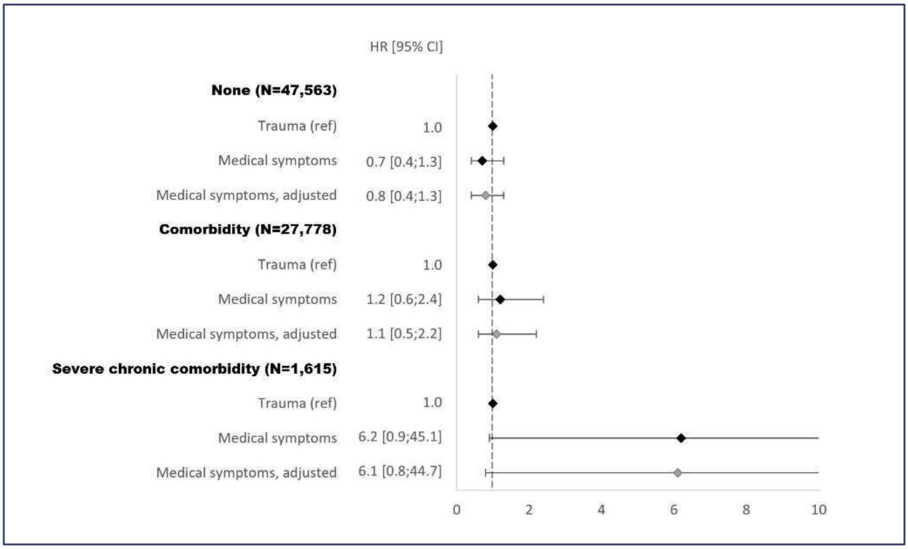


Figure 4.6. *Hazard ratios for 7-day mortality according to reasons for emergency call. 'Medical symptoms' does not include calls regarding paediatric out-of-hospital cardiac arrest. Crude HRs (black) and adjusted for age and sex (grey). Reprint from Paper III (Appendix C).*[38]

Summary

A third of all emergency calls regarding children were initiated because of trauma. Among the non-survivors though, only one in eight patients had calls that regarded trauma, whereas 42.7% had calls regarding medical symptoms or unclear problems excl. POHCA. Half of the children who did not survive a week after an emergency call had pre-existing comorbidity, a quarter of them severe chronic comorbidity. Both in the 'Comorbidity' group, the 'Severe chronic comorbidity' group and group 'None', the majority (>75%) of emergency calls for non-survivors had been made because of various medical symptoms incl. POHCA, and not because of trauma.

4.5 STUDY IV: OUTCOMES AFTER DISPATCH OF HEMS

The 651 HEMS missions were to newborns and infants (9.2%), toddlers (29.0%), preschool and school children (28.3%) and adolescents (33.5%).

Based on the NACA severity score, a third of the patients (29.6%) had critical emergencies, and this proportion did not differ among patients on offshore island missions compared with patients on mainland missions (risk difference 0.08 [-0.02;0.18]).[64]

For 20.1% of the patients, one or more of the following advanced prehospital procedures were performed before arrival at hospital: intubation, ultrasound examination, intraosseous vascular access, mechanical chest compressions, chest tube insertion and/or blood transfusion (listed by frequency).[64] Interventions and NACA scores were not readily available for the full EMS population, only for children attended by HEMS.

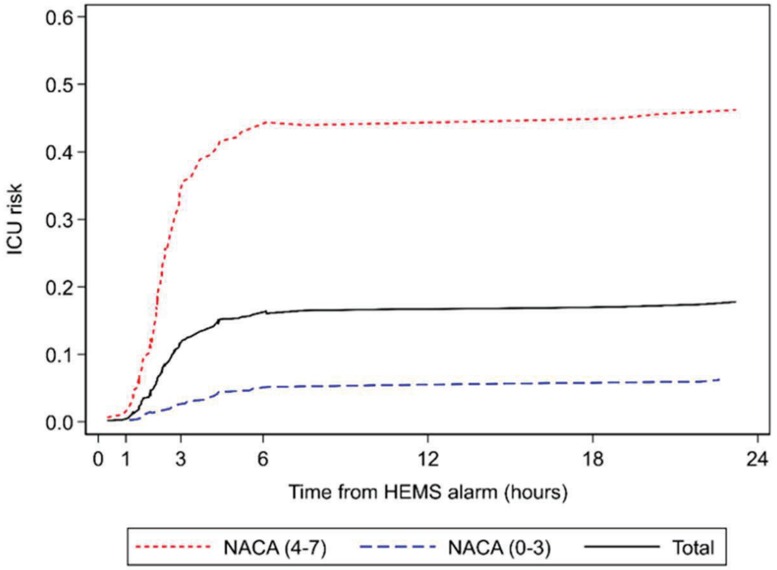
Intensive observation and/or care

Within 24 hours of the mission, 18.1% [14.9;21.7] of the patients brought to a hospital required intensive observation and/or care. Emergencies that were assessed as 'critical' according to the NACA score had an increased risk of intensive observation and/or care (0.06 [0.04;0.09] for NACA scores 0-3 versus 0.47 [0.40;0.56] for NACA scores 4-7 at 24 hours) (Figure 4.7).[64]

24 patients assessed as having 'noncritical emergencies' at the scene required intensive care. A third of these patients were aged 2 years or younger, and two-thirds had hospital diagnoses within the *Injury* chapter.[64]

Mortality

1-day mortality was 5.1% [3.6;7.3]. Most of the deaths that happened before arrival at a hospital (19/23) were among non-trauma patients. The sensitivity analyses indicated that the excluded patients without a valid PIN had higher levels of severity of illness or injuries assessed by NACA scores and performance of advanced prehospital procedures.[64] Yet when mortality was calculated for all patients (regardless of a valid PIN) using the variables from *Hemsfile* only, 30-day mortality did not change (6.2% [4.5;8.5] (35/565) using the validated CRS register versus 6.3% [4.7;8.5] (41/651) using the *Hemsfile* database).



	Time (hours)	ICU risk	[95%	CI]
NACA score 0-3	1	0.000		
	3	0.027	0.014	0.049
	6	0.053	0.035	0.081
	24	0.064	0.043	0.094
NACA score 4-7	1	0.020	0.006	0.061
	3	0.353	0.283	0.436
	6	0.433	0.359	0.516
	24	0.473	0.397	0.556

Figure 4.7. *Time to intensive observation and/or care (black curve, n=95/525 patients). The population is grouped by NACA score assessed at the scene by a HEMS physician. The red curve represents patients with critical emergencies (scores 4-7) (n=73/150 patients) and the blue curve represents patients with noncritical emergencies (scores 0-3) (n=24/375 patients). Cumulative risk estimates for both groups are added below the plot. Reprint from Paper IV (Appendix D).*[64]

Summary

The level of severity of illness or injuries in children attended by HEMS was assessed using several different outcomes. In a third of the missions (29.6%), the patient had a condition denoted as 'critical', and one in five patients brought to a hospital required immediate intensive observation and/or care. The majority of deaths happened on the same day as the HEMS mission or the following day (1-day mortality: 5.1% and cumulative 30-day mortality: 6.2%).

