Disparities in Emergency Care Among Patients with Mental Illness

Mackenhauer, Julie

DOI (link to publication from Publisher):
10.54337/aau499829720

Publication date:
2022

Document Version
Publisher's PDF, also known as Version of record

DISPARITIES IN EMERGENCY CARE AMONG PATIENTS WITH MENTAL ILLNESS

BY
JULIE MACKENHAUER

DISSERTATION SUBMITTED 2022

AALBORG UNIVERSITY
DENMARK

DISPARITIES IN EMERGENCY CARE AMONG PATIENTS WITH MENTAL ILLNESS

by

Julie Mackenhauer

AALBORG UNIVERSITY
DENMARK

Dissertation submitted June 2022

Dissertation submitted: 22nd June 2022

PhD supervisor: Prof. Søren Paaske Johnsen, MD PhD,
Aalborg University

Assistant PhD supervisors: Prof. Jan Mainz, MD PhD MPA,
Aalborg University

Prof. Erika Frischknecht Christensen, MD PhD,
Aalborg University

PhD committee: Clinical Associate Professor Jacob Bodilsen (chair)
Aalborg University, Denmark

Professor Merete Nordentoft
University of Copenhagen, Denmark

Professor Tim Coats
University of Leicester, UK

PhD Series: Faculty of Medicine, Aalborg University

Department: Department of Clinical Medicine

ISSN (online): 2246-1302
ISBN (online): 978-87-7573-878-6

Published by:
Aalborg University Press
Kroghstræde 3
DK – 9220 Aalborg Ø
Phone: +45 99407140
aauf@forlag.aau.dk
forlag.aau.dk

Printed in Denmark by Stibo Complete, 2022

CV

Julie Mackenhauer

I graduated as a Medical Doctor from Aarhus University in 2012. I then completed my foundation year and one year of specialty training in Anaesthesia and Intensive Care. I became part of the Danish Clinical Registries during the establishment of the Danish Database for Acute and Emergency Hospital Contacts. In 2015, I moved to London and worked for six months as a Junior Clinical Fellow in Emergency Medicine at King's College Hospital. Back in Denmark, I completed seven months of specialty training in Geriatrics. I was Vice President of the Danish Society of Emergency Medicine when the medical specialty Emergency Medicine was approved. Working as a clinical doctor and participating in the establishment of a new specialty and a national database of emergency care, I felt something essential was wrong in our healthcare system. Something about the structures, incentives and the distribution of power. I realised that being a doctor could be a job without a white coat – but a job trying to fix the system from the inside. I then completed one year of specialty training in Administrative Medicine working as part of the staff under the director in Psychiatry, North Denmark Region. I am now completing my specialty training and will be a medical specialist in Administrative and Social Medicine by Nov 2023. As a pre-graduate, I completed my research year, spending eight months in Emergency Medicine at the BIDMC, Harvard Medical School, Boston, in 2009. I was co-author of my first scientific paper about sepsis and lactate, based on this work.[1-2] Back in Denmark, I was part of the establishment of the Research Center for Emergency Medicine, Aarhus University, and published several papers with my colleagues.[3-12] After moving to Aalborg in 2016, I became part of the ambitious environment at the Danish Center for Clinical Health Services Research (DACS), where I conduced the studies included in this thesis, at the same time co-authoring other papers.[13-15]

---

1) DUGAS AF, **MACKENHAUER J,** SALCICCIOLI JD., ET AL. (2012). PREVALENCE AND CHARACTERISTICS OF NONLACTATE AND LACTATE EXPRESSORS IN SEPTIC SHOCK. JOURNAL OF CRITICAL CARE, 27(4), 344–350.
2) ANDERSEN, LW, **MACKENHAUER J.,** ROBERTS, JC, ET AL. (2013). ETIOLOGY AND THERAPEUTIC APPROACH TO ELEVATED LACTATE LEVELS. MAYO CLINIC PROCEEDINGS, 88(10), 1127–1140.
3) CHISHOLM GE, **MACKENHAUER J** (2014): "BETYDELIGE REGIONALE FORSKELLE I VISITATION OG INITIAL HÅNDTERING AF AKUTTE KARDIOLOGISKE PATIENTER" UGESKR LÆGER 176(8):757-760 [IN DANISH]
4) **MACKENHAUER J,** CHRISTIANSEN CF, ODBY A, ET AL. (2014): "UDVIKLING AF KVALITETSINDIKATORER FOR AKUTTE PATIENTFORLØB PÅ DANSKE SYGEHUSE". TIDSSKRIFT FOR DANSK SUNDHEDSVÆSEN [IN DANISH]
5) JESSEN MK, **MACKENHAUER J,** HVASS AMSW., ET AL. (2015): PREDICTORS OF INTENSIVE CARE UNIT TRANSFER OR DEATH IN EMERGENCY DEPARTMENT PATIENTS WITH SUSPECTED INFECTION. EUROPEAN JOURNAL OF EMERGENCY MEDICINE, 22 (3), PP. 176-18.0.
6) JESSEN, MK, **MACKENHAUER J,** HVASS AMW., ET AL. (2016): PREDICTION OF BACTEREMIA IN THE EMERGENCY DEPARTMENT: AN EXTERNAL VALIDATION OF A CLINICAL DECISION RULE. EUROPEAN JOURNAL OF EMERGENCY MEDICINE, 23 (1), PP. 44-49.
7) SCHNEGELSBERG A, **MACKENHAUER J**, NIBRO HL, ET AL. (2016) : IMPACT OF SOCIOECONOMIC STATUS ON MORTALITY AND UNPLANNED READMISSION IN SEPTIC INTENSIVE CARE UNIT PATIENTS. ACTA ANAESTHESIOLOGICA SCANDINAVICA, 60 (4), PP. 465-475.
8) KLASTRUP, V., HVASS, AM., **MACKENHAUER J.,** ET AL. (2016): SITE OF INFECTION AND MORTALITY IN PATIENTS WITH SEVERE SEPSIS OR SEPTIC SHOCK. INFECTIOUS DISEASES, 48 (10), PP. 726-731.
9) EISET AH, ERLANDSEN M., MØLLEKÆR AB., **MACKENHAUER J.,** & KIRKEGAARD, H. (2016). A GENERIC METHOD FOR EVALUATING CROWDING IN THE EMERGENCY DEPARTMENT. BMC EMERGENCY MEDICINE, 16(1), 21.
10) SKOV, M. J., DYNESEN, J., JESSEN, M. K., LIESANTH, J. Y., **MACKENHAUER, J**., & KIRKEGAARD, H. (2020). INCLUDING OXYGEN SUPPLEMENT IN THE EARLY WARNING SCORE. SCANDINAVIAN JOURNAL OF TRAUMA, RESUSCITATION AND EMERGENCY MEDICINE, 28(1), 26.
11) M. M., EISET, A. H., **MACKENHAUER, J**., ET AL. (2016). SELECTION OF QUALITY INDICATORS FOR HOSPITAL-BASED EMERGENCY CARE IN DENMARK. SCANDINAVIAN JOURNAL OF TRAUMA, RESUSCITATION AND EMERGENCY MEDICINE, 24, 11.
12) LASSEN, A. T., JØRGENSEN, H., JØRSBOE, H. B., ODBY, A., BRABRAND, M., STEINMETZ, J., **MACKENHAUER, J.,** ET AL.(2016): THE DANISH DATABASE FOR ACUTE AND EMERGENCY HOSPITAL CONTACTS. CLINICAL EPIDEMIOLOGY, 8, 469–474
13) UGGERBY, C., KRISTENSEN, S., **MACKENHAUER, J**., ET. AL. (2021). FROM ACCREDITATION TO QUALITY IMPROVEMENT-THE DANISH NATIONAL QUALITY PROGRAMME. INTERNATIONAL JOURNAL FOR QUALITY IN HEALTH CARE, 33(2), [MZAB071].
14) **MACKENHAUER, J.,** WINSLØV, J. H., HOLMSKOV, JET. AL. (2021). ANALYSIS OF SUICIDES REPORTED AS ADVERSE EVENTS IN PSYCHIATRY RESULTED IN NINE QUALITY IMPROVEMENT INITIATIVES. CRISIS.
15) FRYDENLUND J, **MACKENHAUER J,** CHRISTENSEN EF, ET. AL. (2022) SOCIOECONOMIC DISPARITIES IN PREHOSPITAL EMERGENCY CARE IN A DANISH TAX-FINANCED HEALTHCARE SYSTEM: NATIONWIDE COHORT STUDY. CLIN EPIDEMIOL. 2022 APR 27;14:555-565.

ACKNOWLEDGEMENTS

I would like to express my gratitude to Psychiatry in the North Denmark Region for providing financial guarantee and support throughout my PhD period. The following foundations have supported the PhD project financially, and I would like to sincerely thank:

- Puljen for Klinisk Psykiatrisk Forskning
- Aase og Ejnar Danielsens Fond
- Gangstedfonden
- Region Nordjyllands Sundhedsvidenskabelig Forskningsfond.

Being able to write this section of my thesis is a true honour. So many talented and generous people have inspired me and assisted me along the way. I am proud to have worked with you, discussed with you, learned from you and laughed with you.

I am grateful to my parents for supporting me throughout my life. Especially to you Jens Oluf, my spiritual father, who inspired me to become a doctor. You gave me the opportunity to travel abroad, using your network. Thank you mom for listening and comforting me, when the challenges felt overwhelming and for laughing with me when we got things back on track.

Thank you to Dr. Philip Anderson for inviting me to Boston and for introducing me to Dr. Michael Donnino – my first research supervisor. Working with the dedicated team at Beth Israel Deaconess Medical Center focusing on sepsis in the Emergency Department was a great honour and inspired me to work hard and share my knowledge generously. I am grateful to you, Dr. Niels Jessen. We met at Trader Joe's at Coolidge Corner, when you were buying groceries with your wife Eva. We celebrated 4th of July together in 2009, and you introduced me to all the right people back in Denmark. You made sure I got credit for my work in Boston to start my research career.

Thank you, Dr. Hans Kirkegaard, for supporting my work when I returned to Denmark. Thank you Dr. Else Tønnesen and Dr. Helle Nibro for encouraging me to continue to work with sepsis, and Pia Dreyer for introducing the aspects of socioeconomic disparities in emergency research. Thanks to all my colleagues at the Research Centre for Emergency Medicine and in the Sepsis Network for inspiration. A sincere apology for all the unpublished work and hours wasted entering data. I am glad you all have nice lives now. Not least, thank you to Dr. Marie Jessen for the adventures – personal, cultural and scientific.

Thank you, Dr. Erika Christensen. We met on several occasions discussing emergency research long before I moved to Aalborg. You are a clinician, a scientist and an

administrator. Your power and energy are contagious. Thank you for believing in Emergency Medicine and for becoming my supervisor.

At some point along my way, I realised that something was wrong in our healthcare system. Something about the structures, incentives and the distribution of power in our society and healthcare system. Working with sepsis could not resolve this issue. A special thanks to you, Dr. Jan Mainz, for introducing me to Administrative Medicine and quality improvement and for giving me the opportunity to work with you in Psychiatry. Working with you, the sky is the limit. Thank you for being my mentor, for becoming my supervisor and making everything happen.

At another point along the way, I realised I had been doing a lot of research without a deep understanding of research methodology, epidemiology and biostatistics. Getting the opportunity to work with you, Dr. Søren Paaske Johnsen, is such an honour. Thank you for being my main supervisor. You are building bridges between hardcore science, quality improvement and the clinical reality. I believe this is one of the corner stones in 'fixing' our healthcare system from the inside. Thank you for your patience and for always providing notable, thoughtful and constructive feedback.

Special thanks to my co-authors for their insightful comments and corrections to the papers. I am honoured by the cooperation with field experts – Dr. Grethe Andersen, Dr. Søren Mikkelsen, Chief Statistician Jan Brink Valentin, Dr. Helle Collatz Christensen, Ulla Væggesmose, Dr. Jacob Steinmetz and Dr. Peter Svenningsen. All of you have helped substantially to qualifying this thesis.

Thank you Malene Terp for love and inspiration and Jannie Bang Gram for picking out my research results and starting a movement. Thank to colleagues at DACS for study groups, corona-exercises and all the good advice. Thank to research administrators Mette Munk and Sanne Svendsen for always getting me out of administrative trouble. Thanks to colleagues at the hospital for working my shifts before the submission of this thesis. Thanks to Dr. Ole Mølgaard for noticing that I needed more than a cheer. Thanks to my friends for still being my friends and for coming to my wedding, even though I have not returned your calls or texts over the past weeks (months?).

My warmest thanks and gratitude go to my treasured big family for loving me and the children. A special thanks to you, boys, for accepting that stupid whiteboard and for accepting me. And thanks to Elvira and Lynge for your endless love and for reminding me on a daily basis what is most important in life.

Finally, my love, appreciation and tremendous thanks go to Peter for your support, patience, love and for always being my rock-solid foundation.

Julie Mackenhauer, Skørping 2022

ENGLISH SUMMARY

A mortality gap exists between people with or people without mental illness. Decreasing excess mortality among people with severe mental illness has become a national priority in Denmark and is one of the national goals in the Danish National Quality Programme.

Poor physical health is the main cause of the excess mortality among people with mental illness. Many aspects of society play a role in the overall health of the population. This includes where people are born; where they live, grow up and age; and where they get educated, work and play. However, while not being the main contributor to the overall health of a population, the healthcare system also has an impact on our health. While equity in care is a priority in most healthcare systems, it is well-described that factors such as race, ethnicity and socioeconomic status may influence the care we provide. Stigma and knowledge gaps related to patients with mental health conditions have been described by healthcare providers. Also, poor design of the healthcare system and political demands to reduce healthcare utilisation may cause a systematic failure in the healthcare system to prevent, identify and treat physical diseases among people with mental illness.

Particularly if there are barriers to healthcare access, people may seek care only when acutely ill or injured, if at all. Emergency care is an essential component of universal healthcare and, for some people, it is the primary point of access to the healthcare system. In emergency settings, disparities have been described among people with mental illness suffering from heart attacks or cardiac arrest. However, there is a paucity of detailed data from large population-based studies.

This thesis investigates the association between mental illness and disparities in emergency care. Using nationwide cohort designs, we investigated disparities in three different settings: Study I *'Emergency Medical Services response levels and subsequent emergency contacts among patients with a history of mental illness in Denmark: a nationwide study',* investigated the quality of prehospital care (Emergency Medical Services (EMS)). Study II *'Disparities in reperfusion therapy and time delays among patients with ischemic stroke and a history of mental illness'* and III *'Disparities in early stroke care and clinical outcomes among patients with ischemic stroke and a history of mental illness'* investigated the quality of acute stroke care. Study IV *'Disparities in emergency surgery and emergency care among patients with perforated peptic ulcers and a history of mental illness: A nationwide cohort study'* investigated the quality of emergency surgical care.

Patients were grouped as having major, moderate, minor or no history of mental illness, based on their mental health history.

Study I found that when patients called the EMS with any type of symptom or disease, those who had a history of mental illness were less likely to be transported to a hospital, compared to patients with no history of mental illness. They were also more likely to call the EMS again within 24 hours after receiving telephone advice, or if being released at the scene.

Study II showed that patients with any history of mental illness were less likely to receive reperfusion therapy when admitted with ischemic stroke. Patients with a history of major mental illness had long delays from onset of symptoms to EMS call and to hospital arrival and were less likely to be identified with stroke symptoms.

Study III found that the overall performance of acute stroke care was equally high in all groups of patients admitted with ischemic stroke to a specialised stroke unit. Patients with a history of mental illness had several patient characteristics associated with more severe strokes, higher mortality and a higher risk of death and recurrent stroke compared to patients without a history of mental illness.

Study IV found that patients with a history of major mental illness underwent surgery significantly later and had a higher risk of death, when admitted with a perforated peptic ulcer. Patients with a history of major or moderate mental illness had longer delays from onset of symptoms to hospital arrival, were less likely to be recognised with abdominal pain and less likely to be assigned the highest levels of urgency, if calling the EMS prior to arrival, compared to patients with no history of mental illness.

In conclusion, these studies contribute to shed light on the field of health disparities among people with a history of mental illness. Within the field of emergency care, disparities are identified, contributing to the excess mortality observed among people with mental illness. Monitoring disparities in the healthcare system is important in order to be able to evaluate local, regional and national initiatives targeting this vulnerable groups and keep a political focus on the demand to defeat excess mortality.

DANSK RESUME

Mennesker med psykiske sygdomme lever kortere tid end den øvrige befolkning. Dårligt fysisk helbred blandt psykisk syge er den væsentligste årsag til de mange tabte leveår. Bekæmpelse af overdødelighed blandt psykisk syge er blevet en del af det Nationale Kvalitetsprogram i det danske sundhedsvæsen. Dette forpligter alle sundhedsvæsenets aktører til at bidrage til at nedbringe overdødeligheden.

En befolknings fysiske og psykiske helbred afhænger af mange faktorer. Således påvirker genetik, den tidlige barndom, opvækst, levevilkår, omgivelser og miljø alle i væsentlig grad til det enkelte menneskes sundhed og helbred. Sundhedsvæsenet er også en vigtig aktør, men faktisk bidrager sundhedsvæsenet kun med en mindre andel i forhold til den samlede folkesundhed. Der er både internationalt og nationalt fokus på ulighed i sundhed. Det skyldes, at mange undersøgelser har vist, at mennesker enten behandles forskelligt eller oplever forskellige resultater af behandlingen, afhængigt af bl.a. etnicitet og social status. Stigmatisering og uopmærksomhed kan være en del af forklaringen på, hvorfor nogle udsatte grupper modtager behandling af dårlig kvalitet. Selve indretning af sundhedsvæsenet, tilgængeligheden af relevante ressourcer og modsatrettede politiske krav kan også betyde, at rammerne i sundhedsvæsenet ikke kan tilgodese de behov, som en udsat befolkningsgruppe kan have. Det kan betyde, at udsatte befolkningsgrupper, som eksempelvis mennesker med psykiske sygdomme, ikke systematisk tilbydes og modtager de nødvendige sundhedsydelser.

En række tidskritiske tilstande (fx hjertestop eller blodpropper i hjerte eller hjerne) kræver øjeblikkelig handling fra både patienten, pårørende og sundhedsvæsenet. Man taler om ”overlevelseskæden”, hvor kæden som bekendt ikke er stærkere end det svageste led. Det betyder, at ethvert led i kæden, fra symptomdebut, patientens reaktion på symptomer, kontakten til sundhedsvæsenet, sundhedsvæsenets respons, iværksættelse af behandling osv., er helt afgørende for at sikre patientens overlevelse uden mén. To større danske undersøgelser har vist, at mennesker med psykiske sygdomme, som får hjertestop, ikke modtager samme behandling som andre borgere. Internationale studier har vist samme resultater, bl.a. i forhold til behandling af mennesker med psykisk sygdom, som får en blodprop i hjertet. Den samlede litteratur er dog sparsom, og store befolkningsundersøgelser er blevet efterlyst for at komme tættere på en forståelse af årsager og mekanismer.

Denne afhandling undersøger sammenhængen mellem psykisk sygdom og kvaliteten af de akutte sundhedsydelser i Danmark. I et populationsbaseret studiedesign sammenlignede vi personer med og uden psykisk sygdom inden for følgende områder:

1) Blandt borgere, der ringer 1-1-2
2) Blandt patienter, der indlægges med blodprop i hjernen (stroke)
3) Blandt patienter, der opereres for mavesår (perforeret ulcus).

I alle fire studier fandt vi, at der var forskel enten på behandlingen eller på resultatet af behandlingen afhængigt af, om personen i forvejen var psykisk syg eller ej.

I studie I fandt vi, at personer med psykisk sygdom, som ringede 112, i højere grad blev afsluttet telefonisk eller på skadestedet, fremfor at blive bragt på hospitalet.

I studie II fandt vi, at personer med psykisk sygdom havde lavere sandsynlighed for at få reperfusionsbehandling, hvis de blev indlagt med stroke. Patienter med en svær grad af psykisk sygdom oplevede desuden lange forsinkelser fra symptomdebut, til de ringede 112, og fra symptomdebut til hospitalsankomst. De blev heller ikke identificeret med strokesymptomer i lige så høj grad som personer uden psykisk sygdom.

I studie III fandt vi, at der var en meget høj kvalitet i den akutte, specialiserede strokebehandling blandt alle grupperne. Patienter med psykisk sygdom havde dog nogle grundlæggende karakteristika, som var forbundet med højere dødelighed og mere alvorlige strokes, hvorfor de også havde en højere 30-dages dødelighed efter et stroke.

I studie IV fandt vi, at patienter med psykisk sygdom, som indlægges med perforeret ulcus, modtager antibiotika senere og opereres senere i forhold personer uden psykisk sygdom. Personer med moderat eller svær grad af psykisk sygdom oplevede forsinkelser fra symptomdebut til hospitalsindlæggelse og blev ikke identificeret med mavesmerter eller fik tildelt en ambulance med udrykning i lige så høj grad som personer uden psykisk sygdom.

Konklusionen på denne afhandling er, at der er ulighed i den akutte behandling blandt psykisk syge i Danmark. Vi finder dette i flere af de kritiske faser af overlevelseskæden – fra symptomdebut til akutbehandling, specialiseret behandling og rehabilitering. Dårligere kvalitet af den akutte behandling kan bidrage til overdødelighed blandt mennesker med psykisk sygdom. Det er nødvendigt med målrettede indsatser for at komme problemet til livs.

PAPERS IN THE THESIS

Study I

Mackenhauer, Julie; Valentin, Jan Brink; Mikkelsen, Søren; Steinmetz, Jacob; Væggemose, Ulla; Christensen, Helle Collatz; Mainz, Jan; Johnsen, Søren Paaske; Christensen, Erika Frischknecht: '**Emergency Medical Services response levels and subsequent emergency contacts among patients with a history of mental illness in Denmark: a nationwide study**', *European Journal of Emergency Medicine: October 2021 - Volume 28 - Issue 5 - p 363-372 doi: 10.1097/MEJ.0000000000000806*

Study II

Mackenhauer, Julie; Christensen, Erika Frischknecht; Andersen, Grethe; Mainz, Jan; Johnsen, Søren Paaske: **'Disparities in reperfusion therapy and time delays among patients with ischemic stroke and a history of mental illness'.** *Manuscript conditionally accepted. Stroke.*

Study III

Mackenhauer, Julie; Christensen, Erika Frischknecht; Andersen, Grethe; Mainz, Jan; Johnsen, Søren Paaske: **'Disparities in early stroke care and clinical outcomes among patients with ischemic stroke and a history of mental illness'.** *Manuscript submitted.*

Study IV

Mackenhauer, Julie; Christensen, Erika Frischknecht; Mainz, Jan; Valentin, Jan Brink; Foss, Nicolai Bang; Svenningsen, Peter Olesen; Johnsen, Søren Paaske: **'Disparities in emergency surgery and emergency care among patients with perforated peptic ulcers and a history of mental illness: A nationwide cohort study'.** *Manuscript under preparation.*

ABBREVIATIONS

ADHD – Attention deficit hyperactivity disorder

ASA - American Society of Anaesthesiologists Classification

ATC - Anatomical Therapeutic Chemical Classification

COPD – Chronic Obstructive Pulmonary Disease

COVID-19 - Coronavirus disease 2019

DAG – Directed Acyclic Graph

Danish Index – Danish Index for Emergency Care

DES – Danish registry of Emergency Surgery

DSR – Danish Stroke Registry

ED – Emergency Department

EMS – Emergency Medical Services

GP – General Practitioner

ICD-10 - International Statistical Classification of Diseases and Related Health Problems 10th Revision

IQR – Inter quartile Range

PREM – Patient experience measures

PROM – Patient Reported Outcome Measure

RKKP – Danish Clinical Registries

RR – Risk Ratio

TIA – Transient Ischemic Attack

WHO – World Health Organisation

TABLE OF CONTENTS

TABLES AND FIGURES

Tables

Figures

CHAPTER 1. INTRODUCTION

1.1. MENTAL HEALTH

1.1.1. THE MAGNITUDE OF MENTAL ILLNESS IN OUR SOCIETY

The prevalence of self-reported poor mental health in the Danish population has increased from 10% in 2010 to 17% in 2021.[1] In 2021, the highest prevalence of poor mental health was seen among people aged 16-24 years, including 34% of women and 21% of men in this age group.[1] It is estimated that globally, one in three individuals experiences mental illness during their lifetime[2] with varying prevalence of specific mental illness depending on the instrument used to measure.[3, 4] If excluding substance abuse disorder, the most common mental illnesses in females are depression, anxiety and eating disorders are, while ADHD (attention deficit hyperactivity disorder) and autism spectrum disorders are more common in males.[5]

Mental illnesses account for at least 20% of the global disease burden due to a combination of high prevalence, lifetime mental illnesses arising before adulthood, and a broad range of impacts across health, education, employment, social relationships, crime, violence and stigma.[6] The Global Burden of Diseases, Injuries, and Risk Factors Study from 2019 showed that among young adults aged 10-24 and adults aged 25-49, depression and anxiety are amongst the top 10 leading causes of disability.[7] Also, mental illnesses remained among the top ten leading causes of burden worldwide, with no evidence of global reduction of the burden since 1990.[7]

1.1.2. EXCESS MORTALITY AND PHYSICAL HEALTH

A significant mortality gap exists between people with and people without mental illness.[8] Poor physical health is the main cause of the excess mortality among people with mental illness.[8, 9] Despite international and national calls for action[10-14] – and the increasing knowledge of excess mortality and inequalities in the quality of care of physical illnesses[8, 15, 16] – it is uncertain how comprehensive our understanding of potential inequalities in mental healthcare is, or how the interplay between mental health and physical health works in detail.

