

**A DESCRIPTIVE STUDY OF PATIENTS PRESENTING WITH A CHIEF  
COMPLAINT OF SEIZURES TO THE PREHOSPITAL EMERGENCY CARE  
PRACTITIONER OF THE WESTERN CAPE**

By

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## **ACKNOWLEDGEMENTS**

My family – Thank you for your continuous support throughout this chapter of my life and for encouraging me every step of the way.

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## **ABBREVIATIONS**

AEA:	Ambulance Emergency Assistant
AED:	Antiepileptic drug
ANT:	Ambulance Emergency Technician
BAA:	Basic Ambulance Assistant
CAD:	Computer Aided Dispatch
CoCT:	City of Cape Town
ECG:	Electrocardiogram
ECP:	Emergency Care Practitioner
ECT:	Emergency Care Technician
EMS:	Emergency Medical Services
ePCR:	Electronic Patient Care Report
GTC:	Generalized Tonic-Clonic
HR:	Heart rate
ILAE:	International League Against Epilepsy
IM:	Intramuscular
IN:	Intranasal
IV:	Intravenous
LMIC:	Low and middle income countries
MEDLINE:	Medical Literature Analysis and Retrieval System Online
NICE:	National Institute for Health Care Excellence
PR:	Per rectum
RR:	Respiratory rate
SA:	South Africa
SBP:	Systolic blood pressure
SE:	Status Epilepticus
SpO2:	Peripheral capillary oxygen saturation
WC:	Western Cape
WCG:	Western Cape Government

## **PART A: LITERATURE REVIEW**

## **Introduction**

Seizures are considered to be time-sensitive and potentially life-threatening conditions. In low resource countries approximately 2.4% of seizure patients utilize prehospital services as an entry point into healthcare and, from in-hospital data, up to 1% of emergency calls attended to are due to seizures (1–3). In the Western Cape province (WC) of South Africa, we are unaware of what the current impact of seizures is upon prehospital emergency care practitioners' workload. Seizures often result in autonomic changes resulting in cardiovascular, respiratory, pupillary and urinary manifestations (4). Whilst prehospital practitioners are able to treat many of the symptoms of seizures, they are under pressure to meet rapid response time targets (5).

## **Literature review objectives**

This literature review will focus on the classification of seizures, describing the epidemiology and aetiology of seizures within the South African (SA) context and how this relates to seizures amongst different populations. Secondly, it aims to describe how the autonomic nervous system is impacted by seizures as well as subsequent convulsions on baseline vital signs and identifies current best practice management of seizures within the prehospital environment. Finally, this review will identify any information gaps and determine the fields for future research, especially within the South African context.

## **Search strategy**

A literature search of the MEDLINE and Google Scholar databases was conducted on January 4<sup>th</sup> 2019 using Medical Subject Headings terms and Boolean search operators. The search was filtered to English only texts, published between January 1990 and January 2019, involving human species, and a population of 13 years and older.

The following three broad search categories were used:

- Seizures
- Prehospital care
- South Africa

Search terms in the seizure category included: “seizures”, “convulsions”, “epilepsy”, “fits”, “postictal”, and “status epilepticus”. The terms relating to prehospital care were: “advanced life support”, “emergency medical services”, “emergency medical technicians”, “out-of-hospital”, “out-of-hospital discharge”, “oxygen”, “paramedics”, “pharmacological management”, “prehospital”, “point of care glucose”, “airway”, “benzodiazepines”, “blood glucose levels”, “spinal”, “treatment”, and “vital signs”. Finally, the terms related to South Africa included: “South Africa”, “causes”, “definition”, “epidemiology”, “epileptological emergencies”, “aetiology”, and “mortality”.

## **Definitions**

### Seizures

Seizures are defined as a transient occurrence of altered or abnormal signs and/or symptoms, due to an abnormally excessive or synchronous change in the electrical activity within the brain (6,7).

Generalized tonic-clonic (GTC) seizures are defined as any seizure activity which originates and rapidly affects bilaterally distributed cortical and subcortical networks, often resulting in generalized stiffening and subsequent rhythmic jerking of the limbs (8). GTCs are the most common seizure type resulting in activation of the emergency care system (8).

### Convulsions

Convulsions are defined as abnormal, excessive motor activity (9). Although convulsions are commonly associated with seizures, it is important to understand that not all seizures present with convulsions nor are all convulsions a result of seizures (9).

## Status Epilepticus

Status Epilepticus (SE) in adults and children over the age of five years has been defined as having (i) continuous seizures or (ii) two or more discrete seizures between which there is incomplete recovery of consciousness (7,10). Any seizure event has the potential to become an emergency and includes a spectrum of events ranging from brief, isolated seizures to recurrent unprovoked serial seizures to status epilepticus (9). Furthermore, most seizure activity would have terminated prior to emergency medical services (EMS) arrival, further complicating the identification and recognition of seizures, especially in the absence of a known seizure disorder (8). As a result of the latter, the literature suggests diagnosing any on-going seizure activity upon arrival as status epilepticus (8).