5 DISCUSSION

5.1 PRINCIPAL FINDINGS

In *Study I: Severity of illness or injuries*, we outlined levels of severity of deviating vital signs among children attended by the North Denmark EMS. Initially, 28.0% of children had 'life-threatening' or 'urgent' emergencies decreasing to 18.2% at hospital arrival. Oxygen saturation and heart rate were the most frequently deviating vital signs, and hypoxia was most frequently observed in patients aged ≤2 years. A third of the patients had triage scores that progressed to a lower level of urgency during ambulance transport and concurrent care. Missing vital sign data were unevenly distributed across age groups with decreasing completeness with younger age.[36] To explore possible reasons for this pattern, we initiated a dialogue with the North Denmark EMS and launched various educational initiatives in collaboration.

Following the initiatives described in *Study II: Prehospital monitoring*, we learned that mandatory educational initiatives for EMS professionals were associated with an increase in the extent of vital sign registration in paediatric patients aged 7 years or younger.[56] Although the a priori targets were achieved, even in the post-intervention period, incomplete vital registration was not limited to non-urgent cases.

Study III: Outcomes after emergency calls explored the diagnostic pattern and short-term mortality after emergency calls regarding children in Denmark. Almost forty percent of the children had diagnoses within the *Injury, poisoning and certain other consequences of external causes* chapter. For the subgroup of patients attended by HEMS, the diagnostic pattern was similar to that of the full EMS population except that HEMS was more frequently dispatched for burn victims, drowning victims and patients with diseases of the circulatory system. The ICD-10 chapter *Injury, poisoning and certain other consequences of external causes* accounted for 51.6% in the HEMS population versus 38.0% overall, including burns, which accounted for 11.2% in the HEMS population versus 1.3% overall.

Because most studies conducted in the prehospital setting concerning children focus on subgroups of trauma or POHCA patients, we had thought that most early deaths would be the result of trauma or injury-related conditions. Even though injuries were dominant among the primary hospital diagnoses, trauma only accounted for one in eight of the deaths within 7 days after an emergency call. Among all 255 children who did not survive a week after the emergency call, 42.7% of calls were related to medical symptoms or a problem that was unclear to the medical dispatcher, while 36.5% concerned paediatric out-of-hospital cardiac arrest.

Since more than 40% of the early deaths from paediatric emergencies were not attributable to neither trauma nor POHCA, a more accurate understanding of these emergency patients' medical history was needed.

Around 40% of all EMS patients *did* have previous or chronic diseases, conditions, or perinatal complications. *Study III* demonstrated that 47.5% of the non-survivors had no comorbidity, while 25.1% had previous or chronic diseases. An additional 27.5% had severe chronic diseases with potentially reduced lifespan, which in part could explain the extent of emergency calls regarding medical symptoms among the non-survivors.

Nevertheless, in the majority (>75%) of non-survivors *without* any pre-existing comorbidity, the emergency call had been made because of various medical symptoms incl. POHCA, and not because of trauma. The same was true among the non-survivors with comorbidities without a marked alteration in life expectancy.

5.2 INTERPRETATION

5.2.1 CAUSE OF EMERGENCY CALL

Study III outlined the diagnostic pattern of all paediatric patients, for whom an emergency call had been made, based on a systematic, consecutive and comprehensive data collection from national databases. We used dispatch criteria for categorising reasons for emergency call because diagnoses are rarely known at the point in time when EMS professionals encounter the patient.

In the total EMS cohort, some patients did not have severe illnesses or injuries, indicated by the findings of 80.3% having hospital stays <24 hours and 44.9% having a 'non-urgent' triage score upon ambulance arrival. Length of hospital stay is a proxy measure for severity, as some life-threatening conditions do not require lengthy hospital stays (e.g. foreign body airway obstruction or food allergies). Some of the patients with short hospital stays may have received appropriate care at one of the 24-hour operative out-of-hospital primary care services that exist in every region. Initiatives like the 'Tips from paediatricians' is also an example of health professionals trying to promote self-management at home of a variety of common symptoms.[97]

More than every third emergency call regarding a paediatric patient was caused by injuries, which is in line with a study describing paediatric missions in a regional Danish physician-staffed ground-based EMS.[98] However, it means that two-thirds of the patients had emergency calls regarding medical issues, some of them evidently serious, as described in detail in section 5.2.3.

Patients with medical conditions or symptoms are more frequent than trauma patients in the Danish HEMS compared with what is reported from HEMS systems in other countries.[64,65,67,69,71,99] The proportion of patients with critical emergencies in our HEMS system (29.6%) is well in line with the proportion in some other European HEMS.[64,65,67,69,72,100]

Dispatch of HEMS for island missions

Children account for a larger proportion of offshore island missions for tourists than for missions to resident islanders.[64,74] The Danish HEMS may be dispatched for offshore island missions to patients with low acuity conditions.[64,101] In *Study IV: Outcomes after dispatch of HEMS*, NACA scores did not differ between paediatric patients on offshore island missions and mainland missions. Children situated on offshore islands needed a physician-level EMS resource to the same extent as the children situated on the mainland.

5.2.2 PREHOSPITAL MONITORING IN CHILDREN

Normal ranges for vital signs

How is it determined if a vital sign is 'out of range'? The Danish Regions' Paediatric Triage Model considers one set of ranges to be 'normal', while the European Paediatric Advanced Life Support (EPALS) manual has other limits for 'normal ranges'. The correct way to determine these ranges would be empirically, as our colleagues Ramgopal et al.[102,103], Fleming et al.[49] and Brennan et al.[104] did.

The four vital signs of interest in our studies were respiratory rate, SpO_2, heart rate and level of consciousness.[56] Heart rate and SpO_2 were the most frequently deviating vital signs, especially in toddlers. Fever may induce tachycardia or tachypnea,[26,105] and while the educational material explained this correlation, the Danish Regions' Paediatric Triage Model did not correct heart or respiratory rates in the presence of fever.