Figure 1: Domains in the action plan from the World Psychiatric Association 2020-2023[6]

Both system- and patient-related factors may contribute to the poorer outcomes in patients with comorbid mental illness. Patient-related factors may include low socioeconomic status, poor social network, impaired bodily sensation, disturbed perception of pain, adverse lifestyle factors and physical comorbidities.[17-23] System-related factors result in the healthcare system systematically failing to prevent, identify and treat physical diseases.[12, 24, 25] Also, health professionals, including surgeons and emergency care professionals, still demonstrate stigmatising behaviours towards patients with severe mental illness[26-29] which may explain some of the described variation.

1.1.3. MENTAL HEALTH AS A POLITICAL PRIORITY

2022, the Danish Health Authorities published a proposal for a 10-year plan for mental health in Denmark.[30] Also, a White Paper from the Danish Society for Psychiatry was published in 2021 with a demand for political action to cure the psychiatric system.[10, 31] Improving mental health has been on the global agenda over the past years and in 2019, the World Psychiatric Association launched their action plan 2020-2023 (Figure 1). Their plan is in line with other global and national initiatives identifying access, prevention, inequality, stigma, excess mortality and lack of action as the major threats to this area.[11-14]

In Denmark, the area is being monitored as part of the Danish National Quality Program (Figure 2)[32] and in five dedicated clinical registries under the Danish Clinical Registries, including databases regarding the hospital-based care for patients with schizophrenia,[33] depression,[34] children and young adults with ADHD, forensic psychiatry and dementia.

1. **Excess mortality:** Patients with schizophrenia compared to the background population.
2. **Hospital readmissions** within 30 days for patients admitted to a psychiatric hospital.
3. **Labour market attachment** for patients aged 25-64 six months after the time of first psychiatric diagnosis.
4. **Completing an education** by the age of 25 among patients with a hospital-based contact in psychiatry between ages 15-25.
5. **Belt restraint –** proportion admitted to a psychiatric ward where belt restraints are used.
6. **Waiting time** for outpatient psychiatric assessment.
7. **Patient satisfaction** with mental healthcare.
8. **Patient involvement in own care –** self-perceived involvement.
9. **Fulfilment of quality indicators** in the Danish Clinical Registries.

Figure 2: Examples of national measures of the quality of care for patients with mental health illness from the Danish National Quality Programme regarding Mental Health

1.2. EMERGENCY CARE

Emergency care is defined by the World Bank as the delivery of *'health services for conditions that require rapid intervention to avert death and disability, or for which delays of hours can worsen prognosis or render care less effective*'.[35]

The World Health Organization (WHO) describes emergency care as *'an effective strategy to reduce the global burden of disease'* and argues that *'Emergency care cross cuts traditional disease-focused disciplines to manage a wide range of the acute illnesses and injuries that contribute substantially to death and disability'.*[36]

Another way to define the area is to consider the definition of the medical specialty Emergency Medicine in Europe.[37] However, while most countries consider Emergency Medicine primarily as a hospital-based medical specialty, many aspects of emergency care are closely linked to other urgent healthcare systems outside the hospital, e.g., prehospital services, general practitioners and other community-based services.

While there is no consensus on which diseases to define as 'emergency diseases',[38] the focus is often diseases requiring medical intervention within minutes to hours from symptom onset. Often, the area has been organised around the most severe diseases and injuries such as trauma, cardiac arrests, myocardial infarction, stroke or major disasters. The 'Chain of Survival' has been used to describe the series of actions that are required to reduce morbidity and mortality of a time-dependent disease. The symbol of the chain is used to stress the importance of each individual chain, since a chain is only as strong as its weakest link. The first description of the Chain of Survival from 1991 focused on four elements: Early access, early cardio-pulmonary resuscitation, early defibrillation and early advanced care in cardiac arrest.[39] Since then, the importance of prevention, early rehabilitation and recovery has been added to the Chain of Survival,[40] and the chain analogy has been adopted by other time-dependent diseases, e.g., severe sepsis and stroke.[41, 42] All chains include a variation of the same steps: Early recognition of symptoms, activation of a fast emergency response, early treatment, early advanced care, rehabilitation and recovery (Figure 3).

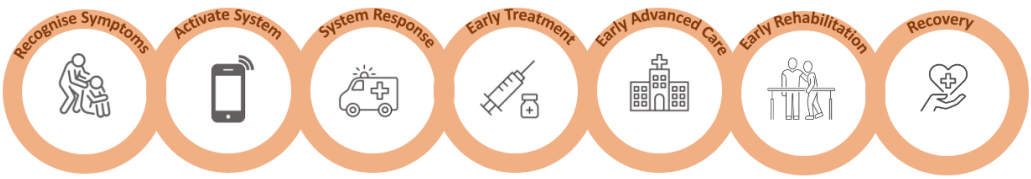

Figure 3: The Chain of Survival (adapted from several authors[39-41]): The series of actions required to reduce morbidity and mortality from a time-dependent disease such as cardiac arrest, myocardial infarction, stroke or severe sepsis.

Only a minority of emergency department (ED) patients require immediate treatment and advanced care. Thus, in 2018, only 12% of all ED patients in the US were admitted to the hospital after ED evaluation.[43] In 2020, in Denmark, the median length of stay at the hospital was four hours (IQR, 1;23) among patients with any unplanned (emergency) hospital contact including both injuries and diseases.[44] This finding is supported by other authors,[45] meaning than less than 25% of patients with an unplanned hospital contact will need a hospital stay lasting more than 24 hours. This indicates that most patients will have critical diseases ruled out or will be diagnosed with less urgent diseases not requiring hospital admission, advanced care or critical care. Also, some patients are thought not to need emergency care at all.[46-49] Nevertheless, improving the organisation of emergency care with respect to the time-dependent diseases is thought to benefit the entire group patients perceiving the need for emergency care services.[38] Some countries have organised hospitals and EDs around a specific time frame of, e.g., four or six hours from hospital arrival, to ensure an effective flow and support the need for sufficient resources around the clock.[50, 51] However, it is widely acknowledged that urgent and emergency care may also be defined as the initial 24-72 hours of hospital admission.[52, 53]

1.2.1. BURDEN OF EMERGENCY DISEASES

Robust emergency care systems are critical to addressing public health challenges and priorities. Globally, the mechanisms causing death and lost life years due to emergency diseases differ significantly.[38] In high-income countries, emergency diseases account for 40% of all deaths and 25% of lost life years.[38] In the European region, injuries, ischemic heart disease, lower respiratory infections and ischemic strokes made up 85% of lost life years due to emergency diseases in 2015.[38]

If comparing the 21 diseases (chronic or emergency diseases) associated with the highest healthcare costs in Denmark, ischemic heart disease and stroke are two the emergency diseases associated with the highest number of lost life years, causing 13,600 (ischemic heart diseases) and 8,500 (strokes) lost life years in a population of 5.9 million people.[54] While substance abuse, anxiety and schizophrenia are the diseases associated the highest number of ED visits, lower respiratory infections and ischemic heart disease account for the highest number of hospital admissions. However, the total cost, including all care expenses, remain the highest for patients with schizophrenia, arthrosis and stroke.[54]

1.2.2. EMERGENCY CARE AS A POLITICAL PRIORITY

Across the World, there is an increasing focus on emergency care.[36] While COVID-19, natural disasters and war have increased the public attention on the key societal role of the healthcare system, there has also been an increasing demand for emergency healthcare services over the past decade due to ageing populations and increasing prevalence of multi-morbidity.[55, 56]

In 2020, the Danish Health Authorities published an extensive update of their recommendations for the emergency care system in Denmark.[57] The recommendations embrace the entire urgent care system and aim to integrate and strengthen the collaboration between primary healthcare services, prehospital services, psychiatric hospitals and non-psychiatric hospitals. The goal is to ensure a high quality of emergency care for all patients contacting emergency care services and reduce the variation due to sociodemographic factors.

Since the Danish Health Authorities published their first recommendations for the emergency care system in Denmark in 2007,[58] the hospital-based emergency care system has been restructured.[59, 60] The emergency services reform was created due to an observed geographical variation of the organisation of emergency services in 2005.[61, 62] A corner stone in the recommendations was reducing the number of emergency hospitals receiving emergency patients around the clock from more than 44 to 21.[45, 59, 60] Also, in the same period, the increasing evidence regarding the association between higher patient volumes and better outcome of emergency care in, e.g., trauma,[63, 64] myocardial infarction[65, 66] and stroke[67-69], created a need to reorganise and centralise the treatment of selected time-dependent diseases in even fewer specialised centres. This resulted in the selection of four Danish trauma centres, four centres offering acute coronary interventions and six (later ten) stroke centres. However, the relationship between the highest patient volume and better patient outcome is not found in all emergency disease, e.g., patients with severe sepsis[70] or hip fracture.[71]

1.3. QUALITY OF HEALTHCARE

Quality of care is highly prioritised in most healthcare systems.[14, 72] It is well-described how not all patients receive evidence-based care (underuse), while others receive unnecessary care (overuse).[14, 73, 74] While reaching consensus on the 'right care' can be challenging, it is acknowledged that unwanted variation regarding both underuse and overuse is a major challenge from a public health perspective.[72, 75]

To evaluate quality improvement initiatives, information on the current quality of care is needed. Methods for measurement of quality of care have therefore been developed over the past decades.[72]

1.3.1. MODELS FOR QUALITY

The most widely used approach to assess quality of healthcare has been Donabedian's model for quality.[76, 77] The Donabedian model characterises quality of healthcare according to structure, process and outcome. Since Donabedian developed the model, clinicians, researchers and policy makers have added domains and details to the model (Figure 4). Based on each domain, quality indicators can be defined. Please see examples within each domain in the following sections.

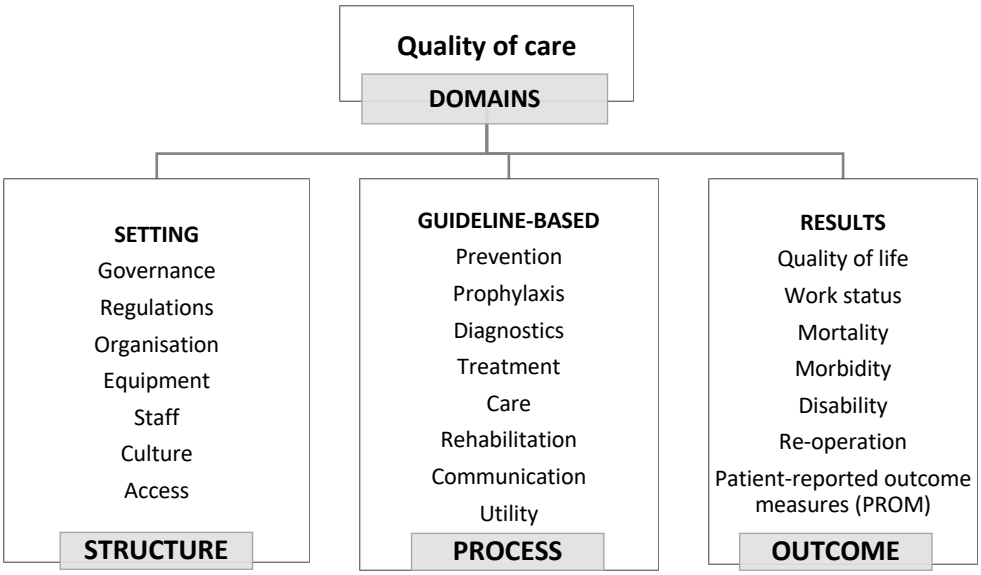

Figure 4: Modified Donabedian model assessing quality of healthcare according to structure, process and outcome.[76]

Care *structure* is defined as the infrastructure of the healthcare services. Structural measures assess the characteristics of a care setting, e.g., facilities, equipment, capacity and access, but also of the society, e.g., governance, regulation and organisation of the healthcare system. An example of a structural indicator is the national recommendation regarding the minimum number of patients (volume) per centre treating patients with ischemic stroke using thrombolysis, i.e., each centre should see 2,000 patients with ischemic stroke each year to qualify as a specialised stroke centre.[78]

Care *processes* are the delivered care and the accordance of this care in relation to clinical guidelines. Processes can also be measured as utility of services (e.g., number of ED visits or EMS calls). An example of a process indicator is the proportion of patients receiving reperfusion therapy if admitted with ischemic stroke. For one disease, several process measures can be relevant, e.g., in acute stroke care there are clinical recommendations for completing swallowing tests, mobilising patients and assessment by physiotherapist and occupational therapist. Process measures (as well as outcome measures) can be combined into a composite score, to assess the overall quality of care delivered for selected patient group.[79]

Outcome is the impact of care on the patient's health status. An example of an outcome measure is 30-day mortality in ischemic stroke or re-operation in patients with perforated peptic ulcers. Outcome can also be measured as disability,

readmission, quality of life or return to work. Over the past 5-10 years, Patient-reported outcome measures (PROM) have been developed. PROM provide standardized assessments for collecting data directly from patients about their health or experience with a health condition and is being used in both primary and secondary health care setting, across a variety of diseases.[80]

The three dimensions of quality supplement each other and will in theory interact so that a care structure affects the patient outcome through care processes. Variation in care processes may be explained by lack of structure to ensure compliance with the processes which, in turn, will affect patient outcome.

1.3.2. QUALITY OF EMERGENCY CARE

Defining measures of quality in the emergency care area has been evolving over the past 10 years.[81-88] Some generic outcome measures, such as 7- or 30-day mortality and 72-hour return/readmission rates, and generic process measures such as ambulance response time and waiting times in the ED have been widely used. Structural measures in emergency care are often defined as ED bed capacity, availability of MR/CT scanners, availability of operating theatres or availability of staff with specific competencies.[19, 88]

Disease-specific measures such as time-to-treatment of emergency diseases (e.g., myocardial infarction, trauma or stroke) are also commonly used process measures. Since the time-dependent diseases are dependent on all factors from the Chain of Survival, it may be useful to monitor each step in the chain and focus on the steps with the largest variation, e.g., time from symptom onset to EMS call in order to understand patient delays, or time from hospital arrival to treatment in order to understand the hospital-dependent factors.

Another example of a disease-specific process measure is the proportion of patients receiving reperfusion therapy. This is a complex measure since it is dependent on patients arriving within 4.5 hours from onset of symptoms (the treatment window in ischemic stroke, please see below). Hence, recognition of symptoms, the role of a bystander/the society, contacting the healthcare system and system response are crucial for the patient to be considered for this type of treatment.

An example of a measure dependent on both structure and process is the proportion of patients admitted to a specialised stroke unit on the day of admission which is dependent on prehospital dispositions, identification of the right stroke patients and bed availability in the stroke units.[89, 90]

In recent years, PROMs assessing the quality of care from the patient perspective rather than a system perspective, have been developed.[91-93] Symptom relief, mobility and return to social activities have been used as PROM in emergency care, while

measures related to the process of care, i.e., communication, understanding, reassurance and having a plan, have also been selected as good emergency care measures by the patients (named PREM (Patient experience measures)),[91-93] Further, more complex measures related to equity and quality of healthcare services delivered to patients with complex needs or patients' frequent use of ambulances or frequent emergency department visits are being implemented.[87, 92, 94-96]

1.3.3. MONITORING QUALITY OF EMERGENCY CARE IN DENMARK

In 2017, the Danish Regions launched three new clinical databases under the Danish Clinical Registries: A Prehospital Database, a Trauma Database and a Danish Database for Acute and Emergency Hospital Contacts.[97, 98] Prior to this, starting in 2003, the only opportunity to monitor the quality of emergency care on a national level in Denmark was through selected measures from the Danish Stroke Registry, the Danish Register of Emergency Surgery and the Danish Multidisciplinary Hip Fracture Registry under the Danish Clinical Registries.[99-101] Also, the prehospital organisations in Denmark have been monitoring patients with out-of-hospital cardiac arrest since 2001,[102] while the semi-national Western Denmark Heart Registry and the semi-national DANARREST have been collecting data on invasive cardiac procedures since 1999 and in-hospital cardiac arrest since 2013, respectively.[103, 104] Starting in 2017, the Heart Registry and DANARREST are now including nationwide data and have been part of the Danish Clinical Registries.[104, 105]

In 2020, the Danish Register of Emergency Surgery implemented a wider approach to abdominal emergencies, no longer restricting their population to peptic ulcers, but adopting quality measures from the British NELA programme.[106, 107] Currently, both the Prehospital Database and the Danish Database for Acute and Emergency Hospital Contacts are under revision. The Prehospital Database is moving towards more patient-oriented measures such as pain management, timely prehospital treatment and collaboration between emergency care services for patients with time-dependent diseases (e.g., stroke, myocardial infarction or trauma), rather than focusing on generic timestamps and response times.[108] The Danish Database for Acute and Emergency Hospital Contacts is implementing more time-to-treatment measures, including both ischemic stroke, hip fractures, myocardial infarction, emergency surgery and severe sepsis, along with measures of pain management and time-to-doctor for all emergency department patients *(unpublished)*. Also, this database is implementing subgroup analyses of selected frail or disadvantaged groups *(unpublished)*.

Quality of emergency care is also being monitored under the Danish National Quality Programme.[32] Selected measures include fulfilment of quality measures from the Danish Clinical Registries, survival after sudden cardiac arrest, overall cardiovascular mortality, patient satisfaction, acute hospital admission for diabetes or chronic obstructive pulmonary disease (COPD), preventable admissions among elderly and

hospital length of stay per admission. National quality improvement collaboratives have been established under the Danish National Quality Programme aiming to improve quality of care for selected patient groups. Among others, collaborations have been established focusing on patients with hip fractures, ischemic strokes and patients undergoing emergency surgery.

In Table 1, selected measures of emergency care demonstrate the development over the past 10 years. While mortality after myocardial infarction has been reduced, and the proportion of patients receiving reperfusion therapy has increased, the healthcare system is still struggling to reduce time-to-surgery for patients with perforated peptic ulcer.

Table 1: Examples of indicators monitoring quality of emergency care in Denmark over time using the available, national/semi-national registries available to the public. Annual reports from the previous years can be requested without permissions from registries.

Data source	**Name of registry**	**Indicator**	**2010-2012**	**2013-2015**	**2018-2020**
Heart Registry/ RKKP[105, 109, 110]	Hearth registry	30-day mortality after primary percutaneous coronary intervention (PCI) N*ational average, 95% confidence interval (CI) (Range between the included regions)*	7.9%* N/A Range (6.2-10.9)	7.1%* CI (5.8;8.6) Range (8.4-10.2)	5.0% CI (4.2;6.0) Range (3.9-7.3)
RKKP[111]	Danish Stroke Registry	Proportion of patients with ischemic stroke receiving reperfusion therapy N*ational average (Range between 98 municipalities)*	13%**	15%** Range (4-39)	24% Range (12-37)
RKKP[107]	Danish Register for Emergency Surgery	Time-to-surgery for patients with perforated peptic ulcer P*roportion operated within three hours, 95% confidence interval (CI) (Range between the five regions)*	27% CI (23;32) Range (18-53)	32% CI (28;38) Range (17-41)	32% CI (26;38) Range (13-54)

**semi-national **only thrombolysis*

1.4. PUBLIC HEALTH, SOCIAL POSITION AND EQUITY IN CARE

Several factors influence the overall health of a population. Most importantly, it depends on a complex interplay of individual factors, including genetics, early childhood, economic, social and psychological conditions in the family, health behaviour, environment and living conditions.[112, 113] A mediating factor between illness and health outcome is the quality of healthcare services delivered to each individual. The literature indicates that the healthcare system contributes with approximately 20% of the health outcome in a population, while societal and environmental factors contribute with 80%.[114]

Social inequality in health comprises a scenario where health status is systematically unequally distributed amongst groups with different social positions.[14] Obviously, the healthcare system cannot change a person's social position. However, the healthcare system has the potential to even out or balance some of the inequalities determined by social position by addressing them directly. Unfortunately, the social position in itself can be associated with differences in the quality of care delivered within the healthcare system.[115, 116] As other social determinants of health, mental health conditions are distributed in such a way that increased rates of mental health conditions are associated with more disadvantaged social positions.[117, 118]

With respect to the overall health of the population, politics, public health priorities, financial incentives and organisation all have a major impact on the structures, processes and/or outcome in the emergency and urgent healthcare system.[119-124] Also, when trying to understand variation in emergency care, factors such as deprivation, race/ethnicity and social position are often thought to explain a major part.[18-23, 116, 125-131] Even in countries with free access to healthcare, socioeconomic disparities in e.g., stroke care persists, and disadvantaged groups experience may experience an underuse of advanced technologies and a worse outcome, compared to more advantaged groups.[21, 22, 116, 126, 129, 131-133]

For patients with mental health, stigma may be a particular problem.[26, 27, 134]. Likewise, diagnostic overshadowing, i.e., '*assuming that a symptom is due to co-existing mental health conditions rather than exploring the cause of the patient's symptoms'* is being reported for this patient groups.[29, 134-139]

In summary, the Chain of Survival can be seen as dependent on a complex interplay between mental health, social position, the society, the healthcare system and the emergency care system. Figure 5 summaries the evidence from Chapter 1 in this thesis.

Figure 5: An overview of the potential negative societal factors and individual factors on the Chain of Survival, based on the evidence presented in sections 1.1, 1.2 and 1.4 (e.g., mental health, social position, race, ethnicity)

1.5. RATIONALE FOR THIS THESIS

For the purpose of this thesis, specific areas of emergency care were selected: Prehospital care, acute stroke care for patients with ischemic stroke and emergency surgical care for patients with perforated peptic ulcer.

When investigating the association between mental illness and quality of emergency care, the contribution of physical diseases to the excess mortality among patients with mental illness is an essential motivation. The evidence around excess mortality primarily concerns chronic, medical disease or does not differentiate between the contributions from emergency or chronic conditions. However, managing emergency diseases and chronic diseases require something very different from both a system level and a patient level, and should be investigated separately.

Poorer outcome among patients with stroke or perforated peptic ulcer and co-morbid mental illness has been described (please see below). However, information on each step in the Chain of Survival, explaining this variation, is sparse. Considering the available evidence of, e.g., less assistance from bystanders, lower hospitalisation rates and fewer invasive cardiac procedures among patients with cardiac arrest, myocardial infarction and comorbid mental illness,[140-142] each step in the Chain of Survival should be investigated. Without this knowledge, interventions targeting these steps cannot be designed. Emergency care is a complex area in healthcare, and interventions must be tailored to this setting.

The following section will summarise the evidence and identify knowledge gaps within the literature related to mental health and quality of *prehospital care, acute stroke care* and *emergency surgery*.

1.5.1. PREHOSPITAL CARE

Prehospital care: Definition

Prehospital care is the care that a patient receives from an emergency medical service (EMS) before arriving at the hospital. EMS form an integral part of a public health care system: their primary function is to deliver emergency medical care in all emergencies, including disasters.[143] The services often include an emergency number (e.g., 112 or 911) received at an Emergency Medical Coordination Centre. From here, relevant resources (ambulances, helicopters etc.) are dispatched according to the level of urgency. Several other systems cooperate with the EMS and can activate or can be activated by the EMS, e.g., general practitioners (GP), out-of-hour GPs, volunteer layperson first aiders, national defence, e.g., the Joint Rescue Coordination Centre Denmark.[143, 144] From a policy perspective, EMS are one of the higher profile aspects of the health system as they are the first point of contact with the health system for many people.[145] EMS also serve as a sentinel for weaknesses in the wider health

system, such as financial or organisational barriers to accessing primary care or shortcomings in the provision of care for people with long-term conditions.[145]

An increasing number of patients seeking emergency care has created a political demand to reduce the numbers of ambulance dispatches and hospital admissions by reducing 'preventable' or 'avoidable' contacts.[127, 145-148] The use of emergency services for non-emergent situations may be addressed by health campaigns intended to change behaviours of the population or by offering alternative pathways to these groups. However, even high-cost interventions (campaigns, case-based management) often fail to maintain behavioural changes in the vulnerable groups who will reach out to the healthcare system through the emergency system.[149-151] Utility measures are also part of the Danish Quality Improvement Programme,[32] e.g., 'avoidable hospital contacts among elderly' and 'acute hospital admission for diabetes or COPD'.

Mental illness and prehospital care

People with a mental illness use emergency services more than the general population,[54, 152-154], and a large proportion of EMS-calls concerns mental health-related issues.[55, 155] Presentation to the EMS with a mental health-related complaint is associated with non-conveyance[156-158] (i.e., not being transported to hospital). While non-conveyance has also been related to unclear symptoms (i.e., non-specific complaints), information on the EMS response and presenting complaints for patients with a history of mental illness calling the EMS regarding non-mental health-related issues have not been described. In out-of-hospital cardiac arrest, patients with comorbid mental illness receive poorer care in the entire Chain of Survival from bystander care to advanced inpatient care.[159] Detailed information on patient characteristics, reason for the EMS call and EMS dispositions may contribute to our understanding of the variation in utility of EMS services and describe any weak links in the Chain of Survival. It may also provide important information to tailor future interventions aiming to improve the overall quality of EMS services as well as the outcome for patients with time-dependent diseases who are calling the EMS.

1.5.2. ISCHEMIC STROKE

Ischemic stroke: Definition

The WHO definition of stroke is *'A disease of the blood vessels supplying the brain', 'an acute event mainly caused by a blockage that prevents blood from flowing to the brain', 'a disease of the blood vessels supplying the brain'* and *'the most common reason for this is a build-up of fatty deposits on the inner walls of the blood vessels that supply the heart or brain. Strokes can be also caused by bleeding from a blood vessel in the brain or from blood clots'.*[160] (Figure 6).

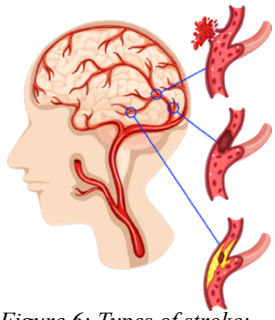

Figure 6: Types of stroke: Haemorrhagic or ischemic, affecting the vessels of the brain and the brain tissue.

Stroke is one the leading causes of death and disability among adults, both globally and in Denmark, and is associated with one the of highest health-related expenses per disease.[7, 54] In a high-income countries, 65% of all strokes are due the ischemia.[161] Stroke mortality has decreased significantly over the past 20 year.[20] In Denmark, 30-day mortality following ischemic stroke and intracerebral haemorrhage were 6% and 27%, respectively, in 2020.[111] Preventing stroke (both ischemic and haemorrhagic) by improving the health has the highest potential to reduce stroke mortality, e.g., decreasing cardiovascular risk factors such as smoking, high blood pressure, poor diet and obesity.[160-162] However, due to the large burden of risk factors in the society – and the poor chances eliminate these - early identification and treatment is essential for patients with stroke. Timing is crucial and in stroke care, the Chain of Survival is dependent not on hours, but rather minutes from onset of symptom to EMS contact and hospital admission.[163, 164] Patients with ischemic stroke can be treated with reperfusion therapy, either thrombolysis or thrombectomy. While thrombolysis is primarily offered to patients arriving within 4.5 hours from onset of symptoms, thrombectomy can be used for selected patients arriving up to 24 hours from onset of symptoms.[163]

Mental illness and ischemic stroke

People with mental illness have an increased lifetime risk of stroke compared to the general population.[165] Previous studies have focused on the prognosis for patients with stroke and comorbid mental illness, finding an association to longer hospital stays, higher risk of death and higher risk of readmission compared with people without mental illness.[166-170] The few existing studies focusing on initial management and protocol adherence found patients with comorbid mental illness to be less likely to receive cerebrovascular arteriography, carotid endarterectomy and thrombolysis compared to patients with no mental illness.[171, 172] Detailed information about the potential barriers, including time delays, was not available in these studies, and further studies have been called for. Investigating each step in the Chain of Survival may strengthen our possibilities to improve both quality of acute stroke care and patient outcomes.

1.5.3. PEPTIC ULCER PERFORATION

Peptic ulcer perforation: Definition

The World Society of Emergency Surgery defines peptic ulcer as *'ulceration due to acid peptic damage to the gastro-duodenal mucosa, resulting in mucosal erosion that exposes the underlying tissues to the digestive action of gastro-duodenal secretions*.'[173] (Figure 7)

Figure 7: Peptic ulcers disease affecting the stomach and duodenum, with symptoms from the abdomen and upper gastrointestinal system.

The disease has traditionally been related to gastric acids, dietary factors and stress. However, the increasing incidence of the Helicobacter pylori

infection and an increasing use of NSAIDs, alcohol and smoking have changed the epidemiology of this disease. Complications of peptic ulcer disease include perforation and bleeding. Recent evidence suggests that haemorrhage is the most common complication.[173] However, perforation is the most common indication for emergency surgery and causes about 40% of all ulcer-related deaths.[173] Having a perforated peptic ulcer is associated with a high mortality as 20-40% of patients are expected to die within 30 days.[173] For patients with perforated peptic ulcers, the timing of surgery is crucial – for each hour of delay, the risk of complications and death increases significantly.[174]

Mental illness and perforated peptic ulcer

People with severe mental illness have an increased risk of developing peptic ulcers.[175] Patients with comorbid mental illness experience an underuse of major abdominal surgery compared to patients without comorbid mental illness.[176] Further, the diagnosis of an abdominal emergency in a patient with comorbid mental illness may be missed by the health professionals due to diagnostic overshadowing and stigma.[26, 27, 29, 134, 135] Previous studies have focused on prognosis after surgery, finding greater post-operative morbidity, longer hospitals stays and higher risk of readmissions compared to patients without comorbid mental illness.[137, 139, 177-179] One study discussed the impact of mental illness and late hospital arrival and the risk of disease urgency and complications.[139] To improve the quality of care, it is important to investigate each chain in the Chain of Survival. Further, investigating patients with different severities of mental illness may be important to describe variation across subgroups.

CHAPTER 2. AIMS OF THE THESIS

2.1. OVERALL OBJECTIVE

The overall objective of this thesis was

1) to investigate if a history of mental illness is associated with the quality of emergency care. The hypothesis was that patients with a history of mental illness had a lower chance of receiving high quality emergency care compared to patients with no history of mental illness when presenting with time-dependent diseases in a healthcare system with universal healthcare.
2) to explore unwanted variations in the quality of emergency care delivered to patients with a history of mental illness.
3) to contribute with new knowledge regarding patients' characteristics, information on the different links in the Chain of Survival from onset of symptoms to advanced hospital-based care.

2.1.1. AIM STUDY I

The aim of this study was to compare the level of Emergency Medical Services (EMS) response and subsequent contacts to prehospital and in-hospital emergency services between patients with and without a history of mental illness.

2.1.2. AIMS STUDY II-III

The aim of these studies was to compare treatment delays, the use of reperfusion therapy, the quality of acute stroke care and clinical outcomes in patients with ischemic stroke with and without a history of mental illness.

2.1.3. AIM STUDY IV

The aim of this study was to compare treatment delays, quality of emergency care and clinical outcomes in patients with perforated peptic ulcers with and without a history of mental illness.

CHAPTER 3. METHODS

This chapter describes the methods of the four studies that this thesis was based on. To reduce repetition of the information in the articles, some details have been left out of the thesis. Thus, details not presented here may be found in the specific papers. Table 2 gives an overview of the study methods.

3.1. STUDY POPULATION AND DESIGN

The four studies were all designed as nationwide cohort studies based on the Danish clinical registries and national databases. The study populations were identified through three clinical registries (described under data sources):[180]

- The Danish Quality Database for Prehospital Emergency Medical Services (Prehospital Database):[98] All EMS calls from 2016-2017 were included.
- The Danish Stroke Registry (DSR):[99] Patients registered with an acute ischemic stroke were included. Study II included patients from 2016-2017, while Study III included patients from 2007-2018.
- The Danish Register of Emergency Surgery (DES):[100] Only patients with a diagnosis of perforated peptic ulcer in combination with a surgical procedural code from 2004-2018 who had the initial surgery performed within 48 hours from hospital arrival were included.

In all four studies, patients were excluded if they were registered as dead more than one day prior to hospital admission or EMS call, if the patient had immigrated to Denmark less than 10 years prior to admission or EMS call, or if the patient was not registered as living in Denmark at the time of admission or EMS call. Patients with more than one admission or EMS call during the study period were not excluded. If several EMS calls were made regarding the same person on the same date, events were merged into a single event using an identifier when possible.

In Study II and IV, we connected admissions with ischemic stroke or perforated peptic ulcer to EMS calls. Patients calling 72 hours prior to hospital arrival were defined as ‘EMS patients’, while patients with no EMS call registered within 72 hours were defined as ‘non-EMS patients’. The cut-off was selected due to our finding in Study I that patients with a history of mental illness were more likely to receive telephone advice only and call again within 24 hours[181] (as presented below).

Table 2: Overview over the definition of the study population, exposure, outcome and analysis in Study I-IV

	Study 1	**Study II**	**Study III**	**Study IV**
Population	Patients calling the EMS identified in the Danish Prehospital Database **2016-2017**	Patients admitted with ischemic stroke identified in the Danish Stroke Registry **2016-2017**	Patients admitted with ischemic stroke identified in the Danish Stroke Registry **2007-2018**	Patients admitted with perforated peptic ulcer identified in the Danish Register of Emergency Surgery **2004-2018** who had surgery performed within 48 hours from hospital arrival.
Exposure Major mental illness Moderate mental illness Minor mental illness or vulnerability No mental illness	- In- or outpatient hospital contacts with schizophrenia or bipolar *(ever).* - Inpatient hospital contact (>2days) with depression or personality disorder *(within the last 10 years).* - Other in- or outpatient psychiatric hospital contacts (other diagnosis than 'major') *(past 5 years).* - Consultations at a practicing psychiatrist *(within the last 5 years).* - None of the above. Reimbursement of at least two prescriptions of selected drugs (antidepressants or benzodiazepines) or two or more sessions of talk therapy or psychometric testing in a primary care setting or referral to a practicing psychologist *(within the past 12 months).* - None of the above *Please see details about definitions and data sources in Supplementary table S1*			
Outcomes	Process measures from the *Danish Prehospital Database:* <u>Process measures</u> - Time-to-arrival of first EMS unit. - Level of urgency registered	Reperfusion therapy, prehospital delay and in-hospital delays from the *Danish Stroke Registry* and the *Danish Prehospital Database:* <u>Reperfusion therapy</u> - Thrombolysis or	Guideline-recommended care using process measures and outcome measures from the *Danish Stroke Registry:* <u>On first day of admission</u> - CT/MR scan of the head. - Mobilisation. - Swallowing test. <u>Within 2nd day of</u>	Process measures and outcome measures from the *Prehospital Database* and *Danish Register of Emergency Surgery:* <u>Process measures</u> - % assigned highest levels of urgency (EMS) - % identified with abdominal pain

	according to Danish Index - Patients calling EMS again within 24 hours if given telephone advice only or released at scene. - Patients with an unplanned hospital contact within 7 days if given telephone advice only or released at scene.	thrombectomy. Total delay - Time from symptom onset to hospital arrival. Patient delay - Time from symptom onset to EMS call. EMS delay - Time from EMS call to hospital arrival. Door-to-imaging - Time from hospital arrival to CT/MR-scan. Door-to-needle - Time from hospital arrival to thrombolysis.	admission: - Assessed by physiotherapist and an occupational therapist. - Nutritional risk assessment. - Admission to a stroke unit. - Treatment with platelet-inhibitor therapy. Within 2 weeks - Treatment with oral anti-coagulation therapy. Composite outcomes - % of received process measures (opportunity-based). - % of patients receiving all measures (all-or-none). Outcome measures - Recurrent stroke (1 year). - 30-day mortality.	when calling the EMS - Time-to-antibiotics. - Time-to-surgery. - Preoperative care. Outcome measures - 30-day mortality. - Days-alive-and-out-of-hospital.
Method of analysis	Regression analysis: *Time differences and combined measure (opportunity-based composite outcomes, defined in section 3.5.3)* - Robust regression for continuous outcomes with serious outliers. - Multiple linear regression for continuous outcomes without serious outliers applying the clustered Huber estimator to account for patients occurring multiple times (robust variance). *Risk Ratios:* - Poisson regression applying the clustered Huber estimator to account for patients occurring multiple times (robust variance).			

3.2. SETTING

The study was conducted in Denmark, which has a population of 5.8 million. The healthcare system is primarily financed through taxation, and citizens have free access to healthcare services, including access to EMS, GP and hospital care.[144, 182, 183]

The healthcare system is divided into three administrative levels.[184] The state is responsible for legislation, health financing and national guidelines through the Ministry of Health and the Danish Health Authority. The five Danish regions are responsible for the delivery of all hospital-based services (psychiatric and non-psychiatric), primary care in general practice, practicing medical specialists (outpatient services based in private clinics), psychologist treatments and the entire EMS, including the regional Emergency Medical Communication Centre and the ambulance services.[144, 184] Finally, 98 municipalities are responsible for prevention, school health, child dental care, nursing homes, homecare, rehabilitation, social psychiatry and treatment of alcohol and drug abuse.[184, 185] A unique ten-digit Civil Personal Register (CPR) number is assigned to all citizens in Denmark. The CPR allows for individual-level record linkage of Danish databases and registers.[182, 186] The clinical registries DSR,[99] DES[100] and the Prehospital Database[98] are organised under the publicly funded organisation, Danish Clinical Registries.[180] Reporting to the Clinical Registries is mandatory for all hospitals, including private hospitals and the EMS.

Since 2004, hospitals and GPs have access to an online Shared Medication Record[187] though their local electronic medical record, providing information on the citizens' medication, including the most recent prescriptions, dates of prescription and dates of redemption. Since 2008/10 (depending on region of residency), hospitals and GPs have also had online access to hospital-based health records across hospitals and regions through the National Service Platform (sundhed.dk), providing information on, e.g., diagnosis and discharge letters. Only hospitals use the ICD-10 coding system. Each region has a Patient Administrative System, including ICD-10 diagnosis registered within the region since the 1970s. Information on previous diagnoses is available through the local electronic medical record.

3.2.1. THE ORGANISATION OF EMERGENCY CARE IN DENMARK

The organisation of emergency care system in Denmark has been introduced above in section 1.1.2. Emergency care is only provided in public hospitals in Denmark, including emergency surgical care and acute stroke care.[188] [22] During the study period, more than 90% of all acute stroke patients were treated at specialised multidisciplinary stroke units, including eight centres providing IV thrombolysis and three comprehensive stroke centres providing both IV thrombolysis and thrombectomy. Referrals from a GP or out-of-hours GP are mandatory for all hospital contacts, excluding psychiatric emergencies and patients arriving by ambulance after calling

EMS. Hence, since the patients need to call a health professional prior to admission, GPs and EMS have important roles as gatekeepers for hospital-based care. The annual number of EMS calls is currently 44-64 per 1,000 capita. It has increased over time and depends on the region of residency.[183] About 1/3 of Danish patients admitted with stroke contact the EMS prior to hospital arrival,[189] while 1/2 of patients admitted with stroke out-of-hours contact the EMS prior to hospital arrival.[190]

Police or fire brigade personnel answer all EMS calls. Calls identified as health-related are forwarded to one of the five public Emergency Medical Communication Centres.[183] At the Emergency Medical Communication Centre, healthcare professionals handle these calls. The personnel assess the individual calls using the 'Danish Index for Emergency Care' (Danish Index), a criteria-based dispatch decision support tool.[191] Each call is assigned a main symptom, which can be selected from among 37 standardised symptoms or mechanisms (e.g., symptom card 26 'Impaired consciousness – paralysis – dizziness'). Call-takers mainly focus on the acute symptoms, but may ask for relevant comorbidities. However, they will not obtain, e.g., a complete mental health history from each caller and do not have access to any medical chart. Depending on the type and urgency of the symptoms (e.g., stroke symptoms, breathing difficulties etc.), the call is assigned a priority level from 'A' to 'E'. The highest priority level is urgency level A, corresponding to an immediate response. Call-takers can choose not to send an ambulance, but advice, e.g., to call the patient's GP. The decision to release a patient at scene requires consultation with a physician (on-site or by telephone).

3.2.2. THE ORGANISATION OF MENTAL HEALTHCARE IN DENMARK

Based on recommendations from the Danish Health Authority,[192] patients with mental illnesses are treated in hospitals, by practicing psychiatrists, by practicing psychologists, by their GP and/or through other community-based services (Figure 8).

Severe mental health conditions such as schizophrenia, bipolar disorder, post-traumatic stress disorder and moderate to severe cases of depression are treated in hospital-based facilities offering both in- and outpatient services.[192] Patients with the need for an interdisciplinary effort, complicated comorbidity or other reasons for prolonged processes are often treated in hospital-based facilities. While a few private psychiatric hospitals offer outpatient-based services, patients with severe mental illness are primarily treated in public hospitals in Denmark. No private hospitals in Denmark offer hospital-based inpatient care or emergency psychiatric care.

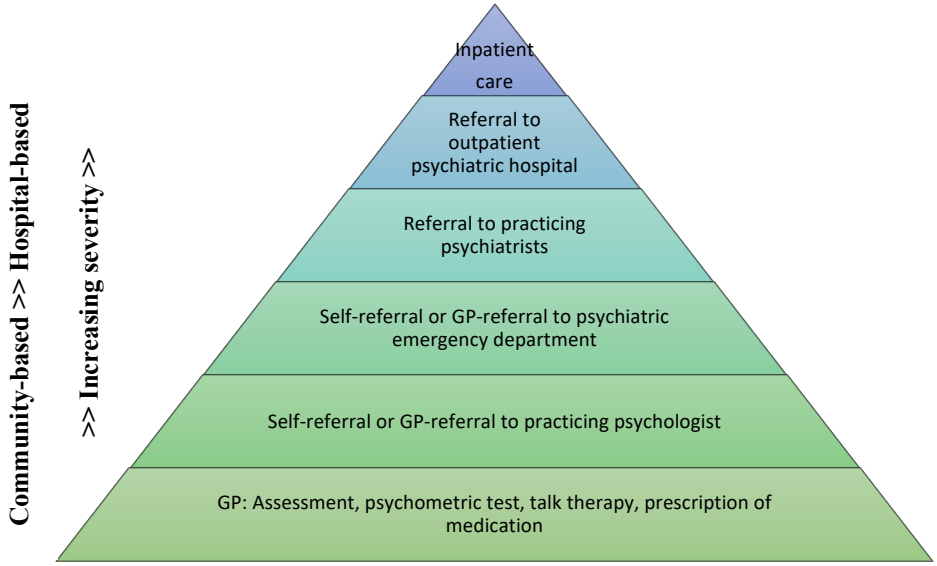

Figure 8: Levels of mental healthcare in Denmark [192-194]

Practicing psychiatrists primarily take care of patients with mental health conditions of moderate severity with no need for interdisciplinary effort, such as anxiety, depression, stress-related conditions, personality disorders and adults with ADHD [192, 195] GPs take care of a broad spectrum of mental health conditions, such as mild to moderate depression and anxiety, crises, dementia and alcohol abuse.[192-194] Moreover, GPs take care of the follow-up of certain psychiatric patients after assessment and treatment at psychiatric hospitals. Private psychologists primarily take care of patients with mild to moderate depression or young adults with mild to moderate anxiety.

As described above, the municipalities also play an important role in the care of citizens with mental illnesses. While some patients with severe mental illness are living in nursing or care homes (regional, private or municipality-based), the municipalities are also responsible for prevention, social psychiatry, home care, rehabilitation and treatment of alcohol and drug abuse.[185, 192]

3.3. DATA SOURCES

3.3.1. DANISH CLINICAL REGISTRIES (RKKP)

In 2001, the administrative infrastructure was established to support the development of the clinical quality registries, embracing the need for monitoring the clinical quality and patient safety.[180, 196] Since 2006, there has been a specific procedure in place to improve and operate the clinical quality registries and since 2011, they have been

organised in an administrative structure, the Danish Clinical Registries.[180] The registries are primarily devoted to the improvement of quality of care and to facilitate accountability and transparency in healthcare.[197] However, the registries also have an important role in the national research infrastructure by providing data to complete important nationwide analyses.[198] The registries contain data related to diagnostic procedures, treatment, rehabilitation and outcomes.[196] They may cover diseases (e.g., ischemic stroke), interventions (e.g., laparotomy) or specific areas of healthcare (e.g., emergency departments and prehospital care). A dedicated group of clinicians and experts appointed by the regions, hospitals and scientific and medical societies determines the process measures and outcomes measures based on evidence and good clinical practice.[199]

The Prehospital Database is a nationwide clinical registry established in 2016.[98] The registry contains data on all EMS calls from all five Danish Regions. The Prehospital Database includes nine process measures.[98, 108] The Prehospital Database is based on information from the regional ambulance dispatch software, containing individual-level information on Danish Index, timestamps for the emergency call, ambulance dispatch time and on-scene times as consecutively registered by the EMS personnel.

The Danish Stroke Registry (DSR) is a nationwide clinical registry established in 2003.[99] The registry contains data on patients (18 years or above) admitted to a Danish hospital with acute stroke (ischemic or haemorrhagic) or Transient Ischemic Attack (TIA). The Danish stroke guidelines, including stroke diagnose, are in accordance with the guidelines of the European Stroke Organisation.[200] The registry contains measures regarding urgent care, non-urgent care, compliance with prescribed medication, long-term outcome and rehabilitation.[111] Since 2003, the definitions of the measures have been updated according to new evidence within the field, e.g., door-to-thrombolysis and proportion of patients receiving reperfusion therapy have been measured since 2009. Based on detailed written instructions, the hospital staff classify every patient as eligible or ineligible for each measure, according to the presence of contraindications. For example, severe dementia in a patient with ischemic stroke and atrial fibrillation can preclude oral anticoagulant therapy, and mobilisation is not relevant, if the patient was immobilised prior to admission. The medical relevance of each measure is therefore incorporated into the registration and consequently included in this study, i.e., patients with contraindications for a specific clinical intervention were not considered eligible for the corresponding performance measure.

