Development of a clinical deterioration prediction tool for adult patients during ambulance transportation in South Africa

by

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Declaration:

I, Wayne Jooste, hereby declare that the work contained in this thesis is my original work and that I have not previously submitted it, in its entirety or in part, at any university for a degree. This work has not been reported or published prior to registration for the abovementioned degree.

Signature: Signed by candidate Date: 11/02/2024

CONTENTS

Acknowledgements and lists of abbreviations, tables, and figures.

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List of acronyms and abbreviations

AEA	Ambulance Emergency Assistant.
AI	Artificial Intelligence
ANT	Paramedic
BAA	Basic Ambulance Assistant.
CD	Clinical Deterioration.
CHAID	Chi-squared Automatic Interaction Detection
ECA	Emergency Care Assistant.
ECP	Emergency Care Practitioner.
ECP	Emergency Care Practitioner.
ECT	Emergency Care Technician.
EWS	Early Warning Score
GCS	Glascow Coma Score
HPCSA	Health Professions Council of South Africa.
ICU	Intensive Care Unit.
MEES	Mainz Emergency Evaluation Score.
MeSH	Medical Subject Headings.
MEWS	Modified Early Warning Score.
MP	Medical Practitioner.
NEWS	National Early Warning Score.
SP02	Pulse oximeter oxygen saturation.

List of Tables

List of Appendices

1. Annexure A-Significant variables used for CHAID tree and binomial regression.
2. Annexure B-List of grouped diagnoses from data received.
3. Annexure C-Human Research Ethics Committee-Ethics Approval.

List of figures

Abstract

Background – Clinical deterioration is a worldwide concern and is associated with increased mortality, hospital stay, and incidence of adverse events. CD also occurs in the pre-hospital setting though few studies describe its occurrence and the factors it is associated with, and no evidence currently exists that describes its occurrence within the South African context. CD is deemed preventable, and although several tools exist to detect early CD, no published evidence was found about validated pre-hospital CD prediction tools.

Aim - The study aimed to describe whether adult patients clinically deteriorate during transportation by private ground and air ambulance, as well as describe which factors may predict clinical deterioration. In addition, it aimed to propose a pre-hospital clinical deterioration prediction tool.

Methods – A data archive analysis was done on physiological parameters and other factors recorded by pre-hospital practitioners of patients during ambulance transportation. A NEWS and MEES score were calculated on physiological parameter trends to observe for the occurrence of CD on 89193 patients. Data from the analysis was subsequently used for the creation of a pre-hospital clinical deterioration prediction tool through binomial regression and Chi-square Automatic Interaction Detector classification.

Results – A CD rate of 15.7% was observed in this sample. Numerous correlating clinical, logistical, and demographic variables emerged. A Chi-Squared Automatic Interaction Detection as well as binomial regression analysis was performed on logistic and clinical variables revealing significant predictive ability. Medical oxygen administration (OR 3.38, 95% CI 3.22-3.55, P-value <0.001) and high clinical risk (OR 2.42, 95% CI 2.26-2.59, p-value 0.000) emerged as the most significant predictors for CD, while senior crew qualification ECP (OR 0.7, 95% CI 0.64-0.77, p-value <0.001) emerged as 30% protective against CD compared to the reference category BAA. These results indicate that there is a significant increase in the probability of CD should a patient be of high clinical risk and receive medical oxygen for example, as well as a decrease in the probability of CD should the patient be treated by higher qualified

providers. The regression analysis was followed by a pre-hospital clinical deterioration prediction tool development, where these variables amongst others were included in a composite score. The score subtracted more points as the qualification of the treating provider increased or if it was a primary case. The score added points should it have been a trauma case, medical oxygen was administered, inotropic support was provided, analgesia or sedation was provided, or if the patients had an increase in level of acuity.

Conclusion

The study aimed to develop through data-archive analysis and regression a pre-hospital clinical deterioration prediction tool. Multiple logistical and clinical variables were identified that are significant predictors for CD in the pre-hospital setting and were ultimately included in a composite score. This tool can practically be implemented into the call centre of an emergency medical service during information gathering for inter-facility transfers, or in an electronic patient report form by a pre-hospital provider. Despite its limitations, we believe this tool could lead to early identification of pre-hospital CD and early implementation of CD mitigation strategies, ultimately improving patient safety and outcomes. We recommend a validation study to be performed in the future.

CHAPTER 1: Introduction

Clinical deterioration (CD) is defined as a patient progressing from one clinical state to a worse clinical state.[1,2] CD in the acute setting, is a worldwide concern and involves physiological decompensation that occurs as a patient's pre-existing condition worsens, or the acute onset of one or more physiological disturbances.[3,4] The occurrence of CD in the in-hospital setting has been described in many studies, and the importance of early recognition, identification, and acknowledgment is a matter of interest.[1,2,4] Evidence suggests that CD is a key contributor to patient mortality, linked to higher incidence of adverse events, and prolonged hospital admission.[5,6] Furthermore, a need exists to understand the cause and events that lead to the occurrence of CD.[7–9] Several studies have attempted to identify aspects related to CD of patients, and one study found that most cardiopulmonary arrest cases were preceded by a period of physiologic abnormality.[9]

CD can also occur during the care and transportation of patients in the pre-hospital environment, and identifying CD in a patient can be challenging.[10,11] The pre-hospital environment poses many risks to the safety and quality of patient care during the transportation phase.[10,11] During this phase, it has been observed that patients often clinically deteriorate, and a high number of adverse events occur. Multiple factors contribute to this, including logistical, demographical, and clinical.[10,11] A Norwegian study reported incidents occurring in 50% of patients transported, all of which possibly contributed to CD.[10,11] A Thailand study using the National Early Warning Score (NEWS), found that 23% of all patients, and 64% of all critical patients transported, showed signs of clinical deterioration during ambulance transportation.[11] In the pre-hospital setting, some risk factors for deterioration include patient age, transport time, patient acuity, and level of qualification of the treating practitioner.[11] An international study described that in cases where CD was observed, it occurred during observations made between minutes 32-45, suggesting that deterioration is linked to longer transportation times.[11] CD was also less likely to occur if the patient was cared for by a practitioner that had received critical care training as well as if the ambulance was equipped with intensive care unit technologies.[11]

A study in Australia found that a lack of working equipment and human factors such as poor communication, delay in care, and poor documentation contributed to most

incidences of CD during patients' stay in an emergency department, but this was not explored in the pre-hospital setting.[12] Evidence suggests that a higher incidence of adverse events occurs in low-income countries as compared high-income countries, and these events contribute to CD.[10]

The NEWS is an early warning score designed to assist medical practitioners in early CD detection by use of physiological parameters.[13,14] The medical practitioner records the patient's physiological parameters, after which the NEWS allocates a score to each parameter that calculates a level of risk for clinical deterioration.[14,15] The NEWS was compared to several other scores and was found to be superior at indicating risk for CD.[16] Recently in the United States, an early detection score was developed and compared to the NEWS score, and even though it showed more accuracy in detecting CD over 24 hours, the study was only done in one hospital and requires the authors' specific software to calculate the risk score.[16] One study showed that the NEWS carried high predictability for 1-day mortality for patients in the pre-hospital setting that fell in the high-risk category, and although no clear pre-hospital definition for CD exists, the NEWS is an accurate and validated tool to attempt assessing for deterioration in this setting.[4,10] An English study described that patients with a NEWS of > or equal to 7 are at high risk of deteriorating in the pre-hospital setting.[17]

The prevalence of CD in the pre-hospital setting is poorly explored in literature with no evidence existing within the South African context, and to the researcher's knowledge, no data with regards to the occurrence of CD exists within the pre-hospital context of South Africa.[11] The need for transportation of critically ill or injured patients is increasing as a consequence of the establishment of specialized facilities to improve outcomes, and out-of-hospital care should be on the same level of safety and quality as in-hospital care.[10] Furthermore, no systems are in place to assist the practitioner to identify or predict CD in the pre-hospital environment. A practitioner's failure to recognize and respond to patients that are deteriorating can lead to an increase in mortality and morbidity, hospital length of stay, and incurred costs on the health care system.[9,16]

This study aims to develop a pre-hospital CD prediction tool for adult patients during ambulance transportation to assist the practitioner in predicting CD early. The format of this thesis will be in a logical manner where the literature review will be presented

first, followed by the research methodology which will explain the methods used, followed by results found and then by discussion. Following the main chapters is a short chapter that describes the clinical deterioration prediction tool and the development thereof during this thesis. The study will then end with the conclusion, limitations, and future recommendations.

CHAPTER 2: Literature Review

The literature review was conducted to establish and describe existing evidence within the known body of knowledge regarding a working definition for clinical deterioration (CD), the occurrence of CD in the pre-hospital setting as well as the factors associated with it.

The literature review aims.

The aims of the literature review are to:

1. Identify a working definition for CD.
2. Describe the current literature on CD occurrence in the pre-hospital setting.
3. Describe the current literature on CD identification models in the pre-hospital setting.
4. Describe risk factors contributing to pre-hospital CD.

Search strategy

Medical Subject Headings (MeSH) and non-MeSH terms were used during the search to create a MeSH query for the literature review. The PubMed search engine was used and included studies from 2014 – 2023. The search was conducted on the 8th of May 2023, it did not include grey literature and only included English studies.

Common terms associated with or describing clinical deterioration (CD) were used to build a MeSH term for the literature review. These terms included: Ambulances, patient transfer, air ambulances, emergency medical services, patient safety, risk management, medical errors, epidemiology, risk factors, mortality, early warning score, incidence, critical illness, health status indicators, critical care, clinical decision rules, and vital signs, The terms were then combined with clinical deterioration or early warning in the query, and all studies within the confines of these terms were included for the review.

On the day, the MeSH search yielded 756 results. The articles were then screened for relevance in two phases: First, all 756 articles were screened for relevance by title, and those deemed relevant were then further screened by abstract. The result was that after both screening processes, 58 articles were deemed to be relevant to the

study, and an additional 28 articles known to the author were reviewed based on topic relevance. Of the 101 articles reviewed by full text, 66 were selected for the literature review (See Table 1)

Table 1: Breakdown of MeSH query and screening for relevance

MeSH query: **(("Ambulances"[Mesh]) OR ("Patient Transfer"[Mesh]) OR ("Air Ambulances"[Mesh]) OR ("Emergency Medical Services"[Mesh]) OR ("Patient Safety"[Mesh]) OR ("Risk Management"[Mesh]) OR ("Medical Errors"[Mesh]) OR ("Epidemiology"[Mesh]) OR ("Risk Factors"[Mesh]) OR ("Mortality"[Mesh]) OR ("Early Warning Score"[Mesh]) OR ("Incidence"[Mesh]) OR ("Critical Illness"[Mesh]) OR ("Health Status Indicators"[Mesh]) OR ("Critical Care"[Mesh]) OR ("Clinical Decision Rules"[Mesh]) OR ("Vital Signs"[Mesh])) AND (("Clinical Deterioration"[Mesh]) OR ("Early Warning Score"[Mesh]))**	**Number screened**	**Number accepted**
Results from MeSH query	**-**	**756**
MeSH results screened for relevance by title	**756**	**156**
MeSH results screened for relevance by abstract	**156**	**73**
Additional topic relevant resources not in MeSH results	**28**	**28**
Total number of articles reviewed by full text	**101**	**66**

Clinical deterioration definition

Clinical deterioration (CD) is defined as a patient progressing from one clinical state to a worse clinical state.[1,2] It involves physiological decompensation that occurs as a patient's pre-existing condition worsens, or an acute onset of one or more physiological disturbances.[5,7] Patients that deteriorate progress to a worse clinical state which incurs escalation of care, increase in hospital length of stay, morbidity, and mortality.[5,16] It is therefore imperative for healthcare facilities or systems to predict and control physiological decompensation when appropriate.[5]

CD can occur as a result of surgery, acute disease, frailty, and chronic conditions. These carry a risk for physiological decompensation resulting in primary consequences such as heart attack, sepsis, pulmonary failure, or kidney failure. In the absence of proper medical intervention, CD can then further occur leading to secondary consequences.[2,5,18]

The major challenge is the development and consensus of a definition for CD. Four frameworks exist for defining CD. Since the 1960's researchers have attempted to develop a working definition by these various frameworks.[19] The first is in the context of the contribution of negligence iatrogenesis in causing adverse events,[19] and was used to study clinical deterioration mainly between the 1960's and 2000's.[19] Adverse events due to medical care were logged and these patients were defined as having suffered CD.[19] Although it enabled researchers to quantify harm due to iatrogenesis and identify contributing factors, it was retrospective in nature and did not include CD possibly caused by the patient's underlying condition.[19] Researchers also went further to include clinical adverse events such as pulmonary embolism and myocardial infarction to the end that clinical deterioration is not only defined by iatrogenesis but also by the underlying medical condition.[19] The disadvantage is that it remains retrospective and does not reliably inform practitioners prospectively of which patients are at risk.

Since 1994, CD has been defined by the presence of physiological instability, and vital signs remain the mainstay within this framework.[19,20] Although it does not consider all factors, the measurement of physiological parameters occurs in real time and response to therapy can be measured and prospectively predict deterioration or death.[8,19,20] Click or tap here to enter text. Disadvantages of this framework is that it does not consider other factors that may predict death and that it must be detected through reliable vital sign measurements.[19]

Risk stratification models have also been implemented to define CD and includes system, patient, physiological and organisational factors that may contribute to risk.[19] This framework places physiological parameters into context of the presenting disease as well setting in which the patient is treated.[19] These models have not been validated yet, and requires advanced mathematical modelling which in real time is still difficult to implement, test, and validate.[19] Research indicate that both adverse events and CD are preceded by deranged vital signs and therefore a definition based on derangement in vital signs still remains the most reliable.[16,19–22] Researchers use the concept of risk stratification to prospectively predict the risk of morbidity based on the degree of derangement of the vital signs, therefore defining it as CD.[3,19] A study that reviewed all these frameworks recommended the following definition: “A deteriorating patient is one who progresses from one clinical state to a worse clinical state which increases their individual risk of morbidity, including organ dysfunction, protracted hospital stay, disability or death”.[19]

Although many theoretical definitions exist, there is still no consensus of an operational definition to measure CD.[6,9] In 2017, Padilla et al recognized the need for the development of an operational definition to assist practitioners to accurately identify patients at risk of CD by use of concept analysis. The study reported that due to variation in uniformity of the concept of CD, a knowledge gap exists necessitating a clarification of this phenomenon.[23] After a thorough review of research, the study recommended the following operational definition: “A dynamic state experienced by a patient compromising hemodynamic stability, marked by physiological decompensation accompanied by a subjective or objective finding”.[23] The conclusion of this definition suggests that physiological parameters play a vital role in defining

CD. Many studies have been done in an attempt to describe a working definition of CD for the in-hospital setting, but few for the pre-hospital setting.[3,6,14,24–263]

The crucial role of physiological parameters in predicting CD has been established repeatedly in literature, and vital signs, through the use of Early Warning Scores remain a key aspect in defining in-hospital and pre-hospital CD.[5,20,22,25,27] According to literature, the increase of one point or more remains a reliable way to define or predict CD in the pre-hospital setting use and development of EWSs remains a reliable way the most reliable method of predicting CD in the pre-hospital setting. [6,11,2766,20,22,26,28 3,16,29] For this study, a realistic operational definition for CD based on the availability of technology, literature, and data would be an increase of one point measured by an EWS, based on physiological parameters recorded by a practitioner caring for a patient.[27]

Occurrence of pre-hospital clinical deterioration

Clinical deterioration (CD) can occur during the transportation of patients in the pre-hospital environment, and identifying CD in these patients can be challenging.[6,10,11,30,31] Studies regarding the occurrence of CD in the pre-hospital setting are limited worldwide, and regardless of the existing studies explaining the burden and need for further research, a gap in the literature exists.[9,30] In 2008 Boyle described that the evidence for management of patients that deteriorate under care of paramedics was limited after a report was released by the Ministerial Review of Trauma and Emergency Services in Victoria, Australia.[32] This report concluded that there remained two major pre-hospital care questions: “Is the mechanism of injury a useful predictor in pre-hospital trauma triage and what is the appropriate triage strategy for patients that severely deteriorate at the scene or during transport? [32] In response to this Boyle conducted a study to determine the number and outcome of patients who suddenly deteriorate in the presence of paramedics.[32] The researcher manually reviewed patient report forms and specifically observed deterioration of physiological parameters to determine if patients clinically deteriorated. It was found that 5.1% of all patients transported showed signs of sudden CD.[32]

During the literature study, only 6 studies were found that have been conducted to determine the prevalence of CD in the prehospital setting. A Canadian study reported critical events in 333 (6.5%) of 5144 urgent ground transportation that led to CD. The study looked at adverse events related to CD during transportation over a period of 5 years and found that patients treated by lower qualified practitioners, who were mechanically ventilated, had longer transport times, and had hemodynamic instability before the transfer had higher adverse event rates leading to possible CD.[33] A Saudi Arabian study in 2017 reported an adverse event rate of 13.7% through a retrospective cohort study of critically ill or injured adult patients undergoing interfacility transfer, and most events were primarily a result of deterioration of physiological parameters such as desaturation and hypotension.[34] The study also described an in-hospital mortality rate of 30.4%, and a 30-day mortality rate of 68.1%, and made use of multiple logistic regression models to assess predictor variables for these events. These are presented in the literature review later.[34]

In 2020, a study in Thailand Srithong et al, reported the incidence of CD as 28.37% in 839 critically ill patients transported by ambulance. A cohort study was done on inter-hospital transfers that included adult patients without obstetrics or psychiatric emergencies for the purpose of observation of CD by use of changes in physiological parameters.[35] To define CD, the study used the NEWS and described it as the most reliable EWS to predict CD. Though the study did not aim to provide a tool for the prediction of CD, it provided valuable insight into the occurrence of CD as well as factors associated with it, yet limitations that should be considered was the quality of documentation of practitioners.[35]

In the UK, Ligtenberg et al reported adverse events occurring in 34% of all transports conducted, some of which had signs of CD. It was found that unstable patients had a CD rate of 63.27%, stable patients with a high risk of CD a rate of 24.33%, and stable patients with a medium risk of CD a rate of 11.76%.[31] The study collected data in the form of physiological parameters before the commencement of inter-facility transportation of a patient via ambulance, and immediately after arrival. It also included other factors such as transfer distance, as well as interventions done. It was found that factors contributing to CD were the presence of adverse events, ignored instructions given by the referring physician, and general technical problems.