The Danish Regions' Paediatric Triage Model had been evaluated in a small single-centre study for children with acute referral to a paediatric department, and concern was expressed about low sensitivity.[106] We did not evaluate the sensitivity and specificity of the Danish Regions' Paediatric Triage Model. The model had already been implemented via expert consensus on the available evidence at the time.[3,49,50,53] And costs related to the change of the software interface would be sizeable. This meant that sensitivity would have to be exceptionally poor if services were to change their current practice. Our agenda was not to replace the module, however, but to facilitate that EMS professionals actually obtained and documented the four vital signs of interest in a confident manner. We chose to make use of the existing triage model, as all of the studies would be conducted in a Danish setting.

The EMS professionals should first and foremost concentrate on the assessment, observation and care for the patient. Incomplete observation exposes the patient to a risk of inappropriate escalation of care.[107] The overall aim of the project was to encourage EMS professionals to use a structured approach to every child, no matter the immediate appearance. In *Study II: Prehospital monitoring*, we interpreted the registration of four specific vital signs as a basic and systematically structured ABCD evaluation of the patient and reevaluation to detect any changes. The exact four vital signs of interest (heart and respiratory rates, SpO_2 and level of consciousness) were chosen because of their association with clinical outcomes in paediatric patients in emergency settings[53,55,108] and because of their simplicity and mild discomfort for the child.[56]

Comparison to other emergency medical services

Study II: Prehospital monitoring added to the body of evidence to support that educational initiatives and training do improve vital sign registration in the prehospital setting.[3,57] The main findings revealed that the younger the patient, the lower the probability of complete vital sign registration.[56] Similar age variations in completeness are well documented in other EMS paediatric populations.[53,57–60,109] Nonetheless, in infants and toddlers, the extent of registration of the four individual vital signs of interest was not poor when results from our service were compared to other prehospital systems'[4,53,56–59,109] (described in detail in Papers I-II, Appendices A and B).[36,56]

Appropriate target level

All of the aforementioned studies reported the registration of single vital signs separately. Compared to these studies, our preset target for complete vital sign registration in *Study II* was ambitious. We chose to study complete vital sign registration as a proxy for a basic ABCD evaluation and reevaluation of the patient. The minimum target level of complete vital sign registration was fulfilled both overall and within four of the five age groups, however with large variations between age groups. But what is an acceptable level? And more importantly, does the difference up to a 100% only represent situations where vital sign registration was not clinically meaningful?

Previously, our colleagues investigated completeness in the recording of vital signs for all EMS patients in the North Denmark Region, i.e. both adults, children and elderly patients. In that study, SpO_2, heart rate, respiratory rate and GCS were entered into the prehospital ePMR in 75-85% of cases when assessed individually.[110] These figures cannot be extrapolated to an EMS population that only consists of children though.

Increasing vital sign registration is not equal to improving outcomes.[56] The focus on educational initiatives to increase vital sign registration in our service was encouraged by the post hoc analyses from *Study I: Severity of illness or injuries*, which suggested that missing vital signs were associated with increased mortality. An important mediator for this association is of course the performance of prehospital treatment and care. The actual act of obtaining vital signs does not affect the patient's condition, however it may lead to initiation of treatments that would not otherwise have been initiated or may increase triage level to a higher level of urgency that includes a forward alert to the receiving hospital.

Increases in vital sign registration were observed within four of the five age groups. Incomplete registration could be a matter of confounding by indication, i.e. EMS professionals may tend to observe and document vital signs only in children whom they assess as having a poor general condition.[36]

Although we never intended to achieve a 100%, did we actually reach a plateau in the post-intervention period where incomplete vital sign registration only represented situations where vital sign registration was not clinically meaningful? Our findings oppose this. Patients with 'non-urgent' conditions were likely to be a contributory cause for not reaching a 100% ('non-urgent' triage score had a relative risk of 0.8 for complete vital sign registration). Yet even after the implementation of the educational initiatives, more than a third of the patients with incomplete vital sign registration had 'less urgent', 'urgent' or 'life-threatening' conditions.[56] Meaning that incomplete vital sign registration does not seem to be restricted to situations where vital signs would not provide clinically meaningful information.

Choosing appropriate outcomes for clinical improvement is complicated, as 'typical' patient-centred outcomes in an adult population, such as ICU admittance or death, are much more infrequent in paediatric populations.[56] As a proxy for change in clinical condition during the prehospital phase, we examined change in triage scores (calculated from the first set of vital signs to the last set). In the intervention region, significantly more patients experienced an improvement in triage score in the post-intervention period than in the pre-intervention period, thus indicating the educational initiatives had had an impact on patient care.[56]

A one-year wonder?

The conduction of educational initiatives does not necessarily translate into a change in work behaviours in several EMS professionals. We made different attempts to particularly target this issue. During the production of the educational materials, we got extensive feedback from two designated paramedics who had been EPALS certified by the European Resuscitation Council. Following the first four weeks after the launch of the initiatives, we met with emergency medical technician representatives in four different cities around the region to understand attitudes to and any concerns regarding the study. These classroom sessions were conducted in a semistructured manner with a short lecture on the background, aims and preliminary results of the study. The lecture was followed by a patient case to facilitate a discussion about motivations for increasing 'paediatric readiness'. Before closing the session, emergency medical technicians had the opportunity to pinpoint certain situations or use of equipment that were often perceived as difficult. As an example, we incorporated a Glasgow Coma Scale into the prehospital ePMR system per request of the EMS professionals, with separate verbal responses in children aged 5 years or younger and 6 years and above, respectively, for those who did not routinely use the Alert – Voice – Pain – Unresponsive scale.[56] In *Study II: Prehospital monitoring*, the positive effects on vital sign registration lasted for more than a year, i.e. throughout the entire 15-month post-intervention period (cf. Figure 4.2), which indicated a sustained impact.

5.2.3 OUTCOMES AFTER EMERGENCY CALL

Mortality rates

Mortality estimates from *Studies III: Outcomes after emergency calls* and *IV: Outcomes after dispatch of HEMS* were divergent (5.1% within one day of HEMS dispatch versus <0.30% overall, no matter the method of computation). This should not be interpreted as the dispatch of HEMS results in poorer outcomes. We consider these estimates to reflect confounding by indication as it is stated in the *Danish Index for Emergency Care* that HEMS must be dispatched to all paediatric emergencies with urgency level A if HEMS is the nearest physician-level EMS resource.

Study III: Outcomes after emergency calls challenges the intuition you would get from reviewing the extensive amount of paediatric trauma studies in prehospital research; that trauma is the dominant cause of death from paediatric emergencies. In our study, *Injury, poisoning and other external causes* accounted for 38.0% of the ICD-10 diagnoses after an emergency call across all ages, while only 13.7% of non-survivors had diagnostic codes within the *Injury* chapter as their last diagnosis before death.