## Epilepsy

Epilepsy is usually diagnosed when a patient has had at least two unprovoked epileptic seizures and their brain “demonstrates a pathologic and enduring tendency to have recurrent seizures” (6).

## **The Epidemiology of status epilepticus and seizures**

### Incidence and prevalence

Status epilepticus is considered the second most common neurologic emergency (11). The annual incidence varies amongst populations but has been reported to be between ten and 41 new cases per 100 000 population in the United States (11). Although there are different classifications of seizures, the convulsive type has been found to account for between 45 and 74% of all cases of status epilepticus (11).

Espinosa-Jovel et al. indicated that epilepsy affects approximately 70 million people worldwide with about 80% of affected individuals residing in low- and middle-income countries (LMIC) (12). Furthermore, studies found that eastern, western and southern sub-Saharan Africa regions were amongst regions with the highest prevalence of epilepsy (13). Pellock reported that approximately 10% of Americans will experience at least one episode of seizures within their

lifetime (9). They estimated that as much as 30% will then be diagnosed with epilepsy without remission, despite treatment with antiepileptic drugs (AEDs) (9). Furthermore, more than half of the patients who present with status epilepticus presented as first-time onset of seizures (9).

Emergency activation of EMS as a result of seizures is extremely common. In one study, the investigators reviewed 87,203 calls received by a 9-1-1 centre in Cleveland, Ohio and found that 5% of all calls were for a chief complaint indicating seizures or convulsions (8). Although no description of this population presenting to prehospital EMS within SA could be found, studies have found an epilepsy incidence of 180-250 per 100 000 population with higher rates in people residing in some LMICs such as SA (12).

### Mortality

The Global Burden of Disease Epilepsy Collaborator group indicated that SA was amongst countries with the highest epilepsy related deaths documented in 2016 (13). A literature review performed by Sánchez and Ricon found that SE is associated with a high mortality rate ranging between 7.2% to approximately 20% amongst populations (14). The literature suggests that the patient's prognosis and responsiveness to treatment decreases inversely with the duration of seizures (11). One article suggested that seizures with a duration of more than 30 minutes might have a mortality rate as high as 19%, depending on the total duration, aetiology and age of the patient (9).

A prospective epidemiological study (n=340) performed by DeLorenzo et al. indicated the causes of mortality amongst status epilepticus patients to be 21% due to anoxia (n=71), 16% due to hypoxia (n=53) and 10% due to cerebrovascular disease (n=33) (9). Pellock also confirmed that the majority of deaths occurring in seizure patients occurred as a result of acute injuries to the brain, including anoxia, hypoxia and traumatic injuries (9).

## Age

Seizures appear to have varying distributions amongst patients of different age groups. Nair et al. observed a bimodal age distribution with most incidences of status epilepticus occurring in the first year of life and in the population aged 60 years and above (15). Dickson et al. determined that their cohort consisted of more calls originating in the younger compared to the older population, with the majority of calls originating in patients aged 16 to 49 years (16).

## Sex

Seizures and SE disproportionately affects males over females. Nair et al. reported that males were affected more frequently than females (15). Reuber et al. similarly found more males (56%) than females (44%) were admitted to emergency departments with epileptological emergencies (17). Dickson et al. determined that 52.6% of their seizure related emergency calls involved male patients (16). Chin et al. determined that males compared to females were more likely (1.7:1) to present with status epilepticus amongst their sample as well (18).

## Incident times

Seizure may occur at any time of the day. Dickson et al. established that the overall call frequency incident rates of patients with a chief complaint of seizures matched that of other calls where the call rates peaked during late morning, plateaued throughout the day and dropped significantly from midnight until 5am (16).

## **The aetiology of seizures and status epilepticus**

Seizures, including status epilepticus, have been found to have many causes (9). A study performed by DeLorenzo et al. investigated the aetiology of status epilepticus amongst patients in the city of Richmond, Virginia (19). They found the five most common aetiologies implicated in status epilepticus amongst the adult population to be (i) low therapeutic levels of AEDs due to noncompliance, (ii) cerebrovascular disease, (iii) previous history of central nervous system

injury such as cerebrovascular accident and traumatic brain injury, (iv) metabolic disturbances, and (v) alcohol related causes (19). Chin et al. performed a systematic review which included the DeLorenzo study and six other population-based studies (18). Their review also agreed that cerebrovascular disease/accidents and withdrawal or low therapeutic levels of AEDs were the most likely causes of status epilepticus (15,18). Reuber et al. determined that 72.6% of patients presenting to the emergency department with seizures had a previous diagnosis of epilepsy (17). Furthermore, they found the most common contributing factors to be unusual or new-onset seizures, an increase in frequency, non-compliance of AEDs and alcohol withdrawal (17).