By monitoring changes in physiological parameters, an American study described CD in 12.2% of patients transported by ground ambulance, and 27.8% transported by helicopter according to a national EMS information database.[36] The study used a decline in physiological parameters such as respiratory rate, Glasgow Coma Scale, and systolic blood pressure to define CD and found that CD was associated with increased pre-hospital time and that HEMS patients were much more likely to deteriorate.[36]

A Hong Kong study described a CD rate of 28% during interhospital transfers by observing changes in physiological decline by use of the MEWS (Modified Early Warning Score). Out of 102 patients transported 28 deteriorated during transport and the incidence of CD was significantly greater with a higher MEWS (Modified Early Warning Score).[37] Another study found that of 47 794 infants transported, 14 722 (30.8%) suffered CD during transport.[36,38]

In summary, the literature indicates that CD does, in fact, occur in the pre-hospital environment with rates reported between 6% to 34% and that there are many factors that contribute to this carrying statistical predictive capacity. Most studies were done in high-income countries such as Canada and Hong Kong, which makes the result difficult to transfer to the South African context. These studies are also mostly observational, and causation could not be established due to the lack of associations and predictions made. The Thailand study was however done in a low to medium-income country and found statistically significant variables through regression that could be related to the South African context.

Early identification of clinical deterioration in the pre-hospital setting

Early identification of clinical deterioration (CD) by in-hospital as well as pre-hospital practitioners is vital and leads to decreased mortality, decreased hospital length of stay, and earlier interventions.[3,8,9,16,22,26,39–41] Pre-hospital care has developed from a simple model of transport to an integral component of the healthcare system, with paramedics often being the first contact for patient care, carrying multiple medications and providing a variety of advanced interventions.[9,42–44] Due to pre-hospital providers playing an integral part in the patient's future pathway, with the inherent risk of patient

transport possessing challenges such as working in a stressful and often unpredictable environment, a good understanding of clinical deterioration and early recognition is vital.[11,40,42,44,45] Evidence shows that 52-94% of all CD incidents are preventable and that early recognition of CD leads to early intervention in preventing fatal events such as cardiac arrest.[11,46]

Despite the need, there is limited knowledge about paramedics' ability to detect or identify CD, and it is a complex issue that according to literature requires further research.[9] Due to the lack of a pre-hospital definition for CD and understanding of the prevalence of CD in the pre-hospital environment, Bourke et al set out to determine the current prevalence of CD as well as develop a working definition through a systematic review.[9] The results showed that there still remains no standardized definition for pre-hospital CD. Only one study showed a definition that did not include CD to be a concept beyond derangements in physiological parameters except examinations of external haemorrhage and cardiac arrest.[9] The lack of a working definition in the prehospital setting leads to CD not being detected or identified in a timely manner by practitioners, and evidence shows that failure to recognize CD even within 15 minutes, contributes to increase in-hospital mortality.[6,41] Two studies reported that paramedics performed sub-optimally at recognition, but that there is an association between the ability to recognize CD and clinician experience. Paramedics often fail to recognize a patient at risk of cardiac arrest, though experienced clinicians were found to be more likely to recognize it early.[6,9]

Bourke et al completed a Delphi study to develop a consensus definition for pre-hospital CD. The consensus was CD primarily takes form in the change of physiological parameters included in most Early Warning Scores (EWS) and that this should be the starting point for further research to create the first consensus-based out-of-hospital CD definition and development of an appropriate EWS.[6]

Patients who suffer from cardiac arrest and unplanned ICU admission often exhibit physiological signs preceding these events, and acute changes in physiological parameters occur before deterioration.[6,16,20,23,28,39,43,47] Vital sign trends have been associated with CD and for these reasons, physiological parameters and systematic or continuous capturing of vital sign trends remain arguably the most important indicators of CD.[3,20,22,26,28,48,49] Due to the lack of a working definition, and

understanding of clinical deterioration by paramedics, there has been an increasing interest to introduce and validate EWS into the pre-hospital environment to aid in facilitating early recognition of CD.[6,9,45,50–52]

A systematic review showed that several studies have used EWS to measure mortality by measuring the National Early Warning Score (NEWS) as example at first patient contact, just before patient transfer via ambulance, and on arrival at hospital. The objective was to determine the evolving prognostic capability of an EWS by monitoring it at three points.[11,42] These studies found that clinical deterioration occurs in the pre-hospital setting and that EWS was reliably used to detect it.[35,45,51] Some studies have been done in the in-hospital setting to detect clinical deterioration through continuous measurement of vital signs by wearable devices, machine learning, and artificial intelligence and have been shown to detect clinical deterioration earlier than conventional EWS.[22,26] However, technological advances have limited these studies and to date, no use of it is described in pre-hospital literature.[26]

Early Warning Scores

Early warning score (EWS) development was started in 1997 and follows the principle of including a threshold score, that triggers a set of actions intended to escalate care.[18,53] An Early Warning Score (EWS) is a score developed to predict the risk of clinical deterioration and is derived from recording of specific physiological parameters.[4,13,24,25] For its use in predicting and identifying clinical deterioration, certain physiological parameters are selected to be monitored and recorded, a threshold is placed on each parameter, and if the physiological parameters exceed these thresholds clinical deterioration (CD) is triggered.[2,14,53,54] EWS are well-established and validated track and trigger tools used to predict and detect clinical deterioration.[18,44–46,53,55] An early warning score is designed based on monitoring vital signs or certain physiological parameters because 80-85% of all serious adverse events are preceded by abnormal vital signs.[5,18,41,46] Most literature found regarding the identification and prediction of clinical deterioration in the pre-hospital setting

describes the use of an EWS for this purpose, and this remains the mainstay of observing, detecting, and predicting CD in the pre-hospital setting.

Any tool that is capable of producing a score that can classify risk of CD before its implementation, can be considered valid for use in the prediction of CD.[56] Although this is the case, limited studies exist that describe its application in the pre-hospital setting, describing it as only accurate in predicting short-term mortality at 24 and 48hrs.[57] It is however evident that EWSs should be implemented for use in the pre-hospital setting, more research is required to determine its accuracy and higher initial scores in relation to the tool used, are associated with a greater risk of CD.[39,45,57]

In-hospital, many facilities complete manual or electronic vital signs tracking charts to detect and predict CD, and studies have found that its use significantly decreases ICU length of stay, distinguishing between patients that are at risk of deteriorating and those who are not.[3,20,24,39,58,59] The use of EWS in the pre-hospital setting is seen as controversial due to a lack of evidence of its effectiveness in this setting, but a recent systematic review described reasonable predictive performance for patient mortality within the first 48 hours.[21,39,53] Although there is no evidence that suggests a difference in patient outcome in pre-hospital settings that use or do not use an EWS, a study showed that a patient with a score of 7 or above on the NEWS describes very high likelihood of deterioration. Another showed that the use of an EWS appears to predict the likelihood of an adverse outcome accurately and that a score of more and equal to 5 is a key trigger point for clinical alert.[21,39] A study performed in Qatar described that an increase of 1 or more points on an EWS, was indicative of CD.[27] A study done in South Africa, determined the stability of HEMS patients after interventions by calculating Mainz Emergency Evaluation Score (MEES) based on certain physiological parameters, and a decrease in 2 or more points was defined as CD.[60]

A review of EWS optimal cutoff was done on the NEWS, and unfortunately, the ideal cutoff score cannot be determined.[53] Scores with 7 and above were associated with a high mortality rate in 24 hours, though the mortality outcome variable was missing for 44% of the sample. A NEWS of 5 is the most adopted cutoff score, but 40% of all patients with a NEWS score of 5 die in the hospital, and although a NEWS of 3 is associated with low risk, 9% of patients with a NEWS score of 3 or less die within the first 24hrs and 16% die ultimately in hospital.[53] Although an increase of 1 point on a

score may trigger unwanted interventions or clinical alerts, it is still associated with mortality and is therefore an indication of CD.[53] Several well-known EWS's have been developed and compared to each other in the pre-hospital setting for the purpose of validation.[14,45,61] A study comparing the National Early Warning Score 2, Modified Early Warning Score (MEWS), Vitalpac Early Warning Score, Worthing Physiological Scoring System, Triage Early Warning Score, Modified Rapid Emergency Medicine Score, and the Prehospital Index, has shown that none of the above mentioned is superior to the other but that the NEWS does have clinical advantages and has been validated, making its use the most ideal in the pre-hospital setting.[25,45,51,53] In North America, an EWS called the Early Deterioration Indicator was developed and shown to be more accurate than the most common EWS such as the MEWS and NEWS. This EWS however has not been validated for clinical application and requires further research and development.[16]

The use of an EWS is recommended from the initiation of pre-hospital care as it may benefit the practitioner and patient by providing an early indication of deterioration risk and is most useful when documentation is accurate.[30,42,45,50,51,62] One study found that clinical judgment alone had a low sensitivity for critical illness and that the use of an early warning score improved detection at the expense of specificity in the pre-hospital environment.[30] EWSs only assist the practitioner to detect CD in addition to their clinical judgment, therefore an EWS should never be a substitute for clinical assessment, judgment, nor the concern of the practitioner, and is rather recommended to be used as a tool in conjunction with the above.[8,18,29,30,45]

Clinical judgment had a sensitivity of 61.8% and a specificity of 94.1% while the Modified Early Warning Score (MEWS) had a sensitivity of 95% and no specificity was reported.[30] One study compared the MEWS score with the Emergency Medical Service Early Warning Score (EMEWS) for applicability in the pre-hospital setting, though found no difference in predicting deterioration[63]. These EWS have however not been validated for pre-hospital use to the extent of the NEWS[63]. Early warning scores are an essential aid to pre-hospital practitioners for their ability to predict CD, assisting in the decision for appropriate patient disposition and decision to escalate the patient for specialist care, though their misuse by practitioners have raised concerns of its validity.[8,30,42,51,58,61,64]

Some studies have shown that automated early warning scores present more accuracy in predicting and detecting CD from 81-100%.[24] These early warning scores are calculated without the manual capturing and completion by a practitioner, but rather an automated vital signs measuring device attached to the patient that calculates an EWS using Artificial Intelligence (AI). By use and development of these technologies, decreased delays and inaccuracies in vital sign measurements were observed and mortality has proven to decrease by up to 8%.[24] Only recording vital signs for the purposes of detecting CD can be limiting as variables such as patient history, and clinical notes may add to the accuracy of prediction and identification.[24] However the implementation of these technologies still faces many challenges and requires validation before it can be used.[4] Due to these reasons, manual recording of physiological parameters despite its limitations remains the most realistic and validated way to complete an EWS for the purpose of predicting and detecting CD, with the NEWS being a validated, and widely used score.[46]

National Early Warning Score (NEWS)

The NEWS (Annexure A) is an early warning score designed to assist a medical practitioner to effectively detect clinical deterioration early by use of physiological parameters, validated for pre-hospital use.[21,25,39,54] It was developed in 2012 as a result of the National Health Service (NHS) in the United Kingdom (UK) experiencing a high number of adverse events and in-hospital patient deterioration.[2,65]

A chart was developed that require the monitoring and capturing of six physiological parameters to determine whether patients are at risk of clinical deterioration during their care in hospital. The purpose of this venture was to make it simple and efficient for any practitioner to complete this score at the patient bedside. Each physiological parameter measured has a specific score allocated to it, and a total score is then calculated based of the score that each parameter received, indicating level of risk for CD.[13,15,42] These physiological parameters include respiratory rate, systolic blood pressure, pulse rate, oxygen saturation (SP02), body temperature, and a Glasgow Coma Score (GCS).[42]

The NEWS was compared to several other EWS and was found to be superior or to have similar performance at indicating risk for CD and was also the most common EWS used in the UK and other settings globally.[2,16,46,47,53] It was also found that EWS had pre-hospital limitations except the NEWS.[9 16,65] One study showed that the NEWS had a high predictability for 1-day mortality for patients in the pre-hospital setting that fell in the high-risk category. Although no clear pre-hospital definition for clinical deterioration exists, multiple studies describe the NEWS as an accurate and validated tool to attempt assessing for prediction and identification of adverse events and CD in this setting.[4,45,51,53,54,66–68]

A recent study done in the UK described that patients transported via ambulance from care homes to an emergency department (ED) had a 14 times higher chance of in-hospital death if they had a high NEWS score as compared to a low score.[40,69] The study also found that an increase in NEWS score via ambulance inter-hospital transfer can indicate CD.[40,69] The NEWS is therefore adequate to act as an adjunct in acute care decision-making due to its indication of the severity of illness.[40,42,45,65,69] A validation study for the use of NEWS in Spain was done and described that in the emergency department, NEWS had 95% accuracy for predictability of adverse events when calculated at the time of triage, as well as had clinical advantages over other EWS.[45]

The NEWS is a validated score that has the capability to stratify risk as compared to other scores and is regarded as the simplest and most ideal practical EWS to use in the pre-hospital setting due to the recording of only basic physiological parameters.[45,55,65,67] Calculation of a NEWS requires easily obtainable physiological parameters as compared to other EWS that require the assessment of the existence of blunt and penetrating trauma, age, mean arterial pressures, immobilization, and factors that are not always easily obtainable at the patient's bedside.[45] In 2023 the same authors published a study that again highlighted the importance of the implementation of this track-and-trigger system into standard practice as its predictability of 2-day mortality was high.[42] In 2020, a study was done in Thailand to determine the incidence of CD during inter-hospital transfers by use of the NEWS, and several other studies described that patients with a NEWS of more or equal to 5 are

of medium risk and more or equal to 7, are of high risk to deteriorate in the pre-hospital setting, accounting for high mortality within 24 hours.[11,17,21,40,45,66,68]

Studies done in Spain and Korea revealed that a pre-hospital NEWS was able to predict adverse events accurately in trauma patients, in patients suffering from traumatic brain injury, and had strong predictive capability for in-hospital mortality, indicating that the higher the pre-hospital NEWS score, the higher the chance of death in hospital.[61,70] A Japanese study found that the NEWS had high predictability for adverse outcomes, could be implemented into the pre-hospital setting reliably, and that the NEWS was clinically useful regardless of age, sex, or the presence of trauma.[66] The use of the NEWS score by paramedics can therefore assist in the appropriate escalation of care, but also early identification of a patient that is at high risk of deterioration.[21,40,42,45,51,65,66]

Some concerns were raised that the NEWS does not accommodate patients in whom a baseline NEWS would be higher than normal due to pre-existing conditions and that some useful diagnostic information, as well as clinical observations, are not accounted for.[40] Some of these claims have been refuted in a recent study showing that 91% of patients seen in the ED and 81% of patients seen by ambulance had a NEWS score of less than 5 which was not considered to be a significant predictor for CD.[40] Much of the criticism of NEWS in the literature is aimed at the response to NEWS and not the score itself, as well as its applicability in low-acuity patients.[53,54] A New Zealand study however, recently came to the conclusion that an EWS such as the NEWS has high predictability for CD within 2 days in low acuity patients, and is therefore a score that is applicable to use in these patients.[54] In 2017, the NEWS score was adapted and was replaced by the NEWS2, incorporating patients on oxygen as well as the presence of chronic obstructive pulmonary disorder (COPD) into the score. However, for pre-hospital use, the two scores were compared, and it was found that both scores had similar predictability for CD.[57] According to the literature reviewed, the NEWS remains the most validated EWS for its use in detecting and predicting CD in the in-hospital as well as pre-hospital setting.[46,67]

Risk factors for pre-hospital clinical deterioration.