In *Study III*, 42.7% of the deaths following paediatric emergencies had happened after calls concerning 'Medical symptoms' or a problem that was unclear to the medical dispatcher. Dispatch criterion 27 'Psychiatry – suicidal' is a diverse criterion with symptoms ranging from suicide attempts to a mere suspicion of mental illness. The 19 patients with this criterion were included in 'Medical symptoms' because self-injury might be preceded by mental health issues, which were considered medical symptoms. Regarding them as trauma might influence results from the Cox regression on reasons for calling. [38]

The reported annual POHCA incidence rate of 3.5 per 100,000 children ≤15 years was comparable, however relatively low, compared to the extensive literature from other high-income countries.[111–114] In children, non-cardiac causes of death such as trauma, drowning or other external causes, respiratory insufficiency, hypovolaemic or distributive shock are more common than presumed cardiac causes.[7,10,26,114,115] Patients who were breathing normally at the time of emergency call could have suffered a POHCA later as the result of the medical condition that led to the call (e.g. chest pain, abdominal pain, seizure, etc.). However, as these patients were not in cardiac arrest at the time of emergency call, they were not categorised as such. In *Study III: Outcomes after emergency calls*, only 3.5% of non-survivors had a last diagnosis of respiratory disease or respiratory failure, however some cases might have been coded as cardiac arrest (ICD-10 code *I46*). Some patients may have been assigned the 'Unconscious child/adult' dispatch criteria even though the call regarded a traumatic POHCA. This would have caused non-traumatic POHCAs to be overestimated in our study.[38] Nonetheless, when we manually reviewed the last diagnoses preceding death and let a cardiac arrest code be 'overruled' by the second to last diagnosis (e.g. in case of drowning), the proportion of deaths attributable to non-traumatic POHCA was also around one third (36.5% using dispatch criteria versus 29.0% using ICD-10 diagnoses (Table 4.2)).[38,73]

Although incidence rates of POHCA in various countries are widely available, nationwide outcomes for unreferred paediatric emergency populations with case-mixes similar to ours (including both trauma and non-trauma patients) are few or not publicly available. In previous studies reporting clinical outcomes of unreferred paediatric EMS populations, comparable short-term mortality rates have been reported.[2,55,58,116] In a study conducted at more than 900 US emergency departments, 2.0% of the injured children died during their hospital stay, while 1.1% of the children with medical illnesses died.[41]
Barker et al reported all-cause 30-day mortality of approximately 8% for children conveyed by an Australian HEMS.[64,66] In that study, as well as in our *Study IV: Outcomes after dispatch of HEMS*, non-traumatic illnesses were proportionally overrepresented among the deceased patients.[64]

Variations with comorbidity

Few and conflicting results have been reported on the occurrence of comorbidity among paediatric emergency patients. In a systematic review of 37 studies, only 6% had what the authors defined as 'Chronic disease' marked as the cause of non-submersion POHCA.[112] In a 10-year single-centre study from Finland, 65% of POHCA patients had 'suspected or diagnosed chronic or otherwise significant conditions'.[117]

Among Canadian atraumatic POHCAs, 16.2% of the patients who did not survive to hospital discharge had been admitted to hospital or visited an emergency department for a 'significant comorbidity' within two years before the arrest.[118] The 'significant comorbidities' were assessed both by predefined ICD-10 codes and by using a previously validated index that included outpatient healthcare encounters and drug prescriptions.[118,119]

Our *Study III: Outcomes after emergency calls* was designed to investigate the prevalence of pre-existing comorbidity among *all* paediatric emergencies. The considerable differences in the proportion of non-survivors with comorbidity may reflect that they were two distinct patient populations.[38]

In *Study III*, we manually reviewed *all* ICD-10 codes to create a separate comorbidity subgroup for diagnoses that entailed a potentially considerably reduced lifespan. We then searched all in-patient *and* out-patient hospital visits *plus* visits to private practitioners in all medical specialities for the five years preceding each emergency call. We found that half of the non-survivors after an emergency call had had some degree of pre-existing comorbidity. Children with 'Severe chronic comorbidity' comprised 2.1% of the study population, yet a quarter of the non-survivors (27.5%).

The sensitivity of triage systems for patients with and without chronic diseases has previously been investigated in a cohort of children who presented to an emergency department with dyspnoea, diarrhoea, vomiting or fever.[120] Sensitivity was lower for children with chronic diseases, i.e. they had an increased risk of 'undertriage'.[120] Artificial intelligence may aid current scoring systems. In a Korean study of >2m paediatric emergency department patients, a deep learning algorithm predicted critical care needs more accurately than a paediatric early warning score.[121]

Variations with age

Age less than 12 months was associated with a higher 7-day mortality and this finding corresponds with international literature.[9,111,114,122–126]

In *Study III: Outcomes after emergency calls*, we found that 41% of the non-survivors aged less than 12 months could be considered dead on arrival of the

EMS, i.e. death date was equal to date of emergency call and the patient had not received any resuscitative efforts. Accordingly, sudden unexpected infant death may be a partial explanation for the higher mortality risk among infants.[127–129] However, it may not exclusively be the cause of this finding, as similar mortality estimates were observed after excluding all patients that could be considered 'dead before arrival of the EMS'. We were notified by EMS professionals that in cases of sudden infant death, an infant may have had discrete signs of death. In such cases, resuscitation would have been initiated upon the arrival of the HEMS or MECU physician, regardless of a dismal prognosis.[64] In this way, some patients undergoing resuscitation may in fact have been dead before arrival of the EMS. This might influence the association between age <12 months and increased mortality reported above.

Death before arrival of the EMS

It can be discussed if a 'true' mortality estimate in children, for whom an emergency call had been made, should exclude patients who were already deceased at the time of the call (i.e. death date was equal to date of emergency call and the patient had not received any resuscitative efforts).

In *Study III: Outcomes after emergency calls*, we learned that 30.2% of the 7-day non-survivors may have died before the EMS had arrived at the scene. This is an approximation though, as the registries do not include any previously validated variables that hold this information. The result implies, however, that patients who had already died before the arrival of the EMS account for a considerable part of the total number of early deaths after paediatric emergency calls. Initiatives to help decrease this number would first and foremost be preventive measures on a public health scale rather than training, education or expanding treatment options in individual services.

5.2.4 HOW THE STUDIES RELATE TO PAEDIATRIC READINESS

'Paediatric readiness' may be associated with survival.[39,41,42] Danish trauma centres and adult emergency departments have acceptable paediatric readiness scores compared to international standards.[39,41,42,130–133] Yet there are opportunities for advancement,[134] and corresponding scores for Danish EMS are not yet available. We have outlined both the frequency and urgency of different types of paediatric emergencies. Based on the four studies in this dissertation, we propose future focuses for training, research and opportunities for increasing paediatric readiness in Danish EMS settings.