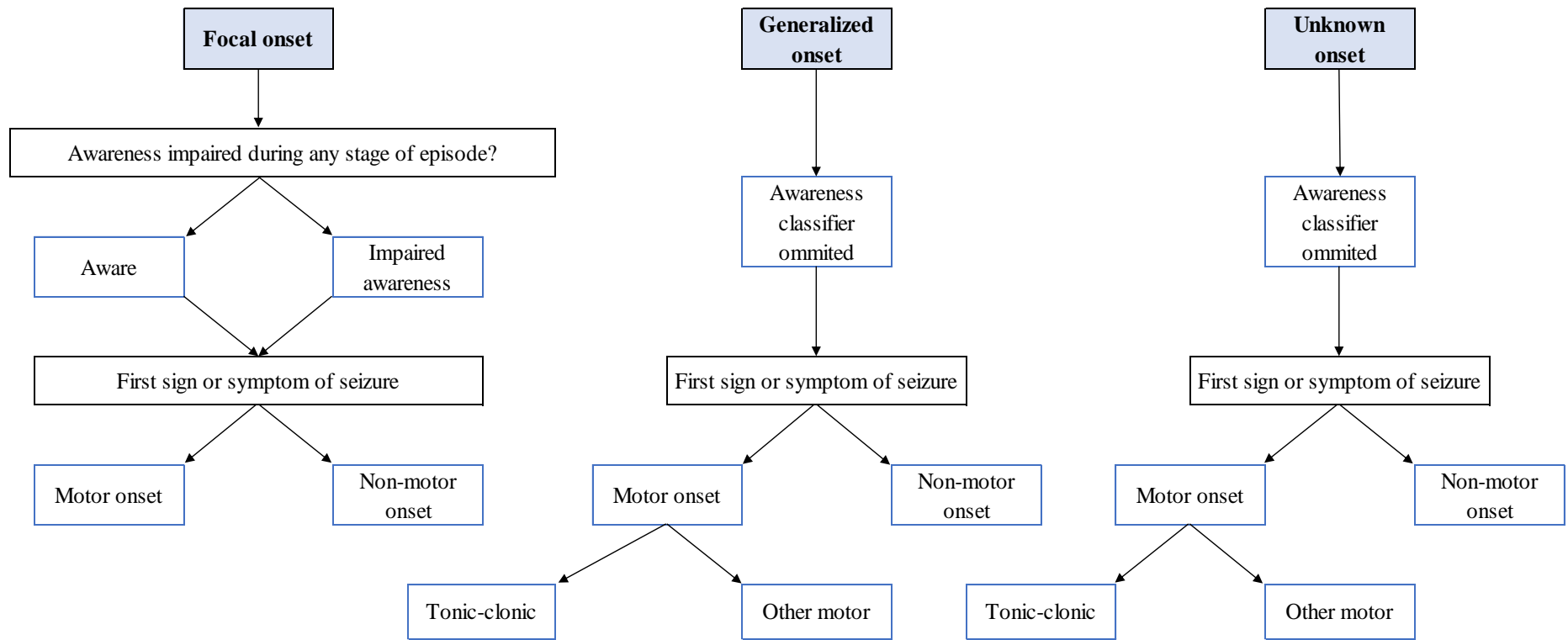
### **Classifications of seizures**

In 1981, the International League Against Epilepsy (ILAE) developed a classification system for seizures which was used until recent years (6). These classifications were often difficult to assign to individual patients and thus they assigned a task force to update the classifications of seizures using a systematic approach to describing the onset of seizures.

The 2017 ILAE classification system (Figure 1) defines seizures as being either “focal”, “generalized”, “unknown”, or “unclassified” in onset (6). The term “unclassified” has remained but should only be used when the seizure activity cannot be classified into either of the other classifications (6). Focal seizures are then classified according to the patient’s level of awareness into either “aware” or “impaired awareness” seizures (6). The ILAE task force emphasized not using the terms “impaired awareness” and “loss of consciousness” synonymously, and thus the first sign or symptom defines the seizure (6). Therefore, if the seizure was focal in onset, the generalized onset cannot be selected, rather the patient should be classified as having a focal, impaired awareness seizure, as the “rule of firsts” applies. Generalized seizures omit the level of awareness step as most generalized seizures present with impaired awareness (6).

The next step is classifying focal seizures, including generalized and unknown seizures, based on their onset as either “motor” or “non-motor” seizures (6). Seizures that start as focal seizures but progress to generalized seizures are classified as “focal to bilateral tonic-clonic seizures” (6). The ILAE further suggests diagnosing seizures where the onset was initially unwitnessed but the episode followed with tonic-clonic activity, as “unknown onset to bilateral tonic-clonic seizures”

(6). However, seizure activity that continues after EMS arrival is provisionally diagnosed as status epilepticus and should be managed as a true emergency. Figure 1 illustrates the current ILAE classification pathway of seizures (6).



