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Innovations in prehospital emergency cardiac care: alleviating the strain on overcrowded hospitals

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Citation

Koning, E. R. de. (2026, January 27). *Innovations in prehospital emergency cardiac care: alleviating the strain on overcrowded hospitals*. Retrieved from <https://hdl.handle.net/1887/4287795>

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**Innovations in Prehospital Emergency Cardiac Care:
Alleviating the strain on overcrowded hospitals**

Enrico R. de Koning

Colofon

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This thesis was written at the Department of Cardiology of the Leiden University Medical Center in Leiden, the Netherlands.

Financial support for the costs associated with the publication of this thesis was received from: Netwerk Acute Zorg West, Hart Onderzoek Nederland, ChipSoft , MSB Gouda and Waleus Bibliotheek

Artwork cover and chapter pages: Hjalmar Haagsman, dachtikhetniet.nl

Provided by thesis specialist Ridderprint, ridderprint.nl

Printing: Ridderprint

Layout and design: Anna Bleeker, persoonlijkproefschrift.nl

Innovations in Prehospital Emergency Cardiac Care: Alleviating the strain on overcrowded hospitals

ter verkrijging van
de graad van doctor aan de Universiteit Leiden,
op gezag van rector magnificus prof. dr. S. de Rijcke,
volgens besluit van het college voor promoties
te verdedigen op dinsdag 27 januari 2026
klokke 16:00 uur
door

Enrico Raun de Koning

geboren te 's-Gravenhage
in 1991

Promotiecomissie

Promotor: Prof. dr. M.J. Schalijs

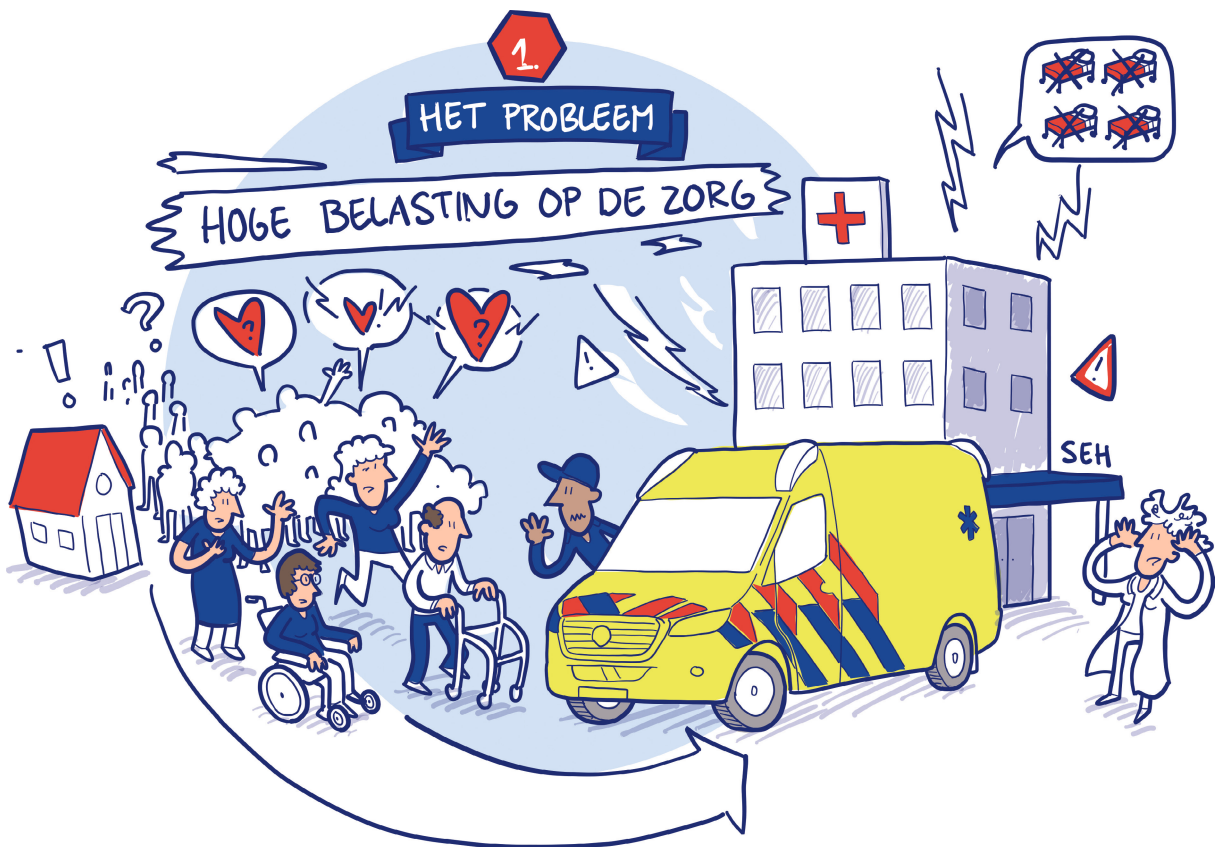
Copromotoren: Dr. J.M.J. Boogers
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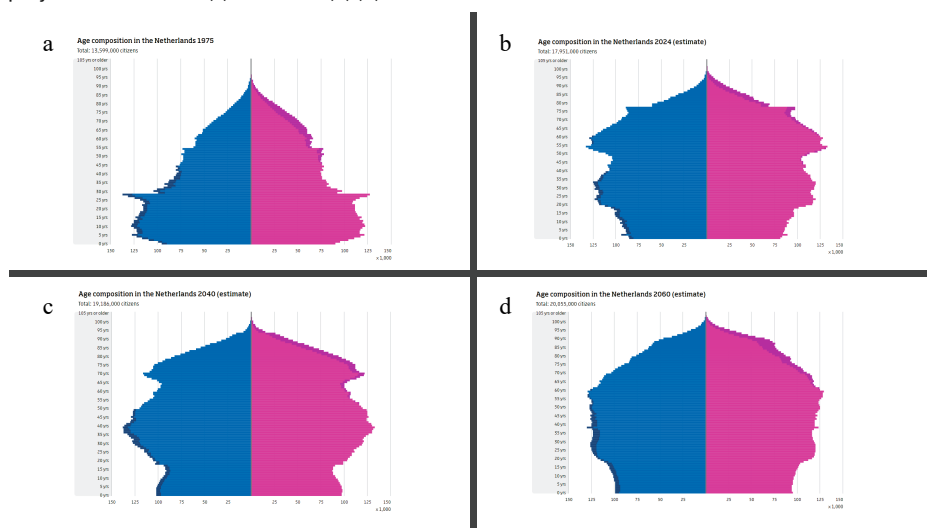
Chapter 1

General introduction

General introduction

The global population is experiencing a significant age distribution shift with people living longer, resulting in a rapid increase in the proportion of elderly individuals (1-2). By 2030, an estimated 1 in 6 people, or 1.4 billion individuals, will be 60 years or older, and this number is projected to reach 2.1 billion by 2050, with over 400 million being 80 years or older (3). High-income countries, including the Netherlands, will face even higher proportions of elderly citizens, with an expected 23% of the population being 65 years or older as early as 2030 (Figure 1) (4).

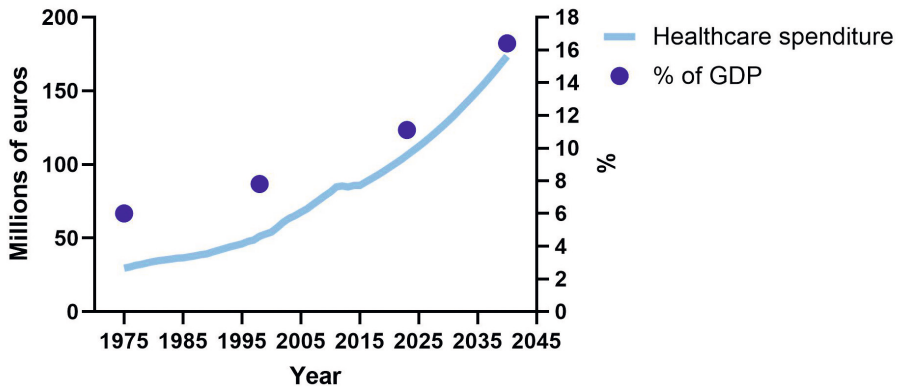
Figure 1. Demographic changes in age composition in the Netherlands from 1975 (a) to 2024 (b), and projections for 2040 (c) and 2060 (d) (5).



The aging population leads to an increased demand for healthcare services, while at the same time the available workforce decreases. Currently, 1 in 7 people work in healthcare with this number projected to increase to 1 in 4 by 2040 (6) to meet the growing demands of the aging population. These demographic changes present considerable challenges in healthcare organization.

In addition, escalating healthcare costs imposes an unsustainable burden on the Dutch gross domestic product (GDP). In 2021, healthcare accounted for approximately 14.3% of the GDP, equivalent to a staggering 124.7 billion euros (7) or 96.6 billion euros (11.1% of GDP) according to the international definition on healthcare expenditure set out in the System of Health Accounts (8). If not addressed, this percentage is projected to climb to 16.4% in 2040 and around 20% by 2060, necessitating urgent measures to control expenditures and ensure the long-term financial stability and effectiveness of the Dutch healthcare system (Figure 2) (9-10).

Figure 2. Healthcare expenditure from 1975 to 2040 in millions of euros per year (light blue line) and the % of GDP (dark blue dots).



A further complication of an aging population is higher rates of comorbidity and complex patient problems (11-12), contributing to longer waiting times for primary healthcare, growing waiting lists for medical specialist care, higher costs and hospital overcrowding. This leads to moments where healthcare is not readily available for every patient, most notably in overcrowded Emergency Departments (EDs). EDs routinely close down and are forced to divert patients to other hospitals further away to provide appropriate care (13).

Overcrowding (in hospitals and EDs) adversely affects patient outcomes due to longer waiting times and reduced attention from healthcare personnel, compromising care quality and resulting in higher healthcare costs. Additionally, it negatively impacts the well-being of overworked healthcare professionals (14-15).

The COVID-19 pandemic underscored the critical importance of healthcare resources, including personnel and hospital capacity. Hospitals worldwide faced overcrowding due to the overwhelming number of infections and subsequent acutely ill patients needing hospitalization and intensive care admission. The Netherlands, like many other countries, experienced a severe strain on Intensive Care Unit (ICU) bed management, disrupting healthcare services and even normal life.

These changes have challenged the accessibility, quality and affordability of the (Dutch) healthcare system. In response the Dutch Government has formulated the Integral Healthcare Agreement (in Dutch: Integraal Zorg Akkoord or IZA) (16) to ensure a sustainable future for healthcare. By prioritizing 'fitting' care on all fronts the IZA aims to address the issues challenging the accessibility, quality and affordability of healthcare. Fitting care is defined as: verifiably effective, in collaboration with the patient, in the appropriate place, with a focus on health instead of disease, and provided in a pleasant working environment. IZA uses this starting point to focus on, among other things, regional collaboration between

healthcare providers, healthcare financiers and the government. Furthermore it aims to tailor healthcare to patients' specific needs, focuses on streamlining data exchange between healthcare providers and the reinforcement of primary care healthcare providers such as general practitioners (GP's)

A fundamental shift in our approach to hospital capacity, - personnel, and further healthcare resources is necessary, with an emphasis on the efficient utilization of existing resources. This requires an innovative, comprehensive logistics strategy incorporating data exchange and triage which are often overlooked in scientific research.

Triage

Given that simple solutions like increasing the number of beds or hospitals are not sustainable, given the demographic changes, nor feasible, it becomes crucial to maximize the utilization of already existing resources in healthcare. One way to achieve this is through triage, which involves allocating care to those individuals who will benefit the most from it. By selecting the appropriate patients for the appropriate care, triage improves outcomes and reduces unnecessary resource consumption. On a further point, not all medical care requires the immediacy and resources of the ED. Many conditions are better managed in primary care, outpatient clinics, or even self-care at home. Utilizing these alternatives appropriately can improve efficiency, reduce strain on emergency services, and ensure patients receive the most suitable care for their needs. Although triage is an essential aspect of medicine, it is primarily based on healthcare professionals' experience.

Risk scores

However, for various diseases or symptoms, risk scores have been developed to assist professionals in triage and provide objective tools for estimating risk both in-hospital and in the pre-hospital setting. Within the field of cardiology the TIMI –(17) and GRACE risk (18) scores are commonly used to predict the risk of death in patients presenting with acute coronary syndrome (ACS). More specifically in triage, to determine the risk of ACS in patients experiencing chest pain, various risk scores are available such as the Emergency Department Assessment of Chest Pain Score (EDACS) (19), the RISTRA-ACS score (20), the Troponin-only Manchester Acute Coronary Syndromes (T-MACS) score (21) and the HEART score (Figure 3) (22). Of these scores, the HEART score is the most widely used. The HEART score is a clinically validated risk assessment tool to evaluate the likelihood of major adverse cardiac events (MACE) in patients presenting with chest pain in the ED. It was developed in the St. Antonius hospital in Nieuwegein, the Netherlands and further validated in 2440 patients from ten hospitals in the Netherlands (23). The acronym (HEART) stands for: **H**istory (or signs and symptoms), **E**lectrocardiogram (ECG), **A**ge, **R**isk factors, and **T**roponin. These factors are scored on a scale of 0, 1, or 2, with a cumulative score ranging from 0 to 10. MACE, defined as ACS, coronary angiography showing procedurally correctable stenosis, percutaneous coronary intervention (PCI), coronary artery bypass graft surgery or all-cause death, occurred in 1.7% of patients in the low-risk group (0-3).

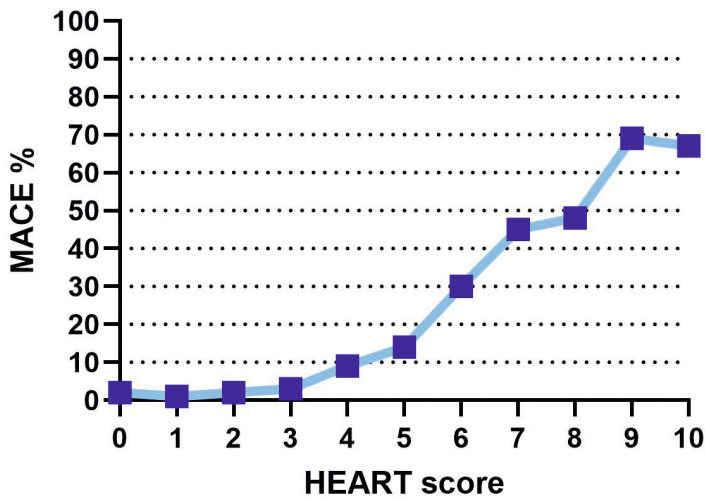
Higher scores indicate elevated risk (Figure 4), aiding healthcare providers in making well-informed decisions regarding patient management and, with lower risk patients, the potential discharge from the ED. The HEART score has been incorporated within the HEART pathway, a clinical algorithm that can be used as a decision-making tool using serial troponin tests (24).

Figure 3. HEART score for chest pain patients.

History (Anamnesis)	Highly suspicious	2	
	Moderately suspicious	1	
	Slightly suspicious	0	
ECG	Significant ST-deviation	2	
	Non-specific repolarisation disturbance / LBBB / PM	1	
	Normal	0	
Age	≥ 65 years	2	
	45 – 65 years	1	
	≤ 45 years	0	
Risk factors	≥ 3 risk factors or history of atherosclerotic disease	2	
	1 or 2 risk factors	1	
	No risk factors known	0	
Troponin	≥ 3x normal limit	2	
	1-3x normal limit	1	
	≤ normal limit	0	
Total			

1

Figure 4. Major Adverse Cardiac Events (MACE) percentage for HEART score 0-10



Cardiac Troponin (cTn) is a key component of the aforementioned risk scores. It is a serum biomarker with high diagnostic accuracy for myocardial necrosis due to ischemia and therefore a cornerstone element in the universal definition of myocardial infarction (25), and in the European Society of Cardiology's (ESC) guidelines for the management of ACS (26).

All the aforementioned risk scores show promising results in ruling out ACS in the ED or shortening ED length of stay. However, they do not address the root cause of overcrowding since patients still need to be presented to the ED. This is especially important for patients with chest pain suspected to be of cardiac origin, as around 80-90% of patients presenting to the ED with chest pain are not diagnosed with ACS (27-30). Thus, risk scores alone are not the solution to overcrowding.

Therefore, attention has shifted towards prehospital triage. Prehospital triage of very high risk patients to hospitals with PCI capabilities, such as patients in cardiogenic shock and prehospitally diagnosed ST-elevation myocardial infarction (STEMI), is routine care within the Netherlands. Prehospitally acquired ECG's are recorded by paramedics and electronically transmitted to the cardiac care unit (CCU) of the nearest hospital with PCI capabilities to determine eligibility for primary PCI (31).

Prehospital risk scores

The shift towards prehospital triage has led to the development of risk scores for chest pain specifically in the prehospital setting, such as the preHEART (prehospital HEART) score (32) and the modified HEART score (33). The developers of the preHEART score analyzed the performance of individual components of the HEART score for MACE. The preHEART score adjusted the thresholds for age, - troponin levels and substituted 'Risk factors' for a single risk factor, namely male sex. It was validated in 435 patients presented to the ED for chest pain via the emergency medical services (EMS) and performed better than the HEART score with a negative predictive value (NPV) of 99.4% and a positive predictive value (PPV) of 50.0%. The modified HEART score was developed to incorporate point-of-care (POC) high-sensitivity cardiac troponin I (hs-cTnI) into the HEART score. It used stored plasma samples from 700 patients included in earlier prehospital studies and assessed the limit of quantitation (LoQ) and the 99th percentile cut-off values of the POC device. Using these cut-off values the modified HEART score with the POC device had an NPV of 99.0% and a PPV of 16.4%.

Prehospital clinical studies

Stratifying patients into low-, medium-, or high-risk categories could enable the subsequent identification of low-risk patients who can safely remain at home following paramedic assessment, at this moment there are no clinical studies supporting this. However, there have been a small number of prospective trials employing clinical decision rules in the prehospital setting.

The Ambulance Cardiac Chest Pain Evaluation in Scotland Study (ACCESS) (34) aimed to determine whether risk stratification in the out-of-hospital setting could effectively identify patients with chest pain at low and high risk, potentially avoiding unnecessary admissions or aiding direct transfer to cardiac centers. Paramedics prospectively enrolled 1,054 patients with suspected acute coronary syndrome, recording the History, ECG, Age, and Risk Factors (HEAR) score and obtaining out-of-hospital samples for cardiac Troponin I (cTnI) on a point-of-care device, enabling calculation of the HEART score. However, because daily quality controls could not be ensured, only 394 patients were available for out-of-hospital cTnI measurement. Of the 1,054 patients, 27% experienced MACE at 30 days. A HEAR score ≤ 3 identified 32% of patients as low risk with 84.9% sensitivity, while a score ≥ 7 identified 3% as high risk with 98.7% specificity. Similarly, a point-of-care HEART score ≤ 3 identified 30% as low risk with 87.0% sensitivity, and a score ≥ 7 identified 14% as high risk with 94.8% specificity. The authors concluded that low HEAR- or HEART scores acquired by paramedics in the prehospital setting could not safely rule out MACE. Importantly, the point-of-care device used, Samsung LABGEOIB10 (Samsung, Seoul, South Korea), required a blood sample drawn from an intravenous cannula and did not measure high-sensitivity troponin, making it more invasive than regular pre-hospital care and having a less sensitive biomarker for ACS than in-hospital (ED) care. On a positive note, the study demonstrated that the HEART score can be incorporated into regular paramedic practice.

Some of the shortcomings of the ACCESS study were investigated in the URGENT 1.5 trial (35). Here, investigators assessed the diagnostic accuracy of the modified HEART score, incorporating fingerstick POC high-sensitivity troponin I (hs-cTnI) testing, in ruling out ACS. Data from 96 patients with chest pain, retrospectively included from a study on a novel POC troponin device, were analyzed. The modified HEART score was determined based on admission data and capillary POC hs-cTnI results. Among the study population, 34% were diagnosed with ACS. The modified HEART score had a sensitivity of 97.0% and a NPV of 97.6%. These findings suggested that the modified HEART score, integrating capillary POC hs-cTnI results, showed promise in ruling out ACS in patients with chest pain presenting to the cardiac emergency department. However, it was not evaluated in the prehospital setting. The URGENT 2.0 trial is currently (as of April 2025) enrolling patients for prospective validation in the prehospital setting.

Another study that prospectively researched prehospital risk stratification was the FamouS Triage study. In phase III (36), the safety and efficacy of referral decisions made by ambulance paramedics based on pre-hospital HEART scores were investigated, aiming to determine if this approach was non-inferior to routine management. The study compared the occurrence of MACE before, which was Phase II of the FamouS study (37), and after the implementation of referral decisions guided by pre-hospital HEART scores. After implementation, patients with a HEART score of <3 were asked to give informed consent to be observed at home instead of being transferred to the hospital. In those patients, a second HEART score was assessed at home 3–12 hours after inclusion. A cardiac Troponin T (cTnT)

assay was performed on the Cobas h232 (Roche Diagnostics, Basel, Switzerland) system. Among the 1236 included patients, there were 149 low-risk patients (28%) not transferred to the hospital. The occurrence of MACE within 45 days for all patients was 16.6% in Phase II and 15.7% in Phase III. The percentage of MACE in low-risk patients was 2.9% and 1.3%, respectively, after which the authors conclude that referral decisions based on pre-hospital HEART scores are non-inferior to standard care. Of note, the FamouS study, much the same as the ACCESS study, did not use hs-cTn assays and thereby used a less sensitive biomarker for ACS than in-hospital (ED) care. Further, to ensure safety, a second visit from a paramedic was necessary. The requirement for a second assessment places a significant strain on ambulance readiness. Additionally, it's important to recognize that this study leaned more towards an observational design rather than a randomized controlled trial.

As a last example, the ARTICA trial (38) assessed the healthcare costs of a pre-hospital rule-out strategy using POC troponin measurement in suspected NSTEMI-ACS patients deemed low-risk based on the HEAR (History, ECG, Age, Risk factors) score ≤ 3 . Blood was obtained by venepuncture or venous line, and cTnT was measured on the Cobas h232. If cTnT was low (<40 ng/L), the patient's care was transferred to the GP, and if cTnT was elevated (≥ 40 ng/L), the patient was transported to the ED. 863 participants were randomized to rule-out in the ED (429 patients) or pre-hospital rule-out with POC troponin measurement (434 patients). The pre-hospital strategy demonstrated significantly lower healthcare costs compared to direct transfer to the emergency department (€1349 vs. €1960). Among the ruled-out ACS population, MACE incidence was very low, with 0.5% in the pre-hospital strategy compared to 1.0% in the ED strategy. Importantly, this study focused on assessing cost-effectiveness, and was not powered for safety outcomes. Therefore, we cannot conclusively state whether it was safe to discharge low-risk patients with low troponin levels to their homes based on the findings of this research.

All of these prospective clinical studies demonstrated success in identifying patients at low risk of MACE in the prehospital setting. However, since the primary aim was not safety (and thus were not powered for safety outcomes), they did not definitively prove to be effective in safely leaving patients at home. It is important to note that the National Protocol for Paramedic Care (in Dutch; Landelijk Protocol Ambulancezorg or LPA) (39) does allow for patients to stay at home when appropriate, meaning it could feasibly be implemented in prehospital care. However, further research is required to conclusively demonstrate the safety of this practice in prehospital triage. Additionally, these studies focused solely on chest pain patients, yet patients with many other presenting (cardiac) symptoms also contribute to ED overcrowding.

Thus, the current situation has proven insufficient in effectively reducing overcrowding, necessitating higher standards. Creating a (national) registry for prehospital triage studies would significantly enhance the power of scientific research to assess safety. Such a registry would provide valuable data on whether patients experience MACE and what

these percentages are across the different levels of risk (low, medium, and high). A potential improvement for prehospital triage could be the ability to consult an in-hospital cardiologist during prehospital care, integrating both prehospital and in-hospital data and expertise. Another approach could involve regional capacity management, where hospitals share data and admission capabilities. Lastly, researching the effectiveness of artificial intelligence (AI) and machine learning (ML) algorithms in predicting acute coronary syndrome, and implementing them if viable, could offer significant advancements.

Data sharing and consultation

1

In both healthcare in general and prehospital cardiac triage specifically, a wealth of data is routinely collected, yet unfortunately, this information often remains siloed among different healthcare providers. Facilitating seamless data-sharing between hospitals, general practitioners, and paramedics emerges as a critical necessity. Establishing efficient channels for communication and information exchange among these stakeholders holds the promise of fostering more effective and well-informed decision-making during critical situations.

As previously discussed, the protocol for paramedic care (LPA) offers the possibility for patients to remain at home after paramedic assessment when deemed appropriate. A suitable option not only for low-risk individuals but potentially for others categorized as medium or high risk by conventional scoring systems. These scoring systems often overlook crucial factors such as frailty, comorbidities, and patient specific wishes, which are all essential for tailoring patient-specific care. For some patients deemed high-risk by clinical risk scores, avoiding hospitalization could be the optimal course of action, highlighting the significance of leveraging data shared between paramedics, GPs, and medical specialists to improve patient care.

Moreover, even among those categorized as low risk, sharing data with an in-hospital cardiologist could offer valuable insights, particularly in cases where uncertainty persisted following paramedic assessment. Given that low-risk scores might not encompass all potential issues, healthcare professionals' intuition or gut feeling could play a significant role in decision-making. Similarly, patients classified as medium risk presented a nuanced scenario with varying individual risks, emphasizing the importance of consulting cardiologists to refine decision-making processes. While multiple risk scores have been developed and validated (as mentioned earlier) for chest pain, such tools are not available for all cardiac symptoms. Effective communication among healthcare providers remains paramount, especially when managing conditions lacking these specific risk scores, such as palpitations or (near)-syncope. Drawing on shared data to facilitate collaborative decision-making is imperative, as highlighted by the efficacy of prehospital triage in identifying and prioritizing severely injured trauma patients (40-41). The success of these triage systems in ensuring appropriate care underscores their potential applicability in cardiac emergencies. This success story indicates the feasibility of extending similar practices to address cardiac-related situations.

Data analysis and Artificial Intelligence

Analyzing numerical parameters such as age, blood pressure, heart rate, and ECG findings has become increasingly streamlined in modern healthcare due to several factors. Numerical data can be easily quantified, standardized, and represented in a structured format, making it conducive to systematic analysis. Additionally, numerical parameters often have well-defined ranges or thresholds that allow for straightforward interpretation, aiding in the identification of patterns or abnormalities.

Conversely, the analysis of textual data poses a greater challenge for humans due to its inherent complexity and variability. Textual data in healthcare often includes free-text notes, medical histories, symptom descriptions, and clinician observations, among other sources. This unstructured nature makes it difficult to extract meaningful information systematically. Unlike numerical data, textual data lacks standardization and may vary widely in language, terminology, and style across different healthcare providers and specialties. As a result, interpreting textual data requires human judgment, context comprehension, and domain expertise, making it more time-consuming and prone to interpretation errors compared to numerical analysis.