Febrile convulsions

In our study population, almost half (46.8%) of all the *Symptoms and signs* (which was the second largest chapter after *Injury, poisoning and other external causes*) were febrile convulsions, which are generally considered a benign condition. In Finland and in Germany, febrile convulsions are highly prevalent in paediatric EMS patients too.[72,135,136] Among non-survivors, some had an infection as their last diagnosis before death. Themes that deserve educational and research attention could be the quality of prehospital seizure management and whether variations in management exist between services. The findings remind us that febrile convulsions are not always benign. Educational material could include objective signs that differentiate febrile convulsions from fever related to central nervous system infections[137–145] or fever related to bacterial infections with complications[146] (e.g. invasive streptococcal disease[147] or multisystem inflammatory syndrome,[148] as the incidences of both have increased in the wake of the COVID-19 pandemic).

Out-of-hospital cardiac arrest

Around one third of the non-survivors after paediatric emergency calls in Denmark had suffered a non-traumatic POHCA. While this research area is already receiving appropriate attention, further studies into risk factors and management are definitely warranted. When POHCAs occur in children with severe chronic comorbidity, they often occur suddenly at an unpredicted time, and EMS professionals may be unprepared for this type of situation.[149] Decision-making about resuscitation in this patient population can be terribly complex. In a multicenter review of cardiopulmonary resuscitation in patients with specialised paediatric palliative home care teams, close to 40% survived POHCA with the same level of quality of life as they had had prior to arrest.[149] The incorporation of EMS professionals in advanced care planning for children is an area where Denmark could lean towards Germany, where training facilities for EMS professionals in paediatric palliative care have been evaluated on a trial basis.[150]

Non-accidental injuries

Infants aged less than 12 months had a higher 7-day mortality risk, even when patients who could be considered 'dead before arrival of the EMS' were excluded. This finding suggests that the increased mortality in infants may only partly be explained by the occurrence of sudden unexpected infant death. Infants can have significant occult injuries, and they have a higher risk of non-accidental injuries than older children,[151] and they might go unnoticed by the EMS. 62% of Danish emergency departments have a policy and a procedure to guide clinicians in cases of suspected non-accidental injuries.[130,152] 'Paediatric readiness' also includes communicating with parents and caregivers in emotional distress and in situations that may be unpleasant.[37] Emergency care providers do not always react sufficiently when they encounter non-accidental injuries,[152–154] even though bruises and other skin lesions are frequently visible on the child's head and neck region or upper limbs.[154,155] EMS professionals encounter the child at the scene of injury. Thereby, they have a unique position to report valuable information regarding the specific mechanism of injury to hospital clinicians. Approach and EMS practices in these types of situations are an unexplored area suitable for further research, and cases can easily be identified from our nationwide cohort with definitive hospital diagnoses.

Derived effects of the educational initiatives

In the educational material produced for *Study II: Prehospital monitoring*, we provided written standardised precalculated dose advice for commonly used medications in paediatric emergency medicine, 'which has been shown to reduce administration errors'.[56,91] The mandatory educational initiatives encouraged EMS professionals to have a standardised approach to clinical examination of children, and this may have increased the caregivers' confidence in the ambulance team.[25,56] Patient or caregiver concerns are valuable in the process of identifying children at risk of clinical deterioration and provision of timely treatment, in addition to 'treatment provider concern' as mentioned in the Introduction section 1.2.[156,157]

5.3 METHODOLOGICAL CONSIDERATIONS

In Paper II (Appendix B)[56], the design of *Study II: Prehospital monitoring* was discussed in detail: "A causal relationship between the educational initiatives and outcomes can only be concluded in randomised trials, and we considered a randomised cluster design within our service using individual ambulance stations. Since 'unlearning' skills is not possible, a crossover design was not suitable. However, a randomised parallel design was not suitable either, as staff could exchange knowledge and create a 'spill-over effect' from intervention to usual care. No movement of staff between regions was expected as regions have different service providers. Consequently, we chose the observational design and divided study groups by period and by regional service level.

EMS professionals may have been inclined to change registration practices as a result of being studied. While it is hard to categorically disprove this possible Hawthorne effect,[158] the fact that the increase in the primary outcome persisted for more than a year (i.e. all through the post-intervention period) suggests otherwise."

5.3.1 PRECISION AND CONFOUNDING

Results are presented with 95% confidence intervals, and insignificant results are described as such. In general, studies with large study populations tend to provide estimates with narrow confidence intervals. This does not necessarily apply to studies with rare occurring outcomes though. In the regression analyses for *Study III: Outcomes after emergency calls*, a type II error might have occurred due to the rarity of the outcome of interest (death). In the 'Severe chronic comorbidity' group, the point estimate for the unadjusted hazard ratio was 6.2 with a wide-ranging confidence interval from 0.9 to 45.1 for calls regarding medical symptoms compared to calls regarding trauma. A study with a larger population might have found an actual difference that could not be detected by our study. Likewise, a larger study population could have enabled us to perform sensitivity analyses without patients who had died even before the EMS had arrived at the scene (identified by call date, death date and no resuscitative efforts). Geographically, the study covers all of Denmark, and the study period ranges back to the first year from which nationwide data are available. Consequently, we had no means of enlarging the study population within our own country.

All observational studies must carefully consider confounding and mediating factors for the reported results. *Study II: Prehospital monitoring* was particularly prone to confounding, which is why we investigated several factors both at organisation and patient level for the outcome of interest (complete vital sign registration). A directed acyclic graph was drawn using the online freeware DAGitty[159] to illustrate possible confounding or mediating factors and to facilitate a discussion among authors about which to control for in the regression model. As data collection for *Study II* took place in the midst of the COVID-19 pandemic, we decided a priori to adjust for COVID-19 incidence peaks. The pandemic led to the obligatory use of personal protective equipment for EMS encounters with patients with a wide variety of symptoms, which could have affected vital sign registration practice. Peaks were defined as months with a national lockdown of schools more than 50% of the time due to the risk of COVID-19 infection.[56] We also decided a priori to adjust for treat-and-release situations, as we hypothesised that vital signs might not have been recorded more than once in such situations.[56]

5.3.2 INTERNAL VALIDITY

All of the studies are strengthened by their population-based design with consecutive inclusion of patients. It follows that the study populations include close to all individuals in the target population which ensures that data reflect routine clinical care.[160] The equal access to free-of-charge emergency care in all of Denmark limits selection bias due to caregivers' socioeconomic resources. Using a registry-based study design also avoids observer biases originating in the process of assessing the outcomes. Danish health registries allow nationwide follow-up on patient-centred hospital outcomes and survival, even after hospital discharge.[160]

For the studies reporting incidences of hospital diagnoses and mortality, data were collected from high-quality, nationwide, centralised databases that are continually maintained as described in the Methods section (3.4.3.). Registry data was used both for the collection of exposures and outcomes and to validate confounding variables.