Studies have shown that there are specific factors that could contribute to CD of patients during the care of paramedics.[31,32] Factors that have been examined in international literature can be classified into patient-related and system-related factors.[11,31,43,54] Patient related factors that have been associated with CD included sex, age, clinical conditions, and level of patient acuity. Older male patients who sustained illnesses with respiratory, circulatory and neurological involvement with high acuity were also found to be factors contributing to CD.[11,38] System related factors that have been associated with CD include a high pre-transfer risk score, ambulance type (whether ICU/helicopter), preparation time, time to hospital, and transfer distance.[11,36,38]

Evidence shows that patients with a high pre-transfer risk score, a lack of adequate protocols for monitoring, interventions for patient care during ambulance transfer, or a lack of adequate patient stabilization and pre-transfer care, increased the risk for clinical deterioration during inter-facility transfers.[11] A Dutch study found that patients cared for by medical doctors, paramedics and nurses who underwent critical care training, as well as patients being transported in an ambulance that was equipped with critical care technologies were less likely to deteriorate.[11,31] It has been described that increased patient preparation time, technical problems, longer transportation distances, as well as increased time to the hospital was associated with an increased incidence of CD.[11,31,36,38] An American study set out to determine the prevalence of CD in neonates during ambulance transportation, and found that the need for helicopter transfer as well as time to facility carried increased risk for CD.[38] In 2020, Srithong et al described multiple significant predictors of CD during inter-facility transfer of patients. These included transfer time where 31-45 min after departure serious CD occurred (OR 0.13, CI 0.015-0.25, p-value 0.02), and patient acuity describing that unstable patients were more likely to deteriorate with a 60% increased risk in comparison to stable patients (OR 1.68, CI 0.66-2.7, p-value 0.001). Mode of transport indicating 15% decreased chance of CD if a patient was transported by an ICU (Intensive care unit) ambulance (OR 0.84, CI (0.3-1.3, p-value 0.001).[35] In 2008, Boyle determined that 5.1% of all patients that were cared for showed signs of sudden

CD, and that specific factors were observed that could serve as risk factors.[32,35] Srithong found that contrary to other studies, gender nor age were risk factors for CD.[11] Boyle et al, however, found that age contributed to CD as they reported higher CD rates with greater age.[32]

Boyle et al found that of all patients who deteriorated, 7.6% had hospital-defined major trauma and 2% died.[32] Of all patients that had had a sudden drop in blood pressure (82%), 32% of them received analgesia such as morphine and methoxyflurane as well as sedation with midazolam.[35] Boyle found that the median time on scene time was 15 minutes, and the mean transport time was around 52 minutes, and communicated that increased occurrence of CD was associated with increased time spent on scene. [32] An American study showed the administration of sedation and analgesia to be a contributor to CD, especially with the use of opioids.[44] This could indicate that iatrogenic factors such as medication administration could serve as risk factors for CD, although it may also have been a physiological consequence of analgesia.[44] Another study found that out of 92 patients who suffered opioid respiratory depression, 77% had severe brain damage or died within 24 hours postoperatively, and were it for timeous recognition and intervention, 97% of these events could have been preventable.[8] Although investigated during surgery, these medications are also administered in the pre-hospital setting and may be relevant in this setting.

CD is closely related to adverse events and a study found that in 50% of cases where CD occurred, transport recommendations for the patient by ICU or treating physician were ignored.[31] This indicated that CD is associated with non-compliance of continuation of intensive care unit (ICU) care during transportation. [31] The monitoring of oxygen saturation via pulse oximeter (SP02) and end-tidal carbon dioxide (ETC02) levels have shown to decrease the incidence of CD, and the same studies revealed that patients who were transported by a specialist retrieval team with these capabilities, resulted in more stable transports and decreased mortality in comparison to transports via standard ambulances.[8,44] Other factors found to have contributed to clinical deterioration were the lack of recognition for an intervention, omitting intubation when indicated, ambulance delay, lack of monitoring of crucial vital signs such as blood pressure, shortage of oxygen availability, new-onset hypotension, frequent sedation, mechanical ventilation, lack of physician accompanying the patient, and

human behavior.[31,41,44,46,71] Human factors found to contribute to a delayed or lack of recognition of CD include lack of knowledge, fear of reprimand, inadequate monitoring and observation, heavy workloads, and limited access to supportive or knowledgeable leaders.[41]

Summary and conclusion

In conclusion, pre-hospital CD remains a critical concern within healthcare settings, as it signifies a patient's transition to a more severe clinical state, often resulting in increased morbidity and mortality. Over the years, various frameworks have been proposed to define CD, each with its strengths and limitations. Despite the advancements, consensus remains elusive, reflecting the complexity and multifactorial nature of CD. Regardless, emphasis on physiological parameters, such as those incorporated in Early Warning Scores (EWS), underscores their pivotal role in defining, predicting, and identifying CD. The literature underscores multiple facets of risk factors contributing to pre-hospital CD among patients attended to by paramedics. Patient-related factors, such as age, sex, clinical conditions, and acuity level, have been consistently highlighted as critical determinants, with older male patients exhibiting respiratory, circulatory, or neurological complications at elevated risk. Concurrently, system-related elements, including ambulance type, preparation time, transfer distance, and the presence of critical care technologies, play pivotal roles in patient outcomes.

Studies have suggested that service-related inefficiencies, such as prolonged patient preparation time, technical issues, and extended transportation durations, amplify the likelihood of CD. Notably, the administration of sedation and analgesia, especially opioids, emerges as a potential iatrogenic risk factor, emphasizing the imperative for meticulous monitoring protocols. Alarmingly, lapses in adherence to transport recommendations, oversight in critical interventions like intubation, and inadequate vital sign monitoring further compound the risk. In essence, a comprehensive understanding of the statistical significance of both patient-specific and systemic risk factors could lead us to improve patient care and decrease mortality.

Yet, literature from the prehospital South African context and other LMICs was limited. Similarly, there was also limited literature related to the prediction of CD in the prehospital transport environment. This master study therefore sought to address this

gap in the literature by describing CD in the South African prehospital context, determine which factors may predict CD, and to propose a pre-hospital clinical deterioration prediction tool as proof of concept.

CHAPTER 3: Thesis aim and methodology.

Problem statement

Clinical deterioration (CD) presents a significant global challenge, marked by increased mortality rates, prolonged hospital stays, and heightened adverse events. While CD occurrences have been documented in various settings, including pre-hospital environments, comprehensive studies detailing its prevalence and associated factors within the South African context remain surprisingly absent. Despite the recognized preventability of CD and the existence of various tools assisting early detection, a critical gap exists in the absence of a validated pre-hospital CD prediction tool tailored for the South African patient population. Addressing this gap is imperative, given the potential to improve patient outcomes and optimize resource allocation in the pre-hospital setting. Thus, this study endeavours to describe the occurrence of CD during ambulance transportation among South African adult patients, employing a robust data-archive analysis. Through regression analyses and Chi-square Automatic Interaction Detector (CHAID) classification, the study seeks to identify pertinent risk factors associated with CD, ultimately paving the way for the development of a pre-hospital CD prediction tool.

Aim of the thesis

The study aimed to describe whether adult patients clinically deteriorate during transportation by private ground and air ambulance, as well as describe which factors may predict clinical deterioration. In addition, it aimed to propose a pre-hospital clinical deterioration prediction tool.

To this end, the objectives were:

1. Retrospective data analysis of patient physiological parameters captured during ambulance transportation of adult patients.

2. To determine what factors, carry statistical significance in predicting clinical deterioration of adult patients during transportation by ambulance.

3. Develop a proposed pre-hospital clinical deterioration prediction tool.

Study context and setting.

The South African EMS system consists of government and private organizations. Government organizations service the public sector and private organizations service patients with medical insurance and these services must be paid for. The EMS system of South Africa provides primary emergency medical response and inter-hospital transport services that range from simple chronic patient transport services to critical care transport. There are 7 different pre-hospital practitioner qualifications ranging from lowest to highest that function within the system and include a Basic Ambulance Assistant (BAA), Ambulance Emergency Assistant (AEA), Emergency Care Assistant (ECA), Emergency Care Technician (ECT), Paramedic (ANT), and Emergency Care Practitioner (ECP). Often in critical care services, you will find Medical Doctors (MP) who do not routinely work full-time in these pre-hospital settings.

A specific private emergency medical service organization from South Africa was approached for the use of their data because they store all the necessary data to complete the study on an electronic data archive and are a nationally based organization servicing a national footprint. The organization has bases in eight of the nine provinces of South Africa and operates 24 hours a day.

There are various divisions within the organization that are staffed by various qualifications of pre-hospital providers. The ground ambulance division is staffed with Paramedic, AEA, and BAA-qualified staff. ECP staff normally function on a rapid response vehicle but may regularly function on an ambulance should there be staff shortages. The helicopter emergency medical services are staffed by ECP or MP and paramedic-qualified practitioners. Fixed Wing ambulances are staffed by ECP or MP and paramedic staff, while ground ICU ambulances are staffed with ECP or paramedic and AEA staff. The average caseload across the entire operation is approximately 12,000 cases per month, with most patients falling in the adult population, and the greatest portion of cases occurring in the Gauteng province.

Research design.

The project encompassed one study with two different phases, with the end goal being the proposal of a pre-hospital clinical deterioration prediction tool for adult ground and air ambulance transportation.

The first part of the study was a retrospective data archive review of patients treated and transported by ground and air ambulance in a private emergency medical service. Data were extracted and described to identify associations between patient physiological parameters, transport factors, and clinical deterioration. Part one also aimed to describe the occurrence of clinical deterioration under the care of paramedics, allowing for the researcher to determine factors that could be associated with cases where CD was highlighted. EWS (Early Warning Score) made use of recorded physiological parameter trends to indicate risk for CD and in progression determines the presence of CD. During review, a NEWS and MEES was calculated on each set of physiological parameters recorded by pre-hospital practitioners. In cases where there was an escalation of 1 point or more of a NEWS or 2 points on the MEES, CD was indicated as CD: Yes, and in cases where there was no escalation or de-escalation of one point or more on the NEWS and no escalation or de-escalation of 2 points or more on the MEES, CD was indicated as CD: No.

In part two of the study, the extracted data from part one of the study, was used to perform a binomial regression to determine variables that carry statistical significance for CD. Additionally, Chi-square Automatic Interaction Detector analysis was undertaken to develop decision trees to classify cases into CD: Yes, and CD: No. The best-performing models and analysis approaches were then selected to propose and CD prediction tool.

Population and sampling

Cases from June 2022 to June 2023 were used to extract the data, to total data for 13 months.

Inclusion criteria

This study included all medical and trauma patients, 18 years or older that were transported by the private emergency medical service. Data collection was done retrospectively for 13 months, and all patient report forms that met the inclusion criteria were included.

Exclusion criteria

Normal physiological parameters within the context of the EWSs used differ for neonates and pediatrics when compared to adults. and during pregnancy, normal parameters for baseline vital signs are also different than the non-pregnant adult patient. and There is also a derangement in physiological parameters during acute psychiatric conditions and therefore data was only included from patients that were 18 years of age and older in the absence of pregnancy and acute psychosis. This prediction tool was only created for the adult population and furthermore, NEWS and MEES were not validated in psychiatric or obstetric populations.[72,73]

Any duplicate cases and any cases with missing critical data points were excluded from the selection. These critical data points included any data variables as identified below, or physiological parameters required to complete a NEWS and MEES. All patients aged 17 and below were also excluded from the study. Any cases where there was an inaccurate recording of blood pressure were also excluded as this was a vital parameter for both the NEWS and MEES score.

Data variables

Defining and noting clinical deterioration (CD) was done so in accordance with the reference used as a working definition for CD. CD is noted as an increase in the National Early Warning Score (NEWS) of 1 point or more as calculated by a set of physiological parameter trends captured by a provider during care in the pre-hospital setting. Both EWSs have been used in similar research studies and especially NEWS has been validated for use in the pre-hospital setting. One physiological parameter of the NEWS score is the inclusion of a body temperature reading and this data could not be provided by the organization. To increase validity, a second Early Warning Score (EWS) was used to calculate CD and compared to the NEWS score to increase the validity of findings. Using the Mainz Emergency Evaluation Score (MEES), an

increase of 2 points or more flagged the case for CD. The MEES early warning score does not require body temperature as a measurement to calculate a score. Before using the final methods for results, 20 cases were manually analyzed to test the accuracy of the data archive results.[27,60]

Any demographical, logistical, or clinical variable obtainable by a patient report form was included in the data-archive analysis to provide the opportunity for as much insight and variation in the analysis of contributing factors as possible. Specific data variables were also selected based on findings in the literature review regarding factors carrying significance in CD. The following variables served as independent variables during data archive analysis. Patient demographic and logistic variables include sex, age, call type, call category, mode of transport, senior crew qualification, time spent on scene in min, transportation time to facility in min, and distance to facility in km.

Call type was subdivided into primary and inter-hospital transport which refers to whether the case was to a scene such as a home residence or accident scene, or inter-hospital transfer from one hospital to another. Mode of transport was subdivided into whether a patient was transported via ground ambulance, intensive care unit (ICU) ambulance, helicopter ambulance, or specialized unit which was either a combination of a paramedic or emergency care practitioner in an ICU ambulance or helicopter.

Senior crew qualification included several senior crew qualifications ranging from lowest to highest including Basic Ambulance Assistant (BAA), Emergency Ambulance Assistant (AEA), Emergency Care Assistant (ECA), Emergency Care Technician (ECT), Paramedic (ANT), Emergency Care Practitioner (ECP), and Medical Practitioner (MP).

For scene time, transportation time, and distance to the facility, the median time and distance results were presented.

Clinical variables included low or medium to high initial clinical risk, whether a patient received medical oxygen, mechanical ventilation, analgesia, or sedation, or was diagnosed with chest trauma. Low clinical risk was defined as an initial NEWS score of 5 or below and medium to high risk of 5 or above.

Data management

Data capturing was done by the treating practitioner of every case and stored in the organization's patient report form data archive. Anonymous data were extracted from this data archive and populated into a Microsoft Excel (Microsoft Corporation, Washington, US) spreadsheet designed by the researcher.