Furthermore, textual data may contain implicit or ambiguous information that necessitates careful consideration and context integration during analysis. For instance, patient symptoms or descriptions of medical events may be subjective and open to interpretation, requiring clinicians to infer underlying meanings or nuances based on their experience and knowledge. Additionally, text-based documentation may contain inconsistencies, abbreviations, misspellings, or grammatical errors that further complicate analysis and hinder data interoperability.

As healthcare systems continue to digitize and accumulate vast amounts of textual data, addressing these challenges through advancements in artificial intelligence (AI) through natural language processing (NLP) and machine learning technologies becomes increasingly crucial for unlocking the full potential of healthcare data analytics.

AI's prevalent application in cardiovascular imaging underscores its potential to revolutionize various realms within cardiology (42-44). Beyond its current focus, AI holds promise for reshaping the landscape of cardiovascular medicine (45-47). By leveraging AI's adeptness at analyzing vast patient datasets, healthcare providers can unveil intricate patterns indicative of medical conditions' severity and urgency, surpassing human capabilities in both speed and accuracy. This pivotal role of AI positions it as a cornerstone in redefining prehospital triage protocols and optimizing patient care delivery. To fully harness the potential of these technologies, healthcare providers must adopt strategies to effectively structure and utilize data for machine learning models. Integrating e-health innovations alongside AI and machine learning solutions not only streamlines processes

but also enhances decision-making capabilities. This becomes increasingly significant in the context of an aging population and escalating healthcare demands, where the need for efficient and effective prehospital triage is paramount.

The embrace of these advancements signifies a transformative shift towards a more patient-centric and data-driven approach in healthcare. Tools like Chat-GPT (OpenAI, San Francisco, United States) and Gemini (Google, Mountain View, United States) exemplify this shift, witnessing a surge in user count over the past year. AI tools will likely persist and significantly transform society and, therefore, influence healthcare. As healthcare continues to evolve, the integration of AI and machine learning technologies offers unprecedented opportunities to improve patient outcomes and revolutionize prehospital care delivery.

Aim and outline

The escalating demand for healthcare due to an aging population will inevitably lead to overcrowding and strain on healthcare systems, which was already notable during the COVID-19 pandemic. While prehospital – and emergent care for cardiology has seen improvements in recent years, notable shortcomings persist. Current approaches predominantly focus on triaging patients with chest pain, overlooking the broader spectrum of cardiac symptoms and failing to integrate the patient perspective. Furthermore, reliance solely on risk scores disregards the potential benefits of shared decision-making between in-hospital and out-of-hospital healthcare providers through enhanced data sharing.

The overarching aim of this thesis is to address the challenges inherent in cardiac care and propose innovative solutions where possible and feasible. First, the thesis seeks to implement and evaluate the effectiveness of a novel prehospital triage method that integrates prehospital data, in-hospital data, and expert cardiologist consultation on a unified data platform. By assessing the impact of this triage method, the research aims to offer valuable insights to optimize prehospital patient management and resource allocation.

Additionally, this study will analyze the effect of (regional) collaboration on hospital capacity management, and study the indirect health effects observed during healthcare stress tests, focusing on the COVID-19 pandemic. By examining these effects, the research aims to enhance our understanding of healthcare system vulnerabilities and glean essential lessons for improved preparedness for future emergencies, including anticipated hospital system overcrowding due to the aging population.

Furthermore, the thesis will explore the future prospects of integrating artificial intelligence (AI) into prehospital triage. This involves validating the application of AI-driven decision-making processes, thereby leveraging technological advancements to further enhance the efficiency and effectiveness of prehospital care.

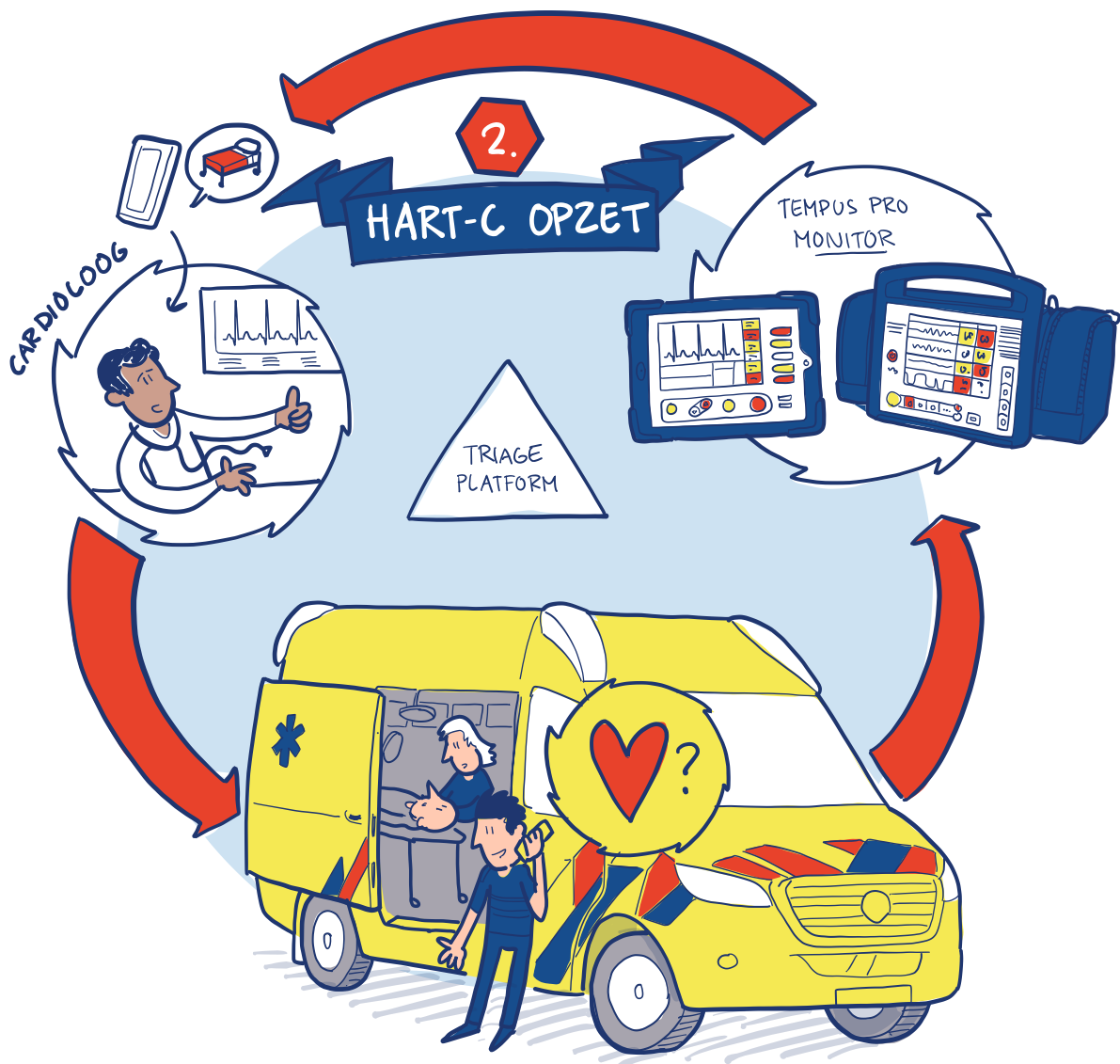
In summary, this thesis aims to contribute to the advancement of cardiac care by addressing existing challenges, innovating solutions in prehospital cardiac triage, and leveraging emerging technologies to improve patient outcomes and healthcare system resilience.

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Chapter 2

Pre-hospital Triage of Acute Cardiac Patients: Study Protocol of HART-c, a multicenter prospective study

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Abstract

Introduction:

Emergency department (ED) overcrowding is a major health care problem associated with worse patient outcomes and increased costs. Attempts to reduce ED overcrowding of cardiac patients have so far focused on in-hospital triage and rapid risk stratification of chest pain patients at the ED. The HART-c study aims to assess the amount of patients left at home in usual ambulance care as compared to the new pre-hospital triage method. This method combines paramedic assessment and expert cardiologist consultation using live-monitoring, hospital data and real-time admission capacity.

Methods and Analysis:

Patients visited by the emergency medical services (EMS) for cardiac complaints are included. EMS consultation consists of medical history, physical examination and vital signs and ECG measurements. All data is transferred to a newly developed platform for the triage cardiologist. Pre-hospital data, in-hospital medical records and real-time admission capacity are evaluated. Then a shared decision is made whether admission is necessary and, if so, which hospital is most appropriate. To evaluate safety, all patients left at home and their GP's, are contacted for 30-day adverse events.

Ethics and dissemination:

The study is approved by the LUMC's Medical Ethics Committee. Patients are asked for consent for contacting their GP's. The main results of this trial will be disseminated in one paper.

Discussion:

The HART-c study evaluates the efficacy and feasibility of a pre-hospital triage method that combines pre-hospital patient assessment and direct consultation of a cardiologist who has access to live-monitored data, hospital data and real-time hospital admission capacity. We expect this triage method to substantially reduce unnecessary ED visits.

Introduction

Emergency Department (ED) overcrowding is a worldwide health care problem associated with worse patient outcomes and increased costs.(1,2) Cardiac complaints are one of the most common reasons for patients to visit the ED, with chest pain as the most frequent complaint.(3) In Europe and the United States, 15-20 million patients with chest pain are seen at the ED every year.(4) The majority will be sent home after ruling out acute cardiovascular disease: previous studies have shown that up to 80% of chest pain patients do not have an acute coronary syndrome.(5-8) However, these patients contribute to overcrowding of EDs and these ED visits substantially increase healthcare costs.

Attempts to reduce ED overcrowding by cardiac patients have so far particularly focused on rapid risk stratification after presentation at the ED. For example, the HEART score stratifies patients as at low, intermediate or high risk of major adverse cardiac events (MACE) based on history, the electrocardiogram (ECG), age, risk factors and troponin levels. (9) However, as it takes 1-2 hours for the latter to be available, patients still spend a long time at the ED after which the majority can be discharged home.

Accordingly, interest has shifted from in-hospital to pre-hospital triage. Preventing patients with cardiac complaints and a very low risk of adverse cardiac events from visiting the ED will substantially help to reduce ED overcrowding. Efforts to prevent ED visits especially involve interventions focused on chest pain patients such as risk score calculation by the ambulance paramedics (for example with the HEART score(10) and HE-MACS(11)) or pre-hospital point of care testing for troponin.(12) In order to improve pre-hospital triage for cardiac patients in the entire chain of acute cardiac care, we developed a comprehensive triage method entitled HART-c ("Hollands-midden Acute Regional Triage - Cardiology").

Innovative in this approach is the combination of pre-hospital patient assessment by the ambulance paramedic and expert consultation of a cardiologist who has access to live-monitored data from the ambulance, in-hospital data and real-time hospital admission capacity in a newly developed triage application. By drafting this triage method, we specifically aimed to safely reduce unnecessary ED visits of patients with all types of cardiac complaints. In addition, we intent to provide patient-tailored care through pre-hospital assessment of patient specific needs and circumstances. The HART-c study was designed to evaluate whether the implementation of the HART-c triage method results in a reduction of unnecessary ED visits.

Methods and analysis

Study design and patient population

The HART-c study is a multi-center prospective study with a historical control group. The intervention group comprises of adult patients visited by the regional emergency medical services (EMS) because of cardiac complaints between 1 September 2019 and 31 August 2020 in whom pre-hospital triage is performed according to the HART-c triage method. The historical control group consists of adult patients visited by the regional EMS because of cardiac complaints between 1 September 2018 and 31 August 2019 (1 year before the start of the HART-c triage method). Of note, in both groups EMS consultation could have been requested directly by the patient, through bystanders or by the patients' general practitioner (GP) who refers patients through EMS. Patients in need for urgent cardiac care, patients with complaints not suspected of cardiac origin as assessed by the ambulance paramedic, and patients unable or not willing to provide informed consent were excluded from triage according to the HART-c method. Table 1 displays the detailed inclusion and exclusion criteria.

Table 1. Inclusion and exclusion criteria

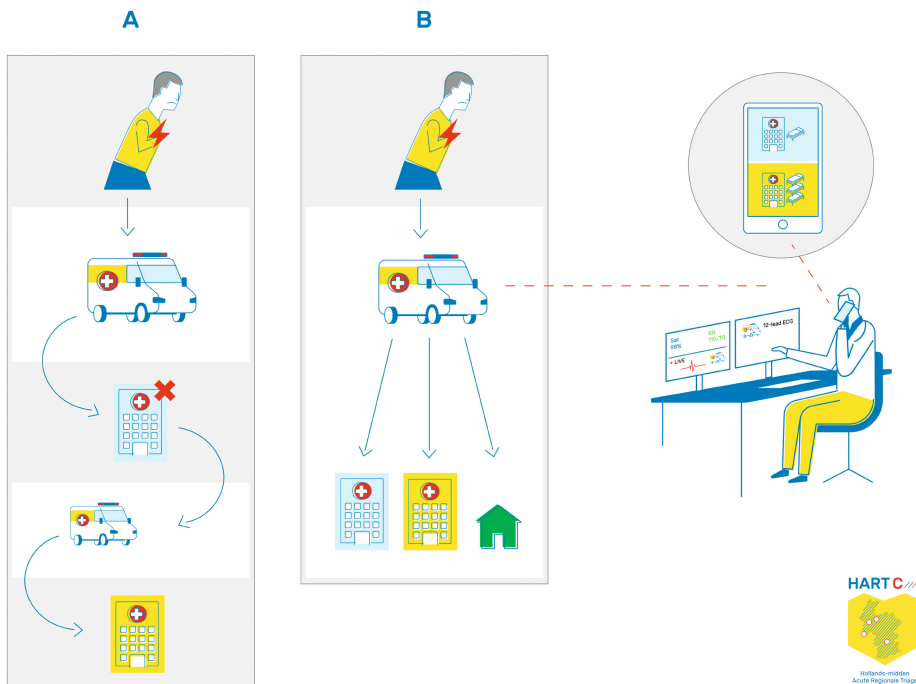
Inclusion criteria
Patients visited by EMS for cardiac complaints
Age over 18 years
Exclusion criteria
Patients in need for urgent cardiac care because of
- ST-elevation myocardial infarction
- Hemodynamic instability
- (Out of hospital) cardiac arrest
- Suspected pulmonary embolism
- Suspected acute aortic syndrome (thoracic or abdominal)
Patients with symptoms not suspected of cardiac origin
Unable or unwilling to provide informed consent

The HART-c study is coordinated by the Leiden University Medical Centre (LUMC) and conducted in the entire EMS region "Hollands-midden" which consists of over 600.000 inhabitants. The hospitals located in this region participate: the Leiden University Medical Centre, the Groene Hart hospital and the Alrijne hospital. The study is performed in close collaboration with the regional EMS (RAVHM) that employs 240 paramedics who are trained in pre-hospital cardiac care and 31 ambulance vehicles equipped with real-time monitoring. In addition, the study was performed and developed with the help of over regional 300 GPs.

Intervention group: Pre-hospital Triage using HART-c method

The intervention group consists of patients visited by the EMS because of symptoms suspected to be of cardiac origin such as chest pain, shortness of breath, palpitations or implanted cardiac device problems. In line with the National Protocol for Emergency Medical Care, patients at first receive standard medical care consisting of a medical history, physical examination with vital sign monitoring (blood pressure, heart rate, pulse oximetry) and a 12-lead ECG.⁽¹³⁾ In patients with chest pain, the pre-hospital modified HEART score (the HEART⁽¹⁴⁾ score without troponin) is calculated. All acquired data are noted on a handheld device and stored on AmbuSuite, an external secure database. Afterwards, the ambulance paramedic directly contacts the on-call triage cardiologist. The right panel in Figure 1 illustrates the entire routing of patients in the intervention group. In total, 43 cardiologist from all three regional hospitals are scheduled so one cardiologist is on duty for the entire region. GPs can refer patients through EMS consultation, however in the intervention period cardiologist consultation is possible. When a GP is in doubt of referral, they can request cardiologist consultation through EMS with the HART-c method. The triage cardiologist evaluates the pre-hospital data, including, medical history, real-time vital parameters and 12-lead ECG and combines them with (if present) previous medical records and the actual hospital admission capacity of the regional hospitals.

Figure 1. Method of triage. (A) Patient routing without pre-hospital selection where patients are referred to the nearest ED or left at home. If hospital admission capacity is insufficient, patients are transferred to another hospital. (B) Patient routing with pre-hospital selection using pre- and in-hospital data where a cardiologist has insight in live vital parameters and regional hospital capacity.



Also, we developed decision aids for chest pain, dyspnoea and arrhythmia as guidance for triage cardiologists. These decisions aids can help the triage cardiologist in decision making and are added, as addendum 1 for chest pain, addendum 2 for dyspnoea and addendum 3 for arrhythmia, to this manuscript. Based on these comprehensive data, the triage cardiologist and ambulance paramedic decide, as a shared decision with the patient, whether transfer to an ED is necessary and, if so, which hospital and which department is most suitable. The triage decision is sent immediately to the concerning ED nursing staff and the capacity of this hospital is updated automatically (Figure 2). Upon arrival at the ED, cardiac assessment is based on in-house clinical decision rules as guidelines prescribe, 12-lead ECG and laboratory findings.(9)

Intervention group: Tempus Pro Monitor, IntelliSpace Corsium, triage platform and data handling

All ambulances are equipped with a Tempus Pro Monitor(15) (Philips, The Netherlands) (Figure 3) that allows recording of a 12-lead ECG and real-time monitoring of the following vital patient parameters: heart rate, blood pressure and pulse oximetry. The monitor can show trends in measurements and stream data for up to 10 hours. All data are encrypted and shared with the on-call triage cardiologist through secure channels.

Figure 2. Mobile phone triage application: Left panel showing overview of a hospital specific capacity. Right panel showing the ability to update capacity.

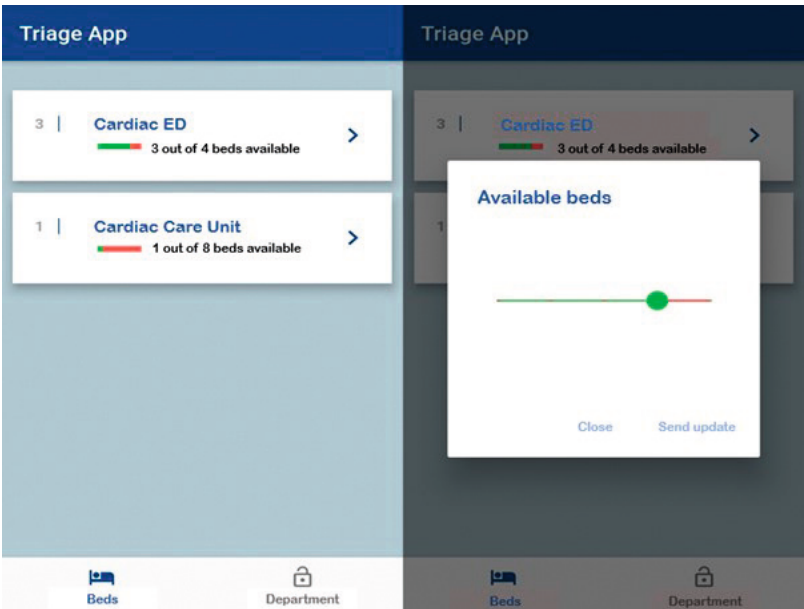
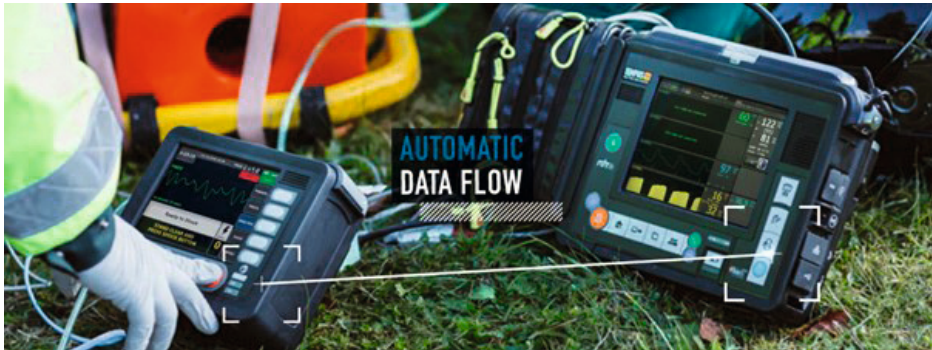


Figure 3. Image of Tempus Pro Monitor.



Using a secure log-in, the on-call triage cardiologist logs in to IntelliSpace Corsium (Philips, the Netherlands) and connects digitally with a patient specific Tempus Pro Monitor. All aforementioned measurements are streamed live. Once the live streaming ends, no patient specific data are stored on the platform. This system of data-transfer is FDA approved.(16,17)

A novel triage platform was developed showing real-time admission capacity of the regional hospitals. The nursing staff in these hospitals continuously updates their admission capacity. Linking these capacity data to a local electronic patient dossier (EPD-Vision; Leiden, The Netherlands), the on-call triage cardiologist has insight into the actual bed occupancy of each hospital. After consultation, the on-call triage cardiologist notes his decision and a message is automatically sent to the nursing staff of the chosen hospital, thereby updating their admission capacity immediately.

Patient data are sent securely from Tempus Monitor to IntelliSpace Corsium. No data are stored on IntelliSpace Corsium. No patient data are transmitted to the mobile phone application. Patient data are transferred from AmbuSuite to our EPD. All patient data and decisions are stored on the EPD of the coordinating hospital and are only accessible for triage cardiologists.

Historical control group: Standard care in pre-hospital setting

The historical control group consists of patients visited by the EMS because of potential cardiac complaints in the year before the onset of the HART-c triage method. Upon arrival by the paramedic, standard medical care consists of medical history, physical examination with vital sign monitoring (blood pressure, heart rate, pulse oximetry) and a 12-lead ECG. All acquired data are noted on a handheld device and stored on AmbuSuite (Topicus, the Netherlands) which is an external secure database. Thereafter, the ambulance paramedic decides, based on predefined national protocols and decision rules for diagnosis, whether transfer to an ED is deemed necessary.(12) Paramedics are able to identify low-risk patient for all medical specialties, and decide whether admission or ED presentation is necessary on every consultation. So, even in the historical cohort group only patients with cardiac

complaints deemed severe enough for presentation are presented to the ED. Of note, at the time of referral, the paramedic has no insight in the previous medical records and the actual hospital admission capacity. The Netherlands has a unique system, where, in the historical cohort in our region, approximately 5% of patients with cardiac complaints aren't referred to a hospital after paramedic assessment, instead these patients are directly referred to their GP or treated at home. However, given the number of unnecessary ED visits, there is still a large cohort of low-risk patients in whom ED presentation could be prevented. After paramedic assessment and hospital transport, cardiac assessment on the ED is based on in-house clinical decision rules as guidelines prescribe, 12-lead ECG and laboratory findings. (9) If evaluation at the ED indicates that hospitalization is mandatory, the patient is admitted in the concerning hospital. However, when admission capacity is insufficient or immediate intervention is not available in the concerning hospital, ambulance transfer to another hospital is mandatory. The routing of patients in the historical control group is illustrated in the left panel of Figure 1.

Objective and outcome measures

The HART-c study is designed to evaluate the efficacy and feasibility of a novel comprehensive pre-hospital triage method which aims to safely reduce unnecessary ED visits in patients with cardiac complaints. The primary outcome is the percentage of patients in who an ED visit can be prevented after EMS consultation. The following secondary end-points will be evaluated:

- Number of ambulance transfers to an ED because of cardiac complaints.
- Number of inter-hospital transfers in cardiac patients.
- Patient, triage cardiologist and GP satisfaction with the HART-c triage method on a 0-10 scale.
- Time from EMS consultation to arrival at the hospital in the both study groups.
- Safety of the HART-c prehospital triage method. This will be evaluated in intervention group patients who are not transferred to an ED after cardiologist consultation. Safety will be assessed by the occurrence of adverse events up to 30 days follow-up. Table 2 displays the pre-specified major and non-major adverse events. To evaluate safety, a dedicated researcher will contact these patients and their GP and evaluate on a case-by-case basis. If a major adverse event is deemed directly attributable to the triage method, the protocol will be adjusted or the study will be terminated prematurely. The study will be deemed safe if the percentage of major adverse events is 1% or lower.
- Feasibility of the HART-c prehospital triage method. This will be evaluated in the intervention group and defined as the absence of technical problems for the ambulance paramedic and the triage cardiologist. This means access to the live-monitored data from the ambulance, hospital data and real-time hospital admission capacity are all available. In order to swiftly manage potential technical problems, the HART-c triage method will start during working hours. If interim analysis reveals that the method is feasible, the time frame in which HART-c triage is available could be extended.

Table 2. Adverse events (30 days after EMS contact)

Major adverse events
Death
Acute coronary syndrome
Other adverse events
Renewed EMS or ED visit for cardiac complaint
Pulmonary embolism
ED visit or hospitalization for acute decompensated heart failure
Ventricular tachycardia or - fibrillation
Cerebrovascular accident (CVA) or transient ischemic attack (TIA)

Statistical analysis

The prevention of an ED visit after EMS consultation will be analysed using a logistic regression analysis. Ambulance transfers and inter hospital transfers in the intervention versus the control group will also be evaluated using logistic regression. Baseline characteristics will be reported as mean and standard deviation or median and interquartile range and compared between historical cohort and intervention. This study will be underpowered to detect differences in mortality and major adverse cardiac events (MACE). Accordingly, these events will only be reported and no further statistics on mortality and MACE will be done. The data will be analysed using IBM SPSS Statistics version 25. A p-value lower than 0.05 will be considered statistically significant.

Patient and public involvement

Patients were involved in the design of the study. During the design stage, representatives from the 'Harteraad', a cardiovascular patient council, were asked for input in study design, choice of outcome measures and methods of recruitment. Also, a dedicated website, www.hartc.nl, was created to inform the public and answer questions from professionals and patients, before and during the study.

Ethics and dissemination

The study is approved by the LUMC's Medical Ethics Committee (P18.213). Patients are requested to provide oral informed consent for contacting their GP at 30 days follow-up. Oral informed consent is requested for cardiologist consultation and study participation by paramedics which is then noted in AmbuSuite. The need for written informed consent was waived by the Medical Ethics Committee. The devices used in this study are FDA and/or CE approved. No manufacturer has a role in study design, data collection, statistical analysis or writing of the manuscript. No financial support is received for this study from any manufacturer. The main results of this trial will be disseminated in one paper.

Discussion

Overcrowding of ED's is a major challenge in healthcare. The HART-c study is a multi-centre prospective study that primarily aims to safely reduce unnecessary ED visits of patients with all types of cardiac complaints. By selecting the hospital best suited for every patient, this method will contribute to more patient-tailored health care and lead to improved utilization of all available healthcare resources in the region.

