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

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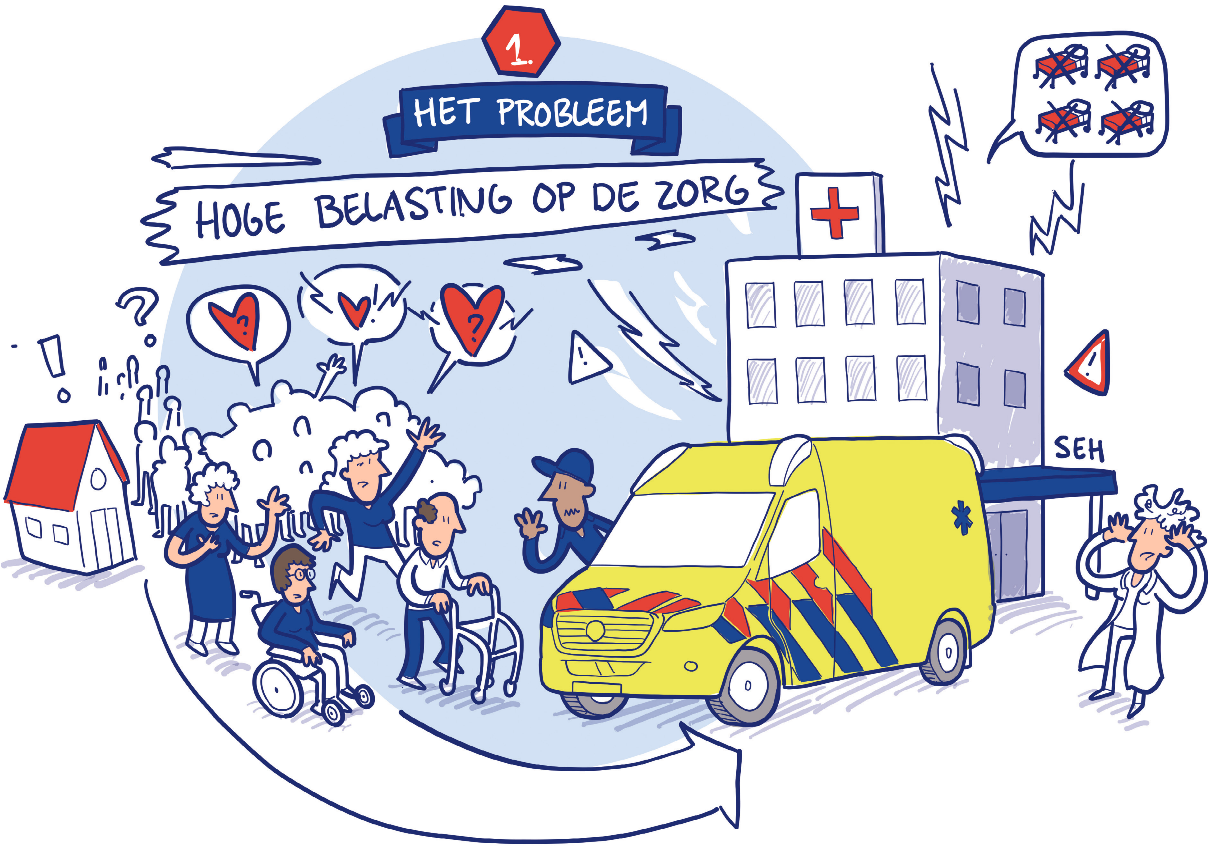
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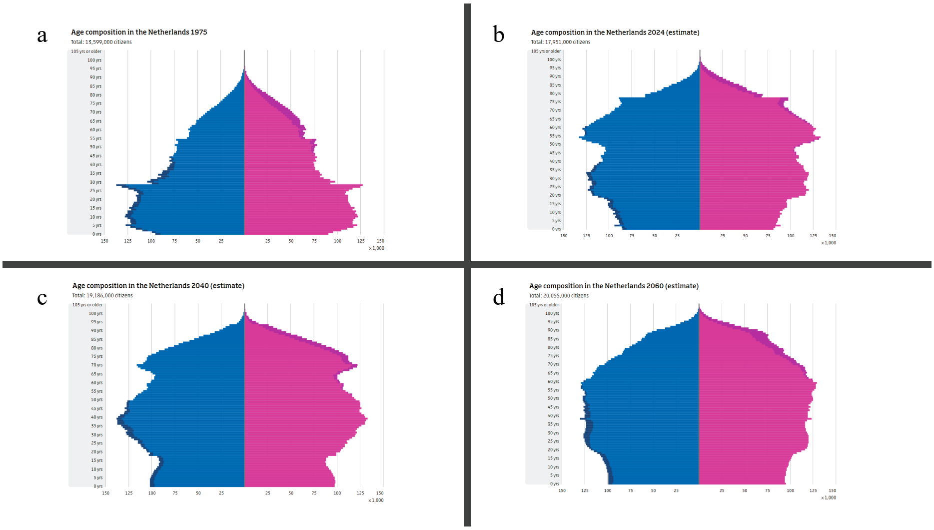
Chapter 1