All cases and data were anonymised and saved onto a password protected computer and backed up onto a secured external hard drive as well as password protected cloud folder. All cases and data will be kept for five years, after which all electronic data will be deleted. By use of a Python code, a research assistant provided data cleaning. The Python code processes all medical response data and performs various analyses, according to the following breakdown of functionalities:

1. Data Processing Loop: The script reads data from an Excel file using the panda's library. For each row (record) in the Data Frame, it creates a case object, extracts relevant information, and performs various analyses and categorizations based on the data.

2. Case Validation: Before proceeding with the analysis, the code implements a comprehensive mechanism for case validation. It starts by defining a set of specific medical diagnoses, and checking their presence in each case. Additionally, certain criteria, such as a minimum age requirement (above 18) and the absence of pregnancy-related conditions, are enforced. Invalid cases are systematically removed from the primary data frame and cataloged in a dedicated 'Not Used Cases' sheet.

3. Excel Workbook Setup: The script initializes an Excel workbook ('Output.xlsx') using the open-pixel library and creates several sheets within the workbook, including 'Not Used Cases,' 'Analysis' sheets, 'Diagnosis Map,' and 'SPSS Keys.'

4. Statistical Analysis: The script aggregates statistics related to different aspects of the emergency cases, such as total cases, valid and invalid cases, clinical

deterioration occurrences, and improvements. These statistics are stored in the stats dictionary.

5. SPSS Data Preparation: The script prepares data for SPSS by mapping values from the case data to SPSS categories and appending the data to the 'SPSS Data' sheet in the Excel workbook. This was for the purpose of the inferential statistics, regression analyses and classification trees.

6. Analysis Sheets Creation: The script creates several analysis sheets with different breakdowns, such as analysis by call type, modes of transport, senior crew qualifications, gender, call category, clinical risk, age groups, time to facility, time on scene, distance to facility, and diagnosis categories.

7. Variability Data: The script calculates, and stores variability data related to time on scene, time to facility, distance to facility, and patient age.

8. Output and Analysis: Finally, the script populates the analysis sheets with the computed statistics and saves the Excel workbook.

In summary, this code processes emergency response data, performs statistical analyses, and organizes the results in an Excel workbook for data archive examination and reporting. During data cleaning, diagnoses were grouped to a total of 35 diagnoses to be used as a variable during the data.

Data archive analyses.

All variables were subjected to descriptive analysis. Continuous variables were summarized using measures of central tendency and dispersion, while categorical variables were presented as median frequencies and percentages. Data were cross-tabulated according to clinical deterioration and are presented in tables.

Clinical Deterioration Prediction tool.

To develop the clinical deterioration prediction, four models were considered using a series of different analytic approaches. The analytic approaches were classification trees and logistic regression. These approaches are reported in detail below. For all models, clinical deterioration (by change in NEWS or MEES) was the dependent variable. Where multiple diagnoses were reported, only the first diagnosis was selected owing to high rates of missingness.

The four models and their independent variables were:

1. Model 1 – Demographics and Logistics
    a. Call type, mode of transport, senior crew, specialized unit, time to facility, distance to facility, scene time, age, and call category.
2. Model 2 – Clinical Characteristics without diagnosis
    a. Call Category, on oxygen, mechanical ventilation, on inotropes or vasopressors, administration of analgesia or sedation, clinical risk category.
3. Model 3 – Clinical Characteristics with Diagnosis
    a. Call Category, on oxygen, mechanical ventilation, on inotropes or vasopressors, administration of analgesia or sedation, clinical risk category, diagnosis.
4. Model 4 – All variables.

In all instances, only the best performing models are reported in the results which includes Model 2 and Model 3 Following these analyses, a composite weighting score was developed which allows for allocation of relative importance and to provide a usable score as final output. This will be reported in more detail in the results where the prediction tool is presented. All analyses were done with IBM SPSS (version 28; IBM; Armonk, New York, United States).

Classification trees

Ch-square automatic interaction detection (CHAID) was used to classify cases into instances where clinical deterioration occurred and where it did not. Clinical deterioration “Yes” was set as the dependent variable of interest target. Growth limits were set at a maximum tree depth of 3 while the minimum number of cases for a parent and child node were set at n=100 and n=50, respectively. A p-value of 0.05 was considered significant to split or merge nodes. The Bonferroni adjustment was applied to correct for multiple comparisons. Pareto (80/20) random split sample validation was undertaken to test the classification tree’s performance and loss of accuracy in unseen data.

As the logistics model (Model 1) included continuous variables, this model was also analyzed using Classification and Regression Trees (CRT) as a growing method for the classification trees. No pruning was applied. Growth limits were set at a maximum tree depth of 5 while the minimum number of cases for a parent and child node were set at n=100 and n=50, respectively. Gini was used as the impurity measure. Again, Pareto random split sample validation was undertaken.

Binomial logistic regression

Binomial logistic regression was also undertaken. In models 1-4, categorical variables were selected for logistic regression based on initial statistical significance ($p<0.05$) in Chi-square testing - all expected cell frequencies were greater than five. For continuous variables, the independent samples Mann-Whitney test was used given an assumption of non-normality. Again, a p-value of < 0.05 was considered significant. The linearity of the continuous variables with respect to the logit of the dependent variable was assessed via the Box-Tidwell procedure. Multicollinearity was also assessed, and no variables had a variance inflation factor of > 10. Appendix A below shows the variables that were selected for each model. Model explanatory power was assessed using Nagelkerke R-square and Hosmer and Lemeshow test was used to determine goodness-of-fit. Significant variables are presented using odds ratios and 95% confidence intervals, along with the p-value.

From the binomial logistic regression, the following formula can be used to develop a clinical deterioration prediction tool:

$$W_i = \log(OR_i)$$

Where:

- W_i: Weight of the ith variable
- |Log|: Natural logarithm's absolute value
- OR_i : Odds ratio of the ith variable

Pre-hospital clinical deterioration prediction tool development

The results from the binomial regression analysis were used to create a questionnaire and composite score from the final p-values, where each variable was distinctively added to the probability of clinical deterioration (CD), and a CD probability percentage could be calculated.

Significant variables were taken from the binomial regression mode that included logistical and clinical variables to develop a proposed CD prediction tool. This model was chosen as the performance was similar to the CHAID trees model and a tool developed from these significant variables will be practically implementable due to its predictive capabilities.

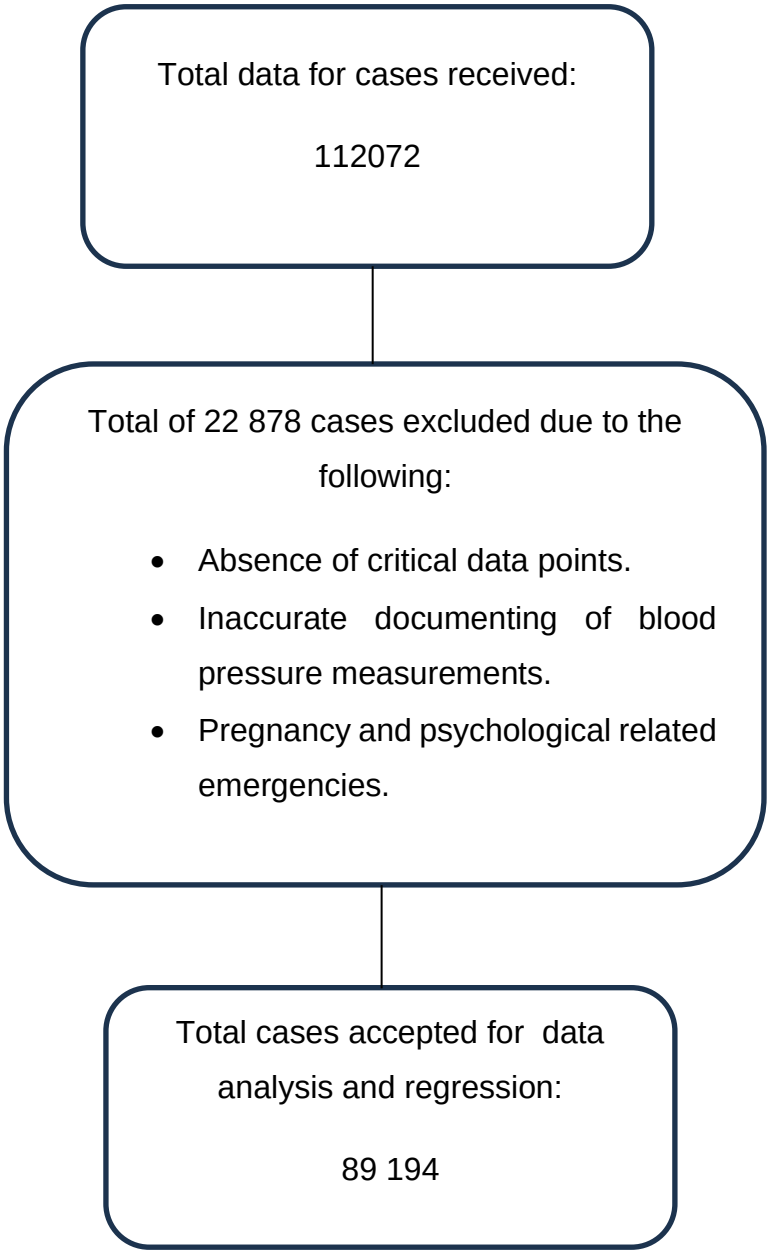
Ethical considerations

Ethical approval was granted from the Human Research Ethics Committee at the University of Cape Town, reference number HREC 294/2023. The study was approved with a waiver of informed consent. A letter of permission was obtained from the organization, allowing access to the requested information.

The data and trends obtained were collected through the approval of the governing clinical entity retrospectively, kept anonymous, and used without the knowledge of the practitioners and patients involved. The organization's name from which data was used was always kept anonymous during the study and will be during the possible publication of findings in a journal. The project posed no harm to patients as no human experiments were conducted. The project posed no risk of presenting harm to any patient, practitioner, or organization that was involved.

CHAPTER 4: RESULTS

A total of 112 072 cases were provided by the organization. Following the exclusion of 22 878 cases for a variety of reasons (See fig. 1 below) a total of 89 193 were eligible for inclusion and data analysis.



Ambulance transportation clinical deterioration rates

This section will present the results for the first phase of the study which was the retrospective data archive analysis, starting with an overview and general results, followed by categorical and specific results.

Patients transported had ages ranging between 18 and 110 years old, 49,4% of cases accounting for male patients (n=45 108), 49.3% accounting for female patients (n=44034). The majority of cases were primary transports 78% (n=69 656), and the balance of cases were interhospital transports accounting for 21.9% (n=19537). Data distinguishing between medical or trauma-related patients were only provided by the organization of 61% (n=55159) of total valid cases. Of the 55159 cases, medical patients accounted for most cases at 68% (n=37806) and the balance of the cases were trauma patients at 31% (n=171353). The rest of the cases used were categorised as unknown call categories accounting for 21% (n=19537) of all cases. Provisional diagnoses data provided by the organization came to 512 different diagnoses and was categorised into 34 different diagnoses by the researcher as presented in Appendix B of this study.

Table 2 describes an overview of data collected and extracted from the data archive review as well as the prevalence of clinical deterioration (CD) according to demographic and logistical factors. For a total of 89193 cases (n=89193), CD was detected in 15.73% (n=17 633) cases according to the National Early Warning Score (NEWS) and 15.05% (n=16871) according to the Mainz Emergency Evaluation Score (MEES). 13.1% (n=14765) of patients showed clinical improvement during transport. Although the CD rates for both EWSs were similar, they only detected CD in around half of the same cases.

Only adult patients from the age of 18 to 110 years were included in the study. The median age of patients transported was 51 years and the median age where CD occurred was 54 years according to the NEWS and 49 years according to the MEES. The median age for patients transported with medium to high risk for CD was 60 years. Age as a variable had a P-value of 0.000 carrying statistical significance.

Patients transported were categorized as call type medical, trauma, or unknown, and carried statistical significance with a P value of 0.003. Medical cases accounted for

42% (n=37806), where 19.4% (n=7339) deteriorated according to NEWS, and 18.2% (n=6894) according to MEES. Patients that deteriorated with an initial NEWS of 5 or > accounted for 26.1% (n=1917). Trauma cases accounted for 19.3% (n=17353) of all patients transported 19.3% (n=3355) of patients deteriorated according to the NEWS, and 20.6% (n=3579) according to the MEES. Patients that deteriorated with an initial NEWS of 5 or > accounted for 13.7% (n=461) of cases. Medical cases accounted for the majority of cases, and the proportion of CD rates was similar for both categories, although medical cases had an increased proportion of initial risk for CD.

Call type was categorized into inter-hospital and primary cases carrying statistical significance with a P-value of 0.004. Inter-hospital transfers accounted for 21.9% of all cases (n=19537), where 20.4% deteriorated according to the NEWS (n=4004), and 18.7% according to the MEES (n=3362). Patients that deteriorated with an initial NEWS 0f 5 or > accounted for 19% of cases (n=762). Primary transports accounted for 78% of all cases (n=69656), where 19.5% deteriorated according to the NEWS (n=13629) and 18.9% according to the MEES (n=13209). Patients deteriorated who had an initial NEWS 5 or > accounted for 22.2% of cases (n=3036). These results indicate that primary calls accounted for the majority of cases and that the proportion of CD rates are very similar for both categories, although the initial risk for CD in primary cases is proportionately higher.

. Mode of transport was found to carry statistical significance with a p-value of <0.001 and was categorized into ground ambulance, helicopter, Intensive Care Unit (ICU) Bus, and specialized units. Ground ambulance transports accounted for most cases at 97.9% (n=87359), Intensive Care Unit (ICU) ambulance for 0.8% (n=781), helicopter for 1.1% (n=1053), and specialized unit transports for 2% (n=1815). CD rates were observed to be proportionally highest with helicopter transports where 44.5% (n=469) deteriorated according to the NEWS and ambulance transports lowest with 19.3% (n=16889). Patients that deteriorated with an initial NEWS of 5 or > that were transported by ambulance accounted for 19.9% (n=3360) of cases, 55.4% (n=259) by helicopter, and 60% by both ICU ambulance and specialized units (n=164, n=442). CD rates according to the MEES were similar to NEWS as displayed below. These results indicate that there is a proportionate increase in CD rates in patients transported by helicopters, ICU ambulances, and specialised units in comparison to

patients transported by ground ambulance. Yet, these units tend to mostly transport patients with proportionately higher risk for CD in comparison to ground ambulances.

Senior crew qualification was found to carry statistical significance with a p-value of <0.001. Senior crew qualification AEA (Ambulance Emergency Assistant) accounted for most of the cases at 50% (n=45462), Paramedic (ANT) at 19.7% (n=176460), Emergency Care Practitioner (ECP) at 9.6% (n=8649), Emergency Care Technician (ECT) at 7.2% (n=6491), Basic Ambulance Assistant (BAA) at 6.7% (n=6000), Emergency care Assistant (ECA) at 3.1% (n=2810), and Ambulance Emergency Assistant (ANA) at 2% (n=1853). CD rates were observed to be proportionally highest with ECP where 28.2% (n=2447) of patients deteriorated according to the NEWS and lowest with BAA where 14.8% (n=890) deteriorated. Patients that deteriorated with an initial NEWS of 5 or < where the senior crew qualification was a BAA accounted for 6% (n=600) and where an ECP accounted for 37.3% (n=3226). CD rates according to the MEES was similar to the NEWS as displayed below. The results indicate that CD rates are proportionately higher as the level of the senior crew qualification increases, yet these qualifications tend to treat patients that have a proportionately higher risk for CD.

Transportation time, distance to the facility, as well as time spent on scene, showed statistical significance with p-values of <0.001. Transportation times to the facility ranged from 1min to >120min, the median time to the facility was 18min and the median time where CD occurred was 19min according to the NEWS. On-scene times ranged from 1min to >120min the median time on scene was 22min, and the median time where CD occurred was 23min according to the NEWS. The median time on scene for patients that had a medium to high risk for CD was 29 minutes. Distances of patient transport to the hospital ranged between 1km to >200km the median distance traveled to a facility was 10km and the median distance where CD occurred was 11km according to the NEWS. The results of median times and distances where CD occurred according to the MEES were similar to the NEWS as displayed in Table 1. It

was found that CD rates were proportionally higher as time on scene, distances to the facility, and transport time to the facility increased.