Recently, interest has shifted from in-hospital - to pre-hospital triage. Pre-hospital cardiologist consultation has been standard procedure for some time in many hospitals in the Netherlands for quick catheterization lab activation when paramedics suspect chest pain patients of STEMI.(18) For all other cardiac complaints no pre-hospital triage procedure is in place for emergency evaluations. However, there have been some studies assessing the possibility of pre-hospital triage and pre-hospital selection of low-risk cardiac patients.

The History and ECG-only Manchester ACS (HE-MACS) decision aid was developed for pre-hospital triage using history, physical examination and ECG. It was derived in 796 patients and validated in cohorts of 474 and 659 patients. 9.4% of all validated patients were identified as 'very low risk' in which ACS could be 'ruled out' with a sensitivity of 99.5%. Its impact, however, was not prospectively evaluated in this study.

The FAMOUS investigators aim to assess the effects of introducing a pre-hospital triage system that stratifies chest pain patients without ST segment elevation into 1) patients at high risk for NSTEMI requiring direct transfer to a PCI hospital, 2) patients at intermediate risk for major adverse cardiac events who could be evaluated at the nearest non-PCI hospital and 3) patients at low risk for major adverse cardiac events who could have further evaluation at home or in a primary care setting.(19) The study was divided in three phases. In the first phase, a venous blood sample was drawn in the ambulance for measurement of the pre-hospital troponin T levels, in order to establish a pre-hospital HEART score and evaluate the possibility of triage at the patient's home. Of the 1127 chest pain patients, 36% had a low modified HEART score and none of them developed a major adverse event.(20) After this first phase proving feasibility, further studies have been done in the pre-hospital setting by the FAMOUS TRIAGE study group. Phase 2, a prospective observational study including 700 patients with suspected NSTEMI-ACS, showed nicely that pre-hospital risk stratification by ambulance paramedics using the HEART score was accurate in differentiating in low and intermediate to high risk.(21) Recently the design of phase 3 has been published, where the FAMOUS study investigators aim to determine if use of the HEART score, including point-of-care Troponin measurement, is non-inferior to routine management. In this phase referral decisions are based on pre-hospital acquired risk stratification. (22)

Another study investigating the added value of point-of-care troponin in the pre-hospital setting is the ARTICA(12) trial. This randomized trial will include patients suspected of

non-ST elevation acute coronary syndrome in whom the modified HEAR score (the HEART score without troponin) is calculated by the ambulance paramedic. If the HEAR score is less than or equal to 3, patients will be 1:1 randomized for 1) presentation at the ED or 2) point-of-care troponin T measurement and transfer of care to the GP in case of a low troponin T value. The primary objective of the ARTICA trial will be healthcare costs at 30 days. The trial is currently ongoing and aims to include 866 patients in 12 months.

The similarity of the currently described HART-c study and the HE-MACS, FAMOUS and ARTICA studies is that all three assess whether patients with chest pain who are at low risk of major adverse events can be identified before presenting to the ED. However, the HART-c study has some added benefit as opposed to earlier known studies. First, the HART-c study does not only identify patients at low-risk for events, but also aims to effectively prevent low-risk patients from actually visiting the ED, as well as further phases from FAMOUS and ARTICA did, by combining pre-hospital risk stratification by the paramedic and real-time cardiologist consultation with insight in live vital parameters and ECG. Secondly, while these studies study only focus on chest pain patients, the HART-c study extends this to all patients with cardiac complaints and could therefore be of benefit for a substantially larger cohort of patients. Furthermore, the HART-c triage method is unique as it combines pre-hospital patient assessment by the ambulance paramedic and direct consultation of an expert triage cardiologist who has access to live-monitored data from the ambulance for all cardiac patients, as opposed to only STEMI patients. Besides these novelties, the HART-c study incorporates hospital data as well as real-time hospital admission capacity to decide which regional hospital is best suited for every patient. In the future, it would be helpful to have pre-hospital information integrated in all hospitals electronic patient dossier. At this moment, however, that is not the case.

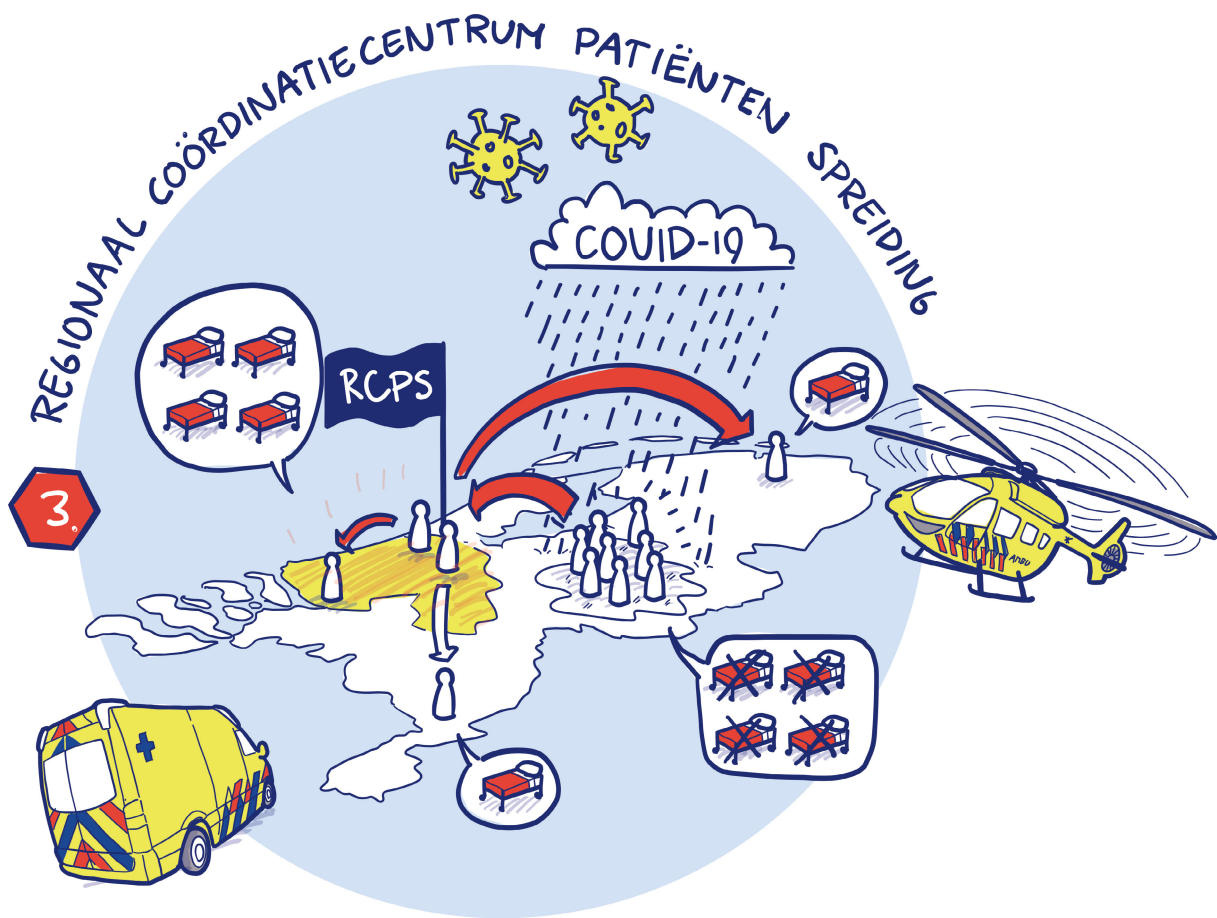
If the results of current study show that the HART-c triage method is effective in safely reducing unnecessary ED visits of patients with all types of cardiac complaints, the next step will be to evaluate cost-effectiveness. When cost-effectiveness can be demonstrated, we feel that the HART-c triage method can be expanded to other EMS regions. Furthermore, last but not least, it may potentially also be useful for other medical specialists aiming to optimize pre-hospital triage of non-cardiac patients. Eventual improvements in pre-hospital triage, such as pre-hospital high sensitive Troponin sampling with a point-of-care test or newly developed and proven risk scores, could always be implemented in this triage protocol.

To conclude, the HART-c study is a multi-center prospective study evaluating the efficacy, and feasibility of a novel comprehensive pre-hospital triage method that combines pre-hospital patient assessment by the ambulance paramedic and direct consultation of a cardiologist who has access to live-monitored data from the ambulance, hospital data as well as real-time hospital admission capacity. If the HART-c study will succeed to safely reduce unnecessary ED visits of patients with all types of cardiac complaints, it may help to decrease ED overcrowding and ultimately reduce healthcare expenditures.

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Chapter 3

Managing Hospital Capacity: Achievements and Lessons from the COVID-19 Pandemic

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Abstract

Introduction:

The coronavirus disease 2019 (COVID-19) pandemic challenged health care systems in an unprecedented way. Due to the enormous amount of hospital ward - and intensive care unit (ICU) admissions, regular care came to a standstill, thereby overcrowding ICUs and endangering (regular and COVID-19-related) critical care. Acute care coordination centers were set up to safely manage the influx of COVID-19 patients. Furthermore, treatments requiring ICU surveillance were postponed leading to increased waiting lists.

Hypothesis:

A coordination center organizing patient transfers and admissions could reduce overcrowding and optimize in-hospital capacity.

Methods:

The acute lack of hospital capacity urged the region West-Netherlands to form a new regional system for patient triage and transfer: the Regional Capacity and Patient Transfer Service (RCPS). By combining hospital capacity data and a new method of triage and transfer, the RCPS was able to effectively select patients for transfer to other hospitals within the region or, in close collaboration with the National Capacity and Patient Transfer Service (LCPS), transfer patients to hospitals in other regions within the Netherlands.

Results:

From March 2020 through December 2021 (22 months), the RCPS West-Netherlands was requested to transfer 2,434 COVID-19 patients. After adequate triage, 1,720 patients with a mean age of 62 (SD = 13) years were transferred with the help of the RCPS West-Netherlands. This concerned 1,166 ward patients (68%) and 554 ICU patients (32%). Overcrowded hospitals were relieved by transferring these patients to hospitals with higher capacity.

Conclusion:

The health care system in the region West-Netherlands benefitted from the RCPS for both ward and ICU occupation. Due to the coordination by the RCPS, regional ICU occupation never exceeded the maximal ICU capacity, and therefore patients in need for acute direct care could always be admitted at the ICU. The presented method can be useful in reducing the waiting lists caused by the delayed care and for coordination and transfer of patients with new variants or other infectious diseases in the future.

Introduction

Health care systems are increasingly under pressure. In Western countries, the ageing population leads to a growing demand for health care and hospital capacity.(1) Paradoxically, the ageing population also results in a decrease in available workforce and thus available health care employees.(2) This, combined with the aim to lower health care expenditures, drives hospitals in the Netherlands to be run efficiently, or in other words, on the minimum required in terms of bed capacity and available staff. Although the system may be efficient, in times of extreme health care demands, the system comes to a halt.

The coronavirus disease 2019 (COVID-19) pandemic challenged the Dutch health care system in an unprecedented way. During the first wave of infections, from March till May 2020, hospitals came under an immense pressure within a few days. As a first step, emergency departments (EDs) and intensive care units (ICUs) tried to increase the number of available beds to obtain extra surge capacity for COVID-19 patients.(3-5) However, this meant regular care came to an abrupt standstill, and even critical non-COVID-19 (ICU) care was difficult to manage safely. Still, a large number of patients was in need of invasive respiratory support and thus ICU treatment. The ICUs were overcrowded, and accordingly, interventions after which ICU surveillance is required were postponed.(6,7) Unfortunately, this pattern repeated during subsequent waves in 2020 and 2021, leading to more postponed care and an increasing waiting list. In April 2022, the Dutch Health Authority (NZA; Utrecht, The Netherlands) estimated that between 100,000-120,000 patients are still on waiting lists for surgical treatment in the Netherlands caused by postponed care during the COVID-19 pandemic.

Before the COVID-19 pandemic, when hospitals had insufficient capacity for patient admissions, patients were transferred between hospitals organized between treating physicians, and the nearest hospital would be the first option for a patient transfer. When this hospital lacked capacity for admission, the physician would contact another regional hospital, and so forth. This system works fine when just one hospital encountered capacity issues. However, when these issues become regional or (inter)national, this system is bound to fail. Clinicians would have to spend an enormous amount of time coordinating patient transfers. Importantly, overcrowding decreases the quality of care, leads to worse patient outcomes, and increases mortality.(8-10) Furthermore, if ICU capacity is insufficient, patients would need to be triaged for access and, the worst-case scenario, would have to be denied access to life-saving care on the ICU based on, for example, age or previous medical history.(11-14) This scenario must be avoided at all cost.

It seems that the coronavirus is here to stay, and furthermore, it is likely that in the future, other variants or entirely different infectious diseases may become wide-spread in the current globalized world. These flare-ups of infectious diseases will put direct pressure on hospital capacity. Optimizing capacity management in moments of acute need is of utmost

importance, since the main issues driving capacity problems (ageing of the population and health care personnel shortages) cannot be changed nor are they easily rectified. Therefore, to prevent hospitals from overcrowding and maintain (ICU) capacity, a new system to adequately coordinate patient transfers between hospitals was (and is) urgently needed. Not solely for COVID-19 patients during this pandemic, but also for other infectious diseases in the future, and to take care of patients whose treatment was postponed or who failed to visit the ED during the COVID-19 pandemic.(15-17)

During the first wave of the COVID-19 pandemic in the Netherlands, acute care coordination center(s) were set up to manage regional and national hospital capacity for COVID-19 patients. This paper presents the achievements of the COVID-19 Regional Capacity and Patient Transfer Service (RCPS) for the region West-Netherlands. Furthermore, the achievements are put in perspective for current and future stress tests of the health care system.

Methods

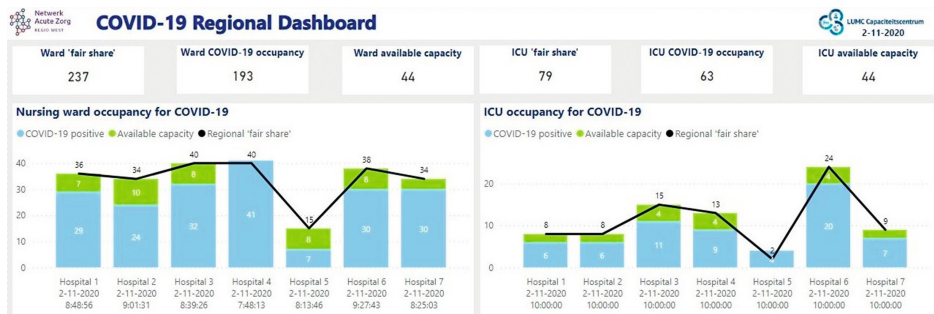
The acute lack of hospital capacity for COVID-19 patients in March 2020 urged physicians, physician-researchers, nurses, data-analysts, general physicians (GPs), nursing homes, and executives to form a new regional system for patient triage and transfer: the RCPS West-Netherlands. The region West-Netherlands is a relatively densely populated urban region comprising seven hospitals servicing approximately 1.5 million people with a regular ICU capacity of 99 beds. The aim of the RCPS West-Netherlands was to ensure that the seven hospitals in the region would share their COVID-19 caseload equally to maximize quality of care for all patients in all hospitals. The presented retrospective observational study assessed hospital capacity and patient transfers throughout the region.

Furthermore, a National Capacity and Patient Transfer Service (LCPS) aimed to equally spread COVID-19 patients among the entire country in corroboration with regional task forces for every region in the Netherlands.(18) Of importance, all patients in the Netherlands are obliged to have health care insurance from one of the available, competing health care insurers. After the first wave (March-May 2020) of the COVID-19 pandemic, all regions in the Netherlands agreed to meet a “fair share” of COVID-19 patients as defined by the LCPS. This fair share was based on the ratio of regular ICU capacity between all 10 regions in the Netherlands. When then the entire region would be overcrowded, the RCPS West-Netherlands contacted the LCPS for patient transfers to hospitals from other regions. The LCPS would then select the appropriate hospital and further arrange transfers in the same way as indicated above. When other regions in the Netherlands were overcrowded, the RCPS received (and distributed) patients within the region. Adequate patient distribution by the RCPS West-Netherlands was based on two pillars: acute and up-to-date information on hospital capacity and a system for triage and transfer.

RCPS – Hospital Capacity Data

For information on hospital capacity, the first step was to provide insight in the number of admitted COVID-19 patients. Initially, automatic aggregating from electronic medical records was not possible as there was no registration standard for COVID-19. Accordingly, each hospital appointed one person to gather data on the number of COVID-19 patients in their hospital, both on the ward and on the ICU. In addition, the number of available ward and ICU beds was registered as well as the ICU occupation of non-COVID-19 patients. These data were automatically uploaded to online spreadsheets developed by the RCPS West-Netherlands, and contact was only needed if data were missing. Based on these data, graphs on COVID-19 occupancy and availability of beds were made. These graphs were openly accessible for all health care professionals in the region on a newly developed platform (Figure 1). After the first COVID-19 wave, from March-May 2020, regional agreements were made on the fair share of COVID-19 patients among the seven regional hospitals. After these agreements were in place, the platform also displayed whether a hospital had sufficient capacity to accept patients from other hospitals (in green) or whether a hospital was over the agreed fair share (black line) and could request transfer of patients. Furthermore, the platform noted the amount of patient movement requests (PMRs) and their current status. Data were requested at fixed times on the day depending on the national and regional risk level (which were developed in June 2020 and changed according to the number of COVID-19 infections and COVID-19 hospital occupancy). The data were updated once on the vigilant level, twice on the worrisome and serious levels, and three times a day on the profoundly serious level.

Figure 1. Overview of Available Beds (green) and Occupied Beds (light blue) for Nursing Ward (left panel) and ICU (right panel) for COVID-19. Note: The black line displays the regional “fair share.”



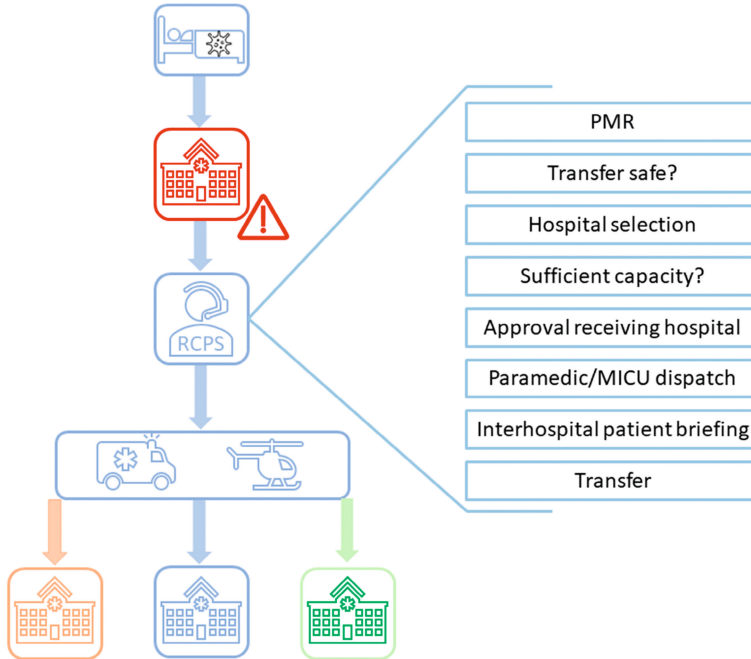
RCPS – Patient Selection for Transfer

The second pillar of the RCPS West-Netherlands was to select patients who were deemed safe for transfer, and subsequently transfer them to the best suited hospital. Physicians, physician-researchers, and nurses were responsible for this triage system (Figure 2) and were continuously available on a central hotline (24/7). When the ED, ward, and/or ICU became overcrowded, a hospital could request patient transfer(s). In the “Patient Movement

Request Form,” all information required to decide whether safe transfer was possible was collected, including age, gender, medical history, current medical status, vital parameters, and, if intubated, mode of therapy used in conjunction with mechanical ventilation. In general, transfers were considered safe if the oxygen suppletion, both for nursing ward and ICU patients, was stable for more than two hours. If the triagist considered transfer safe, the receiving hospital was selected based on the patients’ clinical parameters and/or history. Patients potentially requiring Extra Corporeal Membrane Oxygenation were transferred to an intervention center with these capabilities. Furthermore, patients with prior organ transplants were preferably transferred to a transplant center. Subsequently, capacity was checked in the concerned hospital (as illustrated in Figure 1), whereafter the attending physician from the receiving hospital was contacted. After final approval of this physician, transport was organized by either paramedics (for ward patients) or by Mobile Intensive Care Units (MICU) for ICU patients. The Emergency Medical Services control room was contacted, determined regional ambulance availability, and chose a suitable and available ambulance. Patients would be transported by the nurse paramedics from the region of the receiving hospital. The physician who requested the transfer was contacted to announce the estimated time of pick-up. The patient’s current attending physician would be obligated to contact the physician to which authority the patient would be transferred for a full and up-to-date patient briefing. Furthermore, a printed medical history was brought with the nurse paramedic for the receiving hospital. Physicians could always contact each other themselves or through the RCPS if there were any questions after patient transfer. After this final confirmation, transportation was performed.

Once the RCPS West-Netherlands platform has been developed using both the information on current capacity for COVID-19 patients as well as the system for adequate triage and safe transfer, it is easily activated or inactivated. When COVID-19 infections are scarce, the system is dormant, and when necessary, woken up within a day.

Figure 2. System for Triage of COVID-19 Patients. Note: The overcrowded hospital (red) contacts the RCPS West-Netherlands triage hotline for a PMR (Patient Movement Request). If transfer is safe, the RCPS West-Netherlands selects the best suited hospital for transfer and transfers to one of the available hospitals (orange, blue, green).

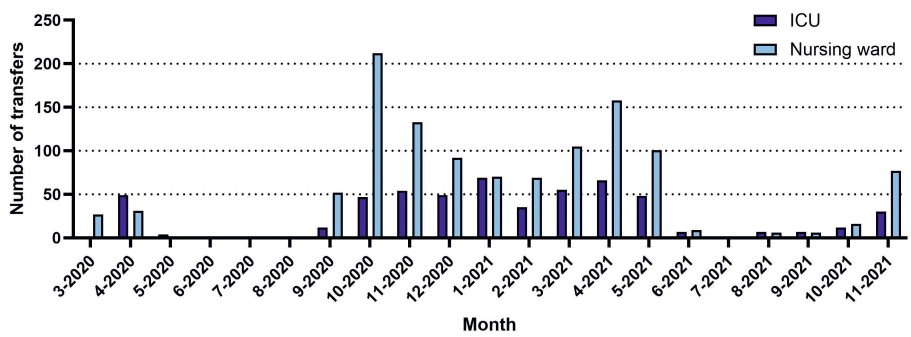


Results

From March 2020 through December 2021 (22 months), the RCPS West-Netherlands was requested to transfer 2,434 COVID-19 patients. Of the 2,434 patients, 714 (29%) were not transferred, either because transfer was considered unsafe ($n = 180$; 25%) or because the transfer request was cancelled ($n = 534$; 75%).

Eventually, 1,720 patients with a mean age of 62 (SD = 13) years were transferred with the help of the RCPS West-Netherlands. This concerned 1,166 ward patients (68%) and 554 ICU patients (32%). Figure 3 shows the number of transfers arranged by the RCPS West-Netherlands for nursing ward and ICU patients per month. Of interest, 830 (48%) patients were transferred from a hospital within the region to another hospital within the region, 733 (43%) patients were transferred from a hospital within the region to a hospital outside the region, whereas 157 patients (9%) were transferred from another region to this region in collaboration with the LCPS.

Figure 3. Number of transfers by RCPS West-Netherlands for ICU (dark blue) and Nursing ward (light blue) per month from March 2020 - November 2021.



RCPS Transfers and ICU/Ward Occupation on a Regional Level

The combined West-Netherlands regional COVID-19 hospital occupation for nursing wards and ICUs is displayed in Figure 4a and Figure 4b. Figure 4a illustrates that the nursing ward occupation (blue) benefitted from RCPS transfers to hospitals outside the region in October-November 2020 and April-May 2021 (as illustrated by the orange highlights). Figure 4b reveals the same phenomenon over time for ICU occupation. Importantly, it also shows that after the first wave, the regional total ICU occupation never exceeded the regional regular (pre-COVID-19) ICU capacity of 99 beds (displayed in red). Accordingly, the RCPS-arranged transfers helped to maintain ICU capacity for non-COVID-19 patients.

Figure 4a. Nursing Ward Occupancy for COVID-19 (blue) in West-Netherlands and the Potential Occupancy if there had been No Patient Transfers (orange).