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).

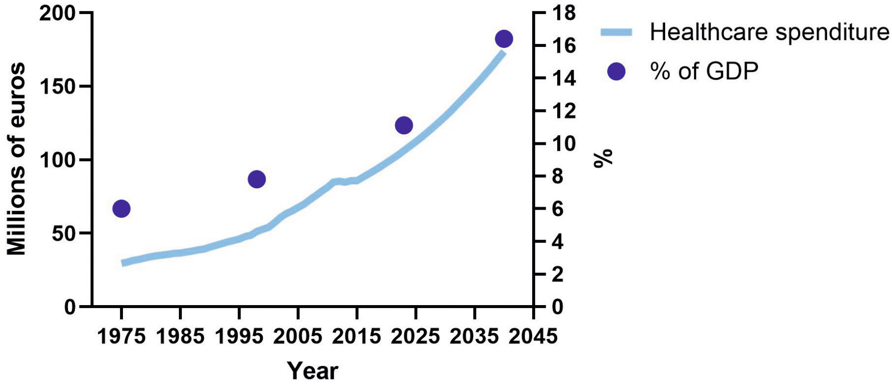
Figure 1. Demographic changes in age composition in the Netherlands from 1975 (a) to 2024 (b), and projections for 2040 (c) and 2060 (d) (5).



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

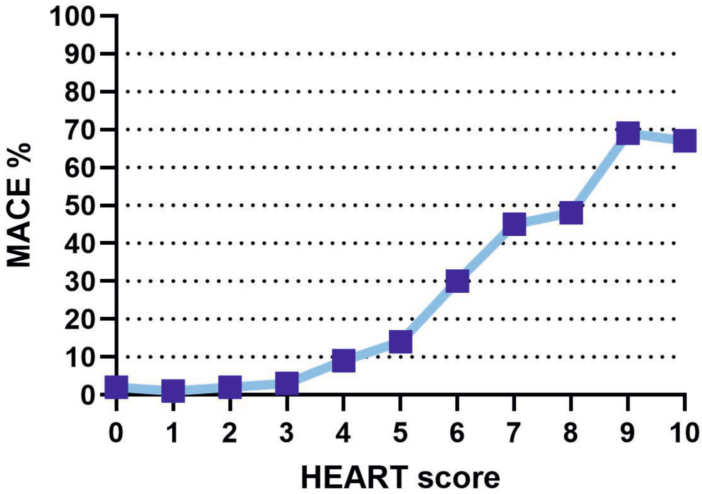
However, for various diseases or symptoms, risk scores have been developed to assist professionals in triage and provide objective tools for estimating risk both in-hospital and in the pre-hospital setting. Within the field of cardiology the TIMI –(17) and GRACE risk (18) scores are commonly used to 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	

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 NSTE-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

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 Status) 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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1