**Figure 1. Representation of the 2017 International League Against Epilepsy Classifications of seizures**

## **Autonomic nervous system changes in seizures**

Seizures often result in autonomic changes which give rise to cardiovascular, respiratory, pupillary and urinary manifestations (4). Studies have suggested that sympathetic responses predominate during most types of seizures and commonly result in increased heart rates, tachypnoea and hypertension (4). However, patients may present with ictal parasympathetic activity or with an inhibited sympathetic response, during which they may present with increased salivation and gastric acid secretions, bradycardia and hypotension (4). Furthermore, the three biochemical abnormalities most commonly associated with seizures are hypo- or hyperglycaemia and hyponatremia (20).

### Respiratory rate

The literature suggests that patients commonly present with respiratory rate abnormalities during or immediately following an episode of seizures. Tachypnoea was reported frequently amongst this population of patients. However, cases of bradypnoea and episodes of apnoea were also documented. A study performed in 2010 observed the respiratory changes amongst 33 patients with localization-related epilepsy whom collectively experienced 187 seizure episodes (21). They recorded the preictal baseline respiratory rates (RR) and monitored for any increases or decreases during each of the episodes (21). The mean preictal baseline RR was  $18.6 \pm 5.2$  breaths per minute (21). Apnea occurred in 45% (n=84) of the episodes with the mean duration of apnea recorded as  $49 \pm 46$  seconds (21). Furthermore, they found that the average RR increased significantly to  $25.7 \pm 10.0$  breaths per minute in the immediate postictal phase ( $p < 0.001$ ) (21).

A cross-sectional study performed by Dickson et al. reviewed recorded clinical data of patients with suspected of seizures (N=4 884) and evaluated the frequency of recorded first vital signs (16). Their results showed that 4.6% (n=227) of patients presented with RRs of equal to or smaller than eight, or equal to or greater than 25 breaths per minute (16). Respiratory rates were not recorded and/or documented in 16.2% (n=792) of patients attended to (16).

### Oxygen saturation

Oxygen saturation forms an important part of establishing the percentage of oxyhemoglobin available in order to maintain adequate tissue perfusion. Respiratory rate disturbances largely affect the percentage of oxygen available to bind to circulating haemoglobin and thus may directly affect tissue perfusion.

Moseley et al. performed a study where 51 adults and 25 children were prospectively observed for oximetric changes during 218 seizure episodes (22). Ictal hypoxemia occurred in 35% of the patients with pulse oximetry data (n=51) and in 25% of their cumulative seizure episodes (22).

A cross-sectional study performed by Dickson et al. also evaluated 4884 electronic and paper report forms for the frequency in which oxygen saturation was measured as part of the first vital signs (16). Their results showed that 3.8% (n=187) of patients had an initial oxygen saturation of equal to or less than 91% and that oxygen saturation was not measured and/or documented in 27.9% (n=1362) of cases (16).

The literature suggest that ictal hypoxemia occurs relatively commonly amongst this population of patients and thus highlights the importance of pulse oximetry measurement and documentation along with the subsequent appropriate management in such cases.

### Systolic blood pressure

Previous studies have suggested that sympathetic responses predominate during most types of seizures and that hypertension is amongst the most common immediate cardiovascular changes noted during or immediately following seizures (4).

Dickson et al.'s results indicated that 2% (n=96) of patients with a chief complaint of convulsions presented with a systolic blood pressure (SBP) ranging between 91 and 100 mmHg, 1.7% (n=81) had a SBP of equal to or less than 90 mmHg, or a SBP of equal to or greater than 220 mmHg (16). Furthermore, SBPs were not recorded nor documented in 20.1% (n=980) of the cases (16).

### Heart rate

Tachycardia is a common autonomic response associated with seizures (23). A study performed by Opherk et al. retrospectively reviewed the changes in heart rate (HR) of 41 patients presenting with 102 cumulative episodes of seizures (23). Their study showed that 99% (n=101) of episodes resulted in an increase in HR (23). Moseley et al. found that 76% (n=57) of their patients also presented with ictal tachycardia and that tachycardia occurred more frequently in generalized compared to non-generalized seizures (22).

Zijlmans et al. also performed a retrospective study during which they set out to determine the onset in HR changes, the minimum and maximum HRs and if there were any electrocardiogram (ECG) abnormalities (24). In their study, 6.4% (n=18) of seizure episodes resulted in a bradycardia, which was defined as a HR less than 60 beats per minute (24). Moseley et al. also found bradycardia to be rare occurring in 5% (n=4) of their sample (22).