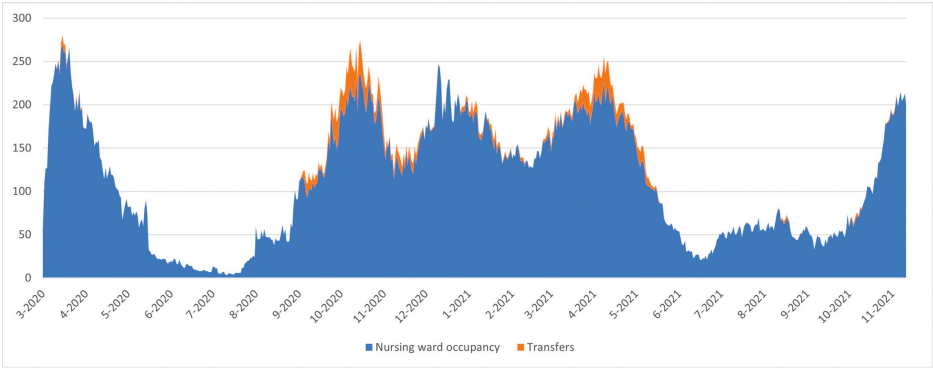
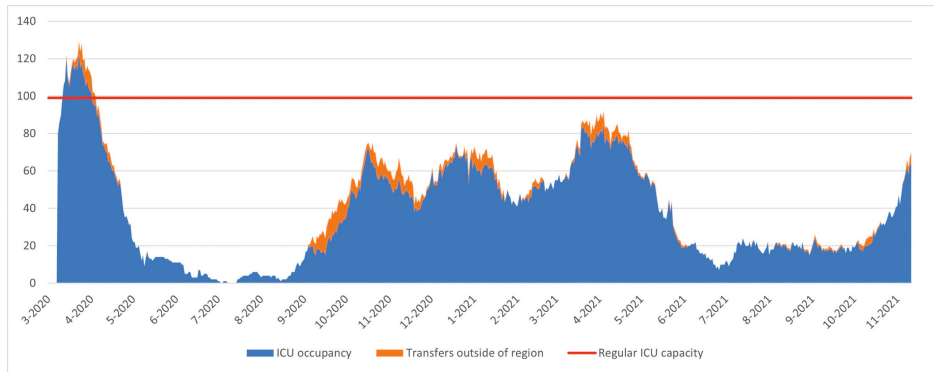


Figure 4b. ICU Occupancy for COVID-19 (blue) in West-Netherlands and the Potential Occupancy (orange). Note: The red line corresponds with the regular ICU capacity for all patients

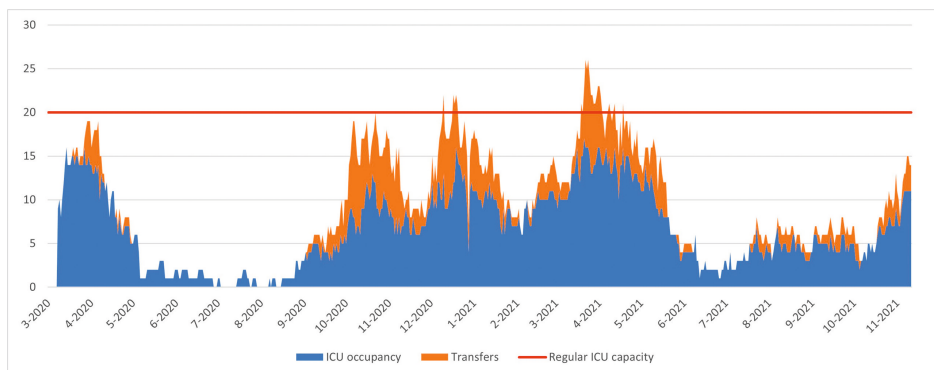


3

RCPS Transfers and ICU Occupation on a Hospital Level

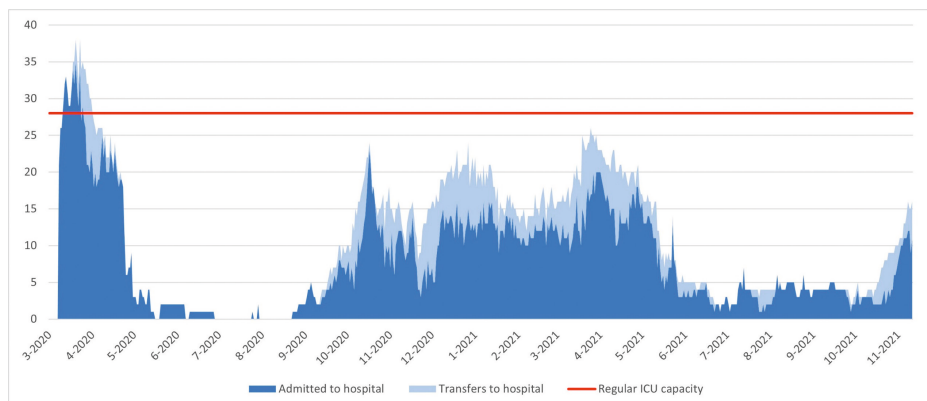
Figure 5a and Figure 5b give more insight into the effect of the RCPS-arranged transfers on the ICU occupation on a single hospital level. The hospital of which these data are displayed in Figure 5a is situated in a highly urban area. The percentage of vaccinated patients in this area was relatively low as compared to the rest of the region. The number of patients from this area far exceeded the available capacity. Pre-COVID-19, this hospital had an average operational ICU capacity of 20 beds. Figure 5a shows the true COVID-19 ICU occupation in blue and the fictitious extra ICU occupation in orange if patients hadn't been transferred. This fictitious occupancy was calculated by multiplying the transfers from this hospital to any other hospital with the average ICU stay for COVID-19 patients (11 days); means were compared with an unpaired t-test. From October 2020 through March 2021, the mean (standard deviation) true ICU occupancy for COVID-19 patients for this hospital was 8.5 (SD = 2.6) beds. However, if patients hadn't been transferred, the potential ICU occupation would have been 12.8 (SD = 4.4) beds ($P < .001$).

Figure 5a. True ICU Occupancy of COVID-19 Patients of a Single Hospital in a Highly Urban Area (blue) and Potential ICU Occupancy if Patients hadn't been Transferred (orange)



The hospital of which the data are displayed in Figure 5b is a tertiary care hospital with advanced intervention capabilities. This hospital has a large reserve capacity because of the large amount of semi-elective interventions that could be postponed. Furthermore, due to the fact this concerns a teaching hospital, teachers and students could be mobilized to help with patient care and logistics. Pre-COVID-19, the hospital had an average operational ICU capacity of 28 beds. Patients directly admitted to this hospital are shown in dark blue and patients transferred to this hospital are shown in light blue. As illustrated, the COVID-19 ICU occupation in this hospital is particularly characterized by the RCPS-arranged transfers towards this hospital. From October 2020 through March 2021, the mean true ICU occupancy for COVID-19 patients for this hospital was 15.1 (SD = 4.6) beds. However, if patients hadn't been transferred, the fictitious ICU occupation would have been 10.5 (SD = 3.9) beds ($P < .001$).

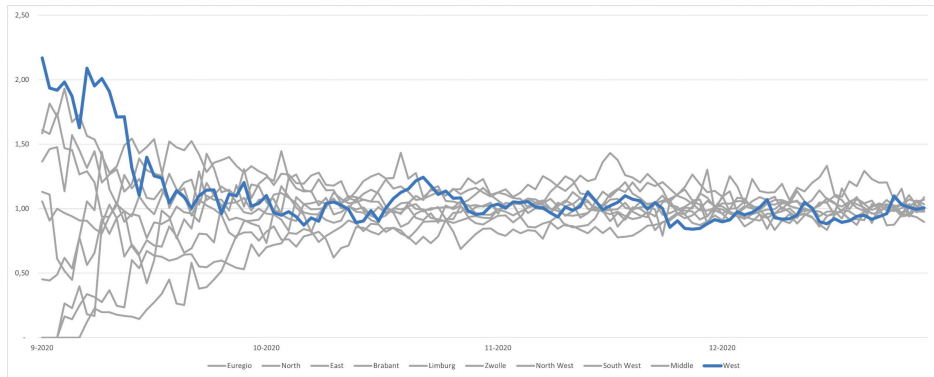
Figure 5b. Total ICU Occupancy of a Tertiary Care Hospital Consisting of Patients Directly Admitted to the Hospital (dark blue) and Patients Transferred to the Hospital (light blue).



RCPS Transfers and ICU Occupation on a National Level

From September 2020 onwards, the national agreements on fair share were established and put in practice through collaboration with the LCPS. Figure 6 displays the ICU occupancy for COVID-19 patients relative to the agreed fair share from September 2020 through February 2021. Initially, the ICU occupancy of hospitals in the region West-Netherlands was more than 2.0-times higher than the agreed fair share, as seen at the start of Figure 6 on the blue line. Transfers from COVID-19 patients to other regions in the Netherlands, a direct effect of close collaboration between the RCPS West-Netherlands and the LCPS, decreased the relative ICU occupancy. As seen in Figure 6, this led to an equal spread of COVID-19 patients throughout the Netherlands.

Figure 6. National ICU Occupancy Relative to “Fair Share” for the Second Wave Starting in September 2020. Note: West-Netherlands in blue, all other regions in the Netherlands in grey.



Discussion

The current study concludes that the health care system benefitted from the RCPS as both ward and ICU occupation were evenly distributed in the region West-Netherlands. After establishing the RCPS, ICU occupation never exceeded the maximal ICU capacity, and accordingly, ICU capacity remained for patients in need of urgent care. By collaborating with the LCPS, the RCPS contributed to an even distribution (or “fair share”) of COVID-19 patients among the country. In future health care capacity stress tests, such as flare-ups of infectious diseases or increasing waiting lists, the RCPS can easily and rapidly be implemented again.

World-wide, the COVID-19 pandemic challenged health care systems, as huge amounts of patients required hospitalization while, at the same time, health care workers dropped out due to illness or quarantine. As a consequence, regular care came to a standstill, acute care was critically endangered, and surgeries after which ICU surveillance is required were postponed. To stop this and prevent recurrence during new flare-ups, building in flexibility in the organization of health care is mandatory. Naturally, various approaches are imaginable.

The most intuitive approach, and first step, for a hospital is to increase the number of available beds for COVID-19 patients, both on ICUs as well as on wards. This can be achieved by using operating rooms for COVID-19 care,(19) building alternate care sites,(20) or quickly training nurses to care for COVID-19 patients.(21) Dutch hospitals are typically run with minimal capacity and personnel in order to minimize health care expenditures, which is illustrated by a relatively low number of available ICU beds (6.7 per 100,000 inhabitants) as compared to other countries, such as Germany (33.4 ICU beds per 100,000 inhabitants).(22) Accordingly, the abilities to increase the number of beds within a hospital in the short and medium term were limited.

Another option to increase the amount of available beds is to discharge patients as early as possible, thereby freeing up capacity for newly admitted patients. E-health applications

allowed patients to be monitored at home, which also helps to reduce the demand of hospital capacity.(23) The GPs and nursing homes in the region West-Netherlands participated in the consultative bodies to set up guidelines for early discharge of patients. Nursing homes even freed up beds especially designed for COVID-19 patients ready for discharge from the hospital, but not ready for discharge home. The next step is critical assessment of which patients benefit most from hospital admission. These assessments should preferably be made in the prehospital setting, before patients are admitted to the ED. Ambulance nurses and GPs can perform this prehospital triage and leave patients at home when ED referral is not necessary, as was done for cardiac complaints in the HART-c study.(24)

When increasing the number of beds and improving prehospital triage offered insufficient solace, collaboration with neighboring hospitals is a next step. The Modena Taskforce response in Italy implemented a dashboard called Pagoda to show the number of positive tests and ICU occupancy throughout the region. Furthermore, the Modena Taskforce took an active role in reallocation of resources to hospitals and in the community.(25) A dashboard was also developed in Picardy, France to coordinate and facilitate the admission of critically ill COVID-19 infected patients. An anesthesiologist, who also functions as an intensivist, was on call for EDs and ICUs of the region. The dashboard showed the occupancy of all regional ICUs and the dispatcher could therefore select the most appropriate hospital for all announced COVID-19 patients.(26) In the Netherlands, regional and national coordination networks were set up; the early experiences of the Acute Care Organization in the Amsterdam region have been published earlier.(18) The method of coordination and transfer in the early experiences in Amsterdam was similar to the method reported in the current study. However, the current study used a newly developed dashboard to gather insight in data of importance for COVID-19 capacity, such as the amount of positive tests, as well as nursing ward and ICU occupancy throughout the entire region. If regional collaboration would not suffice, physicians would have to triage and deny patients access to wards or ICU based on ethical reasons. This worst-case scenario, “code black,” is to be avoided at all costs, although these scenarios were trained in all hospitals within the region.

The RCPS combined information on capacity and triage capabilities to effectively transfer patients throughout the region and the country. Just as the Picardy study, a dispatcher was on call for the ICU in the entire region. However, of added value, the RCPS also arranged (safer and easier) transfers for nursing ward COVID-19 patients. The method of coordination and transfer in the currently presented study was similar to the method reported in the early experiences in Amsterdam and the national network. However, they only presented the experiences of the first two months of coordinating transfers. The current study shows the results from 22 months of coordination during differing numbers of COVID-19 infections. Due to the transfers from the RCPS, the nursing ward and ICU occupancy was lower and vital capacity was maintained for non-COVID-19 patients. Most importantly, the ICU occupancy for the entire region never exceeded the maximal capacity like it did in the first wave. Hospitals with high influx of COVID-19 patients were able to transfer patients to other hospitals in the

region who had a higher reserve capacity or a lower influx of patients. The transfers aided in significantly reducing the ICU occupancy of overcrowded hospitals.

Limitations

Several limitations should be taken into account when interpreting the results. At first, the fictitious ICU occupancy was based on the assumption that an ICU admission would have lasted 11 days if patients would not have been transferred. Therefore, the “true” ICU occupancy could have been lower or higher than the “aggregated” ICU occupancy shown here. Furthermore, it remains to be proven that this system could be replicated in all other countries; however, when data dashboards are available (such as those in Modena and Picardy), dispatch and transferring patients as was reported here is easily implementable. Moreover, the information on capacity requires cooperation between different, sometimes financially competitive, hospitals, which was achieved during this time of crisis. However, it is to be seen whether this system holds up when the crises are less acute.

The currently presented study proves that cooperation between hospitals increases the available capacity through improved use of existing health care resources, thereby preventing critical overcrowding of wards and ICUs. As a further lesson, the RCPS showed that transparency, in this case by making a dashboard available with insight in all COVID-19-related admissions and infections, leads to increased willingness for cooperation for all relevant health care professionals throughout the region and the country.

Although the Omicron variant of SARS-CoV-2 might be less fatal and lead to less hospitalizations, new waves or variants of COVID-19, or indeed other infectious diseases, might cause high numbers of infections and hospitalizations in the future. Also, medical interventions and treatments were postponed to provide capacity for COVID-19 patients on the nursing wards and ICUs. This has led to enormous waiting lists throughout the country for non-COVID-19-related care. Since the presented method of patient transfer and distribution is easily implemented after all logistics are in place, the RCPS and LCPS could potentially aid in eliminating the waiting lists (equally) throughout the country. The data on COVID-19 care could be replaced with information on capacity of postponed interventions, such as operating room, nurse, and surgeon availability, from all hospitals in the Netherlands. The COVID-19 (hospital capacity) crisis has shown that there is strength in cooperation and full transparency of available health care resources.

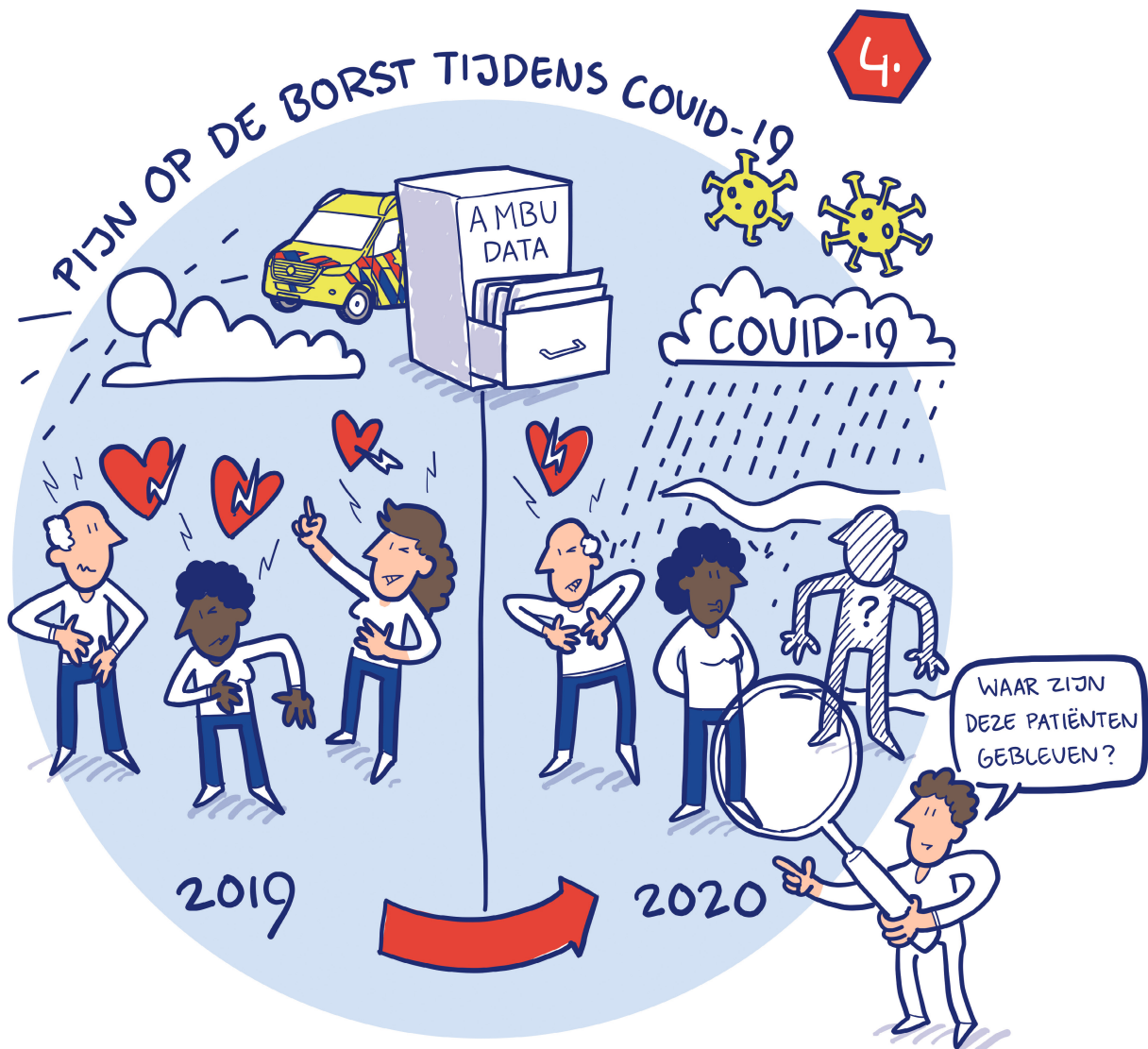
Conclusion

The health care system in the region West-Netherlands benefitted from the RCPS for both ward and ICU occupation. Due to the coordination by the RCPS, regional ICU occupation never exceeded the maximal ICU capacity, and therefore, patients in need for acute direct care could always be admitted at the ICU. The presented method can be useful in reducing the waiting lists caused by the delayed care and for coordination and transfer of patients with new variants or other infectious diseases in the future.

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Chapter 4

Emergency medical services evaluations for chest pain during first COVID-19 lockdown in Hollands-Midden, the Netherlands

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Abstract

Objective To assess whether the COVID-19 lockdown in 2020 had negative indirect health effects, as people seem to have been reluctant to seek medical care.

Methods All emergency medical services (EMS) transports for chest pain or out-of-hospital cardiac arrest (OHCA) in the Dutch region Hollands-Midden (population served >800,000) were evaluated during the initial 6 weeks of the COVID-19 lockdown and during the same time period in 2019. The primary endpoint was the number of evaluated chest pain patients in both cohorts. In addition, the number of EMS evaluations of ST-elevation myocardial infarction (STEMI) and OHCA were assessed.

Results During the COVID-19 lockdown period, the EMS evaluated 927 chest pain patients (49% male, age 62 ± 17 years) compared with 1041 patients (51% male, 63 ± 17 years) in the same period in 2019, which corresponded with a significant relative risk (RR) reduction of 0.88 (95% CI 0.81–0.96). Similarly, there was a significant reduction in the number of STEMI patients (RR 0.52, 95% CI 0.32–0.85), the incidence of OHCA remained unchanged (RR 1.23, 95% CI 0.83–1.83).

Conclusion During the first COVID-19 lockdown, there was a significant reduction in the number of patients with chest pain or STEMI evaluated by the EMS, while the incidence of OHCA remained similar. Although the reason for the decrease in chest pain and STEMI consultations is not entirely clear, more attention should be paid to the importance of contacting the EMS in case of suspected cardiac symptoms in possible future lockdowns.

Introduction

The rapid spread of the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), responsible for coronavirus disease 2019 (COVID-19), urged the Dutch government to announce a national lockdown, starting 16 March 2020. Apart from social distancing, people were encouraged to stay at home as much as possible and schools were closed. These measures were effective in controlling the spread of the virus and reduced the pressure on the Dutch healthcare system.

There is growing interest in the indirect health effects of the COVID-19 lockdown period. On the one hand, improved air quality and reduced work-related stress might have been beneficial. On the other hand, fear of contracting the virus made people cancel, postpone or limit even urgent medical treatments, potentially resulting in life-threatening situations(1). Indeed, during the COVID-19 lockdown period, a significant increase in out-of-hospital cardiac arrest (OHCA) has been observed in Italy and France(2-4).

This finding can be partly attributed to the complications of COVID-19 but may also be related to late presentations of ST-elevation myocardial infarction (STEMI) patients with electrical or mechanical complications. Consistently, a decrease in STEMI admissions in the COVID-19 pandemic period has been observed in Italy, France, Spain and the USA(5-11). Tan et al. analysed cardiac catheterisations in California, USA and reported that the drop in STEMI admissions was paralleled by a decrease in coronary catheterisations for patients with unstable angina or non-ST-elevation myocardial infarction(12). However, it remains to be determined whether chest pain patients across the board were reluctant to seek acute medical care during the COVID-19 lockdown.

The aim of the current study was to investigate the number of chest pain patients evaluated by the emergency medical services (EMS) during the COVID-19 lockdown in the Netherlands in 2020. Simultaneously, EMS alerts for STEMI and OHCA were assessed. These data may attribute to the understanding of the indirect health effects of the COVID-19 lockdown and may contribute to forthcoming guidelines for acute care management during possible future lockdowns.

Methods

The AmbuSuite database (Topicus, the Netherlands) contains data of all ambulance transports performed by the Regional Ambulance Service Hollands-Midden (RAVHM), the EMS of the Dutch security region Hollands-Midden, which has over 800,000 inhabitants. All data in the AmbuSuite database are collected prospectively by the paramedics on the ambulance and include patient data (medical history, main complaint, other symptoms, vital parameters, electrocardiogram and working diagnosis), as well as data regarding the ambulance ride (dispatch time, time of arrival at the scene, time of arrival at the hospital, and address of scene and hospital). The decision to dispatch an ambulance to a patient is made in the regional control centre and is based on the Advanced Medical Priority Dispatch System, Professional Quality Assurance, which was similar in 2019 and 2020(13).

All patients for whom an ambulance was dispatched by the RAVHM during the initial 6 weeks of the first COVID-19 lockdown period in the Netherlands (week 12–17 in 2020) were eligible for inclusion in the current study. Inclusion criteria were: (1) age over 18 years, and (2) ambulance ride because of a main complaint of chest pain or nontraumatic OHCA.

If the paramedics suspected a STEMI, this diagnosis was verified in the central percutaneous coronary intervention centre in the region. A nontraumatic OHCA was defined as any cardiac arrest after exclusion of cases with obvious accidental causes, irrespective of whether resuscitation was attempted or not. To determine the cause of OHCA, the EMS reports of all OHCA cases were analysed on a case-by-case basis by two experienced reviewers (EdK and SB). OHCA cases were divided in shockable rhythm and nonshockable rhythm on arrival by the EMS, with the latter category further subdivided in the following causal categories: cardiac aetiology, related to COVID-19 and unknown aetiology.

For the control group, the same inclusion criteria and definitions were applied to all patients for whom an ambulance was dispatched by the RAVHM in week 12–17 in 2019.

This study complied with the Declaration of Helsinki. The institutional medical ethics committee approved the study protocol (G20.111) and waived the need for individual informed consent.

Statistical analyses

Categorical data were compared using the chi-squared test and are presented herein as number with percentage. Continuous data were compared with a one-way ANOVA or Kruskal-Wallis test and are presented as mean \pm standard deviation. The incidence of chest pain, STEMI and OHCA in the COVID-19 lockdown period were compared with the incidence in the same period in 2019. Incidence rates and relative risk (RR) were estimated based on data on the regional population in 2019 and 2020 from Statistics Netherlands (www.cbs.nl) and compared using the chi-squared test.

The data were analysed using R version 3.6.2. *P*-values <0.05 were considered statistically significant. All data were coded and anonymised.

Results

During the first Dutch COVID-19 lockdown period in 2020, the EMS evaluated 927 chest pain patients, compared with 1041 patients during the same period in 2019. As shown in Table 1, the characteristics of these patients did not differ between both time periods. In particular, gender and age were similar, as well as haemodynamic parameters.

Table 1. Characteristics of chest pain patients evaluated during COVID-19 lockdown in 2020 and during same time period in 2019

	COVID-19 lockdown (n=927)	2019 (n=1041)	P value
Gender (male)	455 (49%)	534 (51%)	0.529
Age (years)	62 ± 17	63 ± 17	0.184
Know coronary disease	215 (23%)	224 (22%)	0.403
Heart rate (bpm)	86 ± 28	86 ± 29	0.415
Systolic blood pressure (mmHg)	152 ± 31	150 ± 31	0.133
Diastolic blood pressure (mmHg)	88 ± 19	88 ± 18	0.487

As illustrated in Figure 1, the incidence of chest pain—defined as the number of chest pain patients evaluated by the EMS divided by the total number of inhabitants in the EMS region—was lower during the COVID-19 lockdown period (927/809,104) than during the same period in 2019 (1041/802,325). This resulted in a significant RR reduction in the incidence of chest pain in the COVID-19 lockdown period of 0.88 (95% confidence interval (CI) 0.81–0.96, *p*= 0.006).

Fig. 1 Incidence of chest pain during COVID-19 lockdown period in 2020 and during same time period in 2019.

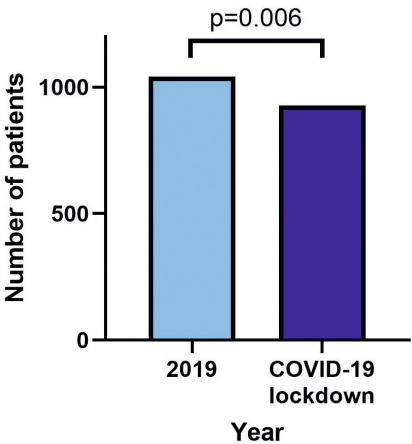
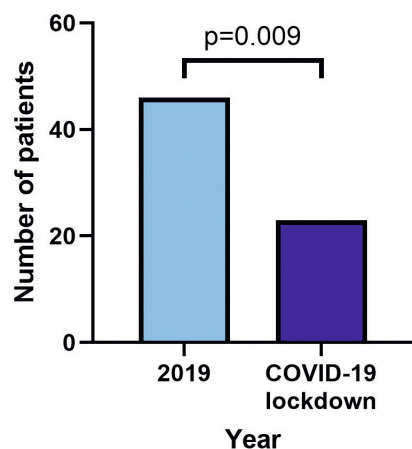


Table 2 displays the characteristics of STEMI patients in the COVID-19 lockdown period ($n=23$) and in the same period in 2019 ($n=46$). The incidence of STEMI—defined as the number of STEMI patients divided by the total number of inhabitants in the EMS region—was lower during the COVID-19 lockdown period (23/809,104) than during the same period in 2019 (46/802,325). Accordingly, during the COVID-19 lockdown period, there was a significant RR reduction in STEMI incidence of 0.52 (95% CI 0.32–0.85, $p=0.009$) compared with the same period in 2019 (Fig. 2).

Table 2. Characteristics of STEMI patients evaluated during COVID-19 lockdown in 2020 and during same time period in 2019.

	COVID-19 lockdown ($n=23$)	2019 ($n=46$)	P value
Gender (male)	20 (87%)	39 (85%)	1
Age (years)	62 ± 10	64 ± 12	0.567
Known coronary disease	18 (78%)	41 (89%)	0.283
Heart rate (bpm)	76 ± 38	77 ± 32	0.945
Systolic blood pressure (mmHg)	140 ± 26	138 ± 46	0.866
Diastolic blood pressure (mmHg)	86 ± 20	83 ± 28	0.614

Fig. 2 Incidence of ST-elevation myocardial infarction during COVID-19 lockdown period in 2020 and during same time period in 2019



The characteristics of OHCA patients in the COVID-19 lockdown period ($n=56$) and in the same period in 2019 ($n=45$) are shown in Table 3. Both groups were comparable regarding gender, mean age and previously known coronary artery disease. Analysis of the EMS reports revealed a trend towards a different cause of OHCA in the COVID-19 lockdown period compared with the same period in 2019 ($p=0.05$). In particular, a shockable rhythm

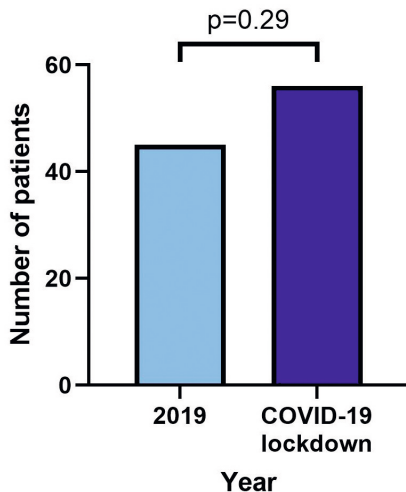
upon arrival by the EMS was found in 15 patients (27%) in the COVID-19 lockdown period and in 18 patients (40%) in the same period in 2019; a cardiac aetiology was found in 10 patients (18%) and in 4 patients (9%), respectively. During the COVID-19 lockdown period, COVID-19 was the probable cause of OHCA in 6 patients (11%).

Table 3. Characteristics of OHCA patients evaluated during the COVID-19 lockdown period and the same period in 2019.

	COVID-19 lockdown (n=56)	2019 (n=45)	P value
Gender (male)	32 (57%)	31 (69%)	0.086
Age (years)	70 ± 14	70 ± 12	0.906
Known coronary disease	15 (62%)	14 (58%)	1
OHCA details			0.050
- Shockable rhythm	15 (27%)	18 (40%)	
- Non-shockable rhythm, cardiac aetiology	10 (18%)	4 (9%)	
- Non-shockable rhythm, COVID-19	6 (11%)	0 (0%)	
- Non-shockable rhythm, unknown aetiology	25 (44%)	23 (51%)	

The incidence of OHCA—defined as the number of OHCA patients divided by the total number of inhabitants in the EMS region—was 56/809,104 during the COVID-19 lockdown period and 45/802,325 during the same period in 2019 (RR 1.23, 95% CI 0.83–1.83, $p=0.29$; Fig. 3).

Fig. 3 Incidence of out-of-hospital cardiac arrest during COVID-19 lockdown period in 2020 and during same time period in 2019



Discussion

The main finding of this study was that the number of patients evaluated by the EMS because of chest pain was lower during the COVID-19 lockdown than during the same period in 2019. This was paralleled by a reduction in the incidence of STEMI, while the incidence of OHCA remained unchanged.

Beyond the harmful effects of COVID-19 on the respiratory and cardiovascular system(14), there have been major concerns about the indirect negative health effects of the COVID-19 lockdown. Fear of being infected when alerting the EMS or attending the hospital, made people cancel, postpone or limit medical treatments, potentially resulting in worse outcomes. To better understand the indirect health effects of the COVID-19 pandemic, previous reports have focused on STEMI and OHCA; however, it is still unknown whether patients with all types of chest pain were reluctant to request acute medical care during a COVID-19 lockdown. In this perspective, the current study provides novel insights, as it showed significantly less chest pain patients were evaluated by the EMS during the Dutch lockdown in 2020 than in the same period in 2019. The current findings are in line with those of Tan et al., which showed a decline of 26% in the number of patients with all types of acute coronary syndrome undergoing cardiac catheterisation in a single centre in California during the COVID-19 pandemic(12).

As part of the broad spectrum of chest pain evaluations, we also evaluated EMS alerts for STEMI and showed a significantly reduced number of STEMIs during the COVID-19 lockdown compared with the same period in 2019. This is in line with the previously reported sharp decrease in STEMIs during the COVID-19 lockdown(5-11). De Rosa et al. reported a clear reduction in acute myocardial infarction in Italy, where the number of hospitalisations halved compared with the previous year, with a 26.5% reduction in STEMI diagnoses(5). Garcia et al. demonstrated a decrease of 38% in STEMI referrals for nine centres in the USA during the COVID-19 period(11).

Our reported decline in the number of chest pain patients as well as STEMI patients admitted to hospitals during the COVID-19 lockdown period may be conceptually attributed to different pathophysiological, environmental and behavioural factors. One can hypothesise that less vigorous physical exercise or reduced physiological stress during a lockdown can result in fewer coronary plaque ruptures. Intense physical exertion reportedly leads to enhanced thrombogenic tendency, increased blood viscosity and increased propensity for thrombocyte aggregation and thereby results in an elevated risk of acute myocardial infarction(15).

Furthermore, changes in the environment may play a role in lowering the incidence of cardiovascular morbidity and mortality, since the COVID-19 lockdown has been associated with a dramatic decline in air pollution(16, 17). Reduced exposure to air pollution due to

less traffic and industrial activities during a lockdown, may lead to fewer cardiovascular events. Studies have shown that even short-term exposure to elevated air pollution or traffic exposure is positively associated with elevated risk of myocardial infarction. The underlying pathophysiology is not completely understood, but fine particulate matter-induced inflammation, oxidative stress, and vascular dysfunction are all named as possible contributing factors(18). Several reports have also shown more hospital admissions for ischaemic heart disease, with short-term elevation of inhalable or particulate matter air pollution(19).

Last, but most probably not least, behavioural changes may contribute to less EMS evaluations for chest pain or STEMIs, since patients may be reluctant to seek medical contact as they fear being infected or are unwilling to burden the healthcare system even further.

Other studies have reported an increase in OHCA during COVID-19 lockdowns(2-4). Marijon et al. suggested that OHCA occurring in patients with respiratory or cardiovascular complications of COVID-19 as well as OHCA related to advanced cardiac injury in late STEMI presenters might explain the observed OHCA increase(4). In the current study, the incidence of OHCA remained unchanged. During the COVID-19 lockdown period, however, there was a trend towards a different cause of OHCA, with less patients with a shockable rhythm upon arrival by the EMS and more patients with cardiac complaints shortly before the occurrence of OHCA. Conceptually, this may concern patients who were reluctant to seek medical help in an earlier phase of acute myocardial infarction. Combined with the fact that the total number of OHCA patients in our study was relatively small and that the number of COVID-19 patients in the Netherlands was relatively low compared with that in Italy and France, this might explain that we only saw a shift in causes of OHCA rather than an increase in OHCA incidence. Of note, the aetiologies were defined through case-by-case evaluation of the EMS reports—and not through postmortem pathology, the golden standard—and are thus subjective.

Strengths and limitations

When interpreting the results of the current study, its strengths and limitations should be taken into account. The most important strength is the use of the AmbuSuite database, which contains prospectively collected data of all ambulance transports in Hollands-Midden, a Dutch 'security region' with over 800,000 inhabitants.

Unfortunately, no data from other regions were available. Further research is needed to conclude if these findings are similar in, for example, regions with less air pollution. Furthermore, this database does not provide insight into people with chest pain who decide not to contact the EMS. In addition, it does not contain individual outcome data. Therefore, it was not possible to analyse whether clinical outcomes of chest pain patients evaluated by the EMS was better or worse during the COVID-19 lockdown period.

Conclusion

We showed a significant decrease in the number of patients with chest pain evaluated by the EMS. As seen in the graphic abstract, available as online supplementary material, this was paralleled by a reduction in the incidence of STEMI, while the incidence of OHCA remained unchanged. While the reason for the decrease in chest pain and STEMI incidence is not entirely clear, there are multiple possible factors. A decrease in physical exertion, a dramatic decrease in air pollution and reluctance to contact medical authorities during the COVID-19 lockdown could have played a role in the reduced number of ambulance transports for chest pain and STEMI. Alerting the public to the importance of contacting the EMS in case of suspected cardiac complaints may help to reduce the secondary health damage in case of possible future lockdowns.

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Chapter 5

Artificial Intelligence Algorithm to Predict Acute Coronary Syndrome in Prehospital Cardiac Care: Retrospective Cohort Study

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Abstract

Background: Overcrowding of hospitals and emergency departments (EDs) is a growing problem. However, not all ED consultations are necessary. For example, 80% of patients in the ED with chest pain do not suffer from an acute coronary syndrome (ACS). Artificial intelligence (AI) is useful in analyzing (medical) data, and might aid health care workers in prehospital clinical decision-making before patients are presented to the hospital.

Objective: The aim of this study was to develop an AI model which would be able to predict ACS before patients visit the ED. The model retrospectively analyzed prehospital data acquired by emergency medical services' nurse paramedics.

Methods: Patients presenting to the emergency medical services with symptoms suggestive of ACS between September 2018 and September 2020 were included. An AI model using a supervised text classification algorithm was developed to analyze data. Data were analyzed for all 7458 patients (mean 68, SD 15 years, 54% male). Specificity, sensitivity, positive predictive value (PPV), and negative predictive value (NPV) were calculated for control and intervention groups. At first, a machine learning (ML) algorithm (or model) was chosen, afterwards the features needed were selected and then the model was tested and improved using iterative evaluation and in a further step through hyperparameter tuning. Finally, a method was selected to explain the final AI model.

Results: The AI model had a specificity of 11% and a sensitivity of 99.5% whereas usual care had a specificity of 1% and a sensitivity of 99.5%. The PPV of the AI model was 15% and the NPV was 99%. The PPV of usual care was 13% and the NPV was 94%.

Conclusion: The AI model was able to predict ACS based on retrospective data from the prehospital setting. It led to an increase in specificity (from 1% to 11%) and NPV (from 94% to 99%) when compared to usual care, with a similar sensitivity. Due to the retrospective nature of this study and the singular focus on ACS it should be seen as a proof-of-concept. Other (possibly life-threatening) diagnoses were not analyzed. Future prospective validation is necessary before implementation.

Keywords: cardiology; acute coronary syndrome; Hollands Midden Acute Regional Triage-cardiology; prehospital; triage; artificial intelligence; natural language processing; angina; algorithm; overcrowding; emergency department; clinical decision-making; emergency medical service; paramedics

Introduction

Overcrowding of emergency departments (ED) and hospitals is a concerning problem in many countries and is associated with increased mortality, delays in the initiation of critical care and dissatisfied patients and health care workers(1,2). The causes of overcrowding are multifactorial, such as a large and growing supply of patients due to ageing, and insufficient capacity in hospitals due to personnel and resource shortages. Cardiovascular disease is the most common cause of mortality and morbidity, and as such contributes enormously to overcrowding. In 2019 there were an estimated 5.8 million new cases of ischemic heart disease in Europe(3). Therefore, a large volume of patients presented to the hospital (around 1.95 million per year in the Netherlands(4)) are presented with symptoms of possible cardiac origin. However, not all patients visiting the ED need to be admitted to the hospital. For example, 80% of patients visiting the ED because of chest pain do not have an acute coronary syndrome (ACS) and can be reassured and discharged after a short analysis(5,6). If these patients could be identified before visiting the ED, this could relieve pressure from EDs and prevent time-consuming and stressful ED visits for patients.

While there is extensive experience with prehospital triage in patients with trauma, the experience with prehospital triage in patients with cardiac symptoms is still limited. Recently, the FamouS Triage(7), ARTICA(8) and Hollands Midden Acute Regional Triage-cardiology(9,10) studies focused on improving triage of cardiac patients when patients contact the emergency medical services (EMS). These studies focused on selecting “low risk” patients who could safely stay at home after paramedic assessment. The FamouS and ARTICA studies used prehospital point-of-care troponin assessments, while the Hollands Midden Acute Regional Triage-cardiology study implemented a novel triage platform combining prehospital and hospital data.

Of note, the decision whether a patient can stay at home or should be transported to an ED in these studies was a purely human decision by health care professionals. The accuracy of these decisions is therefore highly dependent of training and expertise. Within these processes enormous amounts of data were gathered, processed, evaluated, and analyzed.

Artificial intelligence (AI) could be useful in analyzing data in medicine(11,12). In cardiology, AI has mostly been used in integration and analysis of cardiovascular imaging(13). However, there is potential to aid health care professionals in clinical decision-making such as certain apps do(14). AI could be useful in making predictions or risk scores by learning from the available data. It might then be possible to identify low-risk patients through these AI generated risk scores in the prehospital setting. Patients could be reassured and safely stay at home, instead of being presented to the hospital.

The aim of the current study was to develop an AI model able to predict ACS from prehospital data in patients presenting to the EMS. The AI model may be used as a proof

of concept for future research on prehospital decision-making. In order to be a reliable tool, the AI model should have an increased specificity and at least a similar sensitivity as compared to regular care, as this could lead to an increase in patients staying at home after EMS consultation.

Methods

Study Design and Patient Population

The retrospective cohort study included all adults (aged 18 years or older) presenting to the regional EMS Hollands-Midden, servicing around 800,000 inhabitants in a mostly urban area, between September 2018 and September 2020 for symptoms suspected to be of cardiac origin. Patients were recruited in the prehospital setting by nurse paramedics. All data were acquired by a nurse paramedic and noted in AMBUFORMS (Topicus). Baseline characteristics are shown in Table 1.

Table 1. Baseline characteristics of all recruited patients divided between patients who were ultimately presented to the hospital and patients who stayed at home after EMSa consultation in this retrospective cohort study analyzing an AI algorithm in prehospital cardiac care.

	Hospital presentations (n=7386)	Stayed at home (n=72)
Female, n (%)	3991 (54)	37 (51)
Age (year), mean (SD)	68 (15)	67 (12)
Distance to hospital (km), mean (SD)	11.6 (8.3)	14.3 (12.0)
Day of presentation, n (%)		
Monday	1414 (19)	20 (28)
Tuesday	1412 (19)	13 (18)
Wednesday	1224 (17)	15 (21)
Thursday	1196 (16)	5 (7)
Friday	1260 (17)	10 (14)
Saturday	438 (6)	5 (7)
Sunday	442 (6)	4 (6)
Chest pain at presentation, n (%)	2741 (37)	31 (43)
ACS ^b diagnosis, n (%)	980 (13.3)	4 (5.6)

^aEMS: emergency medical service. ^bACS: acute coronary syndrome.

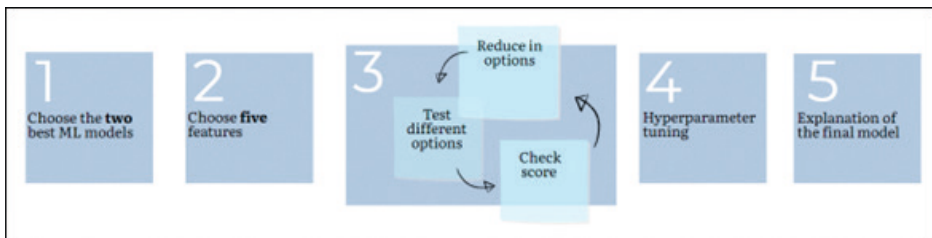
Patients suffering out-of-hospital cardiac arrest, (cardiac) shock, or patients visited by the EMS for noncardiac symptoms were excluded. The final diagnoses for ACS (defined as ST elevation myocardial infarction, non-ST elevation myocardial infarction, or unstable angina pectoris(15)) from all referrals to the ED were acquired through hospital billing data.

AI Model

Separate columns of datapoints, or features, were filled by paramedics for every patient. Patient data were stored on an external secure database AMBUFORMS. Patient data comprise of quantitative data such as oxygen saturation, blood pressure, and heart rate and textual data created by the paramedic, such as the patient's medical history, medication use, current symptoms, and physical examination. Table S1 in Multimedia Appendix 1 shows an overview of all available features evaluated by the AI model.

The 5 steps toward developing the final AI model are shown in Figure 1. The model was developed using Python (version 3; Python Software Foundation). At first, a machine learning (ML) algorithm (or model) was chosen, afterwards the features needed were selected and then the model was tested and improved using iterative evaluation and in a further step through hyperparameter tuning. Finally, a method was selected to explain the final AI model.

Figure 1. In total, 5 steps toward developing the final artificial intelligence model in this retrospective cohort study analyzing an AI algorithm in prehospital cardiac care. ML: machine learning.



In the first step, the 2 best ML models (or algorithms) were selected from 4 algorithms, namely support vector machine (SVM), random forest (RF), k-nearest neighbor (KNN) and logistic regression (LR). These models were preselected because they are well known when applying natural language processing (NLP)(16,17).

The *SVM model* converts the input to a vector in space. If all inputs are plotted, a hyperplane will be created. This plane is able to separate 2 classes of input from each other. The *RF model* is a classification algorithm consisting of many decisions trees. It creates an uncorrelated forest of decision trees from building individual decision trees. The forest of trees is more accurate than any individual tree. The *KNN model* finds distances between queries and examples in the data, selecting the specified number (K) closest to the query. Then the model votes for the most frequent label in the case of classification. The *LR algorithm* can be used for regression as well as classification tasks, for our model the classification tasks are used. LR has a binary response variable, which belongs to one of the classes. It is used to predict categorical variables with the help of dependent variables. Every model generated an F β score by analyzing all available datapoints. The most appropriate models

were selected based on their respective F β score. The F β score was calculated as $(1+\beta^2) \times ((\text{precision} \times \text{recall}) / ((\beta^2 \times \text{precision}) + \text{recall}))$.

Features (or columns of data) were selected in the second step. Further, 3 new features were created; a selection of all available data (CompiledALL), a selection of all textual data (CompiledTEXT), and a selection of all data thought to be relevant by a consulted cardiologist (CompiledSELECT). The CompiledSELECT feature was a combination of medical history, current symptoms, and electrocardiogram description, all of which were textual data noted by a nurse paramedic on the scene. Based on the F β and recall scores, commonly used within AI, the most relevant features were selected.

In the third step, separate parts of the algorithm were tested, after which highest scores were compared and other options were reduced or eliminated. In the first phase of this 'loop' the 2 remaining models are tested, and the model with the lowest recall scores was eliminated. In the second phase, the selected features from step 2 were preprocessed and analyzed. The final feature was selected for the model. Then the threshold for the algorithm was analyzed and determined to find the correct false negative (FN) score.

The fourth step is fine-tuning the hyperparameters. In ML models settings can be altered to change the behavior of the model, and make predictions more accurate. Each model has one or multiple of these settings, called hyperparameters. For example, the SVM model has only 1 hyperparameter, named C. This hyperparameter has the options: 0.01, 0.1, 1, 10, 100, and 1000. During the previous steps, the default settings were used. By changing these settings, through trial-and-error, the final AI model can be optimized and the outcomes altered.

A Python package called 'Explain Like I'm 5' (ELI5) was used to improve understanding of the model(18). ELI5 explains classifiers and predictions in NLP by scoring the importance of words in text. The higher the importance of a word, the more influence it has on the eventual output of the AI model.

Statistics

The following metrics were used to test reliability of the final AI model: precision, recall, and F β score. The F β score combines precision and recall, and the 'beta' highlights the importance of one of the 2 metrics. A beta of 1 means both metrics were equally important, a beta lower than 1 means precision was more important, and a beta higher than 1 means recall was more important.

These metrics were clinically correlated using sensitivity, specificity, negative predictive value (NPV), and positive predictive value (PPV). Sensitivity (=recall) is the ability to correctly identify patients with a disease, in this case meaning no ACS were missed. Specificity is the ability to correctly identify patients without the disease, for the purpose of this study meaning no patients were unnecessarily presented to the hospital. NPV predicts the likelihood of a

correct decision to leave patients at home and PPV (=precision) predicts the likelihood of a correct decision to present a patient to the hospital. The equations are given in Table S2 in Multimedia Appendix 2. All these parameters were calculated using true positives (*TP*), false positives (*FP*), true negatives (*TN*), and *FN*. *TP* was defined as a patient who was presented to the hospital who ultimately suffered ACS. *FP* was defined as a patient presented to the hospital who did not suffer ACS. A *TN* was a patient who could stay at home and did not suffer ACS, and a *FN* was defined as a patient who stayed at home but ultimately did suffer ACS.

Ethics Approval

This study complies with the Declaration of Helsinki and the triage method was approved by the Hospital's Medical Ethics Committee (P18.213). Patients were requested to provide verbal informed consent for participating in the triage method. Data were analyzed anonymously, all patient data were deidentified.

Results

Study Population

In total, 7458 patients (mean 68, SD 15 years, 54% male) were included in this study. For every patient, 270 features were available for the AI model. The primary presenting symptom was chest pain in 4686 (63%) patients, while 2772 (37%) patients had other symptoms (such as dyspnea, palpitations, or near-collapse). The EMS nurse paramedics decided that 72 patients could stay at home (1%); these patients were consequently not transported to the ED. Accordingly, in 7386 patients a medical analysis was performed at the ED: this showed an ACS in 980 patients. From the patients who stayed at home ultimately 4 were diagnosed with ACS within 30 days of staying at home.

AI Model

The RF model had a mean $F\beta$ score of 0.61, and the LR model had a mean $F\beta$ score of 0.63. The 2 best models were the SVM model with an $F\beta$ score of 0.71 and the KNN model with an $F\beta$ of 0.88. The $F\beta$ had a beta of 2 because this would mean that *FN*, an important outcome for the final model, had a higher weight. Table S3 in Multimedia Appendix 3 shows the outcomes from all AI models per feature.

Second, the 5 most relevant features were selected. The $F\beta$ (again with a beta of 2) scores of all 17 features were between 0.75 and 0.89 for both the KNN and the SVM model. The recall scores were used to reduce the starting 17 features to 5. The 'CompiledSELECT', physical examination-, physical survey-, differential diagnosis-, and control room note features had the highest recall scores. For the SVM model these were 0.6, 0.85, 0.71, 0.79, and 0.61, respectively. The KNN model had recall scores of 0.13, 0, 0.02, 0.01, and 0.05.

In the third step recall and *FN* score of both models for the 5 selected features were calculated. The recall scores for SVM were higher (as seen in step 2) and therefore the KNN

model was eliminated. In the second phase the 5 remaining features were preprocessed, reducing the model to 1 single feature. The feature with the highest recall and FN score was 'CompiledSELECT.' Lastly a threshold was selected for the model. A threshold of 0.955, 0.983, and 0.991 gave recall scores of 0.95, 0.995, and 1, respectively.

The final step of the model, step 4, is the tuning of hyperparameters. As mentioned before, the SVM model has 1 hyperparameter, or setting, named C. Recall scores were highest when this hyperparameter was set to 0.1.

The results from analyzing the textual data by the final AI model were shown through ELI5 in Figures 2 and 3. The AI model recognized words that are linked to myocardial infarction in green and words that are not linked to myocardial infarction in red. All textual data were analyzed this way. The final AI model resulted in a recall score of 1.00 and precision score of 0.15 as compared to 1.00 and 0.12 in usual care respectively.

Figure 2. Global explanation of the AI model in this retrospective cohort study analyzing an AI algorithm in prehospital cardiac care. Green shows words which correlate with patients who suffered myocardial infarction, whereas red correlates with patients who did not suffer from myocardial infarction.

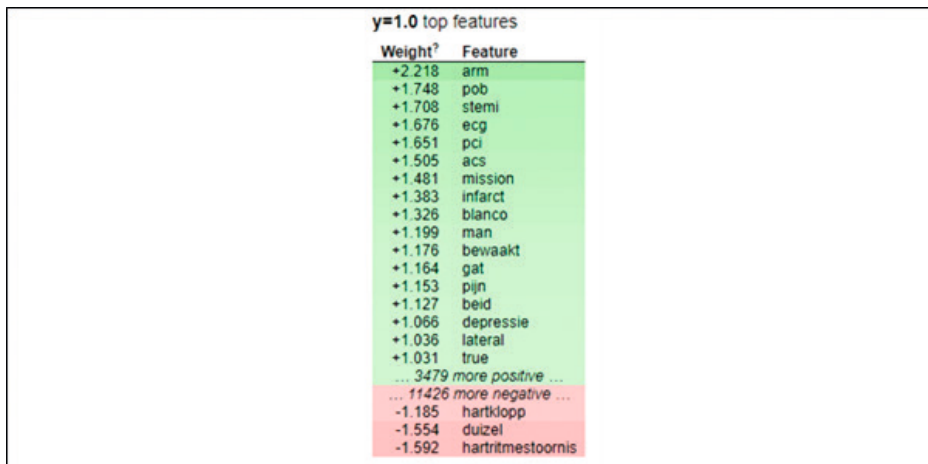
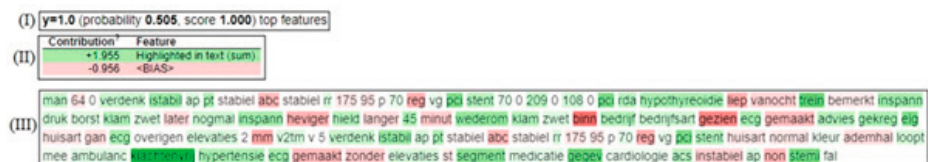


Figure 3. Explanation by ELI5 where red words represent the class 'myocardial infarction' and green 'no-myocardial infarction' in this retrospective cohort study analyzing an AI algorithm in prehospital cardiac care. ELI5: 'Explain Like I'm 5.'



Clinical Results

The AI model was able to identify 713 TNs (patients who could stay at home without suffering ACS) as compared to 68 TNs in usual care. There were 4 FNs (patients who stayed at home but did suffer ACS) in the usual care group and 4 in the AI model, meaning a total of 645 patients could potentially stay at home without missing more ACS. This is an increase in TNs of 945% (n=577). Subsequently, the FPs (patients presented at the hospital without suffering ACS) decreased by 10% (n=645) as there were 5761 patients identified in the AI model and 6406 patients in usual care. TPs remained similar when comparing usual care with the AI model, both comprised of 980 patients. An overview of patients who stayed at home and where presented to the hospital and their subsequent diagnosis is given in table 2 (for usual care) and table 3 (for the AI model)

Table 2. Number of patients who stayed at home and number of patients presented to the hospital in the usual care group and there subsequent diagnosis.

Usual care	Stayed at home	Hospital presentations
ACS diagnosis	4	980
No ACS	713	5761

ACS: Acute Coronary Syndrome

Table 3. Number of patients who stayed at home, and number of patients presented to the hospital in the AI model group and there subsequent diagnosis .

AI model	Stayed at home	Hospital presentations
ACS diagnosis	4	980
No ACS	68	6406

ACS: Acute Coronary Syndrome

The AI model had a specificity of 11% and a sensitivity of 99.5% whereas usual care had a specificity of 1% and a sensitivity of 99.5%. The PPV of the AI model was 15% and the NPV was 99%. The PPV of usual care was 13% and the NPV was 94% (Figure 4a and 4b).

Figure 4a. Sensitivity and Negative Predictive Value (NPV) in the usual care group (light blue) and in the AI model group (dark blue).

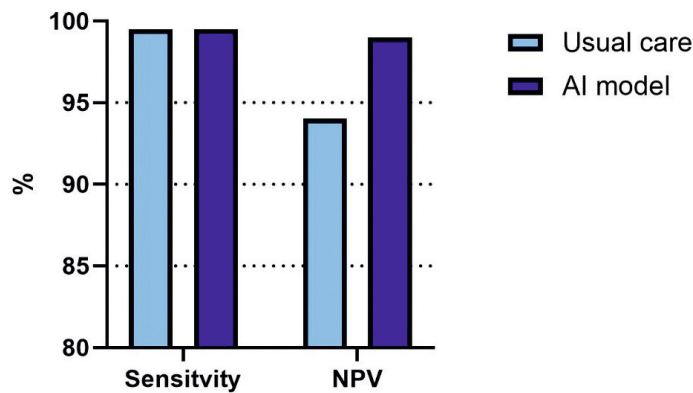
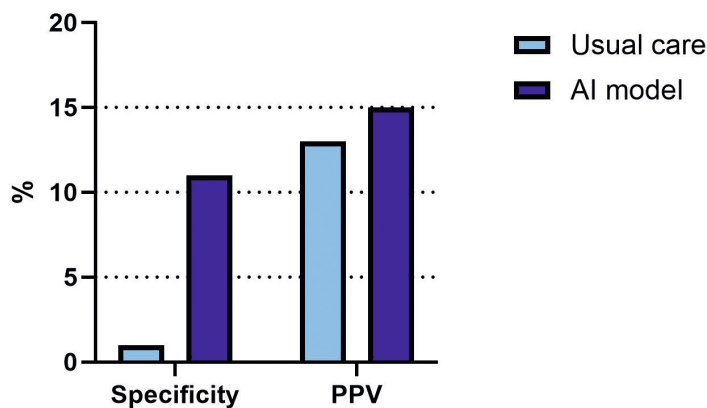


Figure 4b. Specificity and Positive Predictive Value (PPV) in the usual care group (light blue) and in the AI model group (dark blue).



Discussion

Principal Findings

This study evaluates a newly developed AI model to predict ACS in patients presenting to the EMS. The model was developed as a proof of concept for prehospital triage based on large amounts of EMS data. This study demonstrates that the AI model is able to predict ACS with a similar sensitivity and a higher specificity as compared to usual care, which means more patients can stay at home and a low number of ACS are missed.

Resources in health care are scarce, the shortages in health care personnel are increasing and hospitals and ED's are increasingly (at risk of being) overcrowded. With an ageing

population more patients are expected in the near future, putting even more strain on the existing health care resources. It is of utmost importance to correctly allocate (or triage) these scarce resources to the right patient, preferably as early as possible in the health care process, thus, ideally, before patients are presented to the ED. Selecting the appropriate patient to safely stay at home can prevent stressful and time-consuming ED visits for patients. Risk scores developed and analyzed by AI could be useful since the current forms of prehospital triage(8,9,19-21) all depend on health care personnel, such as EMS paramedics, cardiologists, or general practitioners. AI models could reduce costs and decrease the amount of personnel needed while maintaining high quality health care. As a last point, (human) experience-based triage has the potential for errors, whereas AI, by definition, has a lower inter-observer variability. Implementation of AI may therefore potentially limit these errors.

AI within the field of cardiology has mainly been applied in automating the interpretation of cardiac imaging(13,22) and electrocardiography(23). It has also proven to be useful in predicting events in asymptomatic patients and in patients following ACS(24,25), or, when using textual data, by determining cardiovascular disease risk from social media(26). In-hospital AI, outside of the field of cardiology, has been able to identify patients admitted to the ED at risk of clinical deterioration(27), and identify low-severity patients for quick discharge(28). However, the evidence for the use in prehospital triage is scarce. In the prehospital setting, there have been some studies where AI was able to predict the need for critical care or hospital admission for all patients(29,30), and in mass casualty incidents(31). However, prehospital triage for cardiac symptoms with the intention for patients to stay at home after EMS consultation has not been described.

Because of the retrospective nature of this study, the binary outcome (ACS or no ACS) was known and thus supervised ML classification was used. The 4 presented algorithms (SVM, RF, KNN, LR) are most commonly used(16,17) when using supervised classification and analyzing textual data (and thus when applying NLP). Ultimately, the SVM algorithm was implemented in the final AI model.

The model had a specificity of 11% and a sensitivity of 99.5% whereas usual care had a specificity of only 1% and a sensitivity of 99.5%. The AI model led to an 1100% increase in specificity as compared to regular care. The AI model was able to identify more TPs, meaning more patients without ACS could stay at home after EMS consultation. Both methods had a very high sensitivity, meaning there were (almost) no FNs. Thus, a very small number of patients (<0.5% or n=4) were left at home who ultimately suffered ACS. This is important, as delayed care in patients with ACS results in higher mortality and disability rates(32). To the best of our knowledge there are no examples of studies within the field of cardiology that describe the specificity and sensitivity of the clinical use of their AI algorithm as described in this study. As mentioned above, in clinical practice the specificity of prehospital triage for cardiac symptoms is very low, as ACS is a diagnosis that is not to be missed. Of note, sensitivity and specificity of all patients in this study, low-risk, medium-risk and high-risk

combined, are comparable to the sensitivity and specificity of only the low-risk patients in the HEART score (<2), which had a sensitivity of 98.9% and a specificity of 14.7%(33).

This study is the first study to evaluate an AI model in prehospital triage of cardiac patients. The model analyzed routinely collected data from prehospital EMS care and, when applied, could be a useful tool to aid in triage for first responders. The AI model could easily be trained for other purposes, such as different symptoms or cardiac symptoms in different countries. An AI based model is futureproof, since, when available, more advanced techniques, models, and approaches could be built in to the model. The complexity and amount of medical data (and patients) is expected to increase in the future, therefore advanced pattern finding by AI can be hugely beneficial. It seems that an AI model which uses text classification could be useful for other medical specialties as well. Prehospital triage of surgical patients could possibly be improved by an AI model. The model could analyze the textual data from a nurse paramedic and assess whether patients need to be transported and, importantly, which hospital might be best suited for that specific patient. For instance, patients with fever and specific abdominal pain could be presented to a hospital with surgical capabilities, where patients with shortness of breath and a history of coughing up blood could be assessed in a hospital with the capabilities of treatment of pulmonary embolism, thereby improving prehospital triage. Furthermore, it is far less dependent on the (scarcely) available professional workforce. For future research, validation, and eventual implementation it is important to streamline the methods of data collection and analysis. By structuring medical data AI models could be of even greater benefit. Of importance, health care professionals should always have the final say in the decision.

This study has some limitations. The most important limitation is that the AI model was only able to predict ACS or 'no ACS,' a sort of pseudo-diagnosis. It does not take into account important, possible life-threatening causes of chest pain, such as pulmonary embolism or aortic dissection. Therefore, it cannot be said with surety that patients can be left at home if ACS is ruled out. Future research should include all of these possible causes and look for stronger endpoints such as hospital admission for other causes or even 30-day mortality. It is important to note that an AI model should always be used as a tool, or aid, in prehospital decision-making. It should never be used to overrule decisions made by clinicians who are with the patients.

Furthermore, the AI model has only been able to identify patients in a retrospective manner, validation and further research is needed in a prospective setting. Herein also lies the practical limitation, as it is still very difficult to prospectively validate AI models, especially in the prehospital setting. Furthermore, the model needs to be trained regularly and there will always be cases which the model hasn't seen before making it possibly prone to errors.

Conclusions

This retrospective study is a proof-of-concept of an AI model which was developed to identify patients with ACS in the prehospital setting based on textual data. The model had a similar sensitivity and an 1100% increased specificity as compared to usual care

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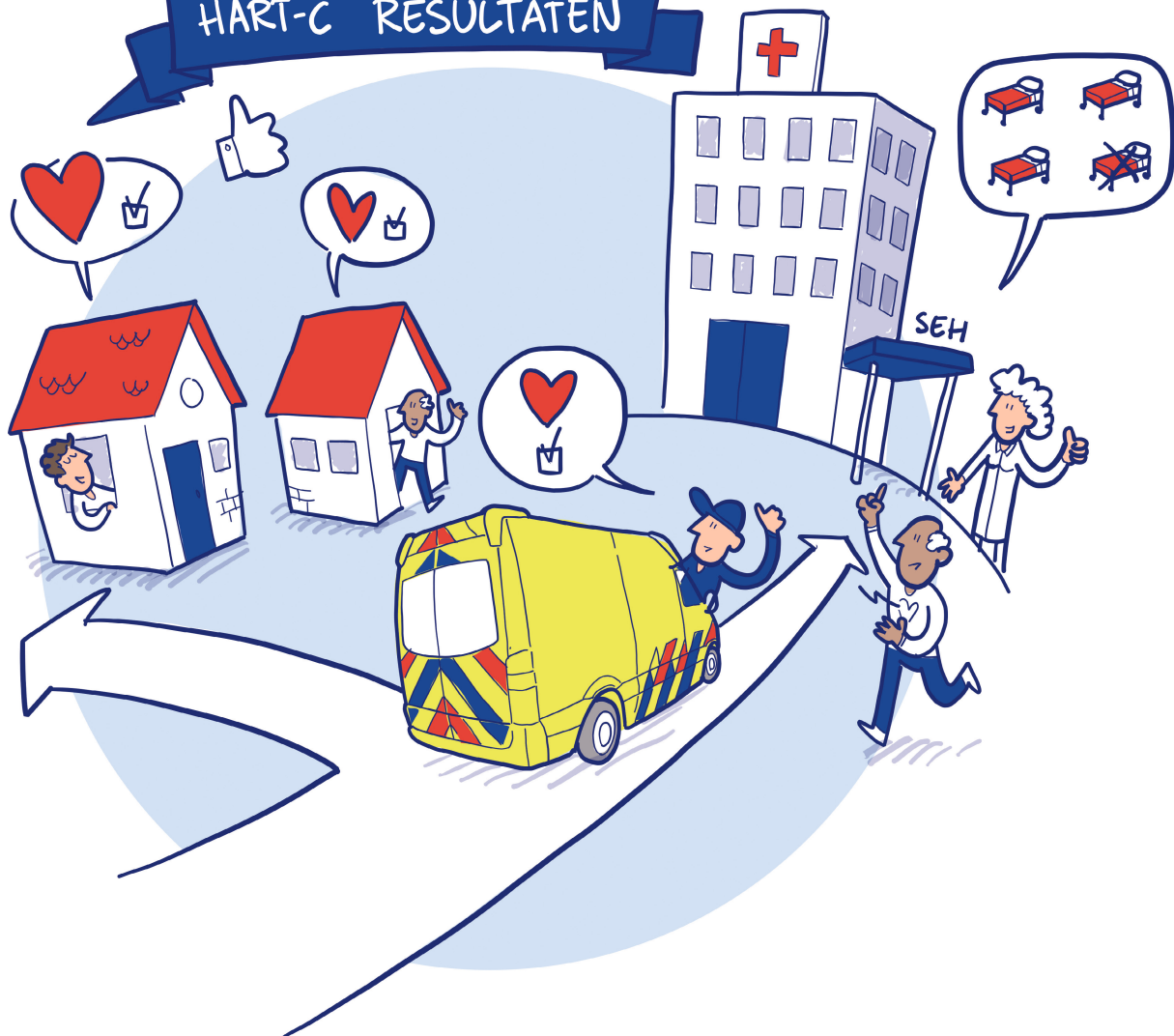
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6.

HART-C RESULTATEN



Chapter 6

Improved Prehospital Triage for Acute Cardiac Care: Results from a Multicentre Prospective Study – Hollands-midden Acute Regional Triage – cardiology (HART-c)

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Abstract

Background: Cardiac symptoms are the most prevalent reason for emergency department visits. However, over 80% of these patients are sent home after ruling out acute cardiovascular disease.

Objective: The HART-c study aims to investigate whether a novel prehospital triage method, combining prehospital and hospital data with expert consultation, can increase the number of patients who could safely stay at home after emergency medical service (EMS) consultation.

Methods: The triage method combined prehospital EMS data, such as ECG and vital parameters in real-time, and data from regional hospitals (including previous medical records and admission capacity) with expert consultation. During the 6 months intervention and control periods 1536 and 1376 patients were consulted by the EMS respectively. The primary endpoint was the percentage change of patients who could stay at home after EMS consultation.

Results: The novel triage method led to a significant increase in patients who could safely stay at home, 11.8% in intervention group versus 5.9% in the control group: odds ratio 2.31 (95% CI 1.74-3.05). Out of 181 patients staying home, only 1 (<1%) was later diagnosed with ACS, no patients died. Furthermore the amount of interhospital transfers decreased: relative risk 0.81 (95% CI 0.67-0.97).

Conclusion: The HART-c triage method led to a significant decrease in interhospital transfers and an increase in patients with cardiac symptoms who could safely stay at home. The presented method thereby reduced overcrowding and, if implemented throughout the country and for other medical specialties, could potentially reduce even more cardiac and non-cardiac hospital visits.

Introduction

Cardiac symptoms are one of the most prevalent reasons for emergency department (ED) visits (1). Interestingly, the vast majority of patients with cardiac symptoms are sent home after ruling out acute cardiovascular disease. Previous studies showed that up to 80% of all patients with chest pain do not have an acute coronary syndrome (ACS) (2-4). This calls for improvement, especially in an era in which the Dutch healthcare system is increasingly under pressure.

Overcrowding of EDs leads to worse patient outcomes, increased healthcare costs and dissatisfied patients and - healthcare workers (5-8). From a cardiologist's perspective, previous attempts to reduce overcrowding mostly focused on rapid risk stratification to rule-out ACS with the development of risk scores, including the frequently used HEART (History, Electrocardiogram, Age, Risk factors, Troponin) score (9, 10). These risk scores, however, do not address the root cause of overcrowding, as it still requires patients to visit the ED. Accordingly, attention shifted from in-hospital triage towards prehospital triage. The recent FamouS Triage(11) and ARTICA(12) studies focussed on prehospital risk stratification. These studies bring progress, but only focus on chest pain patients, whereas patients with other cardiac symptoms also contribute considerably to ED overcrowding. Improved prehospital triage of all cardiac patients, could potentially reduce unnecessary ED visits and contribute to effectively combatting overcrowding throughout the Netherlands.

To improve prehospital triage for all patients with cardiac symptoms a comprehensive novel triage method was developed, entitled Hollands-midden Acute Regional Triage – cardiology (HART-c). This triage method combined *prehospital* real-time emergency medical services (EMS) data with *hospital* data and direct consultation of a cardiologist with insight in the triage platform. The primary aim of the HART-c study was to investigate whether this novel triage method could increase the number of patients who could safely stay at home.

Methods

Study design

The HART-c study was a multicentre prospective cohort study with a historical control group. The intervention group comprised adult patients visited by the EMS in the Dutch region Hollands-Midden, for symptoms of suspected cardiac origin during a six-month period, between 09-09-2019 and 06-03-2020. The historical control period was six months in the year prior, between 09-09-2018 and 06-03-2019. Full details on the study protocol were published previously.(13)

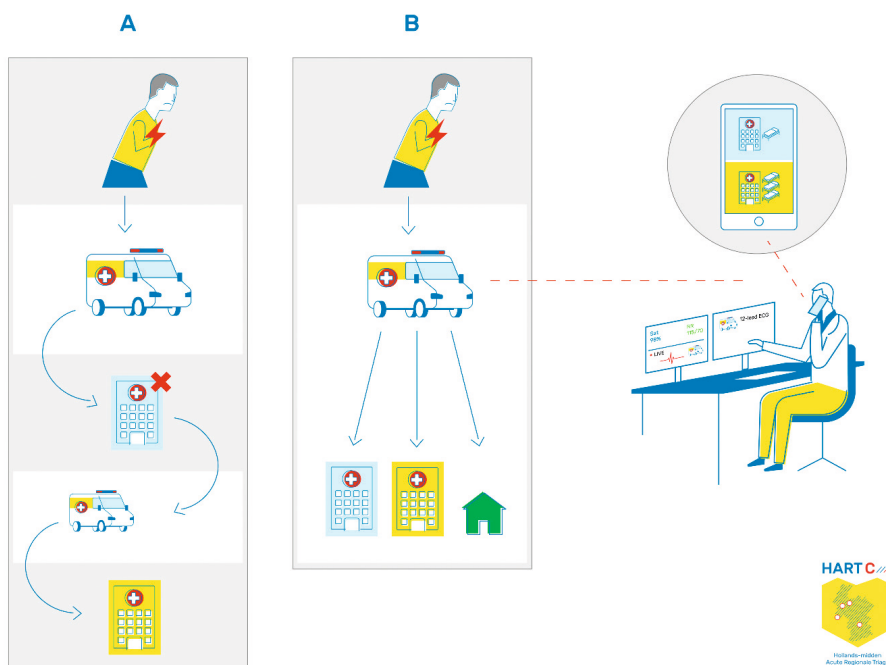
Intervention group – novel triage method

During the intervention period, patients presenting to the regional EMS with symptoms of suspected cardiac origin received standard clinical assessment including medical history,

physical examination and a 12-lead ECG in line with the National Protocol for Emergency Medical Care (LPA version 8.1, June 2016). For the HART-c study, all regional ambulances were equipped with a Tempus Pro Monitor (Philips, the Netherlands) which streams encrypted patient specific pre-hospital data (vital parameters, ECG) to IntelliSpace Corsium (Philips, the Netherlands). All acquired data from the clinical assessment and Tempus Pro Monitor were transferred to the newly developed digital triage platform.

Following informed consent, the nurse paramedic was directly connected to a cardiologist who was on-call. On the triage platform, the patient specific pre-hospital data is combined with in-hospital data (such as real-time admission capacity for the regional hospitals and previous medical history). The paramedic and cardiologist decided whether transfer to a hospital would be of added value and, if so, which hospital suited best. The on-call cardiologist noted the decision in the triage platform and a message was automatically sent to the nursing staff of the chosen hospital, thereby immediately informing them of a new referral and updating the hospital's admission capacity (Figure 1). Notably, in the control group the nurse paramedic's decision was based only on prehospital data without expert cardiologist consultation.

Figure 1. Triage method with (A) standard care and possible interhospital transfers in the case of overcrowded ED or nursing ward and (B) novel triage method combining prehospital data with live streaming of ECG and vital parameters, hospital data such as previous ECG's, medical history and admission capacity and expert consultation.



Outcome measures

The main objective of the HART-c study was to investigate whether the triage method could safely increase the number of patients with suspected cardiac symptoms who could stay at home after EMS consultation. For the purposes of this study, safety was defined as the absence of MACE (death or ACS) 30 days after EMS consultation.

Secondary endpoints were the total amount of hospital referrals, the total number of interhospital transfers, the time from EMS consultation to hospital arrival, final diagnoses, and patient -, GP -, and cardiologist satisfaction.

Interhospital transfers were defined as an EMS transfer from one of the three participating hospitals to any other hospital. The final cardiac diagnoses at the ED were assessed using hospital billing data. EMS consultation, ED admission, hospital admission, or GP consultation for any reason within 30 days after EMS consultation were noted. Cardiologists, patients and their GPs rated their satisfaction with the triage method on a 1-10 scale, where 1 was the least satisfactory and 10 the most satisfactory.

Statistics

Baseline characteristics were reported as mean and standard deviation (SD) or median and interquartile range (IQR) and compared between control and intervention. The proportions of patients staying at home during the intervention and control periods were compared using binary logistic regression analysis, adjusted for age, sex and month (14). The total number of EMS consultations during the intervention and the control period were compared based on incidence rates based on data on the regional population at the time from Statistics Netherlands (www.cbs.nl), 808.860 and 801.600 in intervention and control period respectively, and compared using a chi-squared test. The number of interhospital transfers were compared based on incidence rates from the total number of EMS consultations. The difference in the percentage of final diagnoses per presenting symptom, per ACS diagnosis and in total were evaluated using a chi-squared test. Data were analysed using IBM SPSS Statistics V.25.

Results

Baseline

The intervention group comprised 1536 patients (69±15 years, 51.3% male) and the historical cohort group 1376 patients (68±15 years, 49.9% male). The baseline characteristics of both groups were well comparable (Table 1).

Table 1. Baseline characteristics in control - (n=1376) and intervention group (n=1536).

	Control (n=1376)	Intervention (n=1536)	p-value
Age (years)	68 ± 15	69 ± 15	0.181
Sex (male,%)	49.9	51.3	0.637
<u>Main presenting symptom (n,%):</u>			0.186
Chest pain	733 (53.3%)	880 (57.3%)	
Palpitations	198 (14.4%)	206 (13.4%)	
Dyspnoea	282 (20.5%)	284 (18.5%)	
(Near) syncope	163 (11.8%)	166 (10.8%)	
Sinus rhythm (%)	75.1	77.3	0.182
Breathing frequency (breaths per minute)	19 ± 9	19 ± 8	0.153
Oxygen saturation (%)	97 (96-98)	97 (96-98)	0.611
Pulse (beats per minute)	90 ± 31	88 ± 29	0.102
Systolic blood pressure (mmHg)	148 ± 29	150 ± 28	0.220
Diastolic blood pressure (mmHg)	86 ± 18	86 ± 17	0.987
Distance to hospital (km)	11 ± 8	11 ± 8	0.940

Explanatory footnote: Missing data were excluded. Figures represent mean ± standard deviation, or absolute numbers (%).

Primary objective

In the intervention group, 181 (11.8%) patients could stay at home after EMS consultation, compared to 77 (5.9%) patients in the control group (Figure 2). The percentage of patients who could stay at home per month is shown in Figure 3.

Figure 2. Percentage of patients with cardiac symptoms left at home in control group (5.9%) and intervention group (11.8%).

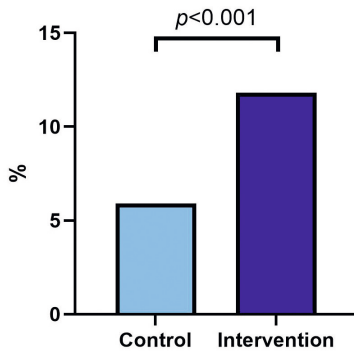
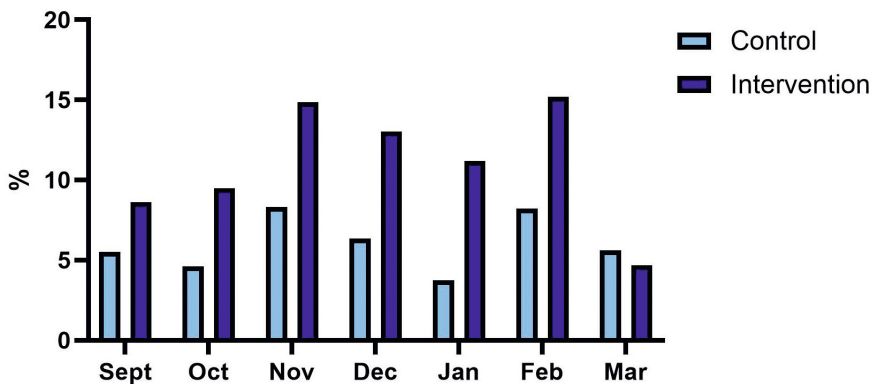


Figure 3. Percentages of patients with cardiac symptoms left at home by the EMS in the control group and in the intervention group per month.



Logistic regression showed an increased odds for staying at home in the intervention group as compared to the control group: 2.31 (CI 1.74-3.05, $p<0.0001$). The logistic regression model was adjusted for age, sex and month of presentation (to account for seasonal patterns) (Table 2). The most prevalent presenting symptom in patients who could stay at home was chest pain (37.6% in control and 48.6% in intervention group), followed by palpitations (36.4% and 27.1%), and dyspnoea (10.4% and 12.2%) ($p=0.31$).

Table 2. Logistical regression model showing the relative risk of staying at home. The final model (in bold) was adjusted for age, sex and month of presentation.

	RR	95% CI lower limit	95% CI upper limit	p value
Prehospital triage	2.31	1.74	3.05	<0.001
Age	0.91	0.87	0.96	<0.001
Age ²	1.07	1.03	1.11	<0.001
Sex (male)	0.70	0.54	0.92	0.007
Month				0.078

*Explanatory footnote: 'Age²' is a composite value of (Age*Age)/100. The p-value of 'Month' is the likelihood ratio of contribution of the variable to the logistic regression model.*

Safety

Of the 181 patients who stayed at home after EMS consultation in the intervention group, 1 patient developed ACS within 30 days after evaluation by the EMS (MACE rate <1%). No patients died. Five (2.8%) patients were lost to follow-up.

Secondary endpoints

There were 1536 EMS consultations in the intervention group and 1376 in the control group. The incidence of EMS consultation did not differ between both groups (190/100.000 vs. 172/100.000 inhabitants) with a relative risk of 1.10 (CI 0.90-1.36, $p=0.344$). In the intervention group, the number of interhospital transfers was lower compared to in the control group (206 vs. 173). The incidence of interhospital transfer was significantly lower in the intervention group (173/1355) as compared to the control group (206/1299) with a relative risk of 0.81 (CI 0.67-0.97, $p=0.023$). Time from EMS consultation to hospital arrival increased by 6 minutes from 37 ± 11 minutes in the control group to 43 ± 14 minutes in the intervention group ($p<0.001$). A triage cardiologist handled an average of 12 calls per day, taking 5-10 minutes each. The total amount of time a cardiologist spends on prehospital triage is therefore around 1-2 hours per day.

In total 126 (9.2%) patients presenting to the EMS ultimately had an ACS in the control group, compared to 127 (8.2%) in the intervention group. All ACS diagnoses are noted in Table 3. There were no differences in ACS diagnoses between control and intervention ($p=0.928$). There were no differences in final diagnoses as shown in Table 4 (Electronic Supplementary Material).

Table 3. Overview of final diagnoses of acute coronary syndrome patients in control - (n=1299) and intervention group (n=1355) presented to the hospitals.

	Control (n)	%	Intervention (n)	%	p-value
ACS	126		127		0,928
STEMI	8	6,3%	8	6,3%	
NSTEMI	85	67,4%	83	65,4%	
Unstable angina	33	26,2%	36	28,3%	

Explanatory footnote: STEMI: ST-elevation myocardial infarction, NSTEMI: non-ST-elevation myocardial infarction.

Satisfaction

Patients who could stay at home averaged a satisfaction score of 8.8. GPs from these patients scored the care given with an average of 7.7. Cardiologists scored each shift, averaging a score of 7.7.

Discussion

Implementing a novel prehospital triage method for patients visited by the EMS for cardiac symptoms combining live-streamed prehospital data, insight in previous medical history, and expert consultation led to a significant increase in the number of patients who could stay at home. The triage method had a MACE rate <1%, none of these patients died. Furthermore, a decrease in interhospital transfers was achieved. Patients and healthcare workers were very satisfied with the presented triage method. These results may help to relief the pressure from the currently overcrowded Dutch EDs.

Overcrowding of EDs is a major healthcare challenge (5-8). Cardiac patients form a large part of all ED consultations, with more than 10% of all ED consultations involving patients experiencing chest pain (1). However, over 80% of these patients do not suffer from acute cardiovascular disease. To reduce overcrowding, in-hospital triage for rapid risk stratification of chest pain patients has been in use for several years with the use of risk scores (9, 15, 16). Although these result in accurate and fast risk stratification, patients are still presented and evaluated at the ED, and thus still contribute to overcrowding. Therefore, scientific focus has shifted on improving prehospital triage.

The ARTICA (12) study assesses whether the addition of POC cTnT measurement is cost-effective in ruling out ACS and leaving patients at home after EMS consultation. The Famous Triage (17) investigators concluded that it seems feasible and non-inferior to rule out myocardial infarction in prehospital chest pain patients using a modified HEART score at the patient's home, incorporating only a single troponin T (cTnT) measurement on intravenously acquired blood samples (18). The PRESTO (19) study seeks to evaluate the diagnostic accuracy of the validated T-MACS decision rule to rule out ACS in the prehospital

environment. This could allow paramedics to rule out ACS for chest pain patients in the very low risk group and avoid the need for transport to the ED.

The present HART-c study differs from the aforementioned studies in its included patients, triage method and main objective. Firstly and uniquely, the HART-c study does not limit its inclusion to chest pain patients, but also includes patients with other cardiac symptoms. Thus, the HART-c study could be of benefit to a larger cohort of patients, and for this reason, could be of greater value in preventing overcrowding of EDs and hospitals. Since the method is not solely focused on chest pain patients, it is easier to recreate, adjust and implement for other medical specialties. Second, the HART-c study is unique in its triage method. The ARTICA, FamouS and PRESTO studies rely solely on prehospital data, whereas the HART-c study is the first study to combine prehospital - and hospital data. Furthermore, the HART-c study includes expert consultation on the scene by having a cardiologist available for the nurse paramedic. Lastly, this is the first study to publish its results regarding *safely* leaving cardiac patients at home after EMS assessment. Appropriate selection of patients at (very) low risk for MACE, who could therefore safely stay at home following EMS consultation, could contribute substantially to providing overcrowded EDs and hospitals with much-needed relief. Of utmost importance, patients who can safely stay at home after EMS consultation are spared the (unnecessary) strain and stress of a ED visit.

The HART-c study has some limitations. First of all, this is not a randomised controlled trial, so selection bias could influence its results and therefore these results should be seen as promising and not definitive. A randomised controlled trial or a study with a stepped wedge design should be conducted in the future to confirm the results presented in the current study. Another limitation is the patients lost to follow-up when not transferred to an ED. Unfortunately, not all these patients (or their GP's) could be contacted after 30 days as some patients did not have a GP (tourists or homeless) or in some cases phone numbers were not noted correctly. Therefore, the true MACE rate could be slightly higher than 1%. Furthermore, the MACE rate might have been this low due to the wide inclusion criteria: 'symptoms of possible cardiac origin'. Chest pain patients with possible ACS have a higher MACE rate than, for example, patients with palpitations or dyspnoea. The intervention was planned for one year, however in March 2020 COVID-19 struck the Netherlands which had a huge impact on acute and non-acute (cardiac) care. As patients might have hesitated to contact the GP, EMS or hospitals this would have introduced too much bias in the study affecting the comparability between the intervention and the (historical) control group. Therefore, the study was closed in March 2020.

In conclusion, the HART-c study evaluated a novel triage method combining prehospital live-streamed EMS data, insight in previous medical records, real-time hospital admission capacity with expert cardiologist consultation. The achieved increase in patients who could safely stay at home after EMS consultation and the reduction in interhospital transfers could help take substantial pressure of the currently overloaded healthcare system. Furthermore, the presented triage method is adjustable and easily implementable for other medical specialties to further reduce overcrowding.

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7.

CONCLUSIES

AI



Chapter 7

Summary, conclusions
and future perspective

Chapter 1 of this thesis provided an extensive examination of the demographic changes, healthcare obstacles, and the imperative for inventive solutions. It stressed the urgency of tackling these issues in light of the predicted surge in the elderly population and the resultant strain on healthcare resources.

The introduction discussed the rising demand for healthcare services amidst a shrinking workforce, leading to considerable challenges in healthcare organization and escalating healthcare costs. The unsustainable burden on the Dutch gross national product due to healthcare expenditure necessitates urgent measures to ensure the long-term financial stability and effectiveness of the healthcare system.

Moreover, it highlighted the complications arising from an aging population, such as higher rates of comorbidity and complex patient problems, contributing to longer waiting times, growing waiting lists, and hospital overcrowding. The adverse effects of overcrowding on patient outcomes and healthcare professionals' well-being were emphasized, especially in the context of the COVID-19 pandemic, which further strained healthcare resources.

To address these challenges, the Dutch government formulated the Integral Healthcare Agreement (IZA) to prioritize fitting care and regional collaboration between healthcare providers, financiers, and the government. The focus on streamlining data exchange, reinforcing primary care or care at home, and tailoring healthcare to patients' specific needs were highlighted as key strategies to ensure sustainable healthcare delivery now and in the future.

The introduction further emphasized the importance of triage and risk scores in optimizing healthcare resource utilization, particularly in the prehospital setting. It discussed various risk scores, such as the HEART score, commonly used in the assessment of patients with chest pain, and highlighted the potential of prehospital risk scores, such as the preHEART and modified HEART scores, in identifying low-risk patients before they are presented to the hospital. Furthermore, it delved into prehospital clinical studies using these (prehospital) risk scores, such as the ACCESS study, URGENT 1.5 trial, FamouS Triage study, and ARTICA trial, which demonstrated the effectiveness of risk scores in identifying low-risk patients in the prehospital setting.

The importance of data sharing among healthcare providers and the potential of AI and machine learning technologies in optimizing prehospital triage protocols were discussed. Data sharing among healthcare providers is critical for effective decision-making, particularly in prehospital cardiac triage. Current practices often resulted in fragmented data, hindering comprehensive patient care. By establishing seamless communication channels between paramedics, general practitioners, and hospitals, crucial information like frailty and patient preferences could be integrated into the decision-making processes, enhancing the accuracy of care plans beyond traditional scoring systems.

As a last point, Artificial Intelligence (AI) holds significant promise in addressing challenges posed by textual data and in optimizing healthcare processes. While numerical data analysis has improved medical care and is current practice for research, textual data remains complex, unstructured and difficult to study. AI-powered natural language processing (NLP) can offer a solution by enabling systematic analysis and interpretation of textual medical information. Integrating AI and machine learning technologies can help form a transformative shift towards a more data-driven and patient-centered healthcare approach, promising to improve prehospital care delivery and patient outcomes in the digital age.

Chapter 2 outlined the study protocol of the HART-c study, a multicenter prospective study evaluating the efficacy and feasibility of a novel comprehensive prehospital triage method. In this triage method patients visited by paramedics for all cardiac complaints were included. Paramedic consultation consisted of a full medical history, physical examination, noting of vital signs, and ECG measurements. All this data was noted on a handheld device and was transferred to a newly developed digital triage platform. An on-shift triage cardiologist was able to log in remotely on the triage platform and view all (live-streamed) data. This prehospital data was combined with in-hospital medical records and real-time admission capacity of all regional hospitals. The consulting paramedic contacted the triage cardiologist and together a shared decision was made whether admission was necessary and, if so, which hospital was most appropriate.

In **Chapter 3**, the recent COVID-19 pandemic and its effect on the healthcare system in the West-Netherlands region were examined. A Regional Capacity and Patient Transfer Service (RCPS) was set up. The RCPS combined information on capacity and triage capabilities to effectively transfer patients throughout the region and the country. Hospitals with high influx of COVID-19 patients were able to transfer patients to other hospitals in the region who had a higher reserve capacity or a lower influx of patients. The RCPS ensured that regional ICU occupation never exceeded maximal capacity and thus allowed patients in need of acute direct care to be admitted to the ICU. The presented method could be useful in reducing waiting lists caused by delayed care and for coordinating and transferring patients with new variants or other infectious diseases in the future.

Chapter 4 aimed to assess the indirect health effects of the COVID-19 lockdown in 2020, focusing on people's reluctance to seek medical care. Evaluation of paramedic consultations for chest pain or out-of-hospital cardiac arrest (OHCA) compared to the same period in 2019 revealed a significant reduction in the number of evaluated chest pain patients and ST-elevation myocardial infarction (STEMI) patients, while the incidence of OHCA remained similar. Possible factors contributing to the decrease in chest pain and STEMI incidence were discussed, including a decrease in physical exertion, a dramatic decrease in air pollution, and reluctance to contact medical authorities during the COVID-19 lockdown. Alerting the public to the importance of contacting EMS in case of suspected cardiac complaints was proposed to reduce secondary health damage in possible future lockdowns.

Chapter 5 showcased the potential of data and AI in healthcare, presenting a retrospective study as a proof-of-concept of an AI model developed to identify patients with ACS in the prehospital setting based on textual data. Prehospital data collected by emergency medical services' nurse paramedics between September 2018 and September 2020 were retrospectively analyzed. A supervised text classification algorithm was employed to develop the AI model, which underwent iterative evaluation, feature selection, and hyperparameter tuning. The AI model demonstrated a specificity of 11% and a sensitivity of 99.5%, with a positive predictive value (PPV) of 15% and a negative predictive value (NPV) of 99%. In comparison, usual care exhibited a specificity of 1%, a sensitivity of 99.5%, a PPV of 13%, and an NPV of 94%. The AI model significantly improved specificity and NPV compared to usual care, while maintaining similar sensitivity levels. The potential for AI to support decision-making in the future was discussed, with the caveat that final decisions on patient management should always rest with a physician or nurse paramedic.

Finally, **Chapter 6** presented the results of the HART-c study of which the protocol was extensively discussed in chapter 2. The intervention group consisted of 1536 patients (69 ± 15 years, 51.3% male), while the historical cohort control group comprised 1376 patients (68 ± 15 years, 49.9% male), with comparable baseline characteristics. In the intervention group, 181 (11.8%) patients were able to stay at home after EMS consultation, compared to 77 (5.9%) patients in the control group. Logistic regression demonstrated increased odds of staying at home in the intervention group compared to the control group (adjusted odds ratio: 2.31, 95% CI 1.74–3.05, $p < 0.0001$), even after adjusting for age, sex, and month of presentation. The most prevalent presenting symptom for patients who could stay at home was chest pain. Only one patient in the intervention group developed ACS within 30 days after EMS evaluation, with no reported deaths and a low rate of loss to follow-up (2.8%). In terms of secondary endpoints, there was no significant difference in the incidence of EMS consultations between the two groups, but the intervention group experienced a lower incidence of interhospital transfers. The time from EMS consultation to hospital arrival increased slightly in the intervention group. Additionally, there were no significant differences in ACS diagnoses or final diagnoses between the control and intervention groups. Patients who could stay at home reported high satisfaction scores, as did their GPs and cardiologists involved in their care. The HART-c study demonstrated an increase in patients who could safely stay at home after EMS consultation and a reduction in interhospital transfers, potentially relieving substantial pressure on the currently overloaded healthcare system. Furthermore, the presented triage method was noted to be adjustable and easily implementable for other medical specialties, further aiding in reducing overcrowding.

Conclusions

This thesis addressed current and forthcoming challenges in (cardiac) healthcare, offering innovative strategies to alleviate overcrowding through enhanced prehospital triage. The newly developed triage method, integrating prehospital and in-hospital data with expert

cardiologist consultation, efficiently identified patients suitable to stay at home post-paramedic assessment, reduced interhospital transfers, and thereby optimized resource allocation. Consequently, this method significantly contributed to decreasing overcrowding by streamlining prehospital patient management.

Additionally, the thesis examined the impact of the recent COVID-19 pandemic on cardiac healthcare, revealing declines in chest pain referrals and STEMI diagnoses. Additionally, the pandemic underscored the importance of effective triage mechanisms and collaborative (regional) approaches to increase healthcare resilience, exemplified by the RCPS.

Lastly, this research provided a glimpse into the future, demonstrating the proof-of-concept of artificial intelligence in prehospital decision-making, promising further advancements in cardiac care delivery.

Future perspectives

In contemplating the future landscape of cardiac prehospital triage, significant improvements emerge, most notably in the management of patients experiencing chest pain. The integration of point-of-care (POC) high-sensitivity cardiac troponin (hs-cTn) assessments into existing triage protocols such as those discussed in this thesis holds promise for further improving prehospital risk assessment. By enhancing prehospital risk scores prehospital patient selection can be elevated to unprecedented levels of precision. However, this integration should also represent a paradigm shift, aiming to redefine prehospital triage as a selective process focused on excluding patients from hospitalization rather than admitting them. When scientifically proven to be safe, implementing POC hs-cTn assessment within the HART-c triage method (or other similar triage methods) can mean low-risk patients are allowed to be managed at home without cardiologist consultation. Expert consultation can then be reserved to ensure patient tailored care for medium- to high-risk categories or in cases where there's uncertainty regarding low-risk patients. Recent studies, including the TRIAGE-ACS study, have demonstrated the efficacy of identifying high-risk patients without ST-elevation on prehospital ECGs for direct transport to hospitals with interventional capabilities. In these instances, prehospital consultation with a cardiologist can further refine patient selection, ensuring that those who would benefit most from rapid intervention are appropriately identified.

Additionally, when point-of-care high-sensitivity cardiac troponin (POC hs-cTn) is measured before hospital arrival, obtaining a subsequent POC hs-cTn measurement upon hospital admission facilitates the calculation of a 'delta' troponin. This enables much faster classification of patients by the 1-hour or 2-hour rule-out algorithms as recommended in the European Society of Cardiology (ESC) guidelines for the management of acute coronary syndromes.

Implementing the combination of prehospital POC hs-cTn with expert consultation would parallel prehospital care to in-hospital assessment in the emergency department (ED),

complete with real-time ECG, monitoring vital signs, high-sensitivity troponin tests, and facilitating consultations with cardiologists. Carrying out this process before patients arrive at the ED would further alleviate hospital- and ED overcrowding. It will also significantly reduce the time patients spend in diagnostic uncertainty by minimizing unnecessary hospital referrals and by enabling faster use of the rule-out algorithm. Once in place, the level and accuracy of prehospital cardiac triage will be unparalleled.

The logical progression from regional improvement and implementation would be towards national dissemination. The Netherlands, because of its geography and healthcare system, is positioned to lead this transformative endeavor. Collaboration among the many currently ongoing clinical studies in prehospital cardiac triage will lay the groundwork for nationwide adoption, with attention to the nuanced needs of individual regions. The triage method discussed in this thesis can be used as a template adaptable to the unique needs of every region within the Netherlands. Different healthcare providers can freely share relevant patient data and look in to data which is shared by others. These regionale platforms could provide a comprehensive and complete view of a patient's medical history, enabling healthcare professionals to make more accurate assessments and prioritize treatment accordingly. Moreover, the development of a triage platform adaptable to various symptoms or medical specialties, such as neurologic symptoms, or pediatric care, holds promise for optimizing triage processes across diverse healthcare contexts.

A central point to this endeavor is the meticulous stewardship of data, crucial for scientifically demonstrating the safety and efficacy of these methods. Combining the eventual outcomes from patients classified as low-, medium- or high risk in a single (prehospital) registry could be of great benefit to assess quality of care and to increase the power for (clinical trial) safety assessments. Furthermore, this would make the development of observational – and randomized clinical trials easier for whoever has ideas to improve prehospital patient care further. Of note, some agreements should be made by healthcare providers and healthcare financiers, such as the (local) government and healthcare insurers, on how to structurally finance these triage platforms and – registries.

Proper data management enables the integration of AI-powered predictive models, promising a future where risk prediction and decision support reach unparalleled levels of sophistication. Accurate storage and annotation of data for AI or ML models are important, as it ensures precise model training, generalization, and bias mitigation, while also enabling model interpretability and compliance with regulations. Such meticulous data management bolsters the reliability, fairness, and security of AI systems, for their successful implementation and public trust. In this thesis an AI algorithm was demonstrated as a proof-of-concept in prehospital triage, however such models should undergo thorough validation before eventual implementation. Furthermore, developers should be forced, by professional associations or national governments, to publicly share the underlying algorithm and data before publication. In this way other researchers have the possibility

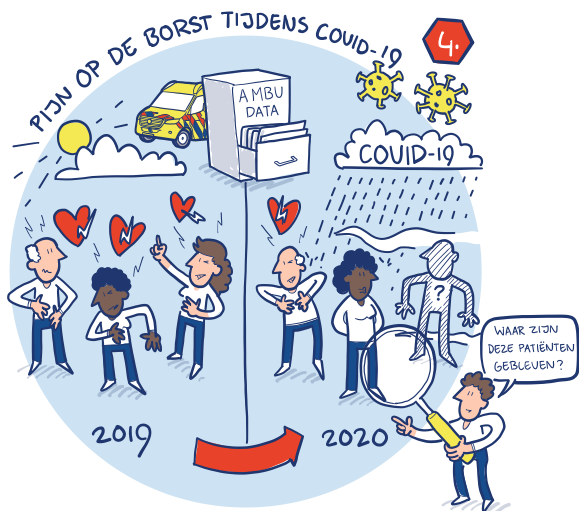
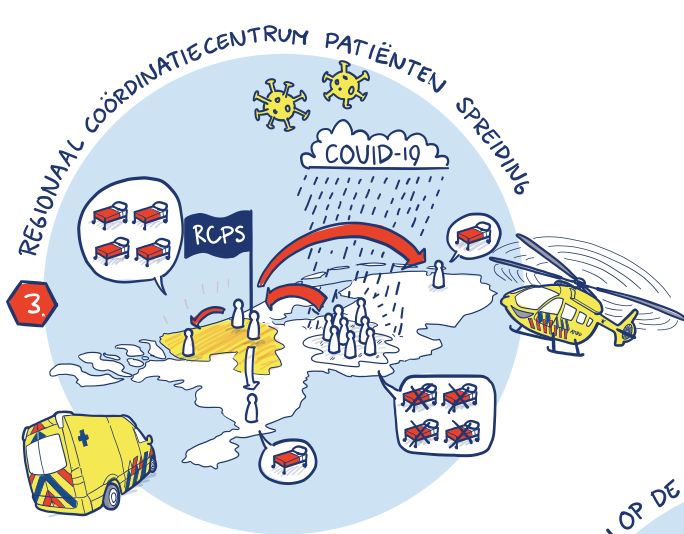
for further improvements to the algorithm, and thus further improvements to patient care. If deemed safe, this approach holds promise for enhancing risk prediction, akin to existing risk score models for conditions like chest pain, providing healthcare professionals with a supportive tool to aid in the decision-making processes. This approach can reduce the reliance on human-based healthcare, thereby alleviating some strain on the system. Consequently, only patients who genuinely require hospital care will be admitted or seen in the emergency department, leading to a higher acuity of patients on average. This shift necessitates corresponding adjustments in healthcare financing.

Improving prehospital cardiac triage in the entirety of the Netherlands will benefit patients experiencing symptoms of cardiac origin. The triage method can further alleviate the strain on healthcare because of its flexibility and therefore adaptability across diverse medical specialties such as neurologic symptoms or pediatric care. One can imagine that for these specialties adaptations might be necessary, such as the ability to examine patients through video calling inside the ambulance to assess neurologic symptoms. However, it will not solve the demographic shifts, rising demand for healthcare, workforce shortages and the resulting strain on healthcare resources. The COVID-19 pandemic underscored the importance of collaboration among healthcare providers, transcending the confines of competition-driven healthcare models. Through working together, healthcare providers have demonstrated their capacity to address significant crises. Embracing transparency in capacity and by sharing resources, they must transcend the prevailing profit-driven model, striving towards a future characterized by equity and sustainability for all. Herein lies a role for government and policymakers as well, to enact policies that support and incentivize collaboration, transparency, and equitable resource allocation in healthcare.

This thesis has demonstrated that collaboration among healthcare providers and subsequent shared decision-making can improve patient outcomes. Although hopeful and definitely useful, even necessary, these endeavors they may serve as temporary solutions to larger systemic challenges. The aging population and subsequent smaller working population will lead to persistent overcrowding in most countries, and efficient resource use will not alleviate escalating healthcare costs. Sustainable healthcare delivery hinges not only on technological advancements but also on the willingness to make difficult decisions in resource allocation. Whether through increased funding or judicious admission criteria, addressing these challenges demands bold action. The thesis offers a preliminary glimpse into the future and highlights the importance of innovation, collaboration, transparency, adaptability and equitable resource distribution. Drawing lessons from the past and implementing scientifically proven advancements, policymakers and healthcare professionals are urged to develop a healthcare system that can stand the test of time.

BETERE ACUTE ZORG BIJ MOGELIJKE HARTPROBLEMEN





Chapter 8

Nederlandse samenvatting,
conclusies en toekomstperspectief

Hoofdstuk 1 van dit proefschrift beschreef de demografische veranderingen, obstakels in de gezondheidszorg en de noodzaak van vernieuwende oplossingen. Het onderstreepte de urgentie van het aanpakken van deze kwesties in het licht van de verwachte vergrijzing en de daaruit voortvloeiende druk op de beschikbare zorgmiddelen.

In de inleiding werd ingegaan op combinatie van stijgende vraag naar zorg en een krimpende beroepsbevolking, wat zal leiden tot aanzienlijke uitdagingen in de organisatie van de gezondheidszorg en in toenemende zorgkosten. Dit vraagt om dringende maatregelen om de financiële houdbaarheid en effectiviteit van het zorgsysteem op de lange termijn te waarborgen.

Daarnaast leidt een vergrijzende bevolking, met meer comorbiditeit en dus complexere patiëntproblemen, tot groeiende wachtlijsten en overvolle ziekenhuizen. Deze overvolle ziekenhuiszalen en spoedeisende hulpen hebben een negatief effect op uitkomsten van patiënten en op het welzijn van zorgverleners zoals gezien werd tijdens de COVID-19-pandemie, die de zorgcapaciteit verder onder druk zette.

Om deze uitdagingen aan te pakken, stelde de Nederlandse overheid het Integraal Zorgakkoord (IZA) op, met als doel passende zorg en regionale samenwerking tussen zorgaanbieders, zorgverzekeraars en de overheid te bevorderen. De nadruk lag op het verbeteren van gegevensuitwisseling, het versterken van de eerstelijnszorg of zorg aan huis, en het afstemmen van zorg op de specifieke behoeften van patiënten als belangrijke strategieën om duurzame zorgverlening nu en in de toekomst te waarborgen.

In dit hoofdstuk werd verder het belang van triage en risicoscores bij het optimaliseren van het gebruik van zorgmiddelen benadrukt, met name in de prehospital setting oftewel voordat patiënten het ziekenhuis betreden. Verschillende risicoscores werden besproken, zoals de HEART-score, die vaak wordt gebruikt bij de beoordeling van patiënten met pijn op de borst. Daarbij werd ook het potentieel van prehospital risicoscores, zoals de preHEART-en aangepaste HEART-scores, belicht voor het identificeren van laag-risicopatiënten vóór aankomst in het ziekenhuis. Verder werd ingegaan op prehospital klinische studies waarin deze (prehospital) risicoscores werden toegepast, zoals de ACCESS-studie, URGENT 1.5-trial, FamouS Triage-studie en ARTICA-trial, die de effectiviteit aantoonden van risicoscores bij het identificeren van laag-risicopatiënten in de prehospital context.

Het belang van gegevensuitwisseling tussen zorgverleners en het potentieel van AI- en machine learning-technologieën bij het optimaliseren van prehospital triageprotocollen werd besproken. Gegevensuitwisseling is cruciaal voor effectieve besluitvorming, zoals ook te zien bij prehospital triage van cardiale patiënten. Op dit moment is er met name veel gefragmenteerde informatie beschikbaar zoals losse huisartsen-, apotheek-, en ziekenhuisdossiers, wat goede patiëntenzorg belemmert. Door het opzetten van communicatiekanalen tussen ambulancemedewerkers, huisartsen en ziekenhuizen, kunnen essentiële gegevens zoals kwetsbaarheid en patiëntvoorkeuren worden geïntegreerd in de

besluitvorming. Dit zal leiden tot betere beslissingen voor de patiënt, ook buiten traditionele scoresystemen om.

Tot slot werd besproken dat kunstmatige intelligentie (AI) grote potentie heeft voor het aanpakken van uitdagingen rondom tekstuele data en het optimaliseren van zorgprocessen. Hoewel data-analyse reeds de medische zorg heeft verbeterd en gemeengoed is binnen onderzoek, blijft tekstuele informatie complex, ongestructureerd en moeilijk te analyseren. AI-gedreven natural language processing (NLP) kan hierin uitkomst bieden door gestructureerde analyse en interpretatie van medische tekstgegevens mogelijk te maken. De integratie van AI- en machine learning-technologieën kan bijdragen aan een verschuiving naar een meer datagedreven en patiëntgerichte aanpak, met als doel de prehospitala zorgverlening en patiëntuitkomsten te verbeteren in het digitale tijdperk.

Hoofdstuk 2 beschreef het studieprotocol van de HART-c studie, een multicenter prospectieve studie die de effectiviteit en haalbaarheid evalueerde van een nieuwe prehospitala triagemethode. In deze triagemethode werden alle patiënten die door ambulancepersoneel werden bezocht vanwege cardiale klachten geïnccludeerd. Het ambulanceonderzoek bestond uit een volledige anamnese, lichamelijk onderzoek, het vastleggen van vitale functies en het maken van een ECG. Al deze gegevens werden genoteerd op een handheldapparaat en verstuurd naar een nieuw ontwikkeld digitaal triageplatform.

Een dienstdoende triagecardioloog kon op afstand inloggen op het triageplatform en alle (live gestreamde) gegevens bekijken. Deze prehospitala gegevens werden gecombineerd met medische dossiers uit het ziekenhuis en de actuele opnamecapaciteit van alle regionale ziekenhuizen. De consulterende ambulanceverpleegkundige nam contact op met de triagecardioloog, en samen werd via gezamenlijke besluitvorming bepaald of opname noodzakelijk was en, zo ja, welk ziekenhuis het meest geschikt was.

In **Hoofdstuk 3** werd de COVID-19-pandemie en de impact ervan op het zorgsysteem in de regio West-Nederland onderzocht. Er werd een Regionaal Coördinatiecentrum Patiëntspreiding (RCPS) opgericht. Het RCPS combineerde informatie over beschikbare capaciteit en triagemogelijkheden om patiënten effectief te kunnen spreiden binnen de regio en het land. Ziekenhuizen met een hoge instroom van COVID-19-patiënten konden patiënten overplaatsen naar andere ziekenhuizen in de regio met meer reservecapaciteit of een lagere instroom. De RCPS zorgde ervoor dat de regionale IC-bezetting nooit de maximale capaciteit overschreed, waardoor patiënten met een acute zorgvraag altijd opgenomen konden worden op de intensive care. De beschreven methode zou in de toekomst van waarde kunnen zijn bij het verminderen van wachtlijsten als gevolg van uitgestelde zorg, evenals bij de coördinatie en spreiding van patiënten met nieuwe virusvarianten of andere infectieziekten.

Hoofdstuk 4 had als doel de indirecte gezondheidseffecten van de COVID-19-lockdown in 2020 te beoordelen, met de nadruk op de terughoudendheid van mensen om medische zorg te zoeken. Een analyse van ambulanceconsulten voor pijn op de borst of een circulatiestilstand buiten het ziekenhuis (OHCA) in vergelijking met dezelfde periode in 2019 liet een significante afname zien in het aantal beoordeelde patiënten met pijn op de borst en presentaties voor (mogelijke) ST-elevatie myocardinfarcten (STEMI's), terwijl de incidentie van OHCA vergelijkbaar bleef. Mogelijke factoren die bijdroegen aan de afname van patiënten met pijn op de borst en STEMI verdenkingen waren onder meer een vermindering van lichamelijke inspanning, een drastische afname van luchtvervuiling en terughoudendheid om medische hulp in te schakelen tijdens de lockdown. In de toekomst zou de bevolking in de toekomst beter geïnformeerd moeten worden voor het belang van het inschakelen van spoedeisende hulp bij verdenking op hartklachten, om zo secundaire gezondheidsschade tijdens mogelijke toekomstige lockdowns te beperken.

Hoofdstuk 5 liet het potentieel zien van data en kunstmatige intelligentie (AI) in de gezondheidszorg, aan de hand van een retrospectieve studie als proof-of-concept van een AI-model dat ontwikkeld werd om patiënten met acuut coronair syndroom (ACS) te identificeren op basis van tekstuele gegevens. Prehospitala gegevens, verzameld door ambulanceverpleegkundigen tussen september 2018 en september 2020, werden retrospectief geanalyseerd. Er werd gebruikgemaakt van een gesuperviseerd tekstclassificatie-algoritme om het AI-model te ontwikkelen.

Het AI-model had een specificiteit van 11% en een sensitiviteit van 99,5%, met een positief voorspellende waarde (PPV) van 15% en een negatief voorspellende waarde (NPV) van 99%. Ter vergelijking, de gebruikelijke zorg had een specificiteit van 1%, een sensitiviteit van 99,5%, een PPV van 13% en een NPV van 94%. Het AI-model verbeterde de specificiteit en de NPV aanzienlijk ten opzichte van de gebruikelijke zorg, terwijl het vergelijkbare sensitiviteitsniveaus behield. Het hoofdstuk besprak het potentieel van AI om besluitvorming in de toekomst te ondersteunen, met als kanttekening dat de uiteindelijke beslissingen over patiëntenzorg altijd genomen moeten worden door een arts of ambulanceverpleegkundige.

In **Hoofdstuk 6** werden de resultaten van de HART-c studie gepresenteerd, waarvan het studieprotocol uitgebreid werd besproken in hoofdstuk 2. De interventiegroep bestond uit 1536 patiënten (69 ± 15 jaar, 51,3% man), terwijl de historische controlegroep 1376 patiënten omvatte (68 ± 15 jaar, 49,9% man), met vergelijkbare uitgangskarakteristieken. In de interventiegroep konden 181 patiënten (11,8%) na consultatie door de ambulanceverpleegkundige thuis blijven, tegenover 77 patiënten (5,9%) in de controlegroep.

Logistische regressieanalyse toonde een verhoogde kans om thuis te kunnen blijven in de interventiegroep ten opzichte van de controlegroep (gecorrigeerde odds ratio: 2,31; 95% BI

1,74–3,05; $p < 0,0001$), zelfs na correctie voor leeftijd, geslacht en maand van presentatie. De meest voorkomende klacht bij patiënten die thuis konden blijven was pijn op de borst.

Slechts één patiënt in de interventiegroep had in de 30 dagen na beoordeling door de ambulance een acuut coronair syndroom (ACS), er werden geen sterfgevallen gerapporteerd, en het aantal patiënten dat uit follow-up raakte was laag (2,8%).

Wat betreft secundaire eindpunten was er geen significant verschil in het aantal EMS-consultaties tussen beide groepen, maar de interventiegroep kende een lagere incidentie van interhospitala overplaatsingen. De tijd tussen ambulanceconsult en aankomst in het ziekenhuis nam in de interventiegroep licht toe. Daarnaast waren er geen significante verschillen in het aantal ACS-diagnoses of uiteindelijke diagnoses tussen de controle- en interventiegroepen.

Patiënten die thuis konden blijven gaven hoge tevredenheidsscores, evenals hun huisartsen en cardiologen die bij de zorg betrokken waren. De HART-c studie toonde aan dat het aantal patiënten dat na ambulanceconsult veilig thuis kon blijven toenam en dat het aantal overplaatsingen afnam, wat mogelijk bijdraagt aan het verlichten van de aanzienlijke druk op het overbelaste zorgsysteem. Daarnaast bleek de gepresenteerde triagemethode aanpasbaar en gemakkelijk implementeerbaar voor andere medische specialismen, wat verdere overbelasting van de zorg kan helpen verminderen.

Conclusies

Dit proefschrift behandelde de huidige en toekomstige uitdagingen in de (cardiale) zorg en presenteerde innovatieve strategieën om overbelasting te verminderen door middel van verbeterde prehospitala triage. De nieuw ontwikkelde triagemethode, waarbij prehospitala - en ziekenhuisdata worden geïntegreerd met consultatie van een triagecardioloog, identificeerde patiënten die na beoordeling door ambulancepersoneel veilig thuis konden blijven. Daarnaast leidde deze aanpak tot een vermindering van overplaatsingen en optimaliseerde zij de inzet van beschikbare zorgmiddelen. Deze methode droeg daarmee aantoonbaar bij aan het terugdringen van overbelasting door een meer gestroomlijnde prehospitala patiëntenzorg.

Daarnaast onderzocht dit proefschrift de impact van de COVID-19-pandemie op de cardiale zorg, waarbij een afname in verwijzingen voor pijn op de borst en STEMI-diagnoses werd waargenomen. De pandemie benadrukte tevens het belang van effectieve triage en regionale samenwerking ter versterking van de veerkracht van de zorg, zoals geïllustreerd door de Regionale Capaciteit- en Patiëntenservice (RCPS).

Tot slot bood dit onderzoek een blik op de toekomst door een proof-of-concept te presenteren van kunstmatige intelligentie in prehospitala besluitvorming, waarmee verdere verbeteringen in de levering van cardiale zorg in het vooruitzicht worden gesteld.

Toekomstperspectief

Bij het overwegen van de toekomstige inrichting van prehospital cardiale triage, zijn er belangrijke verbeteringen zichtbaar, met name in de beoordeling van patiënten met pijn op de borst. Het integreren van point-of-care (POC) metingen van high-sensitivity cardiac troponine (hs-cTn) in bestaande triageprotocollen, zoals in dit proefschrift besproken, biedt mogelijkheden om de risicobeoordeling in de prehospital setting verder te verbeteren. Door het verfijnen van prehospital risicoscores kan patiëntselectie naar een ongekend hoog niveau worden gebracht. Deze integratie zou echter ook een paradigmaverschuiving moeten inluiden, waarbij prehospital triage wordt hergedefinieerd als een selectief proces gericht op het uitsluiten van patiënten van ziekenhuisopname, in plaats van het enkel identificeren van wie opgenomen moet worden. Wanneer het wetenschappelijk veilig wordt geacht, kan de toepassing van POC hs-cTn binnen de HART-c triagemethode (of vergelijkbare methodes) ervoor zorgen dat laagrisicopatiënten veilig thuis behandeld kunnen worden zonder cardiologisch consult. Specialistisch consult kan dan worden gereserveerd voor patiënten met een gemiddeld tot hoog risico, of in geval van onzekerheid bij laagrisicopatiënten.

Recente studies, waaronder de TRIAGE-ACS studie, tonen de effectiviteit aan van het identificeren van hoogrisicopatiënten zonder ST-elevatie op het prehospital ECG voor directe verwijzing naar ziekenhuizen met interventiemogelijkheden. In deze gevallen kan een prehospital cardiologisch consult de patiëntselectie verder verfijnen, zodat degenen die het meest baat hebben bij snelle interventie tijdig worden geïdentificeerd.

Daarnaast maakt het meten van POC hs-cTn vóór aankomst in het ziekenhuis het mogelijk om bij opname een tweede meting te verrichten, waarmee het 'delta'-troponine berekend kan worden. Dit stelt zorgverleners in staat patiënten sneller te classificeren volgens de 1- of 2-uurs 'rule-out'-algoritmes zoals aanbevolen in de richtlijnen van de European Society of Cardiology (ESC) voor de behandeling van acuut coronair syndroom (ACS).

De combinatie van prehospital POC hs-cTn met een consult van een medisch specialist zou de prehospital zorg gelijkwaardig maken aan de beoordeling in het ziekenhuis, inclusief real-time ECG, vitale parameters, hoogsensitieve troponinebepalingen en consultatie van een cardioloog. Door dit proces vóór aankomst op de SEH te laten plaatsvinden, kan ziekenhuis- en SEH-overbelasting worden verminderd. Dit leidt bovendien tot minder (diagnostische) onzekerheid bij patiënten, door onnodige verwijzingen te vermijden en sneller duidelijkheid te hebben over de diagnose. Na implementatie zal het niveau en de nauwkeurigheid van prehospital cardiale triage ongeëvenaard zijn.

De logische vervolgstap na regionale implementatie is landelijke uitrol. Nederland, met zijn geografische compactheid en georganiseerd zorgsysteem, is bij uitstek geschikt om dit proces aan te voeren. Samenwerking tussen de vele lopende klinische studies op het gebied van prehospital cardiale triage kan de basis leggen voor landelijke toepassing,

met aandacht voor de specifieke behoeften van iedere regio. De in dit proefschrift besproken triagemethode kan dienen als een blauwdruk dat aan te passen is aan de unieke omstandigheden in elke regio. Verschillende zorgverleners kunnen relevante patiëntgegevens delen en raadplegen, waardoor een volledig en integraal patiëntbeeld ontstaat. Dit stelt zorgprofessionals in staat om beter onderbouwde keuzes te maken samen met de patiënt en de zorg beter te prioriteren.

Bovendien biedt de ontwikkeling van een triageplatform dat aanpasbaar is aan andere symptomen of voor andere specialismen – zoals neurologie of kindergeneeskunde – perspectief om triageprocessen voor alle ziektebeelden te optimaliseren. Cruciaal hierin is zorgvuldig databeheer, noodzakelijk om de veiligheid en effectiviteit van deze methodes wetenschappelijk aan te tonen. Het combineren van uitkomsten van patiënten die als laag-, midden- of hoogrisico zijn geclassificeerd in één (prehospitaal) register kan de kwaliteit van zorg beter inzichtelijk maken en de kracht van evaluaties verhogen. Dit vergemakkelijkt ook de ontwikkeling van observationele en gerandomiseerde klinische studies voor verdere verbetering van prehospitalische patiëntenzorg. Wel zullen er afspraken moeten worden gemaakt tussen zorgverleners en zorgfinanciers, zoals (lokale) overheden en verzekeraars, over structurele financiering van deze platforms en registratiesystemen.

Goed databeheer maakt de integratie van AI-gestuurde voorspellingsmodellen mogelijk, waarmee risicovoorspelling en besluitvorming naar een hoger niveau worden getild. Nauwkeurige opslag en annotatie van data zijn essentieel voor training, generaliseerbaarheid, biasbeperking, uitlegbaarheid en naleving van regelgeving. Deze aanpak verhoogt de betrouwbaarheid, eerlijkheid en veiligheid van AI-systemen – cruciaal voor succesvolle implementatie en maatschappelijk vertrouwen. In dit proefschrift werd een AI-algoritme als proof-of-concept gepresenteerd in prehospitalische triage, maar dergelijke modellen moeten eerst grondig worden gevalideerd. Bovendien dienen ontwikkelaars – verplicht door beroepsverenigingen of overheden – hun algoritmes en onderliggende data publiek te maken voorafgaand aan publicatie. Zo krijgen andere onderzoekers de mogelijkheid tot verbetering, en daarmee verdere verbetering van patiëntenzorg. Indien veilig bevonden, biedt deze aanpak mogelijkheden om risicovoorspelling te verbeteren, vergelijkbaar met bestaande scores voor bijvoorbeeld pijn op de borst, en kan het zorgprofessionals ondersteunen in hun besluitvorming. Dit zou ook de grote vraag naar zorgpersoneel verminderen en zo de druk op het zorgsysteem verlichten. Alleen patiënten die daadwerkelijk ziekenhuiszorg nodig hebben, worden dan nog opgenomen of gezien op de SEH, waardoor er gemiddeld genomen complexere zorg geleverd moet worden. Dit vraagt echter ook om een aangepaste manier van zorgfinanciering.

Een landelijke verbetering van prehospitalische cardiale triage komt ten goede aan alle patiënten met cardiale klachten. De flexibiliteit van de methode biedt kansen om ook binnen andere medische disciplines toe te passen, zoals neurologische klachten of kindergeneeskunde. Aanpassingen zoals videoconsulten vanuit de ambulance om neurologische symptomen

te beoordelen, kunnen hiervoor nuttig zijn. Deze benadering lost echter de structurele problemen zoals vergrijzing, toenemende zorgvraag en personeelstekorten niet op. De COVID-19-pandemie onderstreepte het belang van samenwerking tussen zorgverleners, voorbijgaand aan concurrerende zorgmodellen. Door krachten te bundelen is bewezen dat de zorgsector grote crises aankan. Door transparantie in capaciteit en door het delen van beschikbare middelen moet worden afgeweken van het winstgedreven model en gestreefd worden naar een toekomst waarin gelijkheid en duurzaamheid centraal staan. Hierbij ligt ook een rol voor overheden en beleidsmakers om samenwerking, transparantie en eerlijke verdeling van middelen te ondersteunen en te stimuleren.

Dit proefschrift heeft laten zien dat samenwerking en gezamenlijke besluitvorming tussen zorgverleners leidt tot betere patiëntuitkomsten. Hoewel veelbelovend en zelfs noodzakelijk, kunnen deze initiatieven slechts tijdelijke oplossingen bieden voor diepere systeemproblemen. De vergrijzing en het krimpend arbeidsaanbod zullen blijven leiden tot overbelasting van de zorg. Efficiënte inzet van middelen zal de stijgende zorgkosten niet volledig kunnen opvangen. Duurzame zorg hangt niet alleen af van technologische vooruitgang, maar ook van de bereidheid om moeilijke keuzes te maken in de allocatie van middelen. Of het nu gaat om meer financiering of strengere toelatingscriteria, deze uitdagingen vragen om moedige beslissingen. Dit proefschrift biedt een eerste blik op de toekomst en benadrukt het belang van innovatie, samenwerking, transparantie, aanpassingsvermogen en eerlijke verdeling van zorgmiddelen. Door te leren van het verleden en (wetenschappelijk) bewezen verbeteringen toe te passen, kunnen beleidsmakers en zorgprofessionals bouwen aan een zorgsysteem dat bestand is tegen de uitdagingen van de toekomst.

List of abbreviations

ACS: Acute Coronary Syndrome
AI: Artificial Intelligence
CCU: Cardiac Care Unit
CI: Confidence Interval
COVID-19: Coronavirus disease 2019
ECG: Electrocardiogram
ED: Emergency Department
ELI5: Explain Like I'm 5
EMS: Emergency Medical Services
EPD: Electronic Patient File (or Elektronisch Patiënten Dossier in Dutch)
ESC: European Society of Cardiology
FDA: United States Food and Drugs Administration
GDP: Gross Domestic Product (or BNP: Bruto Nationaal Product in Dutch)
GP: General Practitioner
HART-c: Hollands Midden Acute Regional Triage
(hs)-cTn: (high sensitivity) Cardiac Troponin
ICU: Intensive Care Unit
IQR: Interquartile Range
IZA: Integral Healthcare Agreement (or Integraal Zorg Akkoord in Dutch)
LCPS: National Capacity and Patient Transfer Service (or Landelijk Coördinatiecentrum Patiënten Spreiding in Dutch)
LPA: National Protocol of Paramedic care (or Landelijk Protocol Ambulancezorg in Dutch)
LUMC: Leiden University Medical Center
MACE: Major Adverse Cardiac Events
MICU: Mobile Intensive Care Unit
ML: Machine Learning
NLP: Natural Language Processing
NPV: Negative Predictive Value
NSTE-ACS: Non ST-elevation Acute Coronary Syndrome
NSTEMI: Non ST-elevation Myocardial Infarction
NZA: Dutch Health Authority (or Nederlandse Zorg Autoriteit in Dutch)
OHCA: Out-of-hospital Cardiac Arrest
OR: Odds Ratio
PCI: Percutaneous Coronary Intervention
PMR: Patient Movement Request
POC: Point-of-care
PPV: Positive Predictive Value
RAVHM: Regional Ambulance Service Hollands-Midden (or Regionale Ambulance Voorziening Hollands-Midden in Dutch)
RCPS: Regional Capacity and Patient Transfer Service (or Regionaal Coördinatiecentrum Patiënten Spreiding in Dutch)
RR: Relative Risk
SD: Standard Deviation
STEMI: ST-elevation Myocardial Infarction

List of publications

1. Prehospital triage of patients with acute cardiac complaints: study protocol of HART-c, a multicentre prospective study. **de Koning ER**, Biersteker TE, Beeres S, Bosch J, Backus BE, Kirchhof CJ, Alizadeh Dehnavi R, Silviu HA, Schalij M, Boogers MJ. *BMJ Open*. 2021 Feb 12;11(2):e041553. doi: 10.1136/bmjopen-2020-041553. PMID: 33579765; PMCID: PMC7883865.
2. Emergency medical services evaluations for chest pain during first COVID-19 lockdown in Hollands-Midden, the Netherlands. **de Koning ER**, Boogers MJ, Bosch J, de Visser M, Schalij MJ, Beeres SLMA. *Neth Heart J*. 2021 Apr;29(4):224-229. doi: 10.1007/s12471-021-01545-y. Epub 2021 Feb 18. PMID: 33599968; PMCID: PMC7890775.
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6. Management of patients suspected for non-ST elevation-acute coronary syndrome in the prehospital phase. Tolsma RT, **de Koning ER**, Fokkert MJ, van der Waarden NW, van 't Hof AW, Backus BE. *Future Cardiol*. 2023 Oct;19(13):639-647. doi: 10.2217/fca-2023-0049. Epub 2023 Nov 2. PMID: 37916603.

Currently under review

7. Prehospital Triage of Patients with Suspected Acute Coronary Syndrome - A Consensus Statement of the National Working group Prehospital Triage under Auspices of the Netherlands Society of Cardiology.
8. A multicentre randomized controlled trial of point-of-care hs-cTnI in prehospital ACS triage: impact on diagnosis and cost-effectiveness.

Other

de Koning, ER. Letter to the Editor: On the importance of publishing. *Donald Duck Weekblad*, 10th ed (2020, February 27). ISSN 0165-1293.

About the author

Enrico Raun de Koning was born on August 9, 1991, in The Hague, the Netherlands. After completing high school at the Maerlant Lyceum, he began studying Medicine at Leiden University in 2009. During his studies, he developed a strong interest in cardiology and cardiac research. Following a successful internship as a student researcher, he started working as a resident not in training (ANIOS) at the Department of Cardiology at Leiden University Medical Center (LUMC).



In 2019, he commenced his PhD research on improving prehospital triage at the same department, under the supervision of Prof. Dr. Martin Schalij, Dr. Mark Boogers, and Dr. Saskia Beeres. The results of this research are presented in this thesis.

In addition to his clinical research, Enrico was active in teaching medical students and obtained his Basic University Teaching Qualification (BKO). He also served as head of the event committee of the LUMC Association for PhD Candidates (LAP). During his time as a PhD candidate, his two children, Jules (2020) and Louise (2022), were born.

After completing three years of research, he began his specialist training in cardiology at Haaglanden Medical Center (locations Westeinde and Bronovo) and the Groene Hart Hospital in Gouda. During this period, he co-founded the cardiology podcast Hart op de Tong, a spin-off of a surgery podcast produced by Orly Media. As of June 2025, he serves on the Junior Council of the Netherlands Society for Cardiology (NVVC), representing all cardiology residents and researchers.

He currently lives in The Hague with his partner Saskia and their two children, Jules and Louise.

Over de auteur

Enrico Raun de Koning werd op 9 augustus 1991 geboren in Den Haag. Na het afronden van zijn middelbare schoolopleiding aan het Maerlant Lyceum begon hij in 2009 met de studie Geneeskunde aan de Universiteit Leiden. Tijdens zijn studie ontwikkelde hij een sterke interesse in cardiologie en onderzoek. Na een succesvolle onderzoeksstage als student begon hij als arts-niet-in-opleiding (ANIOS) op de afdeling Cardiologie van het Leids Universitair Medisch Centrum (LUMC).

In 2019 startte hij met zijn promotieonderzoek naar het verbeteren van prehospital triage, onder begeleiding van Prof. dr. Martin Schalijs, dr. Mark Boogers en dr. Saskia Beeres. De resultaten van dit onderzoek werden in dit proefschrift beschreven.

Naast zijn klinisch onderzoek was Enrico actief betrokken bij het onderwijs aan geneeskundestudenten en behaalde hij zijn Basiskwalificatie Onderwijs (BKO). Ook was hij hoofd van de evenementencommissie van de LUMC Association for PhD Candidates (LAP). Tijdens zijn promotietraject werden zijn twee kinderen geboren: Jules (2020) en Louise (2022).

Na drie jaar wetenschappelijk onderzoek, startte hij zijn opleiding tot cardioloog in het Haaglanden Medisch Centrum (locaties Westeinde en Bronovo) en het Groene Hart Ziekenhuis in Gouda. In deze periode was hij medeoprichter van de cardiologiepodcast Hart op de Tong, een spin-off van een chirurgische podcast geproduceerd door Orly Media. Daarnaast was hij vanaf juni 2026 lid van de Juniorkamer van de Nederlandse Vereniging voor Cardiologie (NVVC), waar hij alle ANIOS, onderzoekers en AIOS binnen de cardiologie vertegenwoordigd.

Hij woont momenteel in Den Haag met zijn partner Saskia en hun twee kinderen, Jules en Louise.



Dankwoord

Dit proefschrift is geschreven op de afdeling Hartziekten van het LUMC. Tijdens het schrijven en opzetten van de hier beschreven onderzoeken heb ik het geluk gehad om samen te mogen werken met collega's uit het Alrijne, Groene Hart Ziekenhuis, RAVHM, ROAZ, RCPS West, LCPS en LAP en daarnaast vertegenwoordigers van zorgverzekeraars en de Harteraad. Ik wil graag iedereen bedanken die direct of indirect meegeholpen heeft aan het tot stand komen van dit proefschrift en de hierin beschreven artikelen. Daarnaast wil ik een aantal personen in het bijzonder bedanken.

Geachte professor Schalijs, beste Martin, dank voor het vertrouwen dat je mij hebt gegeven om aan dit proefschrift te beginnen. Ik heb jouw leiderschapsstijl van dichtbij mogen ervaren—binnen mijn promotietraject, op de afdeling en in het ziekenhuis en de manier waarop jij verantwoordelijkheid draagt en daarmee vertrouwen uitstraalt, is inspirerend en iets dat ik mijn hele carrière met me mee zal dragen.

Geachte dr. Beeres, beste Saskia, zonder jou was ik hier nooit gekomen. Al tijdens mijn studie geneeskunde wees je me het juiste pad, en ook daarna, als beginnend clinicus, wist je me te inspireren voor de cardiologie.

Geachte dr. Boogers, beste Mark, dank voor je eindeloze geduld en vertrouwen in mij. Jouw vermogen om mensen te verbinden en hen ieder op hun eigen manier tot hun recht te laten komen, is bijzonder en bewonderenswaardig en heeft geleid tot de voltooiing van ons onderzoek en dit proefschrift.

Beste Jan, jouw tomeloze inzet voor de goede zaak is van onschatbare waarde geweest voor dit proefschrift. Zonder jou geen patiënten, en zonder de geweldige medewerkers van de RAVHM geen inclusie. Ik heb met eigen ogen gezien wat voor bijzonder en belangrijk werk jij en je collega's dagelijks verrichten. Dit proefschrift had zonder de inzet van alle ambulancehulpverleners simpelweg niet kunnen bestaan—mijn oprechte dank daarvoor.

Ook wil ik alle medewerkers van de afdeling Hartziekten bedanken. De gesprekken met jullie—vaak onder het genot van de beste koffie van het ziekenhuis—maakten zelfs de meest uitdagende dagen draaglijk. Mijn collega arts-onderzoekers van 'de Tuin' droegen daar minstens zoveel aan bij. De vele borrels, skireizen en koffierondjes hielpen niet alleen om scherp te blijven op het eigen werk, maar ook om af en toe even te relativiseren. Ik kijk er enorm naar uit om samen met jullie de toekomst van de (cardiovasculaire) zorg in Nederland vorm te geven.

Dank aan al mijn vrienden die mij de afgelopen jaren hebben gesteund. Edmond en Joep, bedankt dat jullie mijn paranimfen willen zijn. Met twee juristen aan mijn zijde weet ik zeker dat ik mijn verdediging zonder kleerscheuren zal doorstaan. Ook mijn huisgenoten van de Gortstraat—Hidde, Lodewijk en Eric—bedankt. Aan al mijn clubgenoten die tot dit punt in

het proefschrift zijn gekomen: chapeau. Ik kijk nu al uit naar onze volgende reizen—hopelijk de volgende keer weer in volledige bezetting.

Fabian, grote kleine broer, hoewel we misschien niet veel discussies hebben gevoerd over de inhoud van dit proefschrift, geloof ik echt dat al onze (toch vaak onzinnige) gesprekken mijn kritisch denken hebben aangescherpt. Je hebt altijd sterke argumenten, en om bij jou een punt te maken, moet deze wel erg goed onderbouwd zijn. Dank je wel dat je mijn blik op de wereld af en toe uitdaagt.

Lieve pap en mam, er zijn eigenlijk geen woorden die volledig kunnen uitdrukken hoe dankbaar ik ben voor alles wat jullie voor mij hebben gedaan. Pap, dank je wel voor het ontwikkelen van mijn kritische blik—een eigenschap die me enorm heeft geholpen tijdens het schrijven van dit proefschrift. Lieve mam, jij hebt me geleerd hoe belangrijk het is om verbinding te maken met anderen. Die les is van onschatbare waarde geweest, juist in contact met al diegenen die hierboven genoemd zijn. Dank jullie wel voor jullie onvoorwaardelijke steun—vroeger in mijn jeugd, tijdens het schrijven van dit proefschrift, en nu in ons gezin.

Lieve Jules en Louise, heel eerlijk: zonder jullie was dit proefschrift waarschijnlijk een jaar eerder af geweest. Maar elke dag jullie te zien groeien en jullie in mijn armen te mogen houden, heeft me laten voelen wat er écht toe doet in het leven. Jullie aanwezigheid heeft me door de stressvolle en moeilijke momenten heen geholpen.

Allerliefste Sas, dank je wel dat je het al die tijd met me hebt volgehouden. Dank je voor je geduld wanneer ik me weer urenlang had teruggetrokken in de studeerkamer, zelfs op onze gezamenlijke vrije dagen. En dank je dat je mijn eindeloze geratel over cardiologie en dit onderzoek telkens weer hebt aangehoord. Je houdt me met beide benen op de grond en houdt mijn ogen open voor de mooie dingen in het leven. Ik houd ongelooflijk veel van je, en ben elke dag opnieuw gelukkig met jou aan mijn zijde. Jij en ik, voor altijd.