The use of unique PINs for the linkage process and collection of outcomes ensures minimal loss to follow-up, as the national CRS register is updated daily.[82] *Study III: Outcomes after emergency calls* benefitted from the completeness of the DNPR to compare baseline variables between the final study population and the patients who were lost to follow-up. In the studies assessing clinical outcomes, children without a valid PIN were excluded, as a certain age could not be verified and outcomes were assessed using specific age group limits. We hypothesised that registering a PIN on the medical record might not be prioritised in cases of critical emergencies, which would cause us to underestimate mortality rates. Selection bias due to invalid PINs has been scrutinised in *Studies III-IV*. In *Study III: Outcomes after emergency calls*, we acquired data from an additional source that included both patients *with* and *without* valid PINs to evaluate the internal validity of our survival analysis.

In *Study IV: Outcomes after dispatch of HEMS*, we conducted sensitivity analyses for patients without valid PINs by using a predefined variable, 'Mission outcome', from the *Hemsfile* database. This variable was filled by the attending HEMS physician, and one of the options for 'Mission outcome' was 'Patient dead'.

All additional analyses indicated that selection biases attributable to unidentified patients were limited in both studies.

The Danish National Patient Register

The DNPR dates back to 1976 and contains all in- *and* (since 1995) out-patient hospital visits plus visits to private practitioners in all medical specialities, however not visits to a patient's general practitioner. Supposedly, a patient could have suffered from a disease or condition for which they had only consulted a general practitioner (e.g. well-controlled asthma). Patients without *any* prior visits in the DNPR were few. We do not consider it likely that those patients were foreigners with comorbidities visiting Denmark because patients without valid Danish PINs were excluded due to missing follow-up.

Existing comorbidity indexes were not applicable to our data sets, as we did not have access to data on all psychiatric comorbidities, weight or smoking status which is necessary to calculate such an index.[119,161]

In *Study III: Outcomes after emergency calls*, the comorbidity subgroups were susceptible to right censoring. Undiagnosed congenital cardiovascular malformations might have been present in some patients, which would make them incorrectly classified as having no comorbidity. Such malformations may not be diagnosed for several years after birth, i.e. after the end of follow-up.[160]

In 2019, the DNPR was extensively revised for administrative purposes (e.g. simpler creation of clinically meaningful admission flows with sequential contacts and updated standards for content and format of variables reported from private hospitals and clinics). During the data management process for *Study III*, we chose to link PINs and EMS units to the DNPR and generate hospital admission flows using the same conditions both before and after this revision. We manually checked a random sample of patients who had been admitted to a hospital during the quarter that followed the revision in 2019 and found meaningful admission flows. Details can be read in the supplemental material to Paper III (Appendix C).[38]

Using a hospital administrative database like the DNPR may introduce information bias since it is the attending physician who assigns the diagnostic code to a patient's record during daily clinical practice. Variations in coding practice between physicians and between institutions are to be expected. This means that limitations may apply to the consistency and sensitivity of the reported diagnostic codes.[38,160] In the DNPR, however, 3-digit primary diagnosis codes alone (e.g. *Axx.x*) have a positive predictive value of 82% in the paediatric speciality.[38,81] The ICD-10 *Injury* chapter is not graduated by level of severity and does not allow for subdivision into patients with major trauma and patients with minor injuries.[64]

Due to the risk of personally identifiable data, 3-digit diagnostic codes for deceased patients were not possible to disclose (cf. the *Danish Act on Research Ethics Review of Health Research Projects*). Gray et al. recently validated three algorithms applied to health administrative data against the Canadian Resuscitation Outcome Consortium (CanROC) reference standard.[162] Close to all of the ICD-10 hospital admission codes included in their algorithms were also found among the non-survivors' last diagnoses preceding death in our *Study III: Outcomes after emergency calls.*[38]

The outcome of triage score progression

The historical (2006-2018) 'baseline level' for this outcome reported in *Study I: Severity of illness or injuries* was a little higher than in the pre-intervention period of *Study II: Prehospital monitoring* (2019-2020) (32% in *Study I* versus 25% in

Study II). This discrepancy was due to different calculation methods and exclusion criteria in the two studies. Firstly, *Study I* excluded patients without a valid PIN whereas *Study II* did not, and there was a trend toward fewer vital sign registrations in patients without valid PINs. During *Study II*, there were no changes in the process for linking vital signs to a case. This was done via the patient's PIN for >95% of the study population and via a record id for the patients without a valid PIN.

Second and more importantly, the denominator in *Study II* was all patients whereas the denominator in *Study I* was all patients with two triage scores. The important thing to infer from *Study II* is that significantly more patients improved their clinical condition (assessed by triage scores) during the post-intervention period than during the pre-intervention period.

5.3.3 EXTERNAL VALIDITY

Within the research discipline of prehospital medicine, the generalisability of studies is generally limited by differences in case-mixes, sociodemographic background, access to emergency care and organisation of EMS systems +/- physician-staffed EMS units. *Studies I-II* are only generalisable within the country of Denmark as all Danish EMS use this particular paediatric triage model,[36] though it does resemble a lot of other triage systems. As for the missing data pattern for vital signs in relation to age, it seems this is a common finding in different countries' EMS systems.

Studies II: Prehospital monitoring and *III: Outcomes after emergency calls* were conducted during both pre- and peri-COVID-19 periods which adds to the findings' reliability in today's clinical setting. Incidences of the reported diseases may not be generalisable to all healthcare systems, however, particularly not systems that do not have free access to emergency care. The methodology for classification of comorbidity can be applied to research in any other healthcare system that has nationwide health administrative databases.

6 CONCLUSIONS AND PERSPECTIVES

Identifying the few children who are at risk of clinical deterioration remains a challenge for non-paediatric emergency care providers. *Studies I-II* investigated vital sign measurements in children attended by EMS professionals and various initiatives aimed to promote a systematic clinical approach to these children.
In *Study I: Severity of illness or injuries*, a third of the patients (28%) had either life-threatening or urgent conditions upon arrival of the ambulance. Vital sign registration in children was incomplete, especially in patients aged ≤2 years.[36]
Study II: Prehospital monitoring implied that mandatory educational initiatives for EMS professionals contributed to a more thorough examination of paediatric patients ≤7 years as it was associated with an increase in the extent of vital sign registration.[56]

EMS professionals are not meant to practise formal diagnosing, and they are not supposed to be 'light paediatricians'. Nonetheless, a basic ABCDE evaluation of the patient to assess immediate treatment needs is expected.
In the spring of 2022, the North Denmark EMS paramedics had an extra day of brush-up training in paediatric ALS and newborn resuscitation plus repeating of the structured clinical approach to children according to the EPALS principles. The instructional video has been implemented into the formal paramedic educational programme at the University College of Northern Denmark, who are responsible for training paramedics from all five Danish regions.