The Danish Clinical Register of Emergency Surgery (DES) is a nationwide clinical registry established in 2003. The registry contains data on both perforated peptic ulcers and bleeding ulcers requiring hospital-based surgical intervention. The Danish guidelines are in accordance with the guidelines from the World Society of Emergency Surgery.[173] We used the measures from the registry 2004-2018, however, some measures have been updated since 2018 to reflect new evidence and best clinical practice within the field.[107] Until 2018, the registry required manual registration of all

measures (e.g., it was not based on data from other national registries). After 2019, the Danish Register of Emergency Surgery also includes high-risk surgical patients other than patients with perforated peptic ulcers (e.g., ischemic bowel, bowel obstructions, bowel perforations etc.).[107] Also, all measures are now based on data from the Danish National Patient Registry, releasing the clinical staff from the burden of registration. While the new definitions and measures in the most recent version of the registry were not available when we received our dataset in 2019, the original measures from 2004 and 2014-2018 still reflect the provision of the core processes of early surgical care for patients with perforated peptic ulcers.

3.3.2. DANISH HEALTH REGISTRIES UNDER THE DANISH HEALTH DATA AUTHORITIES

The Danish Civil Registration System[201] is an administrative register established in 1968. It contains individual-level information on all persons residing in Denmark. It is updated daily with information on migration and vital status. The data in the Civil Registration System are virtually complete and have high accuracy, allowing for nationwide cohort studies with virtually complete long-term follow-up.

The Danish National Patient Registry[202], *The Danish National Patient Registry-Psychiatry* and *The Danish Psychiatric Central Research Register*[195] all contain patient-level data on all hospital-based contacts (in- and outpatients) and diagnoses according to the ICD coding system – including emergency department visits. The registries contain data from 1977 with complete nationwide coverage since 1978.

The National Register of Medicinal Product Statistics[203] contains data on individual-level redeemed prescriptions according to the Anatomical Therapeutic Chemical Classification System (ATC) since 1994.

The National Registry of Alcohol Treatment is a national registry established in 2008 that contains data on individuals who have been assigned for treatment of alcoholism. The registry provides statistics on admissions. The municipalities may refer clients to public or private institutions for treatment of alcoholism. Both are required to report to the Danish Health Authority.

The Register of Substance Abusers in Treatment contains enrolment statistic on clients enrolled in treatment for substance abuse in community-based settings, dating back to 1996.

3.3.3. STATISTICS DENMARK – SOCIAL AND PRIMARY CARE

Statistics Denmark is an extensive collection of administrative registers, containing individual-level data from governmental agencies.

The Danish National Health Service Register for Primary Healthcare[204] contains information on services provided in primary healthcare settings, including general practice, out-of-hours GPs and referrals to community-based psychologists and practicing psychiatrists, dating back to 1990.

The statistics on households and families (FAM/FAIK) describe the total population living in Denmark. Daily submissions from the Central Population Register provide the basis for the statistics. Statistics are produced covering three different kinds of units: Households, families and individuals. The statistics describe these units based on household- and family-related variables (e.g., type of family, size of family, type of household). The basis for the statistics is data on sex, age, marital status, references to spouses and parents as well as address specification. The address data form the basis of the division into households, municipalities and regions.

The personal income statistics (IND) describes income for individual persons who are at least 15 years old at the end of the year and who are fully liable to pay tax in the year concerned. The earned income (*A-indkomst*) statistics mainly comprise wages and transfers. The earned income amounts to 90 per cent of the total gross income.

The employment registry (RAS) is annual labour market statistics based on the population's connection to the labour market on the last working day in November.

The Educational Attainment Register (UDFF) gathers information about the highest completed education for each single person based on information in the Student Register and the Qualification Register. The primary data source for these statistics is the Student Register with data from 1974 onwards.

3.4. MAIN EXPOSURE

The exposure of all four studies in this thesis was a history of mental illness. Patients were grouped into four categories according to severity of mental health history. The categories were defined based on consensus among local experts in clinical epidemiology, psychiatry, social medicine and GP, supported by knowledge of patient groups experiencing the highest excess mortality,[8, 205] and have also been used in other studies.[206-208] Please see Supplementary Table S1 for details on included ICD-10 diagnoses, ATC codes and other codes. Please see Supplementary Table S2 for information about timing of most recent mental health disease-related activity, prior to admission using data from Study II regarding ischemic stroke as an example.

3.4.1. MAJOR MENTAL ILLNESS

We defined a history of major mental illness as in- or outpatient hospital-based contacts with schizophrenia or bipolar (ever) or inpatient hospital contact of more than two days with depression or personality disorder (within the last 10 years). While

there is no gold standard for categorising mental illnesses, it is generally accepted that severe mental illness may include schizophrenia, bipolar disorder and major depression.[12, 205, 209] While bipolar disorder[210] and schizophrenia[211] are less common and often classified as severe, depression is common[4] and varies in severity.[210] Hospital-based care is recommended for the most severe cases of depression and personality disorders.[192]

3.4.2. MODERATE MENTAL ILLNESS

We defined a history of moderate mental illness as any other in- or outpatient psychiatric-hospital contacts with a diagnosis of DF20-99 (other diagnosis than 'major') (past five years) or a consultation at a practicing psychiatrist (within the last 5 years). Hospital-based diagnoses are often used to identify mental illness in registry-based studies[8] and are considered to be more severe than mental health conditions requiring community-based services only (e.g., GP or psychologist services). While substance abuse and organic disorders are often considered as mental illnesses, we defined substance abuse as a co-variate (see below). In 2010, 184 specialists in psychiatry were working as practicing psychiatrists, mostly treating anxiety, affective and personality disorders and possibly treating up to 20% of the cases referred to psychiatric treatment.[195] These patients are not registered in the Danish National Patient Registry. However, any contact to practicing specialist in psychiatry is registered in the Danish National Health Service Register for Primary Healthcare, also used in the studies.

3.4.3. MINOR MENTAL ILLNESS OR VULNERABILITY

We defined a history of minor mental illness as patients fulfilling none of the above-mentioned criteria but receiving reimbursements of at least two prescription of selected drugs (antidepressants or benzodiazepines), two or more sessions of talk therapy or psychometric testing in a primary care setting or a referral to a practicing psychologist (within the past 12 months). The majority of patients with depression are diagnosed and treated by GPs,[192] and these patients are not included in the Danish National Patient Registry. The need of including other registers to identify depression is also described by other Danish authors.[4]

3.5. OUTCOME

All studies used process and outcome measures from the selected clinical registries (described above). Not all measures in each registry were relevant in the acute stage of the diseases. Therefore, we selected measures relevant within the first hours or days of admission to investigate the quality of acute and emergency care. Also, some aspects of acute care have already been described according to mental health history with data from these registries.[159, 212] These analyses were not repeated, since we use overlapping or exactly the same populations. Please see Table 2 for definitions of

measures. Please see each individual paper regarding detailed definition of each of the selected measures.

Additional measures were added to further explore unwanted variation and compare results to other cohorts or countries. All mortality-related measures were calculated using both data from the Clinical Registries and the Danish Civil Registration System.

3.5.1. STUDY I: PATIENTS CALLING THE EMS

Five measures from the Prehospital Database were included in this study with two additional process measures being defined (unplanned hospital contact within seven days) to explore the quality and outcome of EMS services and compare services to countries with similar prehospital systems.[213] These indicators were based on data from the Danish National Patient Registry. Please see Table 2 for definitions of measures.

3.5.2. STUDY II - ISCHEMIC STROKE: PATIENT DELAY, SYSTEM DELAY, EMS RESPONSE AND EMERGENCY TREATMENT

We defined emergency treatment as reperfusion therapy (thrombolysis or thrombectomy) based on information from the DSR. We defined delays from onset of symptom to hospital arrival, imaging and treatment based on timestamps from the DSR, including delays from onset of symptoms to EMS calls, ambulance arrival and transport time based on timestamps from the Prehospital Database. Please see Table 2 for definitions of measures.

3.5.3. STUDY III - ISCHEMIC STROKE: ADVANCED STROKE CARE AND CLINICAL OUTCOME

We defined guideline-recommended acute advanced stroke care based on nine process measures and two outcome measures from the DSR regarding early diagnostics, advanced care, early rehabilitation and clinical outcome. We added two measures combining all relevant process measures into one composite score as described by other authors[79]. We calculated the proportion of fulfilled process measures for each patient (opportunity-based) and the proportion of all patients receiving all relevant measures (all-or-none). Please see Table 2 for definitions of measures.

3.5.4. STUDY IV - PERFORATED PEPTIC ULCER: EMS RESPONSE, EMERGENCY TREATMENT AND CLINICAL OUTCOMES

We defined prehospital process measures based on two variables from the Prehospital Database regarding EMS response and symptom recognition. We defined guideline-

recommended emergency surgical treatment based on four process measures and two outcome measures from the DES. We added the combined outcome 'days alive and out-of-hospital', using the same methodology as described by other authors.[214] Please see Table 2 for definitions of measures.

3.6. CO-VARIATES

The four studies in this thesis used many common co-variates and a few co-variates that are only relevant for a specific population in each study. Common co-variates were factors related to quality of emergency care, outcome of emergency care or frequent use of emergency services for people living in high-income countries,[19, 22, 23, 116, 126-128, 131, 215, 216] which we also expected to be related to mental illness, e.g., age, sex, place of origin, comorbidity, socioeconomic position, cohabitation, drug abuse and geographical area (rural/metropolitan). Please see each paper for definition of co-variates and data sources.

Not all relevant confounders or mediators were available. Please see directed acyclic graph (DAG) in Supplementary Figure S1 presenting co-variates as confounders, mediators or unmeasured using the association between a history of mental illness and receiving reperfusion therapy from Study II as an example.

3.7. METHODS OF ANALYSIS

We compared all measures according to the severity of mental illness using the group with no history of mental illness as a reference.

For the time delays (e.g., prehospital delays, time-to-treatment) and differences between the composite opportunity-based scores, we compared the four exposure groups applying robust linear regression based on Huber and biweight iterations, as implemented in the Stata routine *rreg*. The purpose of this regression was to limit the effect of serious outliers. Please see boxplot in paper IV illustrating outliers in "time-to-surgery". In Study IV, we performed an additional analysis comparing medians and 75% quartiles to further explore the differences between groups.

For the binary outcomes (e.g., hospital admission after EMS call, reperfusion therapy, all-or-none composite score and 30-days mortality), we calculated a Risk Ratio (RR) using Poisson regression. In Study IV, we further used multiple linear regression to explore the differences in days-alive-and-out-of-hospital. To account for the same patient occurring multiple times in our dataset, we applied the clustered Huber estimator to these regressions.

All estimates were calculated as unadjusted and adjusted for age, sex, comorbidity and other relevant confounders or mediators in different models 1-2-3, depending on the outcome measure (e.g., stroke severity in 30-day stroke mortality). Please see the

methods section in each paper for the included variates in each model. We implemented restricted cubic splines for age with three knots at quantile 0.1, 0.5, and 0.9.

In Study IV, both mortality and the proportion of patients with a history of mental illness decreases in the study period 2004-2018. Hence, analyses regarding days-alive-and-out-of-hospital and 30-mortality were adjusted for calendar year.

3.8. ETHICS AND REGULATIONS

The study was approved by the local institutional review board. According to Danish law, approval from the Danish National Committee on Health Research is not required for register-based studies.

CHAPTER 4. RESULTS

In the following chapters, the results will be presented and discussed across studies. With the Chain of Survival in mind, results regarding patient delays, EMS response, emergency treatment and advanced hospital-based care will be presented.

4.1. BASELINE CHARACTERISTICS ACROSS STUDIES

In Table 3, the number of identified and included patients in each study can be found. Further details, such as detailed flow charts of the study populations and more details on baseline characteristics, can be found in the individual articles. Baseline characteristics will be discussed across the four studies to understand the variation and impact of patient characteristics on the results presented later in the chapter.

In all four studies, at least one-fourth of the study population had a history of mental illness (Table 3). The highest proportion was found in Study I regarding EMS patients, with a total of 35% with any history of mental illness. The lowest proportion was found in Study II regarding patients with ischemic stroke, with a total of 24% with any history of mental illness. Study I regarding EMS patients had the highest proportion of patients with a history of moderate or major mental illness (i.e., 10% and 8% of the study population, respectively) (Table 3). Study IV regarding patients with perforated peptic ulcers had the highest proportion of patients with a history of minor mental illness (i.e., 25% of the study population).

Table 3: Number of identified and included EMS calls or admissions, number of individual patients and proportion of patients in each exposure group in Study I-IV

		Study 1	**Study II**	**Study III**	**Study IV**
Number of admissions/ EMS calls identified and included	*Identified in study period*	637,954 EMS calls 2016-2017	20,178 admissions with acute ischemic stroke 2016-2017	118,902 admissions with acute ischemic stroke 2007-2018	4,943 admissions with perforated peptic ulcer 2014-2018
	Included in analysis	492,388 EMS calls	19,592 admissions	117,548 admissions	4,767 admissions
	Individual patients	342,769 patients	18,773 patients	106,000 patients	4,726 patients

Number of admissions/ EMS calls per patient in the study period	*Median*	1	1	1	1
	IQR	1;3	1;1	1;1	1;1
	Range	1-123	1-5	1-16	1-2
Proportion of patients with a history of mental illness	*None*	64%	76%	72%	67%
	Minor	18%	18%	21%	25%
	Moderate	10%	3%	4%	4%
	Major	8%	3%	3%	4%

For all four studies, significant differences were found regarding baseline characteristics (e.g., age, comorbidity, socioeconomic position) between patients with and without a history of mental health illness as well as between the different severities of mental illnesses (Figure 9).

In general, patients with a history of minor mental illness were older, i.e., median age of 73 years in study I regarding EMS-calls, compared to a median age of 62 years among patients with no history of mental illness. They also had a larger burden of comorbidity (Figure 9), were more likely to be female and more likely to live alone compared with patients with no history of mental illness (Figure 9). Patients with a history of major or moderate mental illness were younger, i.e., a median age of 54 years and 45 years, respectively, in Study I regarding EMS-calls. They were also more likely to have a disadvantaged social position (low income, low level of education, no adherence to work force). They were also more likely to live alone and have a substance abuse compared with patients with no history of mental illness (Figure 9).

The distribution of characteristics was similar across the four studies. However, since Study I regarding EMS patients included patients of all ages (hereunder patients aged 0-17 years), the median age was lower. Also, the proportion of patients with low burden of comorbidity was higher in all four groups in Study I.

The proportion of patients working or undergoing education was higher among patients in Study I regarding EMS patients e.g., 35% of patients with a history of moderate mental illness were part of the labour market. In comparison, 15% of patients with a history of moderate mental illness in Study II regarding ischemic stroke were part of the labour market. (Figure 9). This was also found in Study III-IV regarding patients with ischemic stroke and perforated peptic ulcer. However, for the other measures of social position (income and level of education), patients in Study I

generally had a more disadvantaged social position compared to the populations in Study II-III-IV, e.g., the proportion of patients living in relative poverty in Study I was 21% and 14% among patients with a history of moderate or major mental illness, respectively, compared to 4% and 2% of patients in Study II with a history of moderate or major mental illness, respectively. Also, the proportion of patients with substance abuse was higher in all groups in Study I, e.g., 51% of patients with a history of major mental illness had a substance abuse in Study I, while the number was 23% of patients with a history of major mental illness in Study II (Figure 9).

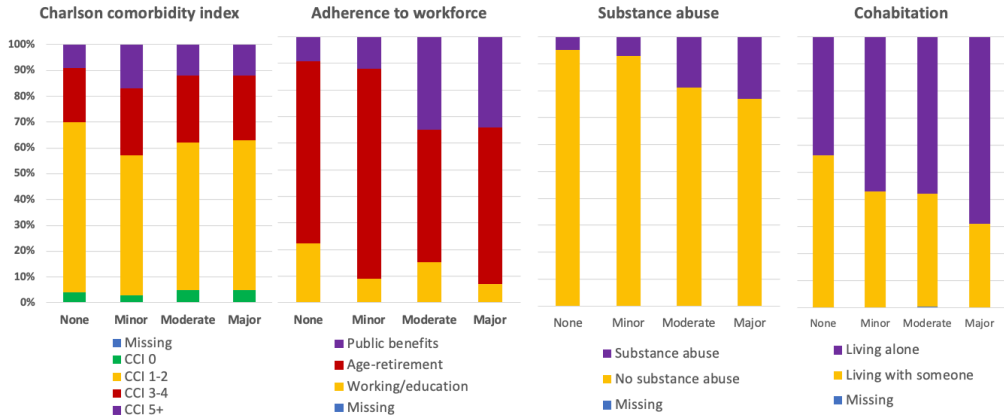

Figure 9: Selected baseline characteristics from Study II according to exposure (history of mental illness)

4.2. RECOGNISING SYMPTOMS, CALLING THE EMS AND EMS RESPONSE

Table 4 contains information on patients calling the EMS prior to admission with stroke (Study II-III) and perforated peptic ulcer (Study IV), including information on presenting symptoms according to the Danish Index and EMS response. In Study II-III-IV regarding patients with ischemic stroke and perforated peptic ulcer, a cut-off of 72 was defined for patients calling the EMS. Since there is no consensus on this cut-off, the differences between a cut-off of 24 hours or 72 hours are presented in Table 4.

Table 4: Presenting symptoms (according to the Danish Index), prehospital dispositions and prehospital delays according to exposure (history of mental illness)

		Study I	**Study II-III****	**Study IV**
Proportion calling the EMS 72 hours *(or 24 hours*)* **prior to hospital arrival**	*None*	Not relevant	33% *(32%*)*	33% *(32%*)*
	Minor	Not relevant	33% *(32%*)*	27% *(27%*)*
	Moderate	Not relevant	34% *(33%*)*	44% *(44%*)*
	Major	Not relevant	31% *(30%*)*	24% *(24%*)*
Presenting symptoms according to the Danish Index for patients calling the EMS	*None*	15% unclear problem 14% chest pain 12% accident (not traffic) 11% impaired consciousness, paralysis, dizziness 8% minor wound, fracture or injury	74% impaired consciousness, paralysis, dizziness 12% unclear problem 14% other symptoms	51% abdominal or back pain 34% other non-abdominal symptom 15% unclear problem
	Minor	16% unclear problem 13% chest pain 13% dyspnoea 12% impaired consciousness, paralysis, dizziness 10% accident, not traffic	72% impaired consciousness, paralysis, dizziness 12% unclear problem 16% other symptoms	48% other non-abdominal symptom 40% abdominal or back pain 12% unclear problem
	Moderate	15% unclear problem 13% chest pain 9% alcohol, intoxication, overdose 9% accident (not traffic) 7% dyspnoea	73% impaired consciousness, paralysis, dizziness 9% unclear problem 18% other symptoms	38% other non-abdominal symptom 31% abdominal or back pain 31% unclear problem
	Major	18% unclear problem 11% chest pain 10% alcohol, intoxication, overdose 9% psychiatry or	60% impaired consciousness, paralysis, dizziness 18% unclear symptom 22% other problem	62% other non-abdominal symptom 25% abdominal or back pain 13% unclear problem

		suicide 8% dyspnoea		
Proportion receiving an EMS response with the highest level of urgency	*None*	53%	86%	48%
	Minor	53%	86%	67%
	Moderate	48%	84%	38%
	Major	45%	83%	25%
Time from onset of symptoms to hospital arrival, median, IQR *Study II-III is reported with Study II above and Study III below*	*None*	Not relevant	344 min (109;1330) *300 min (109;1080)**	330 min (159;718)
	Minor	Not relevant	330 min (120;1110) *300 min (118;960)**	299 min (126;576)
	Moderate	Not relevant	363 min (107;1220) *315 min (133;1045)**	416 min (157;1730)
	Major	Not relevant	480 min (137;1763) *322 min (120;1148)**	658 min (375;4013)

**data not presented in the published article ** overlapping cohorts 2016-2017*

Across the studies, we found that patients with a history of mental illness received a significantly lighter EMS response compared to patients with no history of mental illness. In Study I regarding all EMS patients, patients with a history of mental illness were more likely to receive telephone advice only, i.e., adjusted RRs were 1.08 (CI, 1.04;1.13) for minor, 1.30 (CI, 1.24;1.37) for moderate and 1.61 (CI, 1.53;1.70) for patients with a major history of mental illness, compared to patients with no history of mental illness. They were also more likely to be released at the scene, i.e., adjusted RRs were 1.05 (CI, 1.03;1.07) for minor, 1.03 (CI, 1.01;1.04) for moderate and 1.11 (CI, 1.08;1.13) for patients with a history of major mental illness, compared to patients with no history of mental illness.

In Study II regarding patients with ischemic stroke, 33% of the patients called the EMS prior to admission (Table 4). Of all patients calling the EMS, 86% received an immediate response (urgency level A), and 73% were recognised with stroke symptoms/neurological symptoms (Danish Index card 26 'Impaired consciousness, paralysis, dizziness') (Table 4). Patients with or without a history of mental illness were equally likely to receive an immediate response when calling EMS. However, patients with a history of major mental illness were less likely to be identified with neurological or stroke symptoms and more likely to be registered with unclear

symptoms (Table 4). EMS-related times (response time, on-scene time and transport time) did not differ between patients with or without a history of mental illness.

In Study IV regarding patients with perforated peptic ulcers, 32% of the patients called the EMS prior to admission (Table 4). While 48% of the patients with no history of mental illness were assigned an immediate response when calling the EMS, only 38% and 25% of patients with a history of moderate and major history of mental illness, respectively, were assigned this level of urgency (Table 4). Among patients with no history of mental illness, 51% were identified with abdominal or back pain (Danish Index card 24 'Abdominal pain, back pain'). This number was 40%, 31% and 25% for patients with a history of minor, moderate and major mental illness, respectively (Table 4).

In Study I regarding all EMS patients, patients with a history of mental illness were significantly more likely to call EMS again within 24 hours if given telephone advice only or if released at the scene. If given telephone advice only, adjusted RR for calling again within 24 hours was 1.38 (CI, 1.20;1.60) for minor, 1.96 (CI, 1.20;2.21) for moderate and 2.11 (CI, 1.88;2.40) for patients with a history of major mental illness, compared to patients with no history of mental illness. If released at the scene, adjusted RR of calling the EMS again within 24 hours was 1.57 (CI, 1.35;1.84) for minor, 2.41 (CI, 2.05;2.83) for moderate and 2.86 (CI, 2.44;3.36) for patients with a history of major mental illness, compared to patients with no history of mental illness.

4.3. FROM ONSET OF SYMPTOMS TO HOSPITAL ARRIVAL

In Study I regarding all EMS patients, there were no clinically relevant differences between groups regarding response times for ambulances dispatched with the highest level of urgency. Also, we did not find any difference in the proportion of patients registered according to Danish Index with type of symptom and level of urgency. In Study II, no differences were found between EMS-related times (response time, on-scene time and transport time) between patients with or without a history of mental illness.

In Study II regarding patients with ischemic stroke, the median time from onset of symptoms to hospital arrival among all patients was 245 minutes (IQR, 111;1308) (Table 4). When considering both patients calling and not calling the EMS prior to hospital arrival, patients with a history of major mental illness had the longest prehospital delay of 480 min (IQR, 137;1763). However, if not calling the EMS, patients with a history of major mental illness had a total delay from onset of symptoms to hospital arrival of 811 min (IQR, 197;2845). Adjusting for age, sex, country of origin, comorbidity and stroke severity, the total prehospital delay was 67 minutes (CI, 28;106) longer, when including both EMS and non-EMS patients (Figure 10) and 123 minutes (CI, 49;196) longer when considering non-EMS patients only, compared to patients with no history of mental illness.

For patients calling the EMS, the median time from symptom onset to EMS call (patient delay) for all patients was 120 minutes (IQR, 29;484). Adjusting for age, sex, country of origin, comorbidity and stroke severity, patients with a history of major mental illness called the EMS 27 minutes (CI, 1;52) later, compared to patients with no history of mental illness.

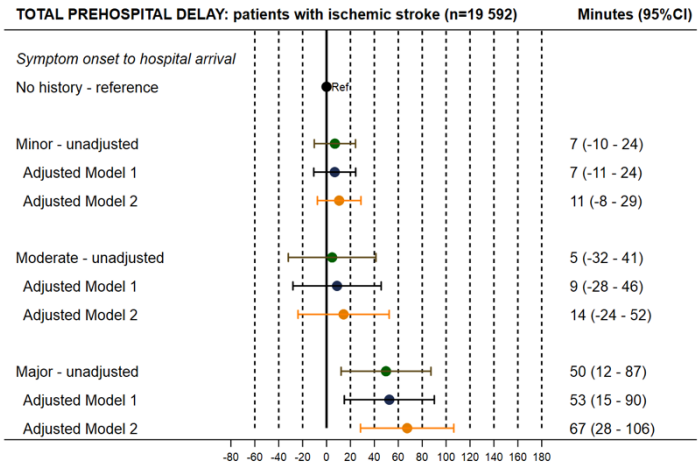

Figure 10: Differences in delays from symptom onset to hospital arrival among patients with ischemic stroke with and without a history of mental illness, including both patients calling and not calling the EMS prior to arrival. Model 1: Age, sex and country of origin. Model 2: Age, sex, country of origin comorbidity and stroke severity.

In Study IV regarding patients with perforated peptic ulcers, the median time from onset of symptoms to hospital arrival among all patients was 330 minutes (IQR, 159;743) (Table 4). Patients with a history of major mental illness had the longest delays of 658 min (375;4013). Adjusting for age, sex and comorbidity, patients with a history of major mental illness arrived 145 minutes (CI-7;296) later, compared to patients with no history of mental illness.

4.4. RECEIVING EMERGENCY TREATMENT AND ADVANCED CARE

In Study II regarding patients with ischemic stroke, patients with a history of mental illness were significantly less likely to receive reperfusion therapy. While 18.5% (CI, 17.4;19.1) of patients with no history of mental illness received reperfusion therapy, 13.9% (CI, 12.8;15.1) with minor, 17.0% (CI, 14.2;20.1) with moderate, and 13.4% (CI, 10.8;16.3) with a history of major mental illness received reperfusion therapy, respectively. Adjusting for age, sex, country of origin, comorbidity, stroke severity and time from symptom onset to admission, the RRs of receiving reperfusion therapy were 0.79 (CI, 0.72;0.86) for minor, 0.85 (CI, 0.72;0.99) for moderate and 0.63 (CI, 0.51;0.77) for patients with a history of major mental illness compared to patients with

no history of mental illness. These differences were less pronounced when considering patients admitted within four hours from onset of symptoms.

Overall, 38.2% (CI, 37.1;39.2) of patients arriving within four hours, received reperfusion therapy. Adjusting for age, sex, country of origin, comorbidity, stroke severity and time from symptom onset to admission, the RRs of receiving reperfusion therapy were 0.85 (CI, 0.79;0.93) for minor, 0.90 (CI, 0.79;1.04) for moderate and 0.83 (CI, 0.69;0.99) for patients with a history of major mental illness arriving within four hours, compared to patients with no history of mental illness (Figure 11).

In Study II regarding patients with ischemic stroke, the median time from hospital arrival to thrombolysis (door-to-needle) was 30 minutes (IQR, 20;44). We found no differences regarding door-to-needle times between patients with and without a history of mental illness or across subgroups. Further, we found no differences regarding door-to-imaging time for patients arriving at the hospital within four hours from onset of symptoms.

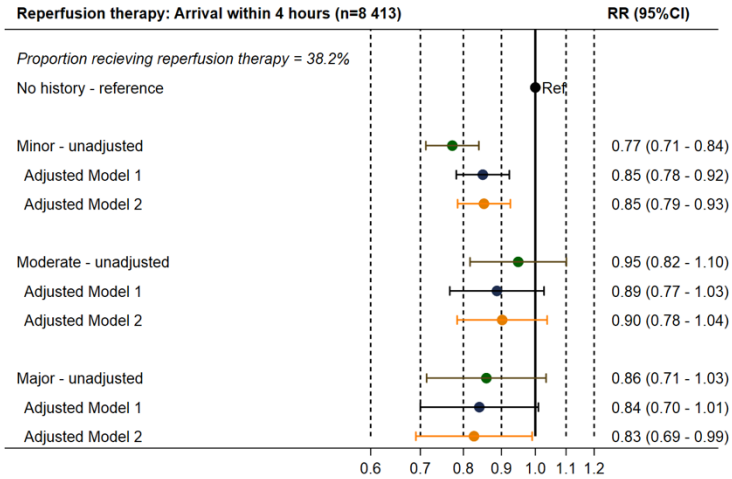

Figure 11: Risk Ratio (RR) of receiving reperfusion therapy among patients with ischemic stroke arriving within four hours from onset of symptoms, with and without a history of mental illness. Model 1: Age, sex and country of origin. Model 2: Age, sex, country of origin, comorbidity and stroke severity.

In Study III regarding patients with ischemic stroke, the overall quality of acute stroke care was high. With only one exception (mobilisation on the day of admission), each process measure was fulfilled for more than 80% of the patients. Looking at the score combining all process measures (composite score), the median opportunity-based composite score was 85.7% (IQR 66.7;100), meaning that of the selected nine process measures reflecting guideline-recommended acute stroke care, 50% of the patients

received 85.7% or more of the selected process measures. Further, 40.9% (40.6;41.2) of the patients received all process measures.

While the absolute differences were small, patients with any history of mental illness were less likely to receive a CT/MR, be mobilised or receive a direct swallowing test on the day of admission and also less likely to receive a nutritional risk assessment and to be assessed by an occupational and a physiotherapist on the second day of admission, compared to patients with no history of mental illness. Further, patients with a history of minor mental illness were less likely to receive indirect swallowing test on the day of admission and receive oral anticoagulation within 14 days if diagnosed with atrial fibrillation, compared to patients with no history of mental illness. Adjusting for age, sex, country of origin, comorbidity and stroke severity, the RRs of all relevant measures (all-or-none) were 0.88 (CI, 0.86;0.09) for minor, 0.89 (CI, 0.86;0.93) for moderate and 0.93 (CI, 0.89;0.97) for patients with a history of major mental illness, compared to patients with no history of mental illness.

In Study IV regarding patients with perforated peptic ulcers, the overall quality of emergency surgery and emergency care was not in accordance with guideline-recommended care. The median time from hospital arrival was 6.0 hours (IQR, 3.6;10.7). Adjusting for age, sex and comorbidity, patients with a history of major mental illness underwent surgery 47 minutes (CI; 7;88) later compared to patients with no history of mental illness. (Figure 12).

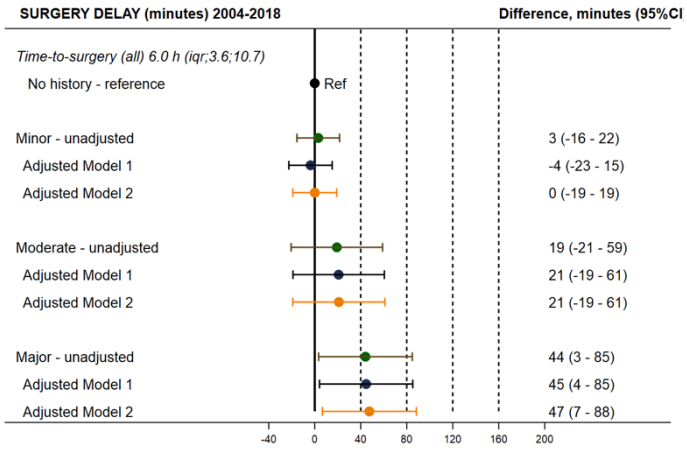

Figure 12: Differences in time-to-surgery for patients with perforated peptic ulcer, according to mental health history. Model 1: Age and sex. Model 2: Age, sex and comorbidity.

The median time from hospital arrival to antibiotics was 207 minutes (IQR, 90;423). While differences regarding time-to-antibiotics were not statistically significant, important differences were observed for patients with a moderate and major mental health history, with a large proportion of patients receiving antibiotics very late (e.g.,

75%-quartile above 500 minutes). Adjusting for age, sex and comorbidity, patients with a history of major mental illness received antibiotics 72 minutes (CI, -10;148) later, compared to patients with no history of mental illness.

4.5. REHABILITATION AND RECOVERY

In Study III regarding patients with ischemic stroke, the overall 30-day mortality outcome was 7.5% (7.3;7.6). Considering age- and sex-adjusted estimates, patients with a history of mental illness had a higher risk of death at day 30 with RRs of 1.31 (CI, 1.26;1.37) for minor, 1.18 (CI, 1.05;1.33) for moderate and 1.44 (CI, 1.30;1.60) for patients with a history of major mental illness compared to patients with no history of mental illness. If also adjusting for stroke severity, differences in the 30-day mortality were less pronounced.

If considering only patients receiving all relevant measures, patients with a history of mental illness had a higher risk of 30-day mortality outcome, compared to patients with no history of mental illness, i.e., adjusting for age, sex and comorbidity, RRs were 1.26 (CI, 1.17;1.35) for minor, 1.12 (CI, 0.92;1.38) for moderate and 1.37 (CI, 1.15;1.62) for patients with a history of major mental illness, compared to patients with no history of mental illness (Figure 13).

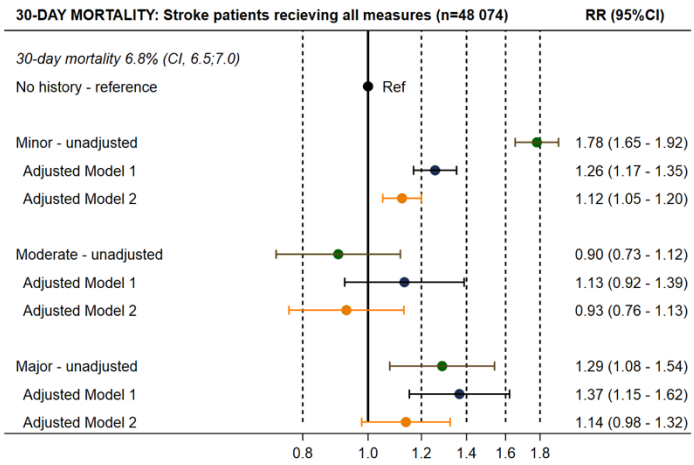

Figure 13: 30-day mortality among patients with ischemic stroke in the subgroup of patients receiving all process measures (100% guideline-based acute stroke care), according to mental health history. Model 1: Age, sex and comorbidity. Model 2: Age, sex, comorbidity and stroke severity.

However, if also adjusting for stroke severity, this was less pronounced, i.e., RR 1.12 (CI, 1.05;1.20) for minor, 0.93 (CI, 0.76;1.12) for moderate and 1.14 (CI, 0.98;1.32)

for patients with a history of major mental illness, compared to patients with no history of mental illness (Figure 13).

In Study III regarding patients with ischemic stroke, the proportion of patients experiencing a recurrent stroke within one year was 4.4% (CI, 4.3;4.5). Considering both age- and sex-adjusted estimates and estimates adjusted for age, sex and stroke severity, patients with a history of mental illness were significantly more likely to have a recurrent stroke within one year. Adjusted RRs were 1.56 (CI, 1.46;1.67) for minor, 1.28 (CI, 1.09;1.49) for moderate and 1.29 (CI,1.10;1.52) for patients with a history of major mental illness, compared to patients with no history of mental illness.

In Study IV regarding patients with perforated peptic ulcers, the 30-day mortality for all patients was 23% (CI, 22;24) and number of days-alive-and-out-of-hospital at day 90 was 67 days (IQR, 0;83). Adjusting for age, sex and comorbidity, patients with a history of major mental illness had a higher risk of death at day 30 with a RR of 1.43 (CI, 1.14;1.80) and 9 days (CI, 4;14) less alive and out-of-hospital at day 90, compared to patients with no history of mental illness. Patients with a minor history of mental illness had a higher risk of death at day 30 with a RR of 1.16 (1.04;1.29) and 2 days (CI, 0;5) less alive and out-of-hospital at day 90. During the study period, 30-day mortality decreased and median number of days-alive-and-out-of-hospital at day 90 increased. We found no differences in 30-day mortality or days-alive-and-out-of-hospital among patients with a history of moderate mental illness.

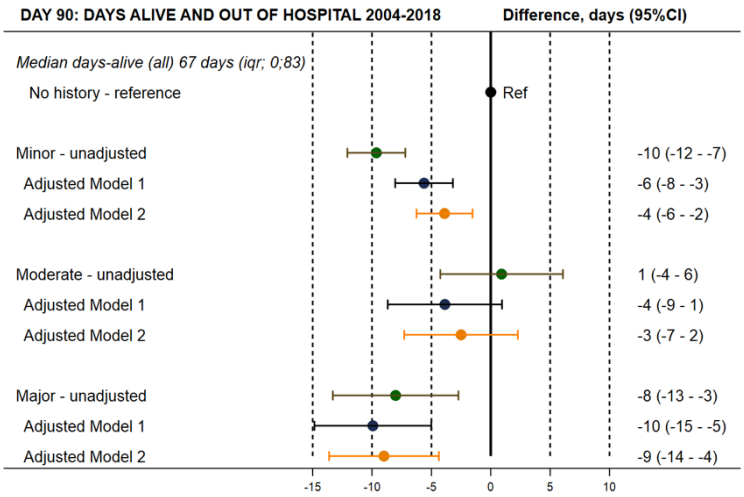

Figure 14: Differences in days-alive-and-out-of-hospital at day 90 in patients with peptic ulcer perforation according to mental health history. Model 1: Age and sex. Model 2: Age, sex and comorbidity.

CHAPTER 5. DISCUSSION

5.1. KEY RESULTS

This thesis shows that patients with a history of mental illness experience a lower quality of emergency care at several steps of the Chain of Survival, from onset of symptoms to emergency treatment, compared to patients with no history of mental illness. It also shows that patients assigned the highest level of urgency when calling the EMS and patients admitted to a specialised stroke unit with ischemic stroke were equally likely to receive high quality of advanced care. Lastly, patients with a history of mental illness were less likely to have a beneficial clinical outcome from their time-dependent disease.

5.2. COMPARISON WITH EXISTING LITERATURE

5.2.1. EMS CALLS AND EMS RESPONSE

We found that patients calling the EMS with any type of symptom or disease with any history of mental illness, to be less likely to be transported to the hospital when calling the EMS, compared to patients with no history of mental illness.[181] They were also more likely to call the EMS again within 24 hours after being given telephone advice or after being released at the scene.[181] For patients with any severity of mental illness, the proportion of patients calling the EMS again after telephone was not in accordance with the national recommendation (i.e., according to the Prehospital database less than 5% should call again with 24 hours). The proportion of patients with a history of minor, moderate or major mental calling the EMS again after telephone advise was 7%, 10% and 12%, respectively, compared to 4% among patients with not history of mental illness.

If admitted with perforated peptic ulcer, we found patients with a history of moderate or major mental illness to be less likely to be assigned an immediate EMS response, if calling the EMS (Table 4). However, if admitted with ischemic stroke, patients with or without a history of mental illness were equally likely to receive an immediate response when calling EMS (Table 4). In both patients with ischemic stroke or perforated peptic ulcer, one-third of patients called the EMS prior to hospital arrival (Table 4). We did not find significant differences between groups regarding proportions calling the EMS prior to hospital arrival (Table 4). However, the urgency, symptoms and EMS response levels differed between groups (Table 4) (discussed below).

The more frequent use of EMS services and more frequent disposition not to transport to a hospital are in accordance with other studies of equal or similar minority or

vulnerable groups (e.g., disadvantaged social position).[128, 154, 156, 215-219] Some investigators believe that this variation may be explained by a more frequent use the EMS for less urgent matters.[220-222] The use of emergency services for non-emergent situations may be addressed by health campaigns intended to change behaviours in the population or by offering alternative pathways to these groups. However, even intensive campaigns often fail to maintain behavioural changes since some patients will keep reaching out to the healthcare system through the emergency system.[149-151] This support the contradictory theories that we may miss the opportunity to assist these patient when they reach out for help, and that emergency services could be better prepared for taking care of these patients.[150, 222-226]

In high-income countries, there is an increasing demand to reduce the number of ambulance dispatches and hospital admissions by reducing 'preventable' or 'avoidable' contacts.[127, 146, 147] In this scenario, it can be seen as contradictory to define an overall 'lower utility of emergency services' as a stand-alone outcome measure, since there may already be an underuse or barriers to access high-quality medical care in these groups. Some evidence suggests that people with mental illness feel misunderstood and may be met by stigmatising behaviour from the staff[28, 224, 225, 227, 228] which may also alter the EMS response, leading to undertriage and underuse of treatment.

5.2.2. TIME FROM ONSET OF SYMPTOMS TO HOSPITAL ARRIVAL

Across studies, we found patients with different severities of mental illness to have different patterns regarding time delays from symptom onset to EMS call (patient delay) and from symptom onset to hospital arrival (combined patient and system delay) (Table 4). For both patients with ischemic stroke and perforated peptic ulcers, we found patients with a history of minor mental illness to have shorter or equal delays compared to patients with no history of mental illness (Table 4). However, patients with a history of moderate mental illness – and especially major mental illness – had significantly longer delays prior to hospital arrival (Table 4).

Across the studies included in this thesis, we found no clinically relevant differences regarding EMS delays (response times, on-scene times or transport time) for ambulances dispatched with the highest level of urgency[181] or ambulances dispatched specifically for patients with ischemic stroke. Hence, in these settings, patients were equally likely to receive high quality of prehospital emergency care.

The shorter delays in both studies among patients with minor mental illness may be explained by the fact that they were older and more comorbid, making their GP or the EMS more likely to admit them to the hospital the first time they call, as also illustrated in Study I.[181] The longer patient delays among patients with moderate or major mental illness may be due to impaired bodily sensation or disturbed perception of reality related to the mental illness of psychopharmacological treatment (discussed

below). If may also be due to their lower socioeconomic position and the fact that a larger proportion of these patients were living alone since this will contribute to lower awareness of warning symptoms.[23, 229, 230] Longer delays (both patient and system delay) prior to hospital arrival have also been described in other minority populations, i.e., racial or ethnic minorities, describing the same theories around living alone, socioeconomic position, health literacy/symptom awareness and area of recidency.[22, 125, 132, 231-233]

5.2.3. PRESENTING SYMPTOMS AND UNCLEAR PROBLEMS

In our Study I regarding all EMS patients, the five most common chief complaints were almost equally distributed between patient groups, with large proportions of patients calling with unclear problems, accidents, chest pain and dyspnoea (Table 4). However, patients with a history of major and moderate mental illness were more often registered with symptoms related to alcohol, intoxications, overdose, psychiatry-related symptoms or suicide/attempt, compared to patients with minor or no history of mental illness (Table 4). Also, patients with a history of major mental illness had the largest proportion of patients presenting with an unclear problem (Table 4). If admitted with ischemic stroke, patients with a history of major mental illness were less likely to be identified with neurological or stroke symptoms and more likely to be registered with an unclear problem (Table 4). If admitted with perforated peptic ulcer, we found patients with a history of moderate or major mental illness to be less likely to be recognised with abdominal pain (Table 4).

Unclear symptoms have been related to increased mortality in both prehospital and in-hospital settings[155, 234-236] In a Swedish study of EMS patients, unclear symptoms were more common among non-transported patients.[218] Other studies confirm our finding of patients with comorbid mental diseases having silent or unspecific symptoms even when presenting with time-dependent diseases, e.g., silent myocardial infarction and atypical presentations in surgical emergencies.[134, 135, 137-139] The reason for these unclear presentations is not well understood, but has been explained by a theory of altered pain response in patients with psychosis/patients taking antipsychotic medication combined with poor health literacy, poor communication between patient and health staff, stigma and diagnostic overshadowing.[29, 134-139]

5.2.4. EMERGENCY TREATMENT: LOWER REPERFUSION RATES AND DELAYED SURGERY

We found that patients admitted with ischemic stroke and any history of mental illness were less likely to receive reperfusion therapy. Even if arriving at the hospital within four hours, reperfusion therapy was still underutilised. According to the DSR, the national recommendation for the proportion of patients with ischemic stroke receiving reperfusion therapy was 25% in 2020.[111] This measure has developed over the past 5

years, hence in 2017 the national recommendation was 20%. However, the proportion of patients with a history of minor or major mental illness receiving reperfusion therapy in our 2016-2017-cohort was 14% and 13%, respectively, compared to 19% among patients with not history of mental illness.

Also, patients admitted with a perforated peptic ulcer and a history of major mental illness had surgery performed significantly later compared to patients with no history of mental illness. According to the DES, the national recommendation 2015-2018 was that more than 60% should be operated within 3 hours, while the 2021-recommandation is that more than 80% should be operated within 6 hours.[107] However, in our 2004-2018-cohort, only 50% of patients within no history of mental illness underwent surgery within 5.8 hours, while this was 6.5 hours for patients with a history of major mental illness.

Two US-based studies also investigated disparities in acute stroke care and found patients with comorbid mental illness to be less likely to receive cerebrovascular arteriography, carotid endarterectomy and thrombolysis.[171, 172] Reperfusion rates in ischemic stroke differ between countries.[161, 237-239] Performance on other measures of acute stroke care is also expected to vary between countries and hospitals.[237] When comparing our rates of reperfusion with the US-based study, it is notable the only 4% of patients received thrombolysis in their nationwide cohort including patients with ischemic strokes 2007-2011 compared to 17% of our population of patients with ischemic strokes received reperfusion therapy (either thrombolysis or thrombectomy) in a nationwide cohort including patients 2016-2017.

While our study seems to be the first study to report on surgical delays for patients undergoing emergency abdominal surgery with comorbid mental illness, an overall underuse of surgical intervention has been described in this polulation.[176] Disparities in the emergency setting has been investigated in other time-dependent diseases, e.g., studies of patients with cardiac arrest or myocardial infarction who are reporting lower hospitalisation rates and fewer invasive cardiac procedures among patients with comorbid mental illness compared to the general population.[140-142] Disparities in reperfusion rates have been also been described in other minority groups, e.g., racial and ethnic minorities.[125, 126]

Lower rates of reperfusion therapy for patients with ischemic stroke are likely to be related to the observed differences in time delays between groups, as described above. The longer delays from symptom onset to hospital arrival and the overall low proportion of patients calling the EMS prior to admission make the patient less likely to be eligible for reperfusion therapy, in particular i.v. thrombolysis, and may cause a higher urgency upon admission (i.e., more severe stroke or perforated peptic ulcer with shock or sepsis). Considering our findings, the decision to call the EMS seemed to be the most crucial since all patients – regardless of mental illness - had even longer delays if not calling the EMS. The longer delays among non-EMS patients have also

been found in other studies,[240] and calling the EMS is part of the clinical guidelines for early stroke management to improve outcome in ischemic stroke.[164] Both the lower reperfusion rates and delayed surgery may be related to unclear symptoms (discussed above) or stigma,[26-28, 225, 228] or treatment may be delayed due to diagnostic overshadowing (defined above).

5.2.5. EARLY STROKE CARE AND REHABILITATION

We found no clinically relevant differences regarding the provision of guideline-recommended acute stroke care during the first days of admission. Hence, on the first day of admission, patients were equally likely to have a CT/MR scan performed and receive relevant swallowing tests. Also, within the second day of admission, patients were equally likely to be assessed by an occupational therapist, a physiotherapist and to be assessed for nutritional risk factors. The only notable difference was found in mobilisation within the first day of admission. While early mobilisation is an important step towards rehabilitation and survival, the Danish standard of mobilisation on the first day of admission is ambitious. According to the national recommendations from DSR in 2020, a minimum of 85% of patients should be mobilized on the first day of admission, which is even more ambitious compared to the recommendations prior to 2018. In our cohort from 2007-2018 this proportion was 57% among patients with no history of mental illness compared to 48% among patients with a history of minor mental illness. However, patients may have been mobilised the following days. Nevertheless, this may be a weak link in the Chain of Survival. While the hospitals seem to be delivering an overall very high quality of acute stroke care during admission to the specialised stroke units, the majority of the rehabilitation is community-based (after hospital discharge). While geographical variation across the regions and municipalities may be an issue for both delayed admission and aftercare in stroke,[111, 241] investigating this was beyond the scope of this thesis.

5.2.6. RECOVERY: SHORT TERM MORTALITY AND LOST LIFE YEARS

In both ischemic stroke and perforated peptic ulcer, we found small or no differences regarding short-term mortality between patients with a history of moderate mental illness compared to patients with no history of mental illness. However, both patients with a history of minor or major mental illness had higher risks of 30-day mortality if admitted with ischemic stroke or perforated peptic ulcer. The national recommendations regarding mortality from the DSR in 2020 was a 30-mortality of less than 15%. Despite significant variation between groups (7-11%), all groups had a 30-mortality within expected range. Howe, since the national recommendations from DES in 2015-2018 was a 30-day mortality of less than 20%, both patients with a history of minor or major mental illness, had a higher 30-mortality with rates of 30% and 27%, respectively.

A chain of events is likely to lead to such disparities in outcomes. Some of the challenges interpreting these results are described above and can be related to the heterogenicity regarding baseline characteristics (e.g., age, sex, comorbidity, cohabitation and social position). While differences in outcome persisted when adjusting for age and sex, differences were less pronounced if also adjusting these estimates for factors thought to be partly caused by the mental illness itself, i.e., potential mediating factors, including physical comorbidity, stroke severity and/or ASA score.

In our cohort, patients had fewer days-alive-and-out-of-hospital at day 90 compared to a similar study of patients ongoing emergency laparotomies in the UK. I.e., in our study, the median number of days-alive-and-out-of-hospital at day 90 was 67 days (IQR, 0;83) compared to 75 days (IQR, 46;82) in the UK-study on patients admitted 2013-2017.[214] However, the UK-study included diagnosis other than perforated peptic ulcers, with an expected lower 30-mortality compared to perforated peptic ulcers alone. In another Danish cohort of all patients undergoing laparotomies, a higher mortality was also noted, when comparing mortality rates to a very similar cohort from the UK, i.e., the 30-day mortality was 19.3% from year 2003-2014 in the Danish cohort compared to 14.9% in a UK-based sample from 2010-2011 and 10% 30-day mortality from 2013-2016.[19, 188, 242] While the differences may be due to case-mix and more a complete follow up in the Danish cohorts, some variation may also be due to less standardised care. This is suggested, since we find a decreasing mortality over time, i.e., a median of 77 days (IQR, 10;84) alive-and-out-of-hospital in out subgroups of patients admitted 2016-2018. This is possibly as a result of several quality improvement initiatives implemented and still ongoing in Denmark within this field.[100, 188]

Worse outcome after emergency surgery or ischemic stroke is well-described among patients with major mental illness compared to the general population.[137, 139, 165, 166, 168, 170, 177-179] Further, lost life years and excess mortality has been described across the entire spectrum of mental illness considering any-cause mortality over a lifetime.[8, 205, 243] A complex interplay between patient, healthcare system and society is likely to cause these differences.[8, 12] While we did not find lost life days among patients with a history of moderate mental illness 90 days after emergency surgery for perforated peptic ulcers, our finding of lost life days among patients with a history of major mental illness is remarkable and concerning.

5.3. METHODOLOGY

All studies in this thesis used an observational design to investigate the association between a history of mental illness and the quality and outcome of emergency care in Denmark. The use of an observational design requires thorough methodological considerations as systematic or random errors may affect the results. Only after

considering the limitations, an overall conclusion can be drawn. The internal validity will be discussed in the following sections.

5.3.1. SELECTION BIAS

Selection bias can error during the process of deciding who is going to be studied, and if some factors influence the continued participation in a study (i.e., loss to follow-up). Bias will occur if the selection probabilities of exposed and unexposed are differential and not proportional from the target population or if outcome is different for those who complete a study compared with those who are in the target population. The consequences of selection bias are that the sample selection does not accurately reflect the target population.

All four studies used a population-based design. Identification of the study populations and the majority of the process and outcome measures was based on data from the Danish Clinical Registries. Reporting to the Clinical Registries is mandatory for hospitals as well as the EMS. The coverage of the registers is high, i.e., 89% for the Emergency Surgery Registry[107] and 94% for the Danish Stroke Registry[111], but has not been described for the Prehospital Database. The other outcome measures regarding e.g., hospital admissions and death collected from the Danish National Patient Registry and the Danish Civil Registration System has been described in section 3.3.2. The very high completeness of both the clinical registries and the national database limited the risk of selection bias and ensure a very number of low loss-to-follow up. The majority of missing data in the clinical registries is thought be proportional if the target population is considered to be hospitalised patients. However, if the target population is considered to be all patients with e.g., ischemic stroke or perforated peptic ulcer, our estimates will not be valid for the target population since patients with mental illness may be more likely to have undetected events of stroke[130], an underuse of surgery[176] and worse outcome.

Also, other reasons for selection may have occurred in all four studies. In Study I regarding EMS patients, selection bias may have been introduced since data from the EMS is incomplete, with 17% of EMS calls is not registered with a valid CPR-number. A missing CPR-number was more common, if only telephone advice was given, and in cases with lower acuity. The patients included in the study may not be proportional with the study population since patients with a history of mental illness may be more likely to call with presumed low-acuity symptoms, which makes the proportion of patients with mental illness more likely not to be registered with a CPR number.

There may be a special concern, that homeless people have been excluded from our analyses in all four studies. In Study I this may have occurred if homeless people are also more likely to not be registered with a valid CPR number. Also, in study II-III-IV 1-4% of the population was excluded due a non-valid CPR or if the patients were

not living in Denmark at the time of admission. Mental illness is associated with homelessness, and homelessness is associated with poor outcome in e.g., stoke care[244] this may be not be proportional with the target population and therefore cause selection bias.

5.3.2. INFORMATION BIAS

Information bias can occur due to a lack of accurate measurements of key variables, i.e., if exposure, outcome, or confounders are inaccurately measured or classified. This will cause a distortion of the estimates measuring the association between exposure and outcome.

All four studies used the same definition of the four exposure groups regarding mental illness. The criteria are related to national recommendations of management of the increasing severities of mental illness, and have been thoroughly described in section 3.4 (Figure 8). Supplementary table S2 provides an example from Study III on how recent the mental health disease-related activity was in each group. By using the Danish National Patient Registry to define our two exposure groups (major and moderate), the risk of misclassification is relatively low, due to accuracy of the national databases. However, the validity of psychiatric diagnoses have not been described, there may be the same type of variation in registration practice among hospital departments and over time, as described for non-psychiatric diagnoses.[202] Also, even severe cases of mental illness may be missed, if patients to not consult a healthcare professional with their symptoms. Further, the definition of the minor group is based on information from other registries, i.e., redeemed prescription and primary cases services. Especially the coding of GP-services may be prone to misclassification, since this data is used for administrative and financial purpures, and the definition of codes and services may dependent on the individual GP as well as political priorities. Especially by including GP-services and psychologist servicers, our definition of minor mental illness may express a state of mental vulnerability rather than mental illness. The potential misclassifications our exposures are most likely nondifferential since the misclassification is expected independent of our outcome. Bias due to nondifferential misclassification is predictable in direction toward or beyond the null value leading to an underestimation of the true association.

Regarding misclassification of the process measures and outcome measures from the clinical registries, some local, and unpublished audits find up to 10% misclassification of the process measures. While the Prehospital Database is entirely based on existing electronic and administrative data, both the Stroke Registry and Emergency Surgery Registry required manual registration of process and outcome measures in the study period. Written instructions are available for reporting of the data. Furthermore, regional and national audits are carried out at a minimum of once a year to ensure the validity of the data. Intentional misclassification (‘gaming’) of the fulfilment of the process performance measure is, however, a possibility because of the public

disclosure of the annual reports, which often is used to benchmark hospitals. Nevertheless, misclassification from gaming or other less intentional reasons are most likely unrelated to our exposure. Bias due to nondifferential misclassification is predictable in direction toward or beyond the null value leading to an underestimation of the true association.

Lastly, our outcome regarding mortality is based on data from the Danish Civil Registration Registry with a very high validity. Hence misclassification of the outcome regarding mortality is expected to be very low.

5.3.3. CONFOUNDING AND MEDIATION

Confounding is a concern in all observational studies; therefore, attention of measured and unmeasured (e.g., residual) confounders is needed. Some potential confounders were adjusted for, such as age, sex and country of origin. These factors are all associated to our outcome (e.g., risk of death), and were unequally distributed between groups. However, they are not mediators of our outcome (e.g., mental illness cannot influence on the patient's sex, age of country of origin, which will than lead to a higher risk of death).

In some analyses we adjusted for factors that are more likely to be mediators rather than confounders, such as physical comorbidity, stroke severity or ASA score (e.g., it is well-known that mental illness is causing higher burden of physical comorbidities, higher stroke severity and higher ASA score, which will lead to a higher risk of death). Hence, some adjusted estimates may have been over-adjusted, i.e., the effect of the exposure on the outcome was limited when adjusting for the mediating path.

Further, several factors, such as socioeconomic position, cohabitation, substance abuse and smoking, may be associated with both mental illness and the examined outcomes, however, they were not adjusted for in the analyses as they were considered to primarily be mediators of the association between mental illness and outcome of emergency care.

In all four studies, unmeasured confounding and unmeasured biasing paths due to mediating factors are expected due to e.g., stigma, homelessness and health literacy/awareness of symptoms. In Study I regarding EMS patients, no data was available regarding disease severity (other than dispatched level of urgency) which is an important factor when deciding the correct EMS response. I.e., information on vital signs, prehospital assessment and treatment could have provided valuable information. In Study II-IV no other lifestyle factors than smoking and substance abuse were available. However, both BMI and physical activity are important factors when considering i.e., risk of recurrent stroke. Residual confounding due to unknown or unmeasured risk factors may also exist in all four studies.

5.3.4. PRECISION

In general, due to the high number of subjects in each study, our estimates come with narrow confidence intervals and have high precision. However, a type I error (finding no difference, where the is an actual difference) may have occurred in e.g., Study III with the very high number of study subjects. However, some estimates, especially in study IV, may be imprecise due to subgroup analyses (e.g., low number of patients with a history of moderate mental illness calling the EMS prior to admission with perforated peptic ulcer in 2016-2017). This causes lower precision of our estimates and may also have caused a type II-error (finding a difference, where this is no actual difference).

5.4. EXTERNAL VALIDITY

When considering the generalisability of our results, the unique Scandinavian tax-financed healthcare setting and the limited distances from the urban cities to the most rural areas in Denmark must be considered. Hence, our results may not be generalized to countries with other barriers to healthcare (e.g., insurance status and geography), other types of healthcare setting (low-income countries) or exceptional circumstances (war, natural disaster, extreme poverty). However, if disparities in emergency care exits in countries with free access to healthcare and high performance, we may have a special concern that countries with barriers to care may have even greater challenges in delivering equity in healthcare. Also, considering the interdependence between mental health and social position, we may have a special concern, that other countries may experience an even greater underuse of advanced technologies and a worse outcome, compared to more advantaged groups.[21, 22, 116, 126, 129, 131, 132] Further, the definition of our exposure groups (especially patients with a minor history of mental illness) is based on data from the primary healthcare system. Other countries with different setups with more liberal or more restrictive access to e.g., benzodiazepines or psychologist referrals may not be able to generalise our results regarding patients with a minor history of mental illness.

CHAPTER 6. CONCLUSION

The aim of this thesis was to investigate if a history of mental illness is associated with the quality of emergency care. Further to explore unwanted variation in each link in the Chain of Survival. In conclusion we found several weak links, but also a few strong links.

Symptom recognition and activation of the system may be a specific challenge for patients with a history of mental illness. Only one-third of patients called the EMS prior to admission with ischemic stroke or perforated peptic ulcer. Patients with a history of major mental illness had longer delays from symptom onset to hospital arrival compared to patients with no history of mental illness. This may be due to a combination of poor symptom recognition, difficulties in activating the system, not having a bystander and having a disadvantaged social position.

Regarding system response, we found that patients with a history of moderate or major mental illness were more likely to receive telephone advice only or be released at scene, if calling the EMS. Also, they were more likely to call the EMS again if given telephone advise. There may be specific challenges for patients with mental illnesses in activating the system and getting a helpful response. Some of this variation may be explained by that fact, that patients with a history of moderate of major mental illness were more likely to call the EMS with unclear problems and more likely to be recognized with atypical symptoms of their time-dependent disease. However, if assigned the highest level of urgency, the ambulance response times, on-scene times and transport times did not differ between groups.

Regarding emergency treatment and advanced care, patients with a history of mental illness showed a consistent tendency to be less likely to receive reperfusion therapy if admitted with ischemic stroke. Also, patients with a history of major mental illness had longer delays from hospital arrival to surgery, compared to patients with no history of mental illness. This may be due to longer patient delays prior to hospital arrival causing a higher urgency of disease upon arrival. These factors combined with a higher burden of co-morbidities, higher proportion of atypical presentations and a higher proportion of substance abuse may challenge the diagnostic process. It may also create a need for stabilization and extended preoperative management, which will delay treatment. However, time-to-imaging and time-to-thrombolysis did not differ between groups. Also, the quality of early stroke care was equally high in all groups.

Regarding recovery, a history of mental illness was associated with worse clinical outcome after ischemic stroke or perforated peptic ulcer compared to patients without a history of mental illness. This may at least partly be due to a more adverse prognostic profile at the time of admission, including a higher disease severity.

CHAPTER 7. PERSPECTIVES

The findings in this thesis suggest disparities in the quality of emergency care across time-dependent diseases among patients with mental illness in Denmark. It also highlights the impact of mental illness on the outcome after emergency care and the contribution of emergency diseases the excess mortality described in this population. Unfortunately, our findings only contribute to the extensive literature regarding excess mortality and disparities in health and healthcare among patients with mental illness. Considering the Chain of Survival, our detailed data regarding patient characteristics, delays, emergency treatment, advanced care and outcome, can be used to design tailored interventions to improve emergency care for these patients. Further research is needed to design and evaluate these interventions.

Recognising symptoms

Our findings regarding longer patient delays and unclear symptoms combined with an unfavourable social position, living alone and having a substance abuse, call for interventions in the society to support this vulnerable groups.

- Population-level interventions could be increasing support from lay-persons in emergency situations. This may be improved by addressing stigma towards persons with mental illness in our society.
- Group-level interventions could be training of relatives, social workers, primary-healthcare workers and staff at housing facilities in recognising symptoms of physical illness and acting accordingly.
- Group-level interventions could be empowerment of persons with mental illness, who should be encouraged to reach out for help, when feeling unwell.

Activating the system

Our findings regarding the low proportion of patients calling the EMS prior to admission with a time-dependent disease is concerning. National campaigns have been conducted to increase the proportion of patients calling the EMS, if experiencing e.g., stroke symptoms. Other campaigns have been targeting the overuse of EMS and out-of-hour GPs, aiming to decrease the number of calls, and only calling if being severely ill or injured.

- Group-level interventions could be tailored interventions and campaigns improving knowledge about emergency symptoms and opportunities for action targeting the most disadvantaged groups and neighbourhoods in our society.

System response, early treatment and advanced care

Our finding regarding patients with a history of mental illness receiving a lighter EMS-response has highlighted a potential access problem to ambulances and hospital admissions through the EMS. When calling the EMS, the GP or out-of-hour GP will

handle all calls very professionally. However, national political and economic incitive may disturb or limit the services available. Obviously, no societies have endless funds, and the increasing demand for hospital admissions due to the change in demographics, must be met by political action. Our finding of less frequent use of reperfusion therapy and delayed surgery is a major finding. While the contribution of late hospital arrival, atypical symptoms and higher urgency of disease has also been mentioned, the role of stigma must be explored.

- Population-level interventions could be redesigning healthcare using co-design and involving patients and service users throughout the process. Using co-design may be a longer process, but a safer way to change the healthcare system, rather than defining short-term outcomes related to utility and so-called 'avoidable contacts'. Instead of letting a patient call the EMS 123 times per year, we may want to ask how we can assist this patient towards relief or recovery.
- Group-level interventions could be conducting research in patient presentations of time-dependent diseases and implementation of training of healthcare staff in atypical presentation and interventions targeting stigma.

Recovery

The importance of addressing excess mortality and disparities among patients with mental illness can no longer be discussed. While it is already a part of the national goals in the Danish National Quality Programme, measures of disparities are still being developed within the Clinical Registries. Considering the contribution of time-dependent diseases to the over-all excess mortality, we may want to handle the contribution of chronic and emergency diseases separately.

- Population-level interventions could be demanding the political reforms to support the recommendations from the Danish Health Authority and White Paper from the Danish Society for Psychiatry.
- Population-level interventions could be development of wise measures of disparities, quality of health care and effect of health care services to continuously evaluate interventions within the field. This includes system-level evidence-based measures of structure, process and outcome, as well as further development of PROM and PREM. A transformation to higher value, lower cost care is dependent on the ability of healthcare systems to leverage data that drive improvements in patient care and population health. Based on this thesis, measures within the clinical registries and the Danish National Quality Programme should be revised to capture variation and support quality improvement within this field.

REFERENCES

1. Danskernes sundhed - den nationale sundhedsprofil 2021 [the national health profile 2021]. 2022
2. Pedersen CB, Mors O, Bertelsen A, Waltoft BL, Agerbo E, McGrath JJ, et al. A comprehensive nationwide study of the incidence rate and lifetime risk for treated mental disorders. *JAMA Psychiatry*. 2014;71:573-581
3. Huijts T, Stornes P, Eikemo TA, Bambra C, HiNews C. Prevalence of physical and mental non-communicable diseases in europe: Findings from the european social survey (2014) special module on the social determinants of health. *Eur J Public Health*. 2017;27:8-13
4. Hvidberg MF, Johnsen SP, Davidsen M, Ehlers L. A nationwide study of prevalence rates and characteristics of 199 chronic conditions in denmark. *Pharmacoecon Open*. 2019
5. Collaborators GBDMD. Global, regional, and national burden of 12 mental disorders in 204 countries and territories, 1990-2019: A systematic analysis for the global burden of disease study 2019. *Lancet Psychiatry*. 2022;9:137-150
6. World psychiatric association. Https://www.Wpanet.Org/public-mental-health [access latest june 22nd 2022].2022
7. Diseases GBD, Injuries C. Global burden of 369 diseases and injuries in 204 countries and territories, 1990-2019: A systematic analysis for the global burden of disease study 2019. *Lancet*. 2020;396:1204-1222
8. Plana-Ripoll O, Pedersen CB, Agerbo E, Holtz Y, Erlangsen A, Canudas-Romo V, et al. A comprehensive analysis of mortality-related health metrics associated with mental disorders: A nationwide, register-based cohort study. *Lancet*. 2019;394:1827-1835
9. Rosenbaum L. Closing the mortality gap - mental illness and medical care. *N Engl J Med*. 2016;375:1585-1589
10. Dansk psykiatrisk selskab - hvidbog 2021-2031 [danish society for psychiatry - white paper 2021-2031]. 2021
11. Firth J, Siddiqi N, Koyanagi A, Siskind D, Rosenbaum S, Galletly C, et al. The lancet psychiatry commission: A blueprint for protecting physical health in people with mental illness. *Lancet Psychiatry*. 2019;6:675-712
12. Liu NH, Daumit GL, Dua T, Aquila R, Charlson F, Cuijpers P, et al. Excess mortality in persons with severe mental disorders: A multilevel intervention framework and priorities for clinical practice, policy and research agendas. *World psychiatry : official journal of the World Psychiatric Association*. 2017;16:30-40
13. OECD. A new benchmark for mental health systems. 2021
14. WHO/OECD/WorldBank. Delivering quality health services: A global imperative for universal health coverage. 2018

15. Plana-Ripoll O, Weye N, Momen NC, Christensen MK, Iburg KM, Laursen TM, et al. Changes over time in the differential mortality gap in individuals with mental disorders. *JAMA Psychiatry*. 2020
16. Erlangsen A, Andersen PK, Toender A, Laursen TM, Nordentoft M, Canudas-Romo V. Cause-specific life-years lost in people with mental disorders: A nationwide, register-based cohort study. *Lancet Psychiatry*. 2017;4:937-945
17. Eugene N, Oliver CM, Bassett MG, Poulton TE, Kuryba A, Johnston C, et al. Development and internal validation of a novel risk adjustment model for adult patients undergoing emergency laparotomy surgery: The national emergency laparotomy audit risk model. *Br J Anaesth*. 2018;121:739-748
18. Hasselager RB, Lohse N, Duch P, Moller MH. Risk factors for reintervention after surgery for perforated gastroduodenal ulcer. *Br J Surg*. 2016;103:1676-1682
19. Poulton TE, Moonesinghe R, Raine R, Martin P, National Emergency Laparotomy Audit project t. Socioeconomic deprivation and mortality after emergency laparotomy: An observational epidemiological study. *Br J Anaesth*. 2020;124:73-83
20. Avan A, Digaleh H, Di Napoli M, Stranges S, Behrouz R, Shojaeianbabaei G, et al. Socioeconomic status and stroke incidence, prevalence, mortality, and worldwide burden: An ecological analysis from the global burden of disease study 2017. *BMC medicine*. 2019;17:191
21. Elfassy T, Grasset L, Glymour MM, Swift S, Zhang L, Howard G, et al. Sociodemographic disparities in long-term mortality among stroke survivors in the united states. *Stroke*. 2019;50:805-812
22. Hyldgard VB, Johnsen SP, Stovring H, Sogaard R. Socioeconomic status and acute stroke care: Has the inequality gap been closed? *Clinical epidemiology*. 2019;11:933-941
23. Iversen AB, Blauenfeldt RA, Johnsen SP, Sandal BF, Christensen B, Andersen G, et al. Understanding the seriousness of a stroke is essential for appropriate help-seeking and early arrival at a stroke centre: A cross-sectional study of stroke patients and their bystanders. *Eur Stroke J*. 2020;5:351-361
24. OECD/EU. Health at a glance: Europe 2016 – state of health in the eu cycle. 2016
25. De Hert M, Correll CU, Bobes J, Cetkovich-Bakmas M, Cohen DAN, Asai I, et al. Physical illness in patients with severe mental disorders. I. Prevalence, impact of medications and disparities in health care. *World psychiatry : official journal of the World Psychiatric Association*. 2011;10:52-77
26. McBride KE, Solomon MJ, Steffens D, Bannon PG, Glozier N. Mental illness and surgery: Do we care? *ANZ J Surg*. 2019;89:630-631
27. McBride KE, Solomon MJ, Lambert T, O'Shannassy S, Yates C, Isbester J, et al. Surgical experience for patients with serious mental illness: A qualitative study. *BMC Psychiatry*. 2021;21:47

28. Solvhoj IN, Kusier AO, Pedersen PV, Nielsen MBD. Somatic health care professionals' stigmatization of patients with mental disorder: A scoping review. *BMC Psychiatry*. 2021;21:443
29. van Nieuwenhuizen A, Henderson C, Kassam A, Graham T, Murray J, Howard LM, et al. Emergency department staff views and experiences on diagnostic overshadowing related to people with mental illness. *Epidemiol Psychiatr Sci*. 2013;22:255-262
30. Sundhedsstyrelsen - fagligt oplæg til en 10-årsplan: Bedre mental sundhed og en styrket indsats til mennesker med psykiske lidelser [danish health authorities - 10-year plan - improving mental health and inproveing care for pateints with mental illnesses]. 2022
31. Dansk psykiatrisk selskab. Gør psykiatrien rask - politisk behandlingsplan for psykiatrien. [danish society for psychiatry. Cure the psychiatric system - action plan for political interventions]. 2021;2022
32. Uggerby C, Kristensen S, Mackenhauer J, Knudsen SV, Bartels P, Johnsen SP, et al. From accreditation to quality improvement-the danish national quality programme. *International journal for quality in health care : journal of the International Society for Quality in Health Care / ISQua*. 2021;33
33. Baandrup L, Cerqueira C, Haller L, Korshoj L, Voldsgaard I, Nordentoft M. The danish schizophrenia registry. *Clinical epidemiology*. 2016;8:691-695
34. Videbech P, Deleuran A. The danish depression database. *Clinical epidemiology*. 2016;8:475-478
35. Reynolds TA, Sawe H, Rubiano AM, Shin SD, Wallis L, Mock CN. Strengthening health systems to provide emergency care. In: rd, Jamison DT, Gelband H, Horton S, Jha P, Laxminarayan R, et al., eds. *Disease control priorities: Improving health and reducing poverty*. Washington (DC); 2017.
36. Burkholder TW, Hill K, Calvello Hynes EJ. Developing emergency care systems: A human rights-based approach. *Bull World Health Organ*. 2019;97:612-619
37. What is em? European society for emergency medicine (eusem). Https://eusem.Org/about-us/emergency-medicine/what-is-em [access latest june 22nd 2022]. 2017
38. Razzak J, Usmani MF, Bhutta ZA. Global, regional and national burden of emergency medical diseases using specific emergency disease indicators: Analysis of the 2015 global burden of disease study. *BMJ Glob Health*. 2019;4:e000733
39. Cummins RO, Ornato JP, Thies WH, Pepe PE. Improving survival from sudden cardiac arrest: The "chain of survival" concept. A statement for health professionals from the advanced cardiac life support subcommittee and the emergency cardiac care committee, american heart association. *Circulation*. 1991;83:1832-1847
40. Merchant RM, Topjian AA, Panchal AR, Cheng A, Aziz K, Berg KM, et al. Part 1: Executive summary: 2020 american heart association guidelines

for cardiopulmonary resuscitation and emergency cardiovascular care. *Circulation*. 2020;142:S337-S357

41. Adams HP, Jr., del Zoppo G, Alberts MJ, Bhatt DL, Brass L, Furlan A, et al. Guidelines for the early management of adults with ischemic stroke: A guideline from the american heart association/american stroke association stroke council, clinical cardiology council, cardiovascular radiology and intervention council, and the atherosclerotic peripheral vascular disease and quality of care outcomes in research interdisciplinary working groups: The american academy of neurology affirms the value of this guideline as an educational tool for neurologists. *Stroke*. 2007;38:1655-1711
42. Rivers EP, Coba V, Visbal A, Whitmill M, Amponsah D. Management of sepsis: Early resuscitation. *Clin Chest Med*. 2008;29:689-704, ix-x
43. Cdc - national hospital ambulatory medical care survey - emergency department summary tables (table 24). Https://www.Cdc.Gov/nchs/ahcd/web_tables.Htm [access latest june 22nd 2022]. 2018
44. Rkkp årsrapport databasen for akutte hospitalskontakter [danish clinical registries - danish database for emergency hospital contacts - annual report]. 2020
45. Gregersen R, Fox Maule C, Husum Bak-Jensen H, Linneberg A, Nielsen OW, Thomsen SF, et al. Profiling bispebjerg acute cohort: Database formation, acute contact characteristics of a metropolitan hospital, and comparisons to urban and rural hospitals in denmark. *Clinical epidemiology*. 2022;14:409-424
46. Christensen EF, Larsen TM, Jensen FB, Bendtsen MD, Hansen PA, Johnsen SP, et al. Diagnosis and mortality in prehospital emergency patients transported to hospital: A population-based and registry-based cohort study. *BMJ open*. 2016;6
47. Pines JM, Hilton JA, Weber EJ, Alkemade AJ, Al Shabanah H, Anderson PD, et al. International perspectives on emergency department crowding. *Acad Emerg Med*. 2011;18:1358-1370
48. Colligan EM, Pines JM, Colantuoni E, Howell B, Wolff JL. Risk factors for persistent frequent emergency department use in medicare beneficiaries. *Ann Emerg Med*. 2016;67:721-729
49. Uscher-Pines L, Pines J, Kellermann A, Gillen E, Mehrotra A. Emergency department visits for nonurgent conditions: Systematic literature review. *The American journal of managed care*. 2013;19:47-59
50. Higginson I, Kehoe A, Whyatt J, Smith JE. The 4-hour standard is a meaningful quality indicator: Correlation of performance with emergency department crowding. *Eur J Emerg Med*. 2017;24:25-28
51. Ngo H, Forero R, Mountain D, Fatovich D, Man WN, Sprivulis P, et al. Impact of the four-hour rule in western australian hospitals: Trend analysis of a large record linkage study 2002-2013. *PLoS One*. 2018;13:e0193902
52. Cooke MW, Higgins J, Kidd P. Use of emergency observation and assessment wards: A systematic literature review. *Emerg Med J*. 2003;20:138-142

53. Scott I, Vaughan L, Bell D. Effectiveness of acute medical units in hospitals: A systematic review. *International journal for quality in health care : journal of the International Society for Quality in Health Care / ISQua*. 2009;21:397-407
54. Sundhedsstyrelsen. Sygdomsbyrden i danmark [burden of disease in denmark]. 2015
55. Christensen EF, Bendtsen MD, Larsen TM, Jensen FB, Lindskou TA, Holdgaard HO, et al. Trends in diagnostic patterns and mortality in emergency ambulance service patients in 2007-2014: A population-based cohort study from the north denmark region. *BMJ open*. 2017;7:e014508
56. Flojstrup M, Bogh SB, Henriksen DP, Bech M, Johnsen SP, Brabrand M. Increasing emergency hospital activity in denmark, 2005-2016: A nationwide descriptive study. *BMJ open*. 2020;10:e031409
57. Sundhedsstyrelsen. Anbefalinger for organisering af den akutte sundhedsindsats [danish health authorities. Recommandations for the organization of the emergency care system]. 2020
58. Sundhedsstyrelsen. Styrket akutberedskab - et nyt planlægningsgrundlag for det regionale akutberedskab [danish health authorities. Improving emergency care - planning emerency care on a regional level]. 2007
59. Moellekaer A, Duvald I, Obel B, Madsen B, Eskildsen J, Kirkegaard H. The organization of danish emergency departments. *Eur J Emerg Med*. 2019;26:295-300
60. Bogh SB, Flojstrup M, Moller S, Bech M, Johnsen SP, Henriksen DP, et al. Intended and unintended changes in length of stay following reconfiguration of emergency care departments. *International journal for quality in health care : journal of the International Society for Quality in Health Care / ISQua*. 2021;33
61. Winther J. Fremtidens akutbetjening. *Ugeskr Laeger*. 2005;20
62. Sundhedsstyrelsen. Vurdering af den akut medicinske indsats i danmark. 2005
63. MacKenzie EJ, Rivara FP, Jurkovich GJ, Nathens AB, Frey KP, Egleston BL, et al. A national evaluation of the effect of trauma-center care on mortality. *N Engl J Med*. 2006;354:366-378
64. Durham R, Pracht E, Orban B, Lottenburg L, Tepas J, Flint L. Evaluation of a mature trauma system. *Ann Surg*. 2006;243:775-783; discussion 783-775
65. Andersen HR, Nielsen TT, Rasmussen K, Thuesen L, Kelbaek H, Thayssen P, et al. A comparison of coronary angioplasty with fibrinolytic therapy in acute myocardial infarction. *N Engl J Med*. 2003;349:733-742
66. Jakobsen L, Niemann T, Pedersen NT, Nielsen TT, Johnsen SP. Comparison of primary percutaneous coronary intervention in real-world populations versus clinical trial populations. *Am J Cardiol*. 2010;105:1684-1691
67. Bray BD, Campbell J, Cloud GC, Hoffman A, Tyrrell PJ, Wolfe CD, et al. Bigger, faster? Associations between hospital thrombolysis volume and

speed of thrombolysis administration in acute ischemic stroke. *Stroke*. 2013;44:3129-3135
68. Langhorne P, Ramachandra S, Stroke Unit Trialists C. Organised inpatient (stroke unit) care for stroke: Network meta-analysis. *Cochrane Database Syst Rev*. 2020;4:CD000197
69. Wahlgren N, Ahmed N, Eriksson N, Aichner F, Bluhmki E, Davalos A, et al. Multivariable analysis of outcome predictors and adjustment of main outcome results to baseline data profile in randomized controlled trials: Safe implementation of thrombolysis in stroke-monitoring study (sits-most). *Stroke*. 2008;39:3316-3322
70. Shahin J, Harrison DA, Rowan KM. Relation between volume and outcome for patients with severe sepsis in united kingdom: Retrospective cohort study. *BMJ*. 2012;344:e3394
71. Kristensen PK, Thillemann TM, Johnsen SP. Is bigger always better? A nationwide study of hip fracture unit volume, 30-day mortality, quality of in-hospital care, and length of hospital stay. *Medical care*. 2014;52:1023-1029
72. WHO/OECD. Improving healthcare quality in europe: Characteristics, effectiveness and implementation of different strategies. 2019
73. Berwick DM. Avoiding overuse-the next quality frontier. *Lancet*. 2017;390:102-104
74. Elshaug AG, Rosenthal MB, Lavis JN, Brownlee S, Schmidt H, Nagpal S, et al. Levers for addressing medical underuse and overuse: Achieving high-value health care. *Lancet*. 2017;390:191-202
75. Kleinert S, Horton R. From universal health coverage to right care for health. *Lancet*. 2017;390:101-102
76. Donabedian A. The quality of care. How can it be assessed? *JAMA*. 1988;260:1743-1748
77. Donabedian A. Evaluating the quality of medical care. *The Milbank Memorial Fund quarterly*. 1966;44:Suppl:166-206
78. Sundhedsstyrelsen. Specialeplan for neurologi [danish health authorities. Speciality planning neurology]. 2020
79. Kara P, Valentin JB, Mainz J, Johnsen SP. Composite measures of quality of health care: Evidence mapping of methodology and reporting. *PLoS One*. 2022;17:e0268320
80. Austin E, LeRouge C, Hartzler AL, Segal C, Lavallee DC. Capturing the patient voice: Implementing patient-reported outcomes across the health system. *Quality of life research : an international journal of quality of life aspects of treatment, care and rehabilitation*. 2020;29:347-355
81. The royal college of emergency medicine (rcem). Improving quality indicators and system metrics for emergency departments in england. 2019
82. Coleman P, Nicholl J. Consensus methods to identify a set of potential performance indicators for systems of emergency and urgent care. *J Health Serv Res Policy*. 2010;15 Suppl 2:12-18
83. Schull MJ, Guttmann A, Leaver CA, Vermeulen M, Hatcher CM, Rowe BH, et al. Prioritizing performance measurement for emergency department

care: Consensus on evidence-based quality of care indicators. *CJEM*. 2011;13:300-309, E328-343
84. Cameron PA, Schull MJ, Cooke MW. A framework for measuring quality in the emergency department. *Emerg Med J*. 2011;28:735-740
85. Schuur JD, Hsia RY, Burstin H, Schull MJ, Pines JM. Quality measurement in the emergency department: Past and future. *Health Aff (Millwood)*. 2013;32:2129-2138
86. Madsen MM, Eiset AH, Mackenhauer J, Odby A, Christiansen CF, Kurland L, et al. Selection of quality indicators for hospital-based emergency care in denmark, informed by a modified-delphi process. *Scandinavian journal of trauma, resuscitation and emergency medicine*. 2016;24:11
87. Hruska K, Castren M, Banerjee J, Behringer W, Bjornsen LP, Cameron P, et al. Template for uniform reporting of emergency department measures, consensus according to the utstein method. *Eur J Emerg Med*. 2019;26:417-422
88. Yiadom M, Napoli A, Granovsky M, Parker RB, Pilgrim R, Pines JM, et al. Managing and measuring emergency department care: Results of the fourth emergency department benchmarking definitions summit. *Acad Emerg Med*. 2020;27:600-611
89. Morris S, Ramsay AIG, Boaden RJ, Hunter RM, McKevitt C, Paley L, et al. Impact and sustainability of centralising acute stroke services in english metropolitan areas: Retrospective analysis of hospital episode statistics and stroke national audit data. *BMJ*. 2019;364:l1
90. Asplund K, Sukhova M, Wester P, Stegmayr B, Riksstroke C. Diagnostic procedures, treatments, and outcomes in stroke patients admitted to different types of hospitals. *Stroke*. 2015;46:806-812
91. Salinas J, Sprinkhuizen SM, Ackerson T, Bernhardt J, Davie C, George MG, et al. An international standard set of patient-centered outcome measures after stroke. *Stroke*. 2016;47:180-186
92. Vaillancourt S, Cullen JD, Dainty KN, Inrig T, Laupacis A, Linton D, et al. Prom-ed: Development and testing of a patient-reported outcome measure for emergency department patients who are discharged home. *Ann Emerg Med*. 2020;76:219-229
93. van Oppen JD, Alshibani A, Coats TJ, Graham B, Holch P, Lalseta J, et al. A systematic review and recommendations for prom instruments for older people with frailty in emergency care. *J Patient Rep Outcomes*. 2022;6:30
94. Bertoli-Avella AM, Haagsma JA, Van Tiel S, Erasmus V, Polinder S, Van Beeck E, et al. Frequent users of the emergency department services in the largest academic hospital in the netherlands: A 5-year report. *Eur J Emerg Med*. 2017;24:130-135
95. Shy BD, Loo GT, Lowry T, Kim EY, Hwang U, Richardson LD, et al. Bouncing back elsewhere: Multilevel analysis of return visits to the same or a different hospital after initial emergency department presentation. *Ann Emerg Med*. 2018;71:555-563 e551

96. Shy BD, Shapiro JS, Shearer PL, Genes NG, Clesca CF, Strayer RJ, et al. A conceptual framework for improved analyses of 72-hour return cases. *Am J Emerg Med*. 2015;33:104-107
97. Lassen AT, Jorgensen H, Jorsboe HB, Odby A, Brabrand M, Steinmetz J, et al. The danish database for acute and emergency hospital contacts. *Clinical epidemiology*. 2016;8:469-474
98. Christensen EF, Berlac PA, Nielsen H, Christiansen CF. The danish quality database for prehospital emergency medical services. *Clinical epidemiology*. 2016;8:667-671
99. Johnsen SP, Ingeman A, Hundborg HH, Schaarup SZ, Gyllenborg J. The danish stroke registry. *Clinical epidemiology*. 2016;8:697-702
100. Moller MH, Larsson HJ, Rosenstock S, Jorgensen H, Johnsen SP, Madsen AH, et al. Quality-of-care initiative in patients treated surgically for perforated peptic ulcer. *Br J Surg*. 2013;100:543-552
101. Kristensen PK, Rock ND, Christensen HC, Pedersen AB. The danish multidisciplinary hip fracture registry 13-year results from a population-based cohort of hip fracture patients. *Clinical epidemiology*. 2020;12:9-21
102. Danish cardiac arrest registry. Https://hjertestopregister.Dk/?Page_id=428 [access last june 22nd 2022].
103. Schmidt M, Maeng M, Madsen M, Sorensen HT, Jensen LO, Jakobsen CJ. The western denmark heart registry: Its influence on cardiovascular patient care. *J Am Coll Cardiol*. 2018;71:1259-1272
104. Rkkp - danarrest [danish clinical registries - danarrest].
105. Rkkp - årsrapport - hjerteregisteret [danish clinical registries - annual report - danish heart registry]. 2020
106. Aggarwal G, Peden CJ, Mohammed MA, Pullyblank A, Williams B, Stephens T, et al. Evaluation of the collaborative use of an evidence-based care bundle in emergency laparotomy. *JAMA Surg*. 2019;154:e190145
107. Rkkp årsrapport akut kirurgi databasen [danish clinical registries - annual report - registry for emergency surgery].
108. Rkkp - årsrapport - præhospitaldatabsen [danish clinical registries - annual report - prehospital database]. 2020
109. Årsrapport vestdansk hjertedatabase [annual report - western danish heart registry]. 2012
110. Årsrapport vestdansk hjertedatabase [annual report western danish heart registry]. 2010
111. Rkkp årsrapport apopleksidatabasen [danish clinical registries - annual report - danish stroke registry].
112. Diderichsen F, Andersen I, Manuel C, Working Group of Danish Review on Social Determinants of H, Andersen AM, Bach E, et al. Health inequality--determinants and policies. *Scandinavian journal of public health*. 2012;40:12-105
113. Marmot M. Fair society, healthy lives the marmot review. 2010
114. Hood CM, Gennuso KP, Swain GR, Catlin BB. County health rankings: Relationships between determinant factors and health outcomes. *Am J Prev Med*. 2016;50:129-135

115. Diderichsen F, Hallqvist J, Whitehead M. Differential vulnerability and susceptibility: How to make use of recent development in our understanding of mediation and interaction to tackle health inequalities. *Int J Epidemiol*. 2019;48:268-274
116. Lindmark A, Norrving B, Eriksson M. Socioeconomic status and survival after stroke - using mediation and sensitivity analyses to assess the effect of stroke severity and unmeasured confounding. *BMC Public Health*. 2020;20:554
117. Bhalla IP, Stefanovics EA, Rosenheck RA. Social determinants of mental health care systems: Intensive community based care in the veterans health administration. *BMC Public Health*. 2020;20:1311
118. Jeste DV, Pender VB. Social determinants of mental health: Recommendations for research, training, practice, and policy. *JAMA Psychiatry*. 2022
119. Galarraga JE, Black B, Pimentel L, Venkat A, Sverha JP, Frohna WJ, et al. The effects of global budgeting on emergency department admission rates in maryland. *Ann Emerg Med*. 2020;75:370-381
120. Chang AM, Cohen DJ, Lin A, Augustine J, Handel DA, Howell E, et al. Hospital strategies for reducing emergency department crowding: A mixed-methods study. *Ann Emerg Med*. 2018;71:497-505 e494
121. Su Y, Sharma S, Ozdemir S, Chow WL, Oh HC, Tiah L. Nonurgent patients' preferences for emergency department versus general practitioner and effects of incentives: A discrete choice experiment. *MDM Policy Pract*. 2021;6:23814683211027552
122. Lega F, Mengoni A. Why non-urgent patients choose emergency over primary care services? Empirical evidence and managerial implications. *Health Policy*. 2008;88:326-338
123. Cutler DM, Rosen AB, Vijan S. The value of medical spending in the united states, 1960-2000. *N Engl J Med*. 2006;355:920-927
124. O'Hara R, Bishop-Edwards L, Knowles E, O'Cathain A. Variation in the delivery of telephone advice by emergency medical services: A qualitative study in three services. *BMJ quality & safety*. 2019;28:556-563
125. Mkoma GF, Norredam M, Iversen HK, Andersen G, Johnsen SP. Use of reperfusion therapy and time delay in patients with ischaemic stroke by immigration status: A register-based cohort study in denmark. *Eur J Neurol*. 2022
126. Rinaldo L, Rabinstein AA, Cloft H, Knudsen JM, Castilla LR, Brinjikji W. Racial and ethnic disparities in the utilization of thrombectomy for acute stroke. *Stroke*. 2019;50:2428-2432
127. O'Cathain A, Knowles E, Turner J, Maheswaran R, Goodacre S, Hirst E, et al. *Explaining variation in emergency admissions: A mixed-methods study of emergency and urgent care systems*. Southampton (UK); 2014.
128. Sovso M, Bech B, Christensen H, Huibers L, Christensen E, Christensen M. Sociodemographic characteristics associated with contacts to emergency medical services and out-of-hours primary care: An

observational study of 2.3 million citizens. . *Clinical epidemiology*. 2020;12:393-401
129. Vivanco-Hidalgo RM, Ribera A, Abilleira S. Association of socioeconomic status with ischemic stroke survival. *Stroke*. 2019;50:3400-3407
130. Squarzoni P, Tamashiro-Duran JH, Duran FLS, Leite CC, Wajngarten M, Scazufca M, et al. High frequency of silent brain infarcts associated with cognitive deficits in an economically disadvantaged population. *Clinics (Sao Paulo)*. 2017;72:474-480
131. Eriksson M, Glader EL, Norrving B, Stegmayr B, Asplund K. Acute stroke alert activation, emergency service use, and reperfusion therapy in sweden. *Brain Behav*. 2017;7:e00654
132. Faigle R, Ziai WC, Urrutia VC, Cooper LA, Gottesman RF. Racial differences in palliative care use after stroke in majority-white, minority-serving, and racially integrated u.S. Hospitals. *Crit Care Med*. 2017;45:2046-2054
133. Rigsrevisionen. Rigsrevisionen. Forskelle i behandlingskvaliteten på sygehusene [report on differences in the quality of care in danish hospitals]. 2019
134. Retamero C, Paglia C. When patients do not hurt: Silent acute abdomen in a patient with schizophrenia. *Gen Hosp Psychiatry*. 2012;34:210 e219-211
135. Kallur A, Yoo E, Bien-Aime F, Ammar H. Diagnostic overshadowing and pain insensitivity in a schizophrenic patient with perforated duodenal ulcer. *Cureus*. 2022;14:e21800
136. Nishihira Y, McGill RL, Kinjo M. Perforated appendicitis in patients with schizophrenia: A retrospective cohort study. *BMJ open*. 2017;7
137. Tsay JH, Lee CH, Hsu YJ, Wang PJ, Bai YM, Chou YJ, et al. Disparities in appendicitis rupture rate among mentally ill patients. *BMC Public Health*. 2007;7:331
138. Nielsen J, Juel J, Alzuhairi KS, Friis R, Graff C, Kanters JK, et al. Unrecognised myocardial infarction in patients with schizophrenia. *Acta Neuropsychiatr*. 2015;27:106-112
139. Nishihira Y, McGill RL, Kinjo M. Perforated appendicitis in patients with schizophrenia: A retrospective cohort study. *BMJ open*. 2017;7:e017150
140. Laursen TM, Nordentoft M. Heart disease treatment and mortality in schizophrenia and bipolar disorder - changes in the danish population between 1994 and 2006. *J Psychiatr Res*. 2011;45:29-35
141. Schulman-Marcus J, Goyal P, Swaminathan RV, Feldman DN, Wong SC, Singh HS, et al. Comparison of trends in incidence, revascularization, and in-hospital mortality in st-elevation myocardial infarction in patients with versus without severe mental illness. *Am J Cardiol*. 2016;117:1405-1410
142. Druss BG, Bradford DW, Rosenheck RA, Radford MJ, Krumholz HM. Mental disorders and use of cardiovascular procedures after myocardial infarction. *JAMA*. 2000;283:506-511
143. WHO. Emergency medical services systems in the european union. 2008
144. Lindskou TA, Mikkelsen S, Christensen EF, Hansen PA, Jorgensen G, Hendriksen OM, et al. The danish prehospital emergency healthcare system

and research possibilities. *Scandinavian journal of trauma, resuscitation and emergency medicine*. 2019;27:100
145. Sagan A, Richardson E. The challenge of providing emergency medical care. 2015;21(4)
146. Naouri D, Ranchon G, Vuagnat A, Schmidt J, El Khoury C, Yordanov Y, et al. Factors associated with inappropriate use of emergency departments: Findings from a cross-sectional national study in france. *BMJ quality & safety*. 2019
147. Limb M. Ambulances should treat more and transport fewer patients, nhs improvement says. *BMJ*. 2018;362:k4106
148. Torjesen I. Almost 1.5m emergency hospital admissions could have been avoided last year. *BMJ*. 2018;361:k2542
149. Eastwood K, Morgans A, Stoelwinder J, Smith K. The appropriateness of low-acuity cases referred for emergency ambulance dispatch following ambulance service secondary telephone triage: A retrospective cohort study. *PLoS One*. 2019;14:e0221158
150. Snooks HA, Khanom A, Cole R, Edwards A, Edwards BM, Evans BA, et al. What are emergency ambulance services doing to meet the needs of people who call frequently? A national survey of current practice in the united kingdom. *BMC Emerg Med*. 2019;19:82
151. Borg K, Wright B, Sannen L, Dumas D, Walker T, Bragge P. Ambulances are for emergencies: Shifting attitudes through a research-informed behaviour change campaign. *Health Res Policy Syst*. 2019;17:31
152. Mitchell AJ, Malone D, Doebbeling CC. Quality of medical care for people with and without comorbid mental illness and substance misuse: Systematic review of comparative studies. *Br J Psychiatry*. 2009;194:491-499
153. Jansen L, van Schijndel M, van Waarde J, van Busschbach J. Health-economic outcomes in hospital patients with medical-psychiatric comorbidity: A systematic review and meta-analysis. *PLoS One*. 2018;13:e0194029
154. Krieg C, Hudon C, Chouinard MC, Dufour I. Individual predictors of frequent emergency department use: A scoping review. *BMC Health Serv Res*. 2016;16:594
155. Christensen EF, Larsen TM, Jensen FB, Bendtsen MD, Hansen PA, Johnsen SP, et al. Diagnosis and mortality in prehospital emergency patients transported to hospital: A population-based and registry-based cohort study. *BMJ open*. 2016;6:e011558
156. Vloet LCM, de Kreek A, van der Linden EMC, van Spijk JJA, Theunissen VAH, van Wanrooij M, et al. A retrospective comparison between non-conveyed and conveyed patients in ambulance care. *Scandinavian journal of trauma, resuscitation and emergency medicine*. 2018;26:91
157. Forsgarde ES, Elmqvist C, Fridlund B, Svensson A, Andersson R, Roost M. Patients' aged >/=65 years dispositions during ambulance assignments, including factors associated with non-conveyance to hospital: A longitudinal and comparative study. *BMJ open*. 2020;10:e038885