Dickson et al. also reviewed the frequency of recording HR in seizure cases during their cross-sectional study period (N=4 884) (16). Their study found that 13.5% (n=658) of patients presented with a HR between 111 and 130 beats per minute, 5.1% (n=247) of patients presented with a HR equal to or less than 40 beats per minute, or a HR of equal to or greater than 131 beats per minute (16). Furthermore, a HR reading was not recorded nor documented in 15% (n=732) of the patients attended to (16).

From the literature it is clear that tachycardia is a common cardiovascular abnormality occurring during or immediately following seizures. Bradycardia is far less common, however may be of more clinical significance (25).

### Blood glucose

The literature suggests performing a blood glucose test in all patients whom present with status epilepticus of unclear aetiology, as hypoglycaemia is a easily and rapidly reversible cause of seizures (7,26).

A retrospective, observational study included 53 505 EMS calls in which patients presenting with seizures had blood glucose levels measured in order to determine the time delays associated with performing this investigation (27). Hypoglycaemia was only present in 1.2% (n=638) of patients (27). Furthermore, the measurement of a blood glucose level resulted in a mean delay of 5.9 minutes in the administration of benzodiazepines in the seizing patient, compared to patients who had no blood glucose testing prior to administering benzodiazepines (27). This study also determined that testing of the blood glucose level after administration of benzodiazepines only led to a mean delay of 2.1 minutes in the detection of blood glucose levels (27). Due to the low incidence of hypoglycaemia, the authors suggested that benzodiazepine administration should not be postponed until a blood glucose level was determined, but should be checked as soon as possible after benzodiazepine administration (27).

Dickson et al. reviewed the frequency in which blood glucose levels were recorded and documented in a cross-sectional study (16). They reviewed 4 884 cases in which seizures and/or convulsions were documented and found that only 2.0% (n=100) of patients presented with a blood glucose level less than 4 mmol/L (16). Furthermore, they found that 46.4% (n=2 267) of patients had no blood glucose level performed and/or documented (16). Osborne et al. also reviewed the number of patients in whom blood glucose levels were recorded in their sample of 87 patients (28). Their results showed that 35.6% (n=31) patients had no blood glucose levels recorded (28).

Blood glucose measurement is an easy and rapidly performed point of care test in the prehospital environment. The measurement of a blood glucose level easily identifies cases where hypoglycaemia may be the cause of seizures. However, from the literature it is clear that a large proportion had missing blood glucose measurements.

### Electrocardiogram

The National Institute for Health Care Excellence (NICE) recommend that all patients presenting with a transient or prolonged loss of consciousness, including seizures, should have an electrocardiogram (ECG) performed (7). The aim in recording an ECG is to identify any serious cardiac causes, which may manifest as seizures, and to monitor for arrhythmias that may occur

during or following seizure activity (7). It has been well documented that seizures may affect HR which may lead to arrhythmias of which the most common are ictal tachyarrhythmias, said to occur in 80 to a 100% of all seizures (29).

Opherk et al. retrospectively reviewed the ECG findings amongst 41 patients collectively presenting with 102 episodes of seizures (23). ECG abnormalities were common with the predominant ECG abnormality being tachyarrhythmia (23). Potentially serious arrhythmias occurred in 10% (n=4) of the patients (23). They also found that ECG abnormalities were relatively common in the population presenting with generalized seizures when compared to non-generalized seizures (23). ECG abnormalities, other than sinus tachycardia, were also noted in 37% (n=15) of the patients and included the following: prominent ST-segment depression, T-wave inversions, second degree atrio-ventricular block Mobitz 1, and premature ventricular depolarization (23). Zijlmans et al. also found that tachyarrhythmias were amongst the most common arrhythmias associated with seizures (24). Furthermore, they had one patient (one episode) who presented with asystole for a duration of 30 seconds, six patients (16 episodes) who presented with a sinus pause and three patients (10 episodes) who presented with either ST-segment elevation or depression (24). As previously noted, bradyarrhythmias may also occur during the ictal phase, however these are considered far less common (29). Whilst the mechanisms underlying sudden unexplained death in epilepsy patients are still unknown, ictal bradycardia and other seizure related arrhythmias are thought to contribute to this phenomenon (25). Furthermore, bradyarrhythmias may significantly compromise systemic and myocardial perfusion, leading to secondary hypoxic insult of tissues. Therefore, although bradyarrhythmias are less common, they are considered of far greater clinical importance (25).

Dickson et al. reviewed the frequency in which ECG recordings were taken on patients with a chief complaint of seizures and/or convulsions (16). According to their findings, an ECG was not recorded in 97.2% of these cases (16). Osborne et al. also reviewed the number of patients in whom specific investigations were performed (28). Their results showed that 87.4% (n=76) of these patients did not receive cardiac monitoring (28).