The explorative studies outlined in this dissertation add new and exhaustive approaches to the research field of prehospital medicine in several ways:
Reporting of hospital diagnoses for a nationwide and complete cohort of paediatric emergency patients; close to complete follow-up beyond the prehospital phase and regardless of hospital admission; and a novel methodology for reporting paediatric comorbidity using hospital visits that had taken place before the emergency call.

Studies III-IV outlined the diagnostic pattern and mortality after paediatric emergency calls. In Denmark, the annual all-cause mortality rate was 7.0 per 100,000 children aged ≤15 years. Even though *Injury, poisoning and certain other consequences of external causes* was the dominant ICD-10 chapter, trauma only accounted for one in eight of the early deaths after an emergency call.

Study III: Outcomes after emergency calls reported reasons for calling in patients who had died within one week from the emergency call. A third resulted from POHCA, whereas 42.7% had called with various medical symptoms or a problem that was unclear to the medical dispatcher. Our findings indicate that emergency calls regarding medical symptoms were as critical as trauma, as 7-day mortality risk did not significantly differ in patients with medical symptoms (excl. POHCA) compared to trauma, even among the children without any comorbidity.[38] Among non-survivors, 30.2% may have died before arrival of the first EMS unit, which suggests reviewing preventive measures for children. Further research is required on risk factors and circumstances in these early deaths, as only a minority of those were trauma-deaths.

Compared to HEMS in other countries' healthcare systems, more paediatric patients in the Danish HEMS had medical conditions or symptoms than injuries. In *Study IV: Outcomes after dispatch of HEMS*, a third had 'critical' emergencies. However, the condition may change over the course of a few hours, and some of the patients who required intensive care within 24 hours of alarming HEMS had been assessed as having 'noncritical emergencies' by the physician on scene.[64]

The methodology for classifying pre-existing comorbidity has been thoroughly described in the dissertation, and full documentation may be requested from the author. The full documentation is enclosed as supplemental material for Paper III (Appendix C),[38] which makes it easy for researchers to apply to future studies conducted in healthcare systems with health administrative databases. It may be freely adopted and used for differentiation between clinically meaningful comorbidity subgroups.

Pre-existing comorbidity might influence mortality after paediatric emergencies. Among all children in Danish EMS, close to 40% had previous or chronic diseases, conditions, or perinatal complications.[38] A quarter of the non-survivors had chronic diseases so severe that the diagnosis implied a limited life expectancy. Another quarter of the non-survivors had diseases or conditions that were either previous or chronic, however without a marked alteration in life expectancy. This 'Comorbidity' group was very heterogenous. The studies suggest that EMS professionals could benefit from education on how to tailor the management of exacerbations or emergencies in children with commonly occurring comorbidities. Based on the nationwide cohort with definitive hospital diagnoses composed for this dissertation, subgroups of patients with specific chronic diseases or conditions (e.g. diabetes, epilepsy or asthma) can be easily identified if we want to explore the quality of prehospital care for exacerbations or attacks of these chronic diseases in future studies.

Altogether, our work supports that time and resources should be set aside regularly for training non-paediatric emergency care providers in both paediatric advanced life support and in recognition and initial management of paediatric medical emergencies.

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SUPPLEMENT

Table S.1. Primary hospital ICD-10 diagnosis for patients with a hospital visit after an emergency call. *N*=93,081, no missing data. Reprint from supplemental material to Paper III (Appendix C).[38]

	0-2 years			
	Urgency level			
No. (%)	Lights and sirens		**No** lights and sirens	
ICD-10 Chapter				
AB: I - Certain infectious and parasitic diseases	1,208	4.7	647	6.1
CD: II - Neoplasms	23	0.1	≤10	-
D: III - Diseases of blood, blood-forming organs and immune system	30	0.1	≤10	-
E: IV - Endocrine, nutritional and metabolic diseases	277	1.1	84	0.8
F: V - Mental and behavioural disorders	36	0.1	≤10	-
G: VI - Diseases of the nervous system	917	3.6	185	1.8
H: VII - Diseases of the eye and adnexa	27	0.1	21	0.2
H: VIII - Diseases of the ear and mastoid process	316	1.2	177	1.7
I: IX - Diseases of the circulatory system	136	0.5	≤10	-
J: X - Diseases of the respiratory system	4,070	15.8	1,513	14.4
K: XI - Diseases of the digestive system	337	1.3	189	1.8
L: XII - Diseases of the skin and subcutaneous tissue	176	0.7	62	0.6
M: XIII - Diseases of the musculoskeletal system and connective tissue	24	0.1	38	0.4

N: XIV - Diseases of the genitourinary system	144	0.6	50	0.5
O: XV - Pregnancy, childbirth and the puerperium	≤10	-	≤10	-
P: XVI - Certain conditions originating in the perinatal period	676	2.6	112	1.1
Q: XVII - Congenital malformations, deformations and chromosomal abnormalities	151	0.6	36	0.3
R: XVIII - Symptoms, signs and abnormal clinical and laboratory findings	10,858	42.2	2,425	23.0
ST: XIX - Injury, poisoning and other external causes	3,785	14.7	3,680	35.0
S-T14: XIX - Injuries	1,819	7.1	2,686	25.5
T15-T19: XIX - Foreign bodies	633	2.5	395	3.8
T20-T35: XIX - Burns, corrosions and frostbite	492	1.9	240	2.3
T36-T65: XIX - Poisoning	335	1.3	223	2.1
T66-T78: XIX - Effects of external causes	453	1.8	117	1.1
T79: XIX - Early complications of trauma	0	0.0	0	0.0
T80-T88: XIX - Complications of surgical and medical care	50	0.2	18	0.2
T90-T98: XIX - Sequelae of injuries, poisoning and external causes	≤10	-	≤10	-
VXY: XX - External causes of morbidity and mortality	0	0.0	0	0.0
Z: XXI - Contact with health services	2,524	9.8	1,278	12.1
Total	25,720	100	10,526	100

Table S.1. (continued) Primary hospital ICD-10 diagnosis for patients with a hospital visit after an emergency call. *N*=93,081, no missing data. Reprint from suppl. material to Paper III (App. C).[38]