Table 2-Clinical Deterioration rates according to demographic and logistic variables.

VARIABLE	CD NEWS N	%	CD MEES N	%	NEWS >5	P VALUE	Total
Valid Cases	17633	15.7%	16871	15%	22.3 %		89194
Median Age		54		49	60	<0.001	51
Call Category						0.004	
IHT	4004	20.4%	3662	18.7%	19%		19537
Primary	13629	19.5%	13209	18.9%	22.2%		69656
Call Type						0.003	
Medical	7339	19.4%	6894	18.2%	26.1%		37806
Trauma	3355	19.3%	3579	20.6%	13.7%		17353
Unknown	4004	20.4%	3662	18.7%	19%		19537
Mode of transport						<0.001	
Heli	469	44.5%	382	36.2%	55.4%		1053
Ambo	16889	19.3%	16259	18.6%	19.9%		87359
ICU ambulance	275	35.2%	230	29.4%	60%		781
Specialized Unit	737	40.6%	608	33.4%	60%	<0.001	1815
Senior crew qualification						<0.001	
AEA		341	18.4 %	377	20.3 %		1853
ANA	7917	17.4 %	8064	17.7%	16%		45462
ANT	4281	19.7%	3772	21.3%	26.5%		17646
BAA	890	14.8%	964	16%	6%		6000
ECA	515	18.3%	444	15.8%	7.2%		2810
ECP	2447	28.2%	2035	23.5%	37.3%		8649
ECT	1177	18.1%	1164	17.9%	22.6%		6491
MP	3	50%	1	16.6%	50%		6
Median T(Scn)		25		23	29	<0.001	
Median T(Fac)		20		20	19	<0.001	
Median D (Fac)		11		10	10	<0.001	

1. **CD NEWS N %** - Clinical deterioration according to National Early Warning Score number and %.
2. **CD MEES N %** - Clinical deterioration according to Mainz Emergency Evaluation Score number and %.
3. **NEWS >5** -National Early Warning Score above 5.
4. **IHT**-Inter-hospital transfer.
5. **ICU**-Intensive Care Unit.
6. **P-Value**- Probability Value.
7. **AEA**- Ambulance Emergency Assistant.
8. **ANA**- Ambulance Emergency Assistant.
9. **ANT**-Paramedic.
10. **BAA**-Basic Ambulance Assistant.
11. **ECA**-Emergency Care Assistant.
12. **ECP**-Emergency Care Practitioner.
13. **ECT**-Emergency Care Technician.
14. **MP**-Medical Practitioner.
15. **Median T (Scn)**- Median time spent on scene.
16. **Median T (Fac)**-Median transportation time to facility.
17. **Median D (Fac**)-Median distance travelled to facility.

Table 3 provides an overview of the occurrence of clinical deterioration (CD) according to clinical factors that carried statistical significance. Clinical risk was categorized as patients with low, medium, or high risk for CD based on an initial calculated NEWS. These categories all carried statistical significance with p-value <0.001. Patients transported with an initial low risk for deterioration accounted for 80.9% of cases and 19.1% deteriorated according to NEWS (n=13835). Patients transported with an initial high risk for CD accounted for 9.5% of cases (n=8547). These results indicate that most patients transported by ambulance carry an initial low risk for CD and only a slight proportionate increase of CD rates are observed in patients that have proportionally higher risk for CD prior to transport.

Therapeutic intervention variables included in the analysis that carried statistical significance consisted of medical oxygen administration (p-value 0.000), inotropes and vasopressors (p-value <0.001), mechanical ventilation (p-value <0.001), and analgesia or sedation (p-value <0.001). Patients who received medical oxygen accounted for 21% of all cases (n=18772), 33.2% deteriorated according to the NEWS (n=6249), and 52% had medium to high risk for CD (n=3250). Patients transported that required mechanical ventilation accounted for 1.1% of all cases (n=1030), 37.4% deteriorated according to the NEWS (n=386), and 90.9% had medium to high risk for CD (n=319). Patients that required analgesia or sedation accounted for 13.5% of all

cases (n=12106), 28.3% deteriorated according to NEWS (n=3437), and 26.3% had medium to high risk for CD (n=907). CD rates according to MEES were proportionally less as displayed in table 2. The above results indicate that of these interventions patients who received mechanical ventilation had the highest proportion of CD rates, patients on medical oxygen second highest, and those who received analgesia or sedation third. However, interventions that had proportionally higher CD rates also carried a proportionally higher risk for CD.

Diagnoses carried statistical significance with a P value of <0.001. Patients diagnosed with musculoskeletal injury accounted for most cases transported (n=42964, 48.1%), 24.4% deteriorated according to the NEWS (n=10501), and 20.3% and medium to high risk for CD. Table 3 below indicates CD rates of the five most prevalent diagnoses transported.

Table 3-CD occurrence according to Clinical Variables

VARIABLE	CD NEWS N %		CD MEES N %		NEWS >5	P VALUE	Total
Clinical Risk						<0.001	
Low Clinical Risk	13835	19.1%	14078	19.5%	N/A		72173
Medium Clinical Risk	1840	21.7%	1416	16.7%	N/A		8473
High Clinical Risk	1958	22.9%	1377	16.1%	N/A		8547
NEWS 5 or above	3798	22.3 %	N/A	N/A	N/A	N/A	17020
Patient on O2	6249	33.2%	3529	18.7%	52%	<0.001	18772
Mechanical Ventilation	386	37.4%	310	30%	90.9%	<0.001	1030
Analgesia or sedation	3437	28.3%	2908	24%	26.3%	<0.001	12105
Diagnoses						<0.001	
Musculoskeletal Trauma (fractures)	10501	24.4%	9354	21.7%	20.3%		42964
SuperficialInjuries(Abrasions, lacerations)	6625	19.1%	6972	20.1%	20.1%		34658
Abdominal Emergencies	5318	17.8%	5442	18.2%	13.6%		29870
Respiratory Emergencies	5900	24.8%	4043	17.7%	51.7%		23773
Neurological Emergencies	4662	19.9%	4500	19.2%	28%		23408

1. **CD NEWS N %** - Clinical deterioration according to National Early Warning Score number and %.
2. **CD MEES N %** - Clinical deterioration according to Mainz Emergency Evaluation Score number and %.
3. **NEWS >5** -National Early Warning Score above 5.
4. **P-Value-** Probability value

CHAID analysis results

Figure 1 and 2 includes the train and test results of a Chi-squared Automatic Interaction Detection (CHAID) decision tree analysis with a dependent variable clinical deterioration (NEWS): Yes/No and multiple statistically significant logistic independent variables. Both the training and test samples revealed an overall correct prediction percentage of 80.3%. The decision tree reveals that the most significant variable to split the tree is senior crew qualification (Node 0, p-value 0.000), classifying it into 4 nodes (Node 1:<=BAA, Node 2: BAA and ECT, Node 3:ECT and ANT, Node 4: >ANT). Nodes 1-4 indicate a progressive increase in the level of qualification where ECP which is the highest qualification falls under the category >ANT. Node 0 (p-value 0.000) included 14406 patients and 19.8% deteriorated (n=3546). Nodes 1 to 4 revealed deterioration rates between 14.3-27.6% with node 1 being the lowest at 14.3% (n=175) and node 4 the highest at 27.6% (n=1299). The results indicate that senior crew qualification is the most significant variable to influence CD and higher rates of CD are observed with higher senior crew qualifications. Node 1 (<=BAA, p-value 0.011) included 1220 patients and 14.3% (n=175) deteriorated. The tree then splits into 3 classifications, nodes 5,6, and 7 which includes age <=27 years (node 1), 27-81 years (node 2), and >81 years (node 3). The results indicate that under the care of a BAA, the most significant variable for CD is age, and 17.5% of patients <=27 years deteriorated, 14.6% between the ages of 21-81 years, and 10.2% <81 years. After these classifications, the tree further splits into on-scene time as well as call category.

Node 2 (BAA-ECT p-value 0.000) included 11299 patients and 17.7% deteriorated (n=1999). The tree then spits into 4 classifications namely node 8, 9, 10, and 11 which includes a on-scene time <=13min (node 8), 13-19min (node 9), 19-25min (node 10), and >25min (node 11). Patients where time spent on scene was <=13 min accounted for the lowest CD rate at 15.7% (n=392) while >25min highest at 19.1% (n=779). These results indicate that when the senior treating practitioner was of a BAA, ANA or ECT qualification, the next most significant variable for CD is time spent on scene, and it is observed that as time on scene increases, so does the occurrence of CD.

Node 3 (ECT-ANT, p-value 0.000) included 3649 patients and 24.1% deteriorated (n=878). The tree then spits into 5 classifications namely node 12, 13, 14, 15, and 16 which includes on-scene time <=16min (node 12), 16-29min (node 13), 29-35min (node 14), 35-45min (node 15) and >45min (node 16). Patients where time spent on scene was <=16min accounted for the lowest CD rates at 22% (n=172) while highest >45min at 28.3% (n=125). The results indicate that when a senior treating provider was of a in of a ECT, ANT, or ECP qualification, the next most significant variable for CD was again time on the scene, and it was again observed that as time on scene increased, so did CD rates. It was also observed that in general longer time was spent on scene where the senior crew qualifications were ECT or ANT, indicating longer on scene times with higher qualifications.

Node 4 (>ANT p-value 0.000) included 1299 patients and 27.6% deteriorated (n=494). The tree then splits into 2 classifications namely nodes 17 and 18 which includes mode of transport per ground ambulance or Intensive Care Unit (ICU) ambulance (node 17) and helicopter (node 18). Patients that were transported by ground or ICU ambulance accounted for the lowest CD rates at 25.5% (n=403) and helicopter the highest at 42.3% (n=91). These results indicate that should the senior crew qualification be higher than ANT which includes ECP and MP, the most significant variable for CD is mode of transport, and the highest CD rates were observed on the helicopter.

Figure 1-CHAID – logistics - Train

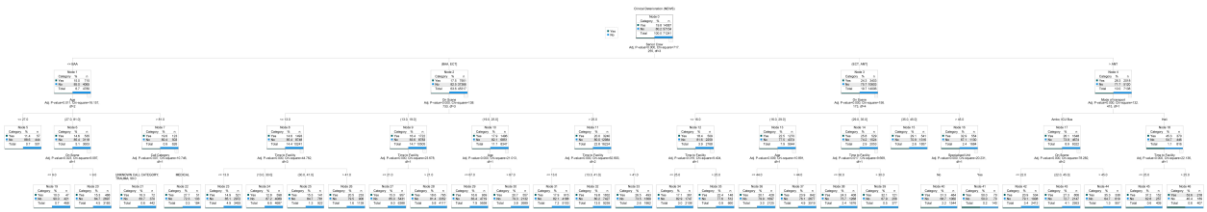
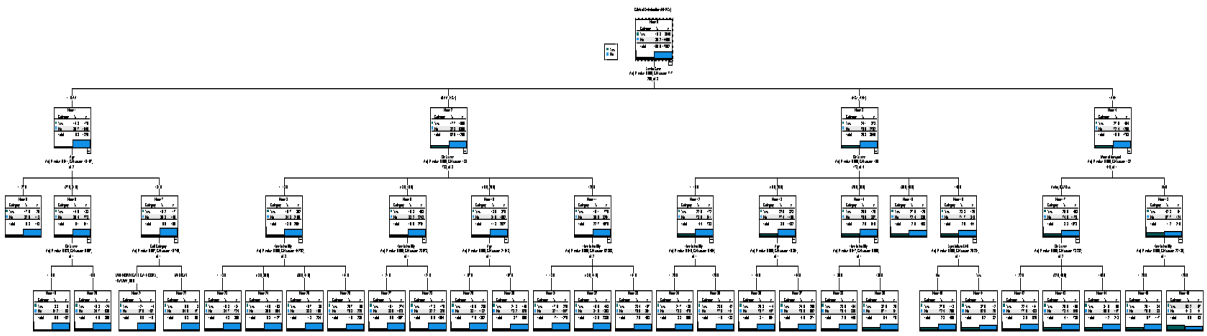


Figure 2-CHAID – logistics - Test



Figures 3 and 4 include the train and test results of a Chi-squared Automatic Interaction Detection (CHAID) decision tree analysis with dependent variable clinical deterioration (NEWS): Yes/No and multiple statistically significant clinical independent variables. Both the training and test samples revealed an overall correct prediction percentage of 80.6%. The decision tree reveals that the most significant variable to split the tree is whether the patient received medical oxygen (Node 0, p-value 0.000). From a total of 14277 patients, 19,8% (n=3522) deteriorated, 79.2% (n=14090) did not receive medical oxygen (node 1), and 16.5% (n=2319) deteriorated. The decision tree then reveals when patients did not receive medical oxygen, the most significant variable for CD is whether the patient received analgesia or sedation (p-value 0.000), or not. The tree then spits into 2 nodes, namely node 3 (Yes: analgesia or sedation) and node 4 (No: analgesia or sedation). A total of 1690 patients received analgesia or sedation, 20.6% (n=348) deteriorated and 12400 did not receive analgesia or sedation and 15.9% (n=1971) deteriorated. For these patients the tree then splits again, indicating the next significant variable for CD as clinical risk.

Patients that did receive medical oxygen accounted for a total of 3709 patients and 32.4% (n=1203) deteriorated. The decision tree reveals that for patients who did receive medical oxygen, the next most significant variable for CD is clinical risk, splitting into 3 nodes namely node 5 (<=low clinical risk), node 6 (low-medium clinical

risk) and node 7 (>medium clinical risk). Patients that had <= low clinical risk accounted for 1383 and 41.7% (n=577) deteriorated, low to medium clinical risk for 936 where 30.9% (n=289) deteriorated, and >medium clinical risk for 1390 where 24.2% (n=337) deteriorated. The tree then further splits into multiple nodes indicating the administration of analgesia or sedation being the next most significant variable for CD. The above results indicate that the most significant variable for CD is whether patients received medical oxygen, and if they did not, the administration of analgesia or sedation. For those patients who did receive medical oxygen, the level of clinical risk is the next most significant variable.