From the literature it is evident that tachyarrhythmias are the most common cardiovascular autonomic change occurring during the ictus or postictal phase of seizures. As a result, ECG

monitoring should be started as soon as possible within all patients suspected of having seizures in order to identify life-threatening asystolic episodes, bradyarrhythmias and tachyarrhythmias.

### **Prehospital management of seizures and status epilepticus**

Seizures account for approximately 1% of all emergencies seen in emergency centres and are a common complaint attended to by prehospital emergency care practitioners (1,2). Early aggressive management of the actively convulsing patient plays a crucial role in the overall management and secondary long term complications in this population of patients. This literature review will focus solely on the management provided in the prehospital emergency care setting.

#### Airway management

The initial assessment and resuscitation of the actively convulsing patient follows the normal airway, breathing, circulation, disability approach used by advanced life support practitioners during other emergencies (28). Nair et al. suggested that the patient's airway and proper oxygenation are the most important steps in managing a patient in status epilepticus (15). Billington et al. suggested that proper airway management and benzodiazepines remain the cornerstone of therapy for acute cases (30). Nevertheless, both articles place emphasis on ensuring that the patient's airway remains patent.

Michael et al. reported that the gag reflex is suppressed and that vomiting may result in the aspiration of gastric contents in a patient experiencing a generalized seizure (8). They suggest placing the patient in the left lateral decubitus position and removing any loose dentures, when applicable (8). They further mention the risk of rescuers being bitten when attempting to insert a bite block or oropharyngeal airway and advised against it in the actively seizing patient (8). They instead recommend that in cases where an airway adjunct is necessary in order to support ventilations during active seizures, a nasopharyngeal airway provides a safer alternative and should be used (8).

A study performed by Martin-Gill et al. showed that airway adjuncts in the prehospital setting were only used in approximately 1.1% of patients presenting with active convulsions (28).

### Oxygen therapy

It is typical of patients to present with a brief period of respiratory depression and thus hypoventilation during or immediately following seizures (26,31). The latter usually terminates quickly once the seizure terminates as long as the patient's airway remains patent (31). The utilization of supplemental oxygen has been discussed and suggested by emergency care experts, however the value of supplemental oxygen remains uncertain and no evidence could be found showing improved patient outcomes or what doses are required in order to improve outcomes (28).

Silverman et al. suggests that supplemental oxygen should be provided via a nasal cannula or facemask (31). Osborne et al. suggested that oxygen should initially be administered at 15 l/min should the seizure be on-going; thereafter, oxygen therapy should be titrated to achieve a peripheral capillary oxygen saturation (SpO<sub>2</sub>) between 94% and 98% (28). They suggest administering supplemental oxygen to postictal patients only if their SpO<sub>2</sub> is less than 94% (28).

### Circulation interventions in the seizure patient

The literature provides conflicting opinions regarding the routine placement of intravenous (IV) lines in patients who are not actively seizing (31). Silverman et al.'s views are that most patients do not require any medications once they are not actively seizing, there is insufficient evidence to support the placement of routine IV lines (31). Their study reported that the incidence of a second seizure within 72 hours is approximately 6% and that, if they should reoccur, benzodiazepines can be safely administered via alternative administration routes (31).

McArthur et al. performed a retrospective study investigating the average on-scene times associated with the number and types of interventions performed (32). Their study found that the average on-scene times in seizure patients increased by approximately 14 minutes in patients in whom IV access was attempted (32). Interestingly enough, they also noticed that patients who

presented with an IV line already *in situ*, but did not possess the qualifications to administer medication, were less likely to receive IV medications within the first ten minutes after arrival at the emergency department (21% versus 39%, respectively) (32). They thus concluded that the placement of prehospital lines are unnecessary unless IV medications can be administered in the prehospital setting by the attending practitioner (32).

### Pharmacological Agents

Early intervention with first-line drug therapy has been associated with an 80% response rate in terminating seizures; with the response rate decreasing progressively the longer the delay in treatment (9). Early prehospital treatment with benzodiazepines were also associated with a reduction in the likelihood of recurrent seizures when compared to cases where treatment was delayed until arrival in the emergency department (9). Benzodiazepines are considered to be the most effective AEDs and are thus considered the first-line medication in the treatment of SE (26,30). Commonly used benzodiazepines include diazepam, lorazepam and midazolam (15).

Allredge et al. indicated that IV lorazepam was favoured over IV diazepam, terminating SE in 59.1% and 42.6% of patients, respectively, while cessation of seizures prior to arrival at the ED was associated with lower rates of admission to intensive care units (33). Additionally, studies have shown that midazolam has superior first-dose seizure suppression when compared to diazepam (31). Furthermore, intramuscular (IM) midazolam are preferred over other IV diazepam due to their alternative means of administration, not requiring IV placement in seizing patients, shorter onset of action, and ease of storage (31). Simultaneously, the risk for needle-stick injuries and IV complications increase during status epilepticus (31).

The RAMPART trial compared different routes of administration with the time intervals to administration and cessation of seizures (31). The latter suggested that the IV route had shortened intervals to cessation of seizures whereas the IM group had shorted times to medication administration (31). Midazolam intranasal (IN) and via buccal routes has also been gaining popularity over recent years (31). Another study performed amongst adult patients found that buccal midazolam were as safe and effective as per rectum (PR) diazepam in terminating status epilepticus (34). The NICE guidelines suggest that IM midazolam should be considered as

first-line prehospital medication and route of administration in patients without an *in situ* IV line, experiencing status epilepticus (7). In cases where IM routes are contraindicated, IN or buccal midazolam should be considered as preferred alternative routes of administration (7). The NICE guidelines also no longer recommend that IV or rectal diazepam be considered as the initial medication and routes of administration for patients presenting with status epilepticus (7).

There has been relatively few studies that directly compare different dosages of the same medication delivered by the same route, especially amongst adults, much of the existing literature has used similar dosing ranges to demonstrate overall medication efficacy.(31) The NICE guidelines suggest the initial dose of IM midazolam to be 0.2 mg/kg, with a maximum of 10 mg in adults and children weighing more than 40 kg (7). Should IN or buccal midazolam be required, the suggested initial dose for either is 0.2 mg/kg, with a maximum of 10 mg in adults and children greater than 40 kg (7). Lastly, the suggested initial dose of IV midazolam and Lorazepam is 0.1 mg/kg, with a max dose of 4 mg in adults and children greater than 40 kg (7).

#### Prehospital response times in seizures or status epilepticus

Rapid response times play a crucial role in time-sensitive cases. A response unit was dispatched to each of the calls (N=5 139) with 58.9% (n=3 026) of the incidents receiving an eight minute response, 9.1% (n=469) within 20 minutes and 30.9% (n=1 587) within 30 minutes (16).

Dickson et al. analysed the times spent on scene (N=4 884) and found that 12.2% (n=595) of crews spend less than 30 minutes on scene, 11.8% (n=578) spent between 30 and 60 minutes on scene, 37.2% (n=1 819) spent 60 to 90 minutes on scene and 38.7% (n=1 892) of crews spent more than 90 minutes on scene (16).

#### **Summary and conclusions**

Prehospital emergency care practitioners form an important link between communities and definitive health care services. Due to the frequency of patients with seizures accessing the health care system via prehospital services, the onus is placed upon them to ensure that these

time-sensitive and potentially life-threatening conditions are managed appropriately. From the literature it is clear that autonomic nervous system, sympathetic as well as parasympathetic changes, are common amongst the seizing patients and thus warrants early evaluation and identification. Unfortunately, no demographic, epidemiological or aetiological information could be found regarding this population of patients within the SA context. As a result, the evaluation of and identification of potential management challenges within this population of patients are important to the exploration and address of this high burden of disease prevalence within the SA context.

A large knowledge gap has therefore been identified within this population of SA patients. The following study therefore aims to provide information regarding the demographics, clinical presentations and current management patterns of patients presenting with a chief complaint of seizures to the prehospital emergency care practitioner in the WC province of SA.

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**PART B: MANUSCRIPT IN ARTICLE FORMAT**

**A DESCRIPTIVE STUDY OF PATIENTS PRESENTING WITH A CHIEF  
COMPLAINT OF SEIZURES TO THE PREHOSPITAL EMERGENCY CARE  
PRACTITIONER OF THE WESTERN CAPE**

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## **Abstract**

**Background** Seizures are considered one of the most common time-sensitive and potentially life-threatening medical emergencies presenting to emergency centres and attended to by prehospital emergency care practitioners. These require a rapid response, prompt identification and appropriate management. There is a paucity of information describing the demographics and prehospital management of patients presenting with seizures in South Africa.

**Objectives** The aim of this study was to describe the demographics and prehospital management of patients presenting with a chief complaint of seizures and/or convulsions to prehospital emergency care practitioners within the Western Cape Government Emergency Medical Services.

**Methods** This retrospective study included all Western Cape Government Emergency Medical Services calls indicating a chief complaint of seizures and/or convulsions between August 2017 and July 2018. Descriptive statistics were performed to describe basic demographics in this population. A sample of emergency calls originating within the City of Cape Town was selected for a clinical chart review to describe on-scene clinical presentation and vitals, response times, and prehospital treatment provided.

**Results** A total of 24 746 seizure and/or convulsion cases were recorded during the study period. The highest frequency of patients was in the 21 – 40 year age group (31%), and 57% of patients were male. The subsample (n=3 075) yielded 1 571 cases with completed electronic patient care records. The mean dispatch and response times were 20 ( $\pm 36$ ) and 14 ( $\pm 10$ ) minutes respectively with a mean on-scene time of 25 ( $\pm 13$ ) minutes. No on-scene vital signs were recorded in 11.3% of patients. Recorded on-scene vitals indicated that 36% of patients presented with a tachycardia, 14% had an oxygen saturation of  $< 95\%$ . Airway manoeuvres were performed in 30% of cases, and 50% of patients presenting with a  $SpO_2 < 95\%$  received supplemental oxygen. The benzodiazepine Diazepam was the most common medication administered, and 83% of medications were administered through the intravenous route.

**Conclusions** Seizures are a recognised time-sensitive emergency, however in this sample of patients we observed a longer than expected dispatch time. Although the importance of recording baseline vital signs is recognised, there was a large proportion of undocumented vital signs

within the sample. Despite consensus recommendations that intramuscular midazolam are the preferred medication and route, IV diazepam was the most frequently administered. Seizures are an under-recognised burden on Emergency Medical Services within the Western Cape. This study provides an initial description of the epidemiology within this population, allowing for optimization of recognition and management in these patients.

## Introduction

Seizures are considered one of the most common medical emergencies presenting to emergency centres and attended to by prehospital emergency care practitioners.<sup>[1,2]</sup> Seizures are broadly defined as a sudden onset of change in behaviour which may be characterized by an alteration in the patient's sensory perception or motor activity.<sup>[2]</sup> Status epilepticus (SE) is defined as any prolonged seizure activity of more than five minutes, or the presence of multiple seizure episodes without returning to baseline between episodes.<sup>[3]</sup>

Diagnosing seizures remains a challenge in both the in-hospital and prehospital emergency care settings.<sup>[4]</sup> Seizures and SE are both considered time-sensitive and potentially life-threatening conditions. These complaints are therefore usually considered as priority one calls and prehospital emergency services are under pressure to meet rapid response time targets.<sup>[5]</sup> Prior studies have suggested that up to 2.4% of patients with seizures in low- and middle-income countries and up to 5% of patients in high-income countries gain access into the healthcare system through prehospital emergency medical care services.<sup>[6,7]</sup>

Seizures often result in autonomic changes resulting in cardiovascular, respiratory, pupillary and urinary manifestations.<sup>[8]</sup> Studies have suggested that sympathetic responses predominate during most types of seizures.<sup>[8]</sup> Seizures may result in life-threatening arrhythmias and direct structural damage due to excessive autonomic stimulation of the heart.<sup>[9]</sup> Patients may alternatively present with ictal parasympathetic activity or with an inhibited sympathetic response and, although less common, this results in more clinically significant sequelae.<sup>[8]</sup> Furthermore, the three biochemical abnormalities most commonly associated with seizures are hypo- or hyperglycaemia and hyponatremia, two of which can be identified and managed within the prehospital setting.<sup>[10]</sup> As a result, the evaluation and identification of abnormalities in baseline vital signs are a critically important step in managing a patient suspected of having seizures.

The initial assessment and resuscitation of the actively seizing patient follows the normal airway, breathing, circulation, and disability approach used by advanced life support (ALS) practitioners during other emergencies.<sup>[11]</sup> The literature suggested that the patient's airway, proper oxygenation and early aggressive first-line treatment with benzodiazepines are the cornerstone steps in managing a patient in SE.<sup>[12,13,14]</sup> Prehospital emergency care practitioners are obligated

to register with the Health Professions Council of South Africa under one of the following three scopes of practice. The scopes of practice include the Basic Ambulance Assistants (BAA), Advanced Emergency Assistants (AEA) or ALS qualifications with the ALS qualification including Advanced Emergency Technician and Emergency Care Practitioners. Management options vary amongst the different qualifications with BAAs being able to administer oxygen and place patients in the left lateral decubitus position, AEAs providing the same as BAAs in addition to the establishment of intravenous (IV) access and finally, ALS practitioners performing pharmacological management, using benzodiazepines.

At the time of this study, no published literature could be found describing this population of patients within the South African context. This study therefore seeks to describe the demographic characteristics of patients presenting with a chief complaint of seizures and/or convulsions to prehospital emergency care practitioners within the Western Cape Government (WCG) Emergency Medical Services (EMS). This study further investigated this population of patients with regards to their on-scene clinical presentation, the prehospital care provided and emergency care response times associated with such cases.

## **Methodology**

This retrospective, descriptive study investigated all WCG EMS computer aided dispatch (CAD) data for the period 1 August 2017 till 31 July 2018 that indicated a chief complaint of seizures and/or convulsions. Both emergency calls as well as interfacility transfers (IFTs) were included for initial analysis. Basic statistical analyses of all seizure and/or convulsions cases recorded within the Western Cape (WC) were performed in order to describe the demographics of this population of patients with regards to sex, age, incident times, geographical location and number of incidents.