	3-7 years			
	Urgency level			
No. (%)	Lights and sirens		**No** lights and sirens	
ICD-10 Chapter				
AB: I - Certain infectious and parasitic diseases	325	2.9	211	2.9
CD: II - Neoplasms	24	0.2	≤10	-
D: III - Diseases of blood, blood-forming organs and immune system	≤10	-	≤10	-
E: IV - Endocrine, nutritional and metabolic diseases	140	1.2	47	0.6
F: V - Mental and behavioural disorders	53	0.5	13	0.2
G: VI - Diseases of the nervous system	1,114	9.9	246	3.4
H: VII - Diseases of the eye and adnexa	24	0.2	16	0.2
H: VIII - Diseases of the ear and mastoid process	29	0.3	40	0.5
I: IX - Diseases of the circulatory system	84	0.7	20	0.3
J: X - Diseases of the respiratory system	2,234	19.8	706	9.7
K: XI - Diseases of the digestive system	86	0.8	101	1.4
L: XII - Diseases of the skin and subcutaneous tissue	79	0.7	40	0.5
M: XIII - Diseases of the musculoskeletal system and connective tissue	61	0.5	72	1.0
N: XIV - Diseases of the genitourinary system	34	0.3	42	0.6
O: XV - Pregnancy, childbirth and the puerperium	0	0.0	0	0.0

P: XVI - Certain conditions originating in the perinatal period	≤10	-	≤10	-
Q: XVII - Congenital malformations, deformations and chromosomal abnormalities	65	0.6	11	0.2
R: XVIII - Symptoms, signs and abnormal clinical and laboratory findings	2,969	26.3	1,142	15.6
ST: XIX - Injury, poisoning and other external causes	2,991	26.5	4,123	56.5
S-T14: XIX - Injuries	2,018	17.9	3,604	49.4
T15-T19: XIX - Foreign bodies	213	1.9	233	3.2
T20-T35: XIX - Burns, corrosions and frostbite	136	1.2	92	1.3
T36-T65: XIX - Poisoning	172	1.5	99	1.4
T66-T78: XIX - Effects of external causes	303	2.7	61	0.8
T79: XIX - Early complications of trauma	0	0.0	0	0.0
T80-T88: XIX - Complications of surgical and medical care	143	1.3	34	0.5
T90-T98: XIX - Sequelae of injuries, poisoning and external causes	≤10	-	0	0.0
VXY: XX - External causes of morbidity and mortality	0	0.0	0	0.0
Z: XXI - Contact with health services	942	8.4	452	6.2
Total	11,269	100	7,301	100

Table S.1. (continued) Primary hospital ICD-10 diagnosis for patients with a hospital visit after an emergency call. *N*=93,081, no missing data. Reprint from suppl. material to Paper III (App. C).[38]

	8-15 years			
	Urgency level			
No. (%)	Lights and sirens		**No** lights and sirens	
ICD-10 Chapter				
AB: I - Certain infectious and parasitic diseases	223	1.2	212	1.1
CD: II - Neoplasms	38	0.2	20	0.1
D: III - Diseases of blood, blood-forming organs and immune system	21	0.1	15	0.1
E: IV - Endocrine, nutritional and metabolic diseases	232	1.3	152	0.8
F: V - Mental and behavioural disorders	493	2.7	502	2.5
G: VI - Diseases of the nervous system	1,939	10.6	627	3.1
H: VII - Diseases of the eye and adnexa	26	0.1	21	0.1
H: VIII - Diseases of the ear and mastoid process	12	0.1	18	0.1
I: IX - Diseases of the circulatory system	219	1.2	98	0.5
J: X - Diseases of the respiratory system	804	4.4	341	1.7
K: XI - Diseases of the digestive system	165	0.9	259	1.3
L: XII - Diseases of the skin and subcutaneous tissue	72	0.4	39	0.2
M: XIII - Diseases of the musculoskeletal system and connective tissue	236	1.3	398	2.0
N: XIV - Diseases of the genitourinary system	82	0.5	155	0.8
O: XV - Pregnancy, childbirth and the puerperium	≤10	-	≤10	-

P: XVI - Certain conditions originating in the perinatal period	0	0.0	0	0.0
Q: XVII - Congenital malformations, deformations and chromosomal abnormalities	52	0.3	19	0.1
R: XVIII - Symptoms, signs and abnormal clinical and laboratory findings	3,891	21.4	3,310	16.5
ST: XIX - Injury, poisoning and other external causes	8,122	44.6	12,665	63.2
S-T14: XIX - Injuries	6,519	35.8	11,498	57.4
T15-T19: XIX - Foreign bodies	101	0.6	68	0.3
T20-T35: XIX - Burns, corrosions and frostbite	171	0.9	97	0.5
T36-T65: XIX - Poisoning	792	4.3	816	4.1
T66-T78: XIX - Effects of external causes	316	1.7	110	0.5
T79: XIX - Early complications of trauma	0	0.0	0	0.0
T80-T88: XIX - Complications of surgical and medical care	219	1.2	72	0.4
T90-T98: XIX - Sequelae of injuries, poisoning and external causes	≤10	-	≤10	-
VXY: XX - External causes of morbidity and mortality	≤10	-	≤10	-
Z: XXI - Contact with health services	1,587	8.7	1,186	5.9
Total	18,220	100	20,045	100

Chapter *XIX: Injury, poisoning and certain other consequences of external causes (S00-T98)* is presented at both main chapter level and at subchapter level.

APPENDICES A-D

Appendix A. Paper I: Nielsen VML, Kløjgård T, Bruun H, Søvsø MB, Christensen EF. Progression of vital signs during ambulance transport categorised by a paediatric triage model: a population-based historical cohort study. *BMJ Open* 2020;10:e042401.
doi:10.1136/bmjopen-2020-042401

Appendix B. Paper II: Nielsen VML, Søvsø MB, Kløjgård TA, Skals RG, Corfield AR, Bender L, Lossius HM, Mikkelsen S, Christensen EF. Prehospital vital sign monitoring in paediatric patients: an interregional study of educational interventions. *Scand J Trauma Resusc Emerg Med* 2023 Jan 14;31(1):4.
doi: 10.1186/s13049-023-01067-z

Appendix C. Paper III: Nielsen VML, Søvsø MB, Skals RG, Bender L, Corfield AR, Lossius HM, Mikkelsen S, Christensen EF. Mortality in Relation to Comorbidity Among Children Attended by Emergency Medical Services
(*manuscript submitted*)

Appendix D. Paper IV: Nielsen VML, Bruun NH, Søvsø MB, Kløjgård TA, Lossius HM, Bender L, Mikkelsen S, Tarpgaard M, Petersen JAK, Christensen EF. Pediatric Emergencies in Helicopter Emergency Medical Services: A National Population-Based Cohort Study From Denmark. *Ann Emerg Med* 2022 Aug;80(2):143-153.
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