Figure 3-CHAID – Clinical – Train

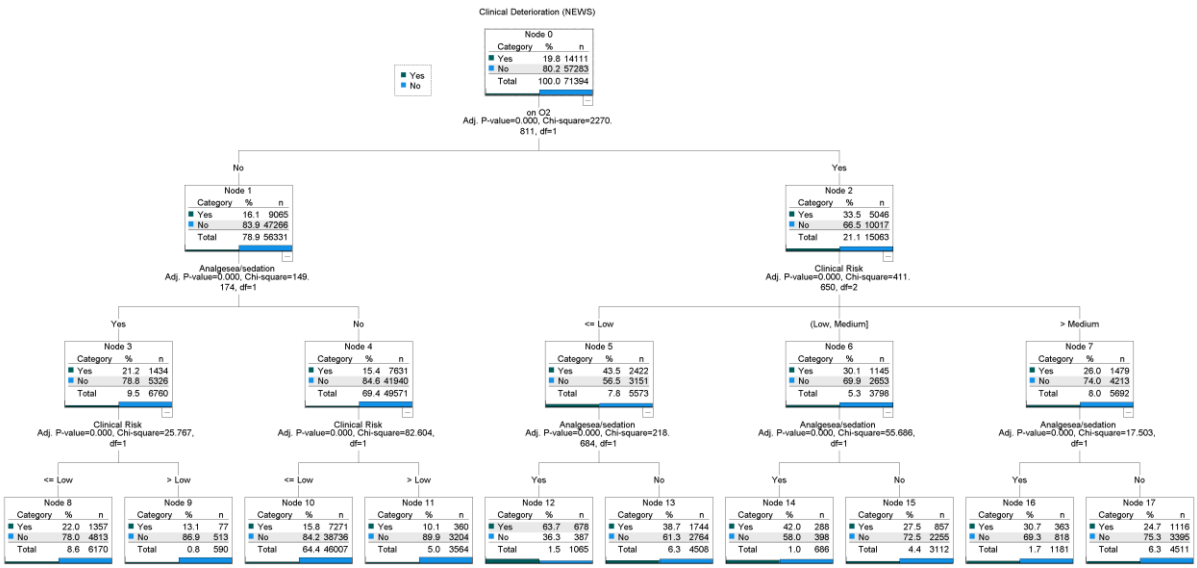
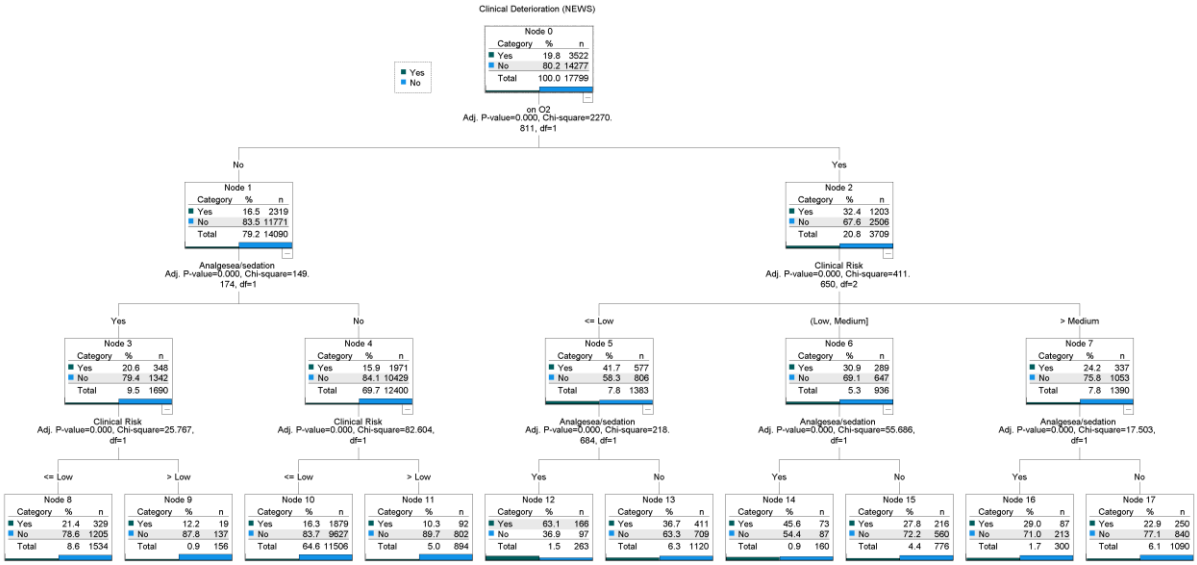


Figure 4: CHAID – Clinical - Test



Binomial regression results

Table 4 provides an overview of demographic and logistic variables included into a binomial regression as well as associated odds ratios (OR), confidence intervals (CI), and p-values for each. A total of 4 models were developed and the model Clinical Deterioration NEWS-Logistics was chosen to be included in the results due to its performance and practical relevance. Model performance according to Nagelkerke R Square was 0.022 indicating a weak relationship between the predictive variables and the outcome: Clinical deterioration. According to the Hosmer Lemeshow test of 0.133, the model is considered to be a good fit. The following variables were found to be significantly predictive of clinical deterioration (CD). Mode of transport emerged as a significant variable with mode of transport-Ambulance being the reference category (P-Value <0.001), and mode of transport 1-Helicopter (OR 0.29, 95% CI 0.11-0.76, P-Value 0.012). These results indicate that there is a 71% decreased probability of CD should a patient be transported by helicopter. All senior crew qualifications emerged as significant predictors for CD (p-value <0.001). Basic Ambulance Assistant being the reference category and lowest pre-hospital provider qualification had a p-value of <0.001 and all other qualifications carried ORs between 0.8-0.5 indicating a decreased probability for CD as senior crew qualification increases against the reference category. Emergency Care Practitioner (ECP) being the highest pre-hospital provider qualification had a p-value of <0.001, OR 0.5 with a 95% CI 0.45-0.54 indicating a 50% less probability for CD should a patient be treated by an ECP in comparison to a BAA. Age was found to be a significant predictor for CD with a 0.6% increase in risk for every 1 years increase in age (OR 0.994, CI 0.99-0.95 p-value <0.001). Call category was found to be statistically significant, and it was found that there is a 6% increase probability of CD (OR 1.061, CI 1.0-1.1 p-value 0.01) if the case was trauma compared to medical.

Table 4-Binomial Regression results-Logistics- NEWS.

Variable	OR	95% CI	P-Value
Call Type-Primary	0.97	0.9-1	0.23
Mode of transport- Ground Ambulance			<0.001
Mode of transport-Helicopter	0.29	0.11-0.76	0.012
Mode of transport-Intensive Care Ambulance	0.42	0.16-1.1	0.079
Senior Crew-Basic Ambulance Assistant			<0.001
Senior Crew-Ambulance Emergency Assistant (AEA)	0.772	0.67-0.87	<0.001
Senior Crew-Ambulance emergency Assistant (ANA)	0.81	0.75-0.88	<0.001
Senior Crew-Emergency Care Assistant	0.77	0.68-0.87	<0.001
Senior Crew-Emergency Care Technician	0.79	0.71-0.87	<0.001
Senior Crew-Paramedic ANT	0.54	0.5-0.59	<0.001
Senior Crew-Emergency Care Practitioner	0.5	0.45-0.54	<0.001
Senior Crew-Medical Practitioner	0.5	0.44-0.78	<0.001
Specialised Unit	0.7	0.27-1.8	0.47
Time to Facility	1	1.0-1.0	0.88
Distance to Facility	1	1.0-1.0	0.3
Age	0.994	0.99-0.95	<0.001
Call Category-Medical			0.01
Call Category-Trauma	1.061	1.0-1.1	0.01
Call Category-Unknown	0.9	0.93-1.0	0.54

Table 5 provides an overview of demographic, logistic and clinical variables included into a binomial regression as well as associated odds ratios (OR), confidence intervals (CI) and p-values for each. The model Clinical Deterioration (CD) NEWS-Clinical was chosen to be included in the results and discussion and was also used to develop a proposed pre-hospital CD prediction tool due to its performance and practical relevance. Model performance according to Nagelkerke R Square was 0.069 indicating a weak relationship between the predictive variables and the outcome: Clinical deterioration. According to the Hosmer Lemeshow test of 0.062, the model is also considered to be a good fit. The following variables were found to be significantly predictive for CD. Mode of transport- ground ambulance was found to be significantly predictive of CD (p-value 0.019) and served as the reference category. Other modes of transport were not found to be significant predictors in comparison to the reference category. indicating an increased probability of CD should patients be transported via this unit. It was shown that senior crew qualification was predictive for CD and there was a decreased probability of CD the higher the qualification of the pre-hospital provider. This is indicated by the progressive decrease in OR with higher qualifications in relation to the reference category BAA. ECP which is the highest pre-hospital provider qualification showed significance (OR 0.7, 95% CI 0.64-0.77 p-value <0.001), indicating that there is a 30% decreased probability of CD should this qualification be the senior crew member. Age was shown to be a significant predictor for CD (OR 0.997 95% CI 0.99-0.99 p-value <0.001) indicating a 0.03% increase in the probability of CD for every 1-year increase in age. Call category was found to be significantly predictive of CD and it was found that there was a 10% increase in probability for CD if a case was a medical (OR 1.1, 95% CI 1-1.1, p-value <0.001) rather than a trauma case. Specific therapeutic interventions were also found to be significant predictors for CD, and it was shown that patients who required medical oxygen administration (OR 3.38, 95% CI 3.2-3.5, p-value 0.000) had a 238% increased probability of CD than those that have not. Those that received inotropes or vasopressors (OR 1.55, 95%CI 1.2-1.8, p-value <0.001) had a 55% increased probability of CD, while analgesia or sedation carried a 41% (OR 1.41, 95% CI 1.3-1.5, p-value <0.001) increased probability for CD. Clinical risk was found to be significantly predictive for CD and the results indicated that the probability of CD increased by 79% if a patient had medium clinical risk (OR 1.79, 95% CI 1.6-1.9, p-value <0.001)in comparison to low clinical risk

(p-value <0.001), and 142% if the patient had high clinical risk (OR 2.42, 95% CI 2.2-2.5, p-value) in comparison to low clinical risk.

Table 5 – Binomial regression results -Logistics and Clinical-NEWS

Variable	OR	95% CI	P-Value
Call type	0.94	0.9-0.99	0.019
Mode of transport-Ground Ambulance			0.019
Mode of transport-Helicopter	0.45	0.16-1.2	0.112
Mode of transport-Intensive Care Unit Ambulance	0.58	0.22-1.54	0.279
Senior crew- Basic Ambulance Assistant			<0.001
Senior crew- Ambulance Emergency Assistant	1	0.88-1.17	0.79
Senior crew-Ambulance emergency Assistant	0.86	0.8-0.93	<0.001
Senior crew-Emergency Care Assistant	0.82	0.73-0.93	0.002
Senior crew-Emergency Care Technician	0.81	0.79-0.97	0.01
Senior crew-Paramedic (ANT)	0.68	0.62-0.74	<0.001
Senior crew-Emergency Care Practitioner	0.7	0.64-0.77	<0.001
Senior crew-Medical Practitioner	0.63	0.47-0.85	0.003
Specialised Unit	0.81	0.3-2.1	0.67
Time to facility	1	1	0.89
Distance to facility	1	1	0.31
Age	0.997	0.99-0.99	<0.001
Call category-Medical			<0.001
Call category-Trauma	1.1	1-1.1	<0.001
Call category -Unknown	1	0.96-1.0	0.52
Patient on medical oxygen	3.38	3.2-3.5	0.001
Mechanical Ventilation	0.97	0.84-1.1	0.781
Inotropes/vasopressors	1.55	1.2-1.8	<0.001
Analgesia and or sedation	1.41	1.33-1.49	<0.001
Clinical risk- low			<0.001
Clinical risk 1-Medium	1.79	1.68-1.91	<0.001
Clinical risk 2-High	2.4	2.26-2.59	<0.001

CHAPTER 5: Proposed pre-hospital clinical deterioration prediction tool.

Chapter 5 aimed to describe the pre-hospital clinical deterioration (CD) prediction tool and composite score that was created as part of this project. Table 6 is the proposed provisional pre-hospital CD prediction tool with a composite score. Model 2 from the binomial regression logistics and clinical National Early Warning Score (NEWS) was selected as the final model, and a simple calculation was made to create a composite score based on model 2's ORs. The following calculation was used to create a score:

$W_i = |\log(OR_i)|$ The log transformation has a few advantages: 1) by providing symmetry, both positive and negative changes are equally weighted. This can be beneficial when combining factors with different directions of effect; 2) it improves interpretability by compressing the range of values, making it easier to compare the magnitudes of different odds ratios; and 3) it can stabilize the variance of the odds ratios, especially in instances of extreme values.

A total score of 230 is obtainable from the composite score and it was found that specific variables carry a positive value which if present and determined by the weight of the value, contributes to an increased probability of CD. Other variables carry a negative value which if present and determined by the weight of the value, contributes to a decreased probability of CD. Senior crew qualification ranging from lowest to highest qualified each subtract a score between 6 and 20 indicating a progressive decrease probability of CD as provider qualification increases. There is slight decreased contribution to probability of CD if it is a primary call subtracting a score of 2, as well as if the patient is mechanically ventilated subtracting a score of 1. It was found that when a patient receives or was already on medical oxygen prior to transport carries the highest score of 53, contributing to increased probability for CD, followed by high clinical risk with a score of 38, medium clinical risk with 26, the presence inotropic or vasopressor support with 19, analgesia and or sedation with 15, and if it is a trauma case with 4.

Table 6: Proposed CD prediction tool and composite score

Variable	OR	Score
Call Type-Primary	0.946	-2
Senior Crew Ambulance Emergency Assistant	0.867	-6
Senior Crew Emergency Care Assistant	0.825	-8
Senior Crew-Emergency Care Technician	0.881	-6
Senior Crew-Paramedic (ANT)	0.683	-17
Senior Crew-Emergency Care Practitioner	0.707	-15
Senior Crew-Medical Practitioner	0,638	-20
Call Category-Trauma	1.1	4
Patient on medical oxygen	3.384	53
On inotropic or vasopressor support	1.551	19
Analgesia or sedation administered	1.412	15
Clinical Risk Medium	1.799	26
Clinical Risk High	2.42	38
Total		230

Variable score- Log of the OR

Table 7 is the proposed CD prediction questionnaire that can be used and populated into a spreadsheet by a call taker in an emergency control center of an emergency medical service, or by a provider into an electronic patient report form. The information can either be gathered by a call taker during the activation of resources for an inter-facility transfer or by a pre-hospital provider during patient contact. The intention is that the information be placed into an electronic patient report form by the provider and a probability score then be automatically calculated. If during call-taking for an inter-facility transfer the information can then be populated in a spreadsheet by the call-taker in order to automatically calculate the probability percentage.

The CD probability was split into three categories: Low (Initial NEWS < or equal to 3), medium(initial NEWS < or equal to 5), and high (initial NEWS > or equal to 7) probability. A case would have a low probability if the percentage were equal or below 35%, medium if 35-65%, and high if above 65%, similar to a risk assessment toolkit.[74]

Whether or not the probability category should be made available to the treating provider, would have to be determined in future research.

Table 7-Proposed CD prediction questionnaire.

Variable	**Answer**	**Probability**
Is it a Primary case?	Yes/No	-2 (if Yes)
Senior Crew- Ambulance Emergency Assistant?	Yes/No	-6 (if yes)
Senior Crew- Emergency Care Assistant?	Yes/No	-8 (if Yes)
Senior Crew- Emergency Care Technician?	Yes/No	-6 (if Yes)
Senior Crew- Paramedic (ANT)?	Yes/No	-17 (if Yes)
Senior Crew Emergency Care Practitioner?	Yes/No	-15(if Yes)
Senior Crew- Medical Practitioner?	Yes/No	-20 (if Yes)
Trauma case?	Yes/No	4 (if Yes)
Patient on medical oxygen?	Yes/No	53 (if Yes)
Patient on inotropic or vasopressor support?	Yes/No	19 (if Yes)
Was analgesia or sedation administered?	Yes/No	15 (if Yes)
Initial Clinical Risk Medium?	Yes/No	26 (if Yes)
Initial Clinical Risk High?	Yes/No	38 (if Yes)

CHAPTER 6: Discussion

The study aimed to describe whether adult patients clinically deteriorate during transportation by private ground and air ambulance, as well as describe which factors may predict clinical deterioration. In addition, it aimed to propose a pre-hospital clinical deterioration prediction tool. Two phases occurred, where the first phase was a retrospective data archive analysis on adult patients treated by pre-hospital practitioners and transported by ambulance spanning over 13 months. Data extracted in phase one of the study were used in phase two of the study where a Chi-Squared Automatic Interaction Detection (CHAID) and binomial regression analysis were performed to determine meaningful relationships between CD and variables. Of all variables used in the retrospective data analysis, 14 were deemed to be statistically significant and practically obtainable telephonically by a call taker during information gathering for an inter-facility transfer, or by a pre-hospital provider during patient contact, and these were used to create the composite score presented in chapter 5 of the thesis.

Ambulance transportation CD rates

CD was defined as an increase in the NEWS of 1 or more and 2 or more on the MEES, resembling a study done by Srithong in 2020.[27,35,60] The study used both Early Warning Scores to improve the validity of overall CD rates and to compare the effectiveness of an EWS in identifying CD. It was interesting to find that overall, both EWS detected CD in almost the same proportion which leads us to believe that our working definition for CD by use of an EWS is valid due to its sensitivity. Although the CD rates for both EWSs were similar, specificity was not similar as they only detected CD in around half of the same cases. This leads us to the conclusion that this may be a result of the specific physiological parameters measured and included in the scores that vary, the threshold for previous research that recommends how many points increase in score constitutes CD, and whether or not the specific tools are valid within the setting they are used It would be interesting to see how other EWSs would compare in sensitivity and specificity when tested within the same setting. The NEWS is the most validated pre-hospital EWS and the main focus was placed on the results by use of this score. To the researcher's knowledge, this study is the first attempt to

report CD occurrence within the South African emergency medical service context. When comparing our results to other studies of a similar nature, the specific study methodologies, systems, and patient population differences should be kept in mind.