158. Lederman J, Lindstrom V, Elmqvist C, Lofvenmark C, Djarv T. Non-conveyance in the ambulance service: A population-based cohort study in stockholm, sweden. *BMJ open*. 2020;10:e036659
159. Barcella CA, Mohr GH, Kragholm KH, Gerds TA, Jensen SE, Polcwiartek C, et al. Out-of-hospital cardiac arrest in patients with and without psychiatric disorders: Differences in use of coronary angiography, coronary revascularization, and implantable cardioverter-defibrillator and survival. *J Am Heart Assoc*. 2019;8:e012708
160. WHO. Who - fact sheet - cardiovascular diseases (cvds). 2021
161. Collaborators GBDS. Global, regional, and national burden of stroke and its risk factors, 1990-2019: A systematic analysis for the global burden of disease study 2019. *Lancet Neurol*. 2021;20:795-820
162. Collaborators GBDRF. Global burden of 87 risk factors in 204 countries and territories, 1990-2019: A systematic analysis for the global burden of disease study 2019. *Lancet*. 2020;396:1223-1249
163. European stroke organisation (eso) guideline directory.
164. Powers WJ, Rabinstein AA, Ackerson T, Adeoye OM, Bambakidis NC, Becker K, et al. 2018 guidelines for the early management of patients with acute ischemic stroke: A guideline for healthcare professionals from the american heart association/american stroke association. *Stroke*. 2018;49:e46-e110
165. Correll CU, Solmi M, Veronese N, Bortolato B, Rosson S, Santonastaso P, et al. Prevalence, incidence and mortality from cardiovascular disease in patients with pooled and specific severe mental illness: A large-scale meta-analysis of 3,211,768 patients and 113,383,368 controls. *World psychiatry : official journal of the World Psychiatric Association*. 2017;16:163-180
166. Chen PH, Kao YW, Shia BC, Lin HC, Kang JH. Adverse stroke outcomes among patients with bipolar disorder. *PLoS One*. 2019;14:e0213072
167. Siddiqui N, Dwyer M, Stankovich J, Peterson G, Greenfield D, Si L, et al. Hospital length of stay variation and comorbidity of mental illness: A retrospective study of five common chronic medical conditions. *BMC Health Serv Res*. 2018;18:498
168. Dossa A, Glickman ME, Berlowitz D. Association between mental health conditions and rehospitalization, mortality, and functional outcomes in patients with stroke following inpatient rehabilitation. *BMC Health Serv Res*. 2011;11:311
169. Lilly FR, Culpepper J, Stuart M, Steinwachs D. Stroke survivors with severe mental illness: Are they at-risk for increased non-psychiatric hospitalizations? *PLoS One*. 2017;12:e0182330
170. Prior A, Laursen TM, Larsen KK, Johnsen SP, Christensen J, Andersen G, et al. Post-stroke mortality, stroke severity, and preadmission antipsychotic medicine use--a population-based cohort study. *PLoS One*. 2014;9:e84103
171. Bongiorno DM, Daumit GL, Gottesman RF, Faigle R. Patients with stroke and psychiatric comorbidities have lower carotid revascularization rates. *Neurology*. 2019;92:e2514-e2521

172. Bongiorno DM, Daumit GL, Gottesman RF, Faigle R. Comorbid psychiatric disease is associated with lower rates of thrombolysis in ischemic stroke. *Stroke*. 2018;49:738-740
173. Tarasconi A, Coccolini F, Biffl WL, Tomasoni M, Ansaloni L, Picetti E, et al. Perforated and bleeding peptic ulcer: Wses guidelines. *World J Emerg Surg*. 2020;15:3
174. Buck DL, Vester-Andersen M, Moller MH, Danish Clinical Register of Emergency S. Surgical delay is a critical determinant of survival in perforated peptic ulcer. *Br J Surg*. 2013;100:1045-1049
175. Momen NC, Plana-Ripoll O, Agerbo E, Benros ME, Borglum AD, Christensen MK, et al. Association between mental disorders and subsequent medical conditions. *N Engl J Med*. 2020;382:1721-1731
176. Copeland LA, Zeber JE, Sako EY, Mortensen EM, Pugh MJ, Wang CP, et al. Serious mental illnesses associated with receipt of surgery in retrospective analysis of patients in the veterans health administration. *BMC Surg*. 2015;15:74
177. McBride KE, Solomon MJ, Bannon PG, Glozier N, Steffens D. Surgical outcomes for people with serious mental illness are poorer than for other patients: A systematic review and meta-analysis. *Med J Aust*. 2021;214:379-385
178. Liao CC, Shen WW, Chang CC, Chang H, Chen TL. Surgical adverse outcomes in patients with schizophrenia: A population-based study. *Ann Surg*. 2013;257:433-438
179. Copeland LA, Zeber JE, Pugh MJ, Mortensen EM, Restrepo MI, Lawrence VA. Postoperative complications in the seriously mentally ill: A systematic review of the literature. *Ann Surg*. 2008;248:31-38
180. Sorensen HT, Pedersen L, Jorgensen J, Ehrenstein V. Danish clinical quality databases - an important and untapped resource for clinical research. *Clinical epidemiology*. 2016;8:425-427
181. Mackenhauer J, Valentin JB, Mikkelsen S, Steinmetz J, Vaeggemose U, Christensen HC, et al. Emergency medical services response levels and subsequent emergency contacts among patients with a history of mental illness in denmark: A nationwide study. *Eur J Emerg Med*. 2021;28:363-372
182. Schmidt M, Schmidt SAJ, Adelborg K, Sundboll J, Laugesen K, Ehrenstein V, et al. The danish health care system and epidemiological research: From health care contacts to database records. *Clinical epidemiology*. 2019;11:563-591
183. Mikkelsen S, Lassen AT. The danish prehospital system. *Eur J Emerg Med*. 2020;27:394-395
184. Mainz J, Hess MH, Johnsen SP. The danish unique personal identifier and the danish civil registration system as a tool for research and quality improvement. *International Journal for Quality in Health Care*. 2019;mzz008
185. The danish approach to mental health. 2021

186. Mainz J, Hess MH, Johnsen SP. The danish unique personal identifier and the danish civil registration system as a tool for research and quality improvement. *International journal for quality in health care : journal of the International Society for Quality in Health Care / ISQua*. 2019;31:717-720
187. Digital health solutions - shared medication record
188. Liljendahl MS, Gogenur I, Thygesen LC. Emergency laparotomy in denmark: A nationwide descriptive study. *World J Surg*. 2020;44:2976-2981
189. Mainz J, Andersen G, Valentin JB, Gude MF, Johnsen SP. Disentangling sex differences in use of reperfusion therapy in patients with acute ischemic stroke. *Stroke*. 2020;51:2332-2338
190. Sovso MB, Christensen MB, Bech BH, Christensen HC, Christensen EF, Huibers L. Contacting out-of-hours primary care or emergency medical services for time-critical conditions - impact on patient outcomes. *BMC Health Serv Res*. 2019;19:813
191. Andersen MS, Johnsen SP, Sorensen JN, Jepsen SB, Hansen JB, Christensen EF. Implementing a nationwide criteria-based emergency medical dispatch system: A register-based follow-up study. *Scandinavian journal of trauma, resuscitation and emergency medicine*. 2013;21:53
192. Sundhedsstyrelsen. Specialevejledning for psykiatri [medical specialty planning: Psychiatry]. 2022
193. Dansk selskab for almen medicin [danish society for general practitioners] unipolar depression - diagnostik og behandling [unipolar depression - diagnistrics and treatment]. 2010
194. Dansk selskab for almen medicin [danish society for general practitioners]: Akuthåndbogen: Psykose, tvangsindlæggelse, krise, angst [acute care: Psychosis, compulsory admission, crisis, anxiety].
195. Mors O, Perto GP, Mortensen PB. The danish psychiatric central research register. *Scandinavian journal of public health*. 2011;39:54-57
196. Mainz J, Krog BR, Bjornshave B, Bartels P. Nationwide continuous quality improvement using clinical indicators: The danish national indicator project. *International journal for quality in health care : journal of the International Society for Quality in Health Care / ISQua*. 2004;16 Suppl 1:i45-50
197. Green A. Danish clinical databases: An overview. *Scandinavian journal of public health*. 2011;39:68-71
198. Norgaard M, Johnsen SP. How can the research potential of the clinical quality databases be maximized? The danish experience. *J Intern Med*. 2016;279:132-140
199. Mainz J. Developing evidence-based clinical indicators: A state of the art methods primer. *International journal for quality in health care : journal of the International Society for Quality in Health Care / ISQua*. 2003;15 Suppl 1:i5-11
200. Berge E, Whiteley W, Audebert H, De Marchis GM, Fonseca AC, Padiglioni C, et al. European stroke organisation (eso) guidelines on

intravenous thrombolysis for acute ischaemic stroke. *Eur Stroke J*. 2021;6:I-LXII
201. Schmidt M, Pedersen L, Sorensen HT. The danish civil registration system as a tool in epidemiology. *Eur J Epidemiol*. 2014;29:541-549
202. Schmidt M, Schmidt SA, Sandegaard JL, Ehrenstein V, Pedersen L, Sorensen HT. The danish national patient registry: A review of content, data quality, and research potential. *Clinical epidemiology*. 2015;7:449-490
203. Pottegard A, Schmidt SAJ, Wallach-Kildemoes H, Sorensen HT, Hallas J, Schmidt M. Data resource profile: The danish national prescription registry. *Int J Epidemiol*. 2017;46:798-798f
204. Andersen JS, Olivarius Nde F, Krasnik A. The danish national health service register. *Scandinavian journal of public health*. 2011;39:34-37
205. Nordentoft M, Wahlbeck K, Hallgren J, Westman J, Osby U, Alinaghizadeh H, et al. Excess mortality, causes of death and life expectancy in 270,770 patients with recent onset of mental disorders in denmark, finland and sweden. *PLoS One*. 2013;8:e55176
206. Heuckendorff S, Johansen MN, Overgaard C, Johnsen SP, Kelly Y, Fonager K. Parental mental health, socioeconomic position and the risk of asthma in children-a nationwide danish register study. *Eur J Public Health*. 2022;32:14-20
207. Heuckendorff S, Christensen LF, Fonager K, Overgaard C. Risk of adverse perinatal outcomes in infants born to mothers with mental health conditions. *Acta Obstet Gynecol Scand*. 2021;100:2019-2028
208. Heuckendorff S, Johansen MN, Johnsen SP, Overgaard C, Fonager K. Parental mental health conditions and use of healthcare services in children the first year of life- a register-based, nationwide study. *BMC Public Health*. 2021;21:557
209. Gissler M, Laursen TM, Osby U, Nordentoft M, Wahlbeck K. Patterns in mortality among people with severe mental disorders across birth cohorts: A register-based study of denmark and finland in 1982-2006. *BMC Public Health*. 2013;13:834
210. Kessler RC, Chiu WT, Demler O, Merikangas KR, Walters EE. Prevalence, severity, and comorbidity of 12-month dsm-iv disorders in the national comorbidity survey replication. *Arch Gen Psychiatry*. 2005;62:617-627
211. McGrath J, Saha S, Chant D, Welham J. Schizophrenia: A concise overview of incidence, prevalence, and mortality. *Epidemiol Rev*. 2008;30:67-76
212. Barcella CA, Mohr GH, Kragholm K, Blanche P, Gerds TA, Wissenberg M, et al. Out-of-hospital cardiac arrest in patients with psychiatric disorders - characteristics and outcomes. *Resuscitation*. 2019;143:180-188
213. Coster J, O'Cathain A, Jacques R, Crum A, Siriwardena AN, Turner J. Outcomes for patients who contact the emergency ambulance service and are not transported to the emergency department: A data linkage study. *Prehosp Emerg Care*. 2019;23:566-577

214. Spurling LJ, Moonesinghe SR, Oliver CM. Validation of the days alive and out of hospital outcome measure after emergency laparotomy: A retrospective cohort study. *Br J Anaesth*. 2022;128:449-456
215. Agarwal G, Lee J, McLeod B, Mahmuda S, Howard M, Cockrell K, et al. Social factors in frequent callers: A description of isolation, poverty and quality of life in those calling emergency medical services frequently. *BMC Public Health*. 2019;19:684
216. Hanchate AD, Paasche-Orlow MK, Dyer KS, Baker WE, Feng C, Feldman J. Geographic variation in use of ambulance transport to the emergency department. *Ann Emerg Med*. 2017;70:533-543 e537
217. Brown JF, Raven MC, Tangherlini NL, Kennedy Hall M. Frequent users of 9-1-1 emergency medical services: Sign of success or symptom of impending failure? *Prehosp Emerg Care*. 2018:1-3
218. Magnusson C, Herlitz J, Axelsson C. Patient characteristics, triage utilisation, level of care, and outcomes in an unselected adult patient population seen by the emergency medical services: A prospective observational study. *BMC Emerg Med*. 2020;20:7
219. Sovso MB, Klojgaard TA, Hansen PA, Christensen EF. Repeated ambulance use is associated with chronic diseases - a population-based historic cohort study of patients' symptoms and diagnoses. *Scandinavian journal of trauma, resuscitation and emergency medicine*. 2019;27:46
220. Booker MJ, Purdy S, Barnes R, Shaw ARG. Ambulance use for 'primary care' problems: An ethnographic study of seeking and providing help in a uk ambulance service. *BMJ open*. 2019;9:e033037
221. Booker MJ, Shaw ARG, Purdy S, Barnes R. 'Primary care sensitive' situations that result in an ambulance attendance: A conversation analytic study of uk emergency '999' call recordings. *BMJ open*. 2018;8:e023727
222. Eastwood K, Morgans A, Stoelwinder J, Smith K. Patient and case characteristics associated with 'no paramedic treatment' for low-acuity cases referred for emergency ambulance dispatch following a secondary telephone triage: A retrospective cohort study. *Scandinavian journal of trauma, resuscitation and emergency medicine*. 2018;26:8
223. Duncan EAS, Best C, Dougall N, Skar S, Evans J, Corfield AR, et al. Epidemiology of emergency ambulance service calls related to mental health problems and self harm: A national record linkage study. *Scandinavian journal of trauma, resuscitation and emergency medicine*. 2019;27:34
224. Wise-Harris D, Pauly D, Kahan D, Tan de Bibiana J, Hwang SW, Stergiopoulos V. "Hospital was the only option": Experiences of frequent emergency department users in mental health. *Adm Policy Ment Health*. 2017;44:405-412
225. Kohn L, Christiaens W, Detraux J, De Lepeleire J, De Hert M, Gillain B, et al. Barriers to somatic health care for persons with severe mental illness in belgium: A qualitative study of patients' and healthcare professionals' perspectives. *Front Psychiatry*. 2021;12:798530

226. De Hert M, Cohen D, Bobes J, Cetkovich-Bakmas M, Leucht S, Ndetei DM, et al. Physical illness in patients with severe mental disorders. Ii. Barriers to care, monitoring and treatment guidelines, plus recommendations at the system and individual level. *World psychiatry : official journal of the World Psychiatric Association*. 2011;10:138-151
227. Ferguson N, Savic M, McCann TV, Emond K, Sandral E, Smith K, et al. "I was worried if i don't have a broken leg they might not take it seriously": Experiences of men accessing ambulance services for mental health and/or alcohol and other drug problems. *Health expectations : an international journal of public participation in health care and health policy*. 2019;22:565-574
228. Henderson C, Noblett J, Parke H, Clement S, Caffrey A, Gale-Grant O, et al. Mental health-related stigma in health care and mental health-care settings. *Lancet Psychiatry*. 2014;1:467-482
229. Reeves MJ, Prager M, Fang J, Stamplecoski M, Kapral MK. Impact of living alone on the care and outcomes of patients with acute stroke. *Stroke*. 2014;45:3083-3085
230. Stack K, Robertson W, Blackburn C. Does socioeconomic position affect knowledge of the risk factors and warning signs of stroke in the who european region? A systematic literature review. *BMC Public Health*. 2020;20:1473
231. Springer MV, Labovitz DL, Hochheiser EC. Race-ethnic disparities in hospital arrival time after ischemic stroke. *Ethn Dis*. 2017;27:125-132
232. Addo J, Ayis S, Leon J, Rudd AG, McKevitt C, Wolfe CD. Delay in presentation after an acute stroke in a multiethnic population in south london: The south london stroke register. *J Am Heart Assoc*. 2012;1:e001685
233. Attenello FJ, Adamczyk P, Wen G, He S, Zhang K, Russin JJ, et al. Racial and socioeconomic disparities in access to mechanical revascularization procedures for acute ischemic stroke. *Journal of stroke and cerebrovascular diseases : the official journal of National Stroke Association*. 2014;23:327-334
234. Møller TP, Kjærulff TM, Viereck S, Østergaard D, Folke F, Ersbøll AK, et al. The difficult medical emergency call: A register-based study of predictors and outcomes. *Scandinavian journal of trauma, resuscitation and emergency medicine*. 2017;25
235. Kellett J, Nickel CH. What are nonspecific complaints and what are their causes and outcomes? The common unknown unknowns of medicine. *Eur J Intern Med*. 2018;47:e12-e13
236. Ibsen S, Lindskou TA, Nickel CH, Klojgard T, Christensen EF, Sovso MB. Which symptoms pose the highest risk in patients calling for an ambulance? A population-based cohort study from denmark. *Scandinavian journal of trauma, resuscitation and emergency medicine*. 2021;29:59
237. Darehed D, Blom M, Glader EL, Niklasson J, Norrving B, Eriksson M. Time trends and monthly variation in swedish acute stroke care. *Front Neurol*. 2019;10:1177

238. Akbik F, Xu H, Xian Y, Shah S, Smith EE, Bhatt DL, et al. Trends in reperfusion therapy for in-hospital ischemic stroke in the endovascular therapy era. *JAMA neurology*. 2020;77:1486-1495
239. Maeda M, Fukuda H, Matsuo R, Ago T, Kitazono T, Kamouchi M. Regional disparity of reperfusion therapy for acute ischemic stroke in japan: A retrospective analysis of nationwide claims data from 2010 to 2015. *J Am Heart Assoc*. 2021;10:e021853
240. Fladt J, Meier N, Thilemann S, Polymeris A, Traenka C, Seiffge DJ, et al. Reasons for prehospital delay in acute ischemic stroke. *J Am Heart Assoc*. 2019;8:e013101
241. Christesen AMS, Vinter N, Mortensen LS, Fenger-Gron M, Johnsen SP, Frost L. Inequality in oral anticoagulation use and clinical outcomes in atrial fibrillation: A danish nationwide perspective. *Eur Heart J Qual Care Clin Outcomes*. 2018;4:189-199
242. Saunders DI, Murray D, Pichel AC, Varley S, Peden CJ, Network UKEL. Variations in mortality after emergency laparotomy: The first report of the uk emergency laparotomy network. *Br J Anaesth*. 2012;109:368-375
243. Weye N, Momen NC, Christensen MK, Iburg KM, Dalsgaard S, Laursen TM, et al. Association of specific mental disorders with premature mortality in the danish population using alternative measurement methods. *JAMA Netw Open*. 2020;3:e206646
244. Wadhera RK, Khatana SAM, Choi E, Jiang G, Shen C, Yeh RW, et al. Disparities in care and mortality among homeless adults hospitalized for cardiovascular conditions. *JAMA Intern Med*. 2020;180:357-366

SUPPLEMENTARY

Table S1: Consensus definition of mental illness and – vulnerability

These groups were defined based on consensus among local experts in clinical epidemiology, psychiatry, social medicine and family medicine/general practice, supported by knowledge of patient groups experiencing the highest excess mortality.[8, 205]

	Definition	Data Source
History of major mental illness	Any in- or outpatient contact (ever) - **ICD-10** DF20-22 and/or **ICD-8** 295: Schizophrenia - **ICD-10** DF30-31 and/or **ICD-8** 296: Bipolar disease Within 10 years prior to admission: In-patient contacts <u>> 2 days</u> - **ICD-10** DF32-34: Uni-polar depression - **ICD-10** DF60.4: Emotional personality disorder	*The Danish National Patient Registry*[202] The Danish National Patient Registry-Psychiatry *The Danish Psychiatric Central Research Register*[195] All three registries contain patient-level data on diagnoses according to the ICD-coding system for all hospital contacts including emergency department visits.
History of moderate mental illness	Within 5 years prior to admission: In- or outpatient contact - **ICD-10** DF23-29: Psychotic disorders, DF38-39: Other affective disorders, DF40-48: Anxiety, and other nonpsychotic disorders, F50-F59 Behavioral syndromes, F60-F69 Disorders of adult personality, F70-F79 Intellectual disabilities, F80-F89 Pervasive and developmental disorders, F90-F98 Behavioral and emotional disorders with onset usually occurring in childhood and adolescence, or F99 Unspecified mental disorder Regarding ICD-10 DF32-34 and DF60.4: only out-patient contacts and in-patient stays <u>≤</u> 2 days	
	OR Within 5 years prior to admission One or more consultations with a private psychiatrist C_SPECIALE =24, 26 or 35	

History of minor mental illness/ vulnerability	Within 1 year prior to admission Two or more consultations with a psychologist C_SPECIALE =63	
	OR Two or more sessions with talk therapy OR Two or more psychometric tests at general practitioner C_SPECIALE = 80 *and* C_YDELSESNR =2149 or 6101 or 4003 or 4021 or 4050 or 4063 or 4106 or 4247 or 4248 or 4249	
	OR Two or more redeemed prescriptions Benzodiazepiner: MN03AE, -05BA, -05CD or -05CF Antidepressants: MN06A02 or -06AX26	*The National Register of Medicinal Product Statistics*[203] contains data on individual-level redeemed prescriptions according to Anatomical Therapeutic Chemical (ATC).
No history of mental illness	None of the above	

Table S2: Available measures of most recent* disease activity prior to admission with ischemic stroke

	Most recent* contact in a psychiatric hospital (any DF-diagnosis)	**Most recent* private psychiatrist**	**Most recent* redeemed prescription benzo-diazepines/anti-depressant**	**Most recent* session talk therapy, psychometrics or psychologist**
History of major mental illness	665 days [185;1546]	1150 days [175;2253]	45 days [14;477]	1044 days [375;2048]
History of moderate mental illness	664 days [259;1158]	662 days [77;1181]	50 days [16;262]	628 days [244;1084]
History of minor mental illness	Not relevant	Not relevant	35 days [13;72]	143 days [57;236]

***** *Disease activity within 10 years for major, 5 years for moderate, 1 year for minor*

APPENDICES

Appendix A: Article of study I – see separate file

Appendix B: Article of study II – see separate file

Appendix C: Article of study III – see separate file

Appendix D: Article of study IV – see separate file

ISSN (online): 2246-1302
ISBN (online): 978-87-7573-878-6

AALBORG UNIVERSITY PRESS