The overall clinical deterioration (CD) rate of all patients transported was 15.7% according to the NEWS and 15% according to the MEES. When comparing our findings to studies worldwide, the overall result shows a lower CD rate than those reported in the UK at 34% and Hong Kong at 23%, but higher than Boyle et al who reported a rate of 5.1% as well as a Canadian study that reported a rate of 6.5%.[31–33,37] The reason for these differences could be because of various system, patient, and study method-related factors.

Our study included all levels of acuity while others reported CD subdivided into categories as critical and stable patients or like most, only reported CD in critically ill or injured patients. CD rates was reported in literature to be greater as the risk for CD or acuity of patients increased, and it was therefore important for us to also report CD rates in critically ill or injured patients only as this was consistent with most existing studies.[33,35,52]

By calculating a NEWS with vital signs measured on arrival, a score of 5 and above allowed us to categorize patients as critical or medium to high risk for CD. Patients in this category accounted for 19% of all patients transported and 22.3% of this population deteriorated. This result is similar to a study done in Thailand which used a similar methodology and reported a CD rate of 28%.[74] A study in Canada reported a CD rate of 6.5% and another in Saudi Arabia 13.7%, though used different methodologies to define and measure CD, making it possibly invalid to compare to our study.[34,36] These results do however lead us to believe that the overall CD rate of critical patients in South Africa is similar or greater than in other countries and that higher CD rates could be directly associated with patient acuity. There are however limitations to these conclusions that need to be considered for it to be valid, though it does provide an indication of the position regarding CD incidence in South Africa and may serve as a starting point for further investigation.

Multiple factors need to be considered for us to compare these studies and CD rates to each other, which may include system, patient, and study method-related factors. An example of this could be practitioner training or level of qualification, as different countries have different scopes of practice, training, and qualifications for pre-hospital providers. The qualification of the treating practitioner is found to be a significant predictor for CD according to existing studies as well as our results during regression, and this factor alone could have a great impact on CD rates reported by different countries.[32,35]

Clinical deterioration rates according to statistically significant variables.

It was interesting to find variables that had statistical significance for clinical deterioration (CD), as well as the proportionate rates of CD where these variables were involved. Some factors did not carry statistical significance such as gender, and weight, though it is important to mention this was dependent on the EWS used, as with the MEES they were found to be significant.

The NEWS is a validated pre-hospital score, that is supported by a vast amount of literature for its use, and therefore the results of CD according to this score were used for discussion. It is interesting to note though that throughout the data archive analysis, the MEES identified CD rates according to specific factors in very similar proportion to that of the NEWS. This as mentioned before, leads us to believe that the working definition for identifying CD rates according to specific factors is valid.

Demographic and logistic factors that were deemed statistically significant with similar CD rates included call category, whether primary or inter-hospital transfers, as well as medical or trauma call types. Primary cases accounted for the most cases, yet, CD rates were proportionally equal in both categories. During regression, it was shown that trauma cases increased the probability of CD by 10% in comparison to medical cases and this may lead anyone to assume that CD rates in trauma patients are proportionality higher, yet this was not the case as rates were the same for both trauma and medical call types. This could not be compared to other studies because no literature could be found that compares rates between these two variables.

The median age for occurrence of CD was 54 years and the median age for patients with a medium to high risk for CD was 60 years, indicating that a higher proportion of CD rates was observed with an increase in age. This was expected to be found based the fact that older persons usually have more co-morbidities, and on those of a previous study by Singh et al that reported similar results.[33,35]

Mode of transport was statistically significant, and it was found that the highest proportion of CD rates were with helicopter transports, and the least with ground ambulance. What was interesting to find was that although CD rates on helicopters were proportionally greater than on ground ambulances, patients transported via helicopter also had proportionally higher risk for CD and therefore it can be expected for the CD rate to be increased. This is valid according to our regression study that showed an increase in the probability of CD between 79-140% with patients that have greater clinical risk. The CD rates that we reported are also consistent with literature that also reported helicopter CD rates to be higher than ground ambulance.[36] Although helicopters, ICU ambulances, and specialized units are generally staffed by highly qualified providers and are equipped with specialized equipment, we found CD rates to be proportionately higher than rates on ground ambulances. This is in contrary to what we found in the literature that reported CD rates to be lower with units that have specialised equipment and practitioners that have critical care training.[31,35] This could possibly be related to the lack of official critical care training, the degree of experience of practitioners, adherence to referring physician instructions during inter-facility transfers, as well as their ability to appropriately use the equipment provided. This requires further investigation, it is valuable to keep in mind that these units are intended to be reserved for the transportation of critically ill or injured patients and that patients transported by these units carry proportionally higher risk for CD, than those that are not.

Senior crew qualification was associated with statistical significance. The results found that CD rates are proportionately higher as the level of the senior crew qualification increases, yet these qualifications tend to treat patients with a proportionately higher risk for CD. It could be speculated that the reason for this is higher qualifications transported more critical patients, requiring advanced interventions and medications to be administered about lower qualifications, and as such an increased risk for CD

can be expected due to high acuity. It was observed that lower qualifications transported lower risk patients and carried greater CD rates in comparison to risk, where higher qualifications had lower actual CD rates in comparison to risk. This indicates that patients are safer with higher qualifications although CD rates are proportionally higher, and this is also supported by the results of our regression study that found a lower probability of CD with higher senior crew qualification.

Attainable qualifications in South Africa vary between short certificates to a degree in paramedicine. Higher levels of qualification receive more in-depth training regarding emergency medical care, and this could be the reason why patients are safer with higher qualified practitioners, probably owing to an ability to recognize, and treat emergencies more appropriately.[75] This requires further investigation. Studies reported a decrease in CD rates with practitioners who had critical care training.[35] In South Africa, there is no postgraduate critical care accreditation attainable, so it was not possible to determine if practitioners perhaps received additional critical care training in any sense, to be able to make a comparison.,

Time spent on scene, transportation time to a facility as well as transportation distance all carried statistical significance. There were proportionally higher CD rates observed with longer time spent on the scene, longer transportation to the hospital, as well as longer distances transported. The results therefore indicate proportionally higher CD rates with increased time spent in the pre-hospital environment, and this may be due to progressively more instability as a result of a delay in definitive care such as blood transfusions, airway management, or emergency surgery. Patients that are unstable may require stabilisation on scene, may be entrapped in a vehicle for example, or may be situated in an environment where it is difficult to remove them, therefore resulting in longer on-scene times. Yet, these patients most likely have inherently high CD risk also possibly explaining the result. Brown et al associated significantly higher patient mortality rates with longer scene times, explained by our results as CD increases mortality.[76] These findings are consistent with a Canadian study done that also reported higher CD rates associated with longer transport times, as well a study done by Srithong et al. which reported an increase of CD of 1.15 times for every additional 10 min of transportation.[34,35,77] No further research exists regarding the contribution of longer scene time as well as longer transport distance to CD rates. [76]

We found that specific clinical interventions also carried statistical significance and included mechanical ventilation, medical oxygen administration, inotropes and vasopressors, and analgesia or sedation administration. A third of all patients who received these interventions either before or during pre-hospital transportation deteriorated, and it was shown 90% of patients who were mechanically ventilated, and 50% of patients on medical oxygen had a high risk for CD. These patients could be regarded as high acuity, and evidence suggests that patients that are critical or unstable before transport have a high risk for CD.[35] We found that administration of analgesia and or sedation during transport was statistically significant, and 28% of patients who received this medication deteriorated. Some of these medications that are within the scope of the South African pre-hospital providers' scope of practice possess increased cardiac and respiratory protective profiles such as fentanyl and ketamine. Others, such as benzodiazepines and morphine can cause respiratory or cardiovascular depression.[77–79] It could be possible that the administration of morphine and benzodiazepines contributed to the reported occurrence of CD, due to their ability to decrease level of consciousness. Also, for patients that were deliberately sedated, this may have caused a decrease in NEWS of at least three, flagging the case as CD, and it is, therefore, questionable if these patients suffered true deterioration.[77–80] These findings are however consistent with the findings of Srithong et al, Boyle et al, and others who found that administration of these medications contributed to CD.[8,32,35,44] The result is however interesting, and further research into analgesia and sedation as risk factors is warranted, possibly looking into CD rates of each medication individually.

Almost all patients who received mechanical ventilation (90%) had medium to high risk for CD, and a third of these patients deteriorated. The results show these patients are usually of high acuity and are transported by more senior qualified practitioners, often in specialized units. It can be expected that they would deteriorate as our findings indicate proportionally increased risk as well as rates of CD risk in higher qualifications and specialized units. The findings are also consistent with those of Walker et al who reported adverse events and CD in patients who were mechanically ventilated.[41] CD rates in mechanically ventilated patients require further investigation based on our definition to establish the actual cause. We hypothesize that it could be inertial forces during transfer, a possible lack of critical care training, as well as adverse events

during transfer such as extubation or equipment failure, as these events have been shown to occur in the pre-hospital setting.[41] To our knowledge there is no evidence of mechanical ventilation as a risk factor for CD specifically, based on our definition. We found that the administration of medical oxygen was also associated with CD, a third of the patients deteriorated, and half of these patients had medium to high risk for CD.

This comprehensive data archive analysis delved into the intricacies of CD rates among patients transported, employing both the NEWS and MEES Early Warning Scores for assessment. Intriguingly, despite the variance in physiological parameters between the two EWS, they exhibited comparable proportionate detection of CD rates, affirming the validity of our working definition. When compared with global studies, our findings indicated a nuanced landscape, with CD rates in South Africa distinctively influenced by various system and clinical-specific factors, including practitioner qualifications, modes of transport, and time spent in pre-hospital environments.

Interesting findings emerged, particularly concerning the proportional CD rates between CD and age, mode of transport, and practitioner qualifications. Older age groups exhibited an increased proportionate CD rate, while helicopter transports revealed elevated CD rates despite possessing specialized equipment and practitioner expertise. This highlights potential areas of concern and necessitates a deeper investigation into the details of these variables, especially considering the absence of postgraduate critical care accreditation in South Africa.

Our analysis pinpointed certain clinical interventions, notably mechanical ventilation, medical oxygen administration, and analgesia and or sedation, as having increased proportionate CD rates. These findings pose critical implications for pre-hospital care protocols, urging evaluation of medication administration practices and their potential repercussions on CD.

In essence, while this analysis offers invaluable insights into CD occurrence within the South African emergency medical service framework, it underscores the multifactorial nature of CD. As such, it serves as a foundational stepping stone, compelling further

research into these factors and refine pre-hospital care strategies, ultimately enhancing patient safety and outcomes.

CHAID and Regression Analysis.

Evidence shows that certain factors are associated with and are statistically significant predictors of CD.[33,35] Our study also highlighted specific demographic, logistical and clinical factors that were found to be significant contributors as well as predictors for clinical deterioration (CD) by use of two statistical methods.

It was interesting to find that both methods highlighted the same variables as the most significant contributors and predictors for CD, indicating that patients on medical oxygen as a clinical factor and senior crew qualification as a logistical factor have the most influence. During the regression analysis, two models were generated where the first included logistical and demographic variables, and in the second clinical variables were added. It was interesting to observe that with the inclusion of clinical variables, these emerged as carrying greater predictability for CD than the logistical and demographic factors. Two models reaching similar conclusions leads us to believe that the variables we deemed to be most significant are valid, and the statistically significant variables from the regression model of logistical, demographic, and clinical variables were included in a proposed pre-hospital prediction tool for CD.

A Chi-squared Automatic Interaction Detection (CHAID) analysis was done to understand relationships between clinical and logistical independent variables and the dependent variable CD: Yes or No. Two decision trees were generated that yielded interesting results. The most significant logistical variable to influence CD was senior crew qualification. It was interesting to find that with different qualifications, variations in the classification of factors associated with these qualifications were observed. For example, should a patient be treated by a Basic Ambulance Assistant (BAA), age became the next significant variable for the occurrence of CD, subdivided into different age groups, showing that an increase in age carried a higher proportion of CD rates, similar to the findings of our data analysis.

As qualification levels increased, scene time became the most significant, and this may be explained by lower qualifications spending much less time on scene. It could also be due to them mostly transporting low acuity patients who required less time for

stabilization, or load-and-go situations as their scope of practice is limited, opting to move to the hospital as soon as possible. Higher qualifications generally treated higher acuity patients, who may have required stabilization on scene, increasing on-scene time and possibly contributing to CD. It may also have been even longer on-scene times were critical for stabilisation, acuity was so high, that CD was inevitable. Though still conflicting, some evidence indicates that longer pre-hospital time in time-sensitive medical conditions increases mortality.[81]With our study describing increased probability for CD, further investigation may be required to establish whether longer on-scene times for stabilization outweigh the benefit of load-and-go situations, despite the level of qualification. It could also simply mean that due to lower qualifications not spending a long time on the scene, it simply was not measured and compared against the CD rate of those cases with higher qualifications. When it came to the highest pre-hospital qualifications though, often transporting the most critical patients, it was interesting to see that mode of transport emerges as the next most significant contributor to CD. During helicopter transports time to facility carried the most significant contribution, and ground or ICU ambulance, time on scene the most. This again highlights increased pre-hospital time as a significant contributor to CD rates, regardless of mode of transport. A South African qualitative study found that pre-hospital providers' perceptions were that factors contributing to extended on-scene time were patient acuity requiring more interventions, awaiting extrication services or law enforcement, multi-casualty incidents, or awaiting air ambulance services.[81] These results reveal the complexities of the reasons why on-scene times could be delayed, confirming that providers do indeed spend more time on the scene with higher acuity patients and warrants further investigation on how to minimize its occurrence. Our logistics decision tree, clearly states that across the board, increased pre-hospital time contributes to CD, which is especially prevalent when higher qualifications are present, most likely treating patients with increased risk.

The clinical decision tree revealed whether a patient received medical oxygen followed by analgesia and sedation administration was most statistically significant for CD. Most patients did not receive medical oxygen, and analgesia or sedation administration became the most significant, followed by the level of clinical risk. For patients who did receive medical oxygen, the level of clinical risk became most significant. These two clinical interventions played the most significant role in

contributing to CD and it was interesting to see that for those who received medical oxygen, the level of acuity contributed to CD rather than administration of analgesia as seen by those who did not. This indicates that despite risk, medical oxygen administration contributes mostly to CD rates, though in comparison to other interventions such as analgesia and sedation, clinical risk contributes to most. This is confirmed by our regression model which indicates that out of all variables, medical oxygen administration serves as the greatest predictor for CD, followed by medium or high clinical risk. Evidence exists that describes a greater occurrence of CD associated with those that are at high risk, so the result was expected as these patients are likely more sick or even unstable due to the requirement of medical oxygen. This was an interesting finding in our study, and to our knowledge not described elsewhere in the literature. A drop in SP02 below 90% would result in an increased score on the NEWS triggering CD. From anecdotal experience, we hypothesize that alternate reasons for this could relate to oxygen supply depletion, inaccurate SP02 readings due to limitations of pulse oximetry devices, or inaccurate recording.[82] Further investigation is warranted.

Our regression analyses revealed variables that are significantly predictive of CD and yielded interesting results, especially with the model that included both logistical and clinical variables. It was observed that when including clinical variables such as medical interventions, these carried the most significant weight in contributing to the probability of CD. For example, should a patient receive medical oxygen, the probability of deterioration increased by 230%, analgesia or sedation by 41%, or inotropes or vasopressors by 55%.

These findings were consistent with our decision tree results which revealed these variables as significant contributors to CD. The clinical risk was found to be predictive of CD, indicating that should a patient carry medium risk the probability increased with 79%, and high risk with 140%. Our findings are consistent with a previous study revealing 68% (OR 1.68, 95% CI 0.63-2.7 p-value 0.001) probability of deterioration with high acuity patients.[35] It makes sense that practically, patients with a higher risk for CD and higher acuity will deteriorate, further investigation may be warranted into the details of why this occurs. This will enable us to identify practical clinical and

logistical areas of improvement in EMS systems to decrease these patients' risk for CD.

Senior crew qualification was found to be protective against the probability of CD as the level of qualification increased. For example, our results show that patients that are treated by an ECP (highest pre-hospital qualifications) have 30% decreased probability of CD in comparison to being treated by a BAA (lowest pre-hospital qualification). This was expected as it could reflect the level of knowledge, ability to optimally stabilize a patient due to higher scope of practice, and possibly the ability to recognize or manage CD more effectively. There was a progressive decrease in the probability of CD observed as level of qualification increased. Previous literature revealed that CD rates were lower with providers that received critical care training, yet we were unable to determine who may have received it from our data sample, and this could not be explored. No evidence could be found of the predictive significance of level of qualification in CD. These findings could warrant further investigation into reasons for this, level of safety in lower qualified providers treating patients, and whether higher qualified providers need to be treating all patients in the pre-hospital environment.

Age was observed to be a significant predictor for CD deterioration indicating a 6% increase in probability of CD for every 10 years increase in age. In essence, this means that a 60-year-old has a 24% more likelihood of deteriorating than a 20-year-old simply based on age. Older age is associated with an increased likelihood of co-morbidities, and evidence suggests that both age and co-morbidities are related to higher CD rates.[83,84] It is therefore likely that older patients who were transported had co-morbidities, increasing their risk for CD. Studies reveal that during geriatric trauma elderly patients are more susceptible to injury and are less able to compensate.[85] Being more suspectable to critical illness, with less physiological reserves, they are also at higher risk of poor short-term mortality.[86] This may in addition to co-morbidities explain our finding of a higher probability of CD associated with age, as they are unable to physiologically compensate as well as younger patients when acutely ill or injured. Similar studies to ours described age as a variable but reported no predictive capacity.[35,83] According to our data, 41% of all patients transported were above the

age of 58 years, and it is therefore imperative for us to further investigate age as a risk factor for CD, enabling us to mitigate CD in this population.

Call category whether trauma or medical revealed a 4% increased chance of deterioration should a patient have suffered a traumatic emergency. No other evidence could be found that reported predictive significance for this variable though we hypothesize that it could be due to the very nature of trauma being associated with high mortality rates.[87,88]

Certain therapeutic interventions revealed to have significantly strong predictive capability for CD, and the most significant of these was medial oxygen administration. A 230% increase in probability for CD was observed should a patient receive oxygen, 41% for those that received analgesia or sedation, and 55% if inotropes or vasopressors were administered. Although interventions such as analgesia and sedation were found to be contributors to adverse events, no literature was found speaking to CD, and we hypothesize that reasons for this could be the desired or normal effects of these medications such as sedation, decreased consciousness which in turn triggered CD on the NEWS. It could also be those adverse reactions such as hypotension occurred which also triggered CD on the NEWS, and which is most likely a true reflection of CD. This is consistent with studies that showed the administration of opioids as an example, resulted in hypotension or respiratory depression.[8] However, a deeper investigation into this is warranted.

An interesting finding, and one that was consistent with the literature, was the predictive capacity of clinical risk for CD. Srithong found that unstable conditions had a 68% increased chance of CD if compared to stable conditions and a 40% increased chance with high clinical risk NEWS of 8 or above.[35] Our regression revealed a significant increase in probability of 79% with medium risk in comparison to low risk and 142% with high risk for CD. The question remains if providers can recognize the risk and intervene appropriately, or if these patients' deterioration is preventable should it be recognized. Could it be related to the level of qualification and knowledge of the providers that reflect such a large increase in probability with high-risk patients? A deeper investigation is warranted.

Other variables such as mode of transport and pre-hospital time did not emerge to have significant predictability contrary to other studies. Srithong found that an ICU ambulance was protective for CD when compared to patients transported by normal ambulance and that longer pre-hospital scene and transport times contributed to the likelihood of CD. [35]

In conclusion, our study delves into the intricate web of factors associated with and predictive of clinical deterioration (CD) in the pre-hospital setting. This comprehensive analysis employing both regression models and decision trees revealed consistent trends across demographic, logistical, and clinical variables. Notably, patients on medical oxygen and senior crew qualifications emerged as pivotal factors influencing CD, with both statistical methods highlighting their significance. The decision tree analysis further unraveled relationships between qualifications, scene times, mode of transport, and CD rates.

The study sheds light on the multifaceted nature of pre-hospital care, indicating that clinical variables, particularly medical interventions like oxygen administration, play a paramount role in predicting CD. The intriguing finding that medical oxygen, when administered, significantly contributes to CD rates emphasizes the need for a closer examination of its implications, potentially beyond the scope of existing literature.

Moreover, the protective effect of higher qualifications, such as Emergency Care Practitioners (ECP), against CD underscores the importance of skill levels and knowledge in pre-hospital care. Age, call category (trauma or medical), and clinical risk were identified as additional predictors, each providing unique insights into the likelihood of deterioration.

While some variables, like mode of transport and pre-hospital time, did not exhibit significant predictability in our study, the nuanced nature of pre-hospital dynamics suggests that these aspects might warrant further investigation. The study’s findings contribute valuable information to the development of a pre-hospital prediction tool for CD, potentially enhancing the efficiency and quality of emergency medical services. Future research should focus on refining our understanding of the intricate interdependence among these variables and their impact on patient outcomes, ultimately aiming for continuous improvement of pre-hospital care systems.

Proposed pre-hospital clinical deterioration (CD) prediction tool.

Variables that were found to be significantly predictive of CD, were used to develop a pre-hospital CD prediction tool. We believe that this tool, with its limitations, could be used in the pre-hospital setting effectively to improve patient outcomes. Predictive and preventative care is shown to improve patient outcomes, and this tool was developed with the aim to aid emergency medical services in identifying patients at risk for CD, prompting strategies and interventions for mitigation.[27,32] We believe that practically, the tool can be used by a call taker during information gathering for inter-facility transfers. A risk for CD can be calculated, and a more informed decision could be made as to whether the patients should be moved, or which resource whether human or system, should be allocated. The tool can also be used by the attending provider, and the information required can be populated into an electronic patient report form, providing them with a risk calculation, aiding them in early recognition of CD, possibly prompting appropriate interventions, request for assistance or additional resources, ultimately improving patient safety and outcomes.

CHAPTER 7 : Conclusion, limitations, and recommendations

Conclusion

The study set out to achieve one specific goal through multiple processes and was divided into several chapters which marked the different steps of the process. The goal was to create a pre-hospital clinical deterioration prediction (CD) tool, that could be used prospectively to predict the probability of CD occurrence.

A literature review was done to describe definitions for CD, the prevalence of CD in the pre-hospital environment, factors that contribute to deterioration as well as strategies that are used to identify CD early in the pre-hospital environment.

A data-archive analysis was done on 89193 patients, and by use of an Early Warning Score, an overall CD rate of 15% was reported. Multiple statistically significant logistic and clinical factors emerged with various proportionate CD rates such as mode of transport, age, pre-hospital scene times, and therapeutic interventions such as medical oxygen administration, analgesia and sedation, as well as clinical risk prior to transport.

These variables were included into multiple statistical models including a Chi-Square Automatic Interaction Detection (CHAID) analysis and binomial regression models. Interesting findings emerged that indicated both logistical and clinical variables contributing to CD, also describing those that have predictive significance. Medical oxygen administration and level of senior crew qualification emerged as factors that significantly contribute to risk for CD warranting further investigation into specific reasons for this.

Lastly, we included our results into a composite score, to develop a proposed pre-hospital CD deterioration prediction tool that can be implemented either into a spreadsheet by a call taker during information gathering for inter-facility transfers, or by a provider attending to a patient, to calculate probability of CD for a specific patients, possibly leading to early suspicion for CD, or strategies to be put in place to prevent it from occurring. This tool is however not validated, and our study therefore further recommends a validation study to be performed, with the goal of ultimately improving patient care and safety.

Limitations

Although the study was done in an organisation that functions across a variety of provinces of the country, as well as the inclusion of a large sample size, it only accounts for the private sector and does not include data from the public sector. Due to possible variations in systems, resources and population samples, this could impact the external validity of the results and may not accurately represent the South African population. A limited number of variables were included into the study and may impact the weighting of significant variables as predictors for CD due to absence of a larger spectrum of variables. The exclusion of pregnant individuals, patients who suffer from psychiatric emergencies and minors further limit the generalisation of the occurrence of pre-hospital CD in South Africa. The use of our proposed prediction model is also not applicable in these patients.

Although the study included the most up to date working definition for CD, the lack of a true consensus for a working definition for CD in literature may influence whether the occurrence of CD reported in our study is a true reflection of actual CD in the patient sample.

The performance of the regression models should be refined for better performance, improving the quality of results for risk factor contributing to the prediction of CD. Further model refinement was beyond the scope of this Master, proof of concept project.

Analgesia and sedation were found to be a significant predictor of CD, though the very nature of these medications with its effect on level of consciousness, may impact the validity of CD rates observed in this population, and leads us to question if these patients truly suffered CD.

Our study reveals that longer on scene times carried significant contribution for CD, though does not specify a reason for this, only that higher qualified personal generally spent longer time on scene. The study does not indicate whether this is due to the requirement for stabilization or whether higher scope of practice unnecessarily delayed scene time due to the ability to provide more interventions that may have not benefited the patient. This is the same for many factors, as our study describes which factors contribute to the probability of CD yet does not always specify the exact reason.

The study simply highlights variables that contribute and predict CD but does not highlight the details or reasons for this. Further investigation into the details of these factors my shed light on whether they contributed to true deterioration, or not.

Another limitation was the use of an early warning score that included body temperature as a physiological parameter where the data was not provided to the researcher. To mitigate for this, the MEES which does not require the measurement of body temperature was also calculated and compared to the results of the NEWS. It was found that overall CD rates were very similar according to both EWSs, yet around half of the cases flagged for CD were not the same cases. There was a 50% deviation in which cases were flagged as patients that suffered CD. The researcher interprets this finding as that the absence of body temperature does not diminish the tool's ability to detect accurately, though the differences in cases flagged can be attributed to the different scoring systems and physiological parameter requirements of different EWSs. The researcher also accepts that due to the omission of this physiological parameter, actual clinical deterioration rates may have been higher than reported.

The goal is for our proposed pre-hospital CD prediction tool to be used in the pre-hospital setting either by a call taker during inter-hospital transfers, or by a provider during patient contact. Firstly, the tool can only be used for adults, in the absence of pregnant, as well as acute psychiatric patients, limiting its use. Although the tool could be used to dispatch adequate resources, it would only be applicable during inter-facility transfers as the information required to calculate a score would not be attainable by a call taker during a primary call. The question remains whether a provider would physically complete the score during patient care, and if this result were to be made available to him during this time, enable him to mitigate the risk of CD. Whether the result increases stress during patient care, or the tool completion adds to cognitive load, could also negatively impact the provider experience with the tool, as well as patient care, and needs further investigation and validation.

Future recommendations.

We recommend further research into the development of an international consensus working definition for pre-hospital clinical deterioration (CD), as this may contribute to future reporting of the occurrence of CD that is a true reflection of actual CD in patients. Further research regarding occurrence of CD rates and factors contributing to CD should be done within the South African context especially within a variety of sectors such as the public sector to come to a more accurate representation of the occurrence of CD in the South Africa. Further investigation should also be done with the inclusion of a wider variety of variables such as comorbidities, specific medications, and other human, service and environmental related factors, as well as a deeper investigation into the reason of these factors contributing to the probability of CD. The inclusion of patients younger than 18 years, pregnant patients, and those suffering from psychiatric emergencies will allow for a more accurate representation of the occurrence of CD in the South African context. We recommend refinement of the regression models used to provide more accurate and reliable results for risk factors that predict probability of CD. We recommend a validation study for the proposed pre-hospital CD prediction tool.

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APPENDICES

1. Annexure A -Significant variables used for CHAID tree and binomial regression analysis.

Variable	Model 1 - Logistics	Model 2 - Clinical 0Dx
	NEWS	NEWS
CallType*	0,004	0,004
Modeoftransport	<.001	<.001
SeniorCrew	<.001	<.001
SpecialisedUnit	<.001	<.001
OnScene	0,000	0,000
TimetoFacility	0,000	0,000
DistancetoFacility	0,000	0,000
Age	0,000	0,000
Gender	0,585	0,585
Weight	0,080	0,080
CallCategory	0,003	0,003
Dx1	<.001	<.001
Dx2	High missing	High missing
Dx3	High missing	High missing
Dx4	High missing	High missing
Dx5	High missing	High missing
Dx6	High missing	High missing
Dx7	High missing	High missing
Dx8	High missing	High missing
Dx9	High missing	High missing
Dx10	High missing	High missing
onO2	0,000	0,000
MechanicalIntervention	<.001	<.001
IntropesVasopressors	<.001	<.001
Anolgosedation	<.001	<.001
ClinicalRisk	<.001	<.001

NEWSOnArival	N/A	N/A
MEESOnArival	N/A	N/A
ClinicalDeteriorationNEWS	DEP	DEP
ClinicalDeteriorationMEES	DEP	DEP
ln_age		
ln_onscene		
ln_timetofac		
ln_distance		

Annexure B-List of grouped diagnoses from data received.

Diagnoses
Superficial Injuries
Respiratory emergencies
Cardiovascular emergencies
Animal bites/Stings
Blood conditions
Congenital conditions
Musculoskeletal Trauma
Pshyciatric disorders
UNKNOWN DIAGNOSIS
Burn Injuries
Sexual Assault
Overdose/Poisening
Chest Trauma
Cardiac Arrest
Spinal trauma/emergencies
Electricution
Abdominal Trauma
Endocrine Emergencies
Near drowning/drowning
GIT emergencies
Obstetric emergencies
Renal emergencies
Seizures/Convulsions
Neurological Emergencies
Abdominal Emergencies
Electrolyte Imbalances
Maxillofacial trauma
Traumatic brain injuries
Allergic Reactions
CVA

Infectious disease
Stab wounds
Gun shot wounds
Mechanism of injury present
Cancer
General body pains

Annexure C-Human Research Ethics Committee-Ethics Approval

UNIVERSITY OF CAPE TOWN
Faculty of Health Sciences
Human Research Ethics Committee

Room 45 E-52-E-Floor- Old Main Building
Groote Schuur Hospital
Observatory 7925
Telephone [021] 406 6492
Email: hrec-submissions@uct.ac.za
Website: www.health.uct.ac.za/home/human-research-ethics

08 May 2023

HREC REF: 294/2023

Dr W Stassen
Division of Emergency Medicine
F-51 OMB
Email: willem.stassen@uct.ac.za
Student: Wjooste07@gmail.com

Dear Dr Stassen

PROJECT TITLE: DEVELOPMENT OF A CLINICAL DETERIORATION PREDICTION TOOL FOR ADULT PATIENTS DURING AMBULANCE TRANSPORTATION IN SOUTH AFRICA- (MSC CANDIDATE-MR WAYNE JOOSTE)

Thank you for submitting your study to the Faculty of Health Sciences Human Research Ethics Committee (HREC) for review.

It is a pleasure to inform you that the HREC has **formally approved** the above-mentioned study.

Approval is granted for one year until the 30 May 2024.

Please submit a progress form, using the standardised Annual Report Form (FHS016) if the study continues beyond the approval period. Please submit a Standard Closure form if the study is completed within the approval period.
(Forms can be found on our website: www.health.uct.ac.za/fhs/research/humanethics/forms)

The HREC acknowledge that the student: Mr Wayne Jooste will also be involved in this study.

Please quote the HREC REF 294/2023 in all your correspondence.

Please note that the ongoing ethical conduct of the study remains the responsibility of the principal investigator.

Please note that for all studies approved by the HREC, the principal investigator **must** obtain appropriate institutional approval, where necessary, before the research may occur.

Yours sincerely

Signed by candidate

PROFESSOR M BLOCKMAN
CHAIRPERSON, FACULTY OF HEALTH SCIENCES HUMAN RESEARCH ETHICS COMMITTEE

Federal Wide Assurance Number: FWA00001637. Institutional Review Board (IRB) number: IRB00001938 NHREC-registration number: REC-210208-007

HREC/ref 294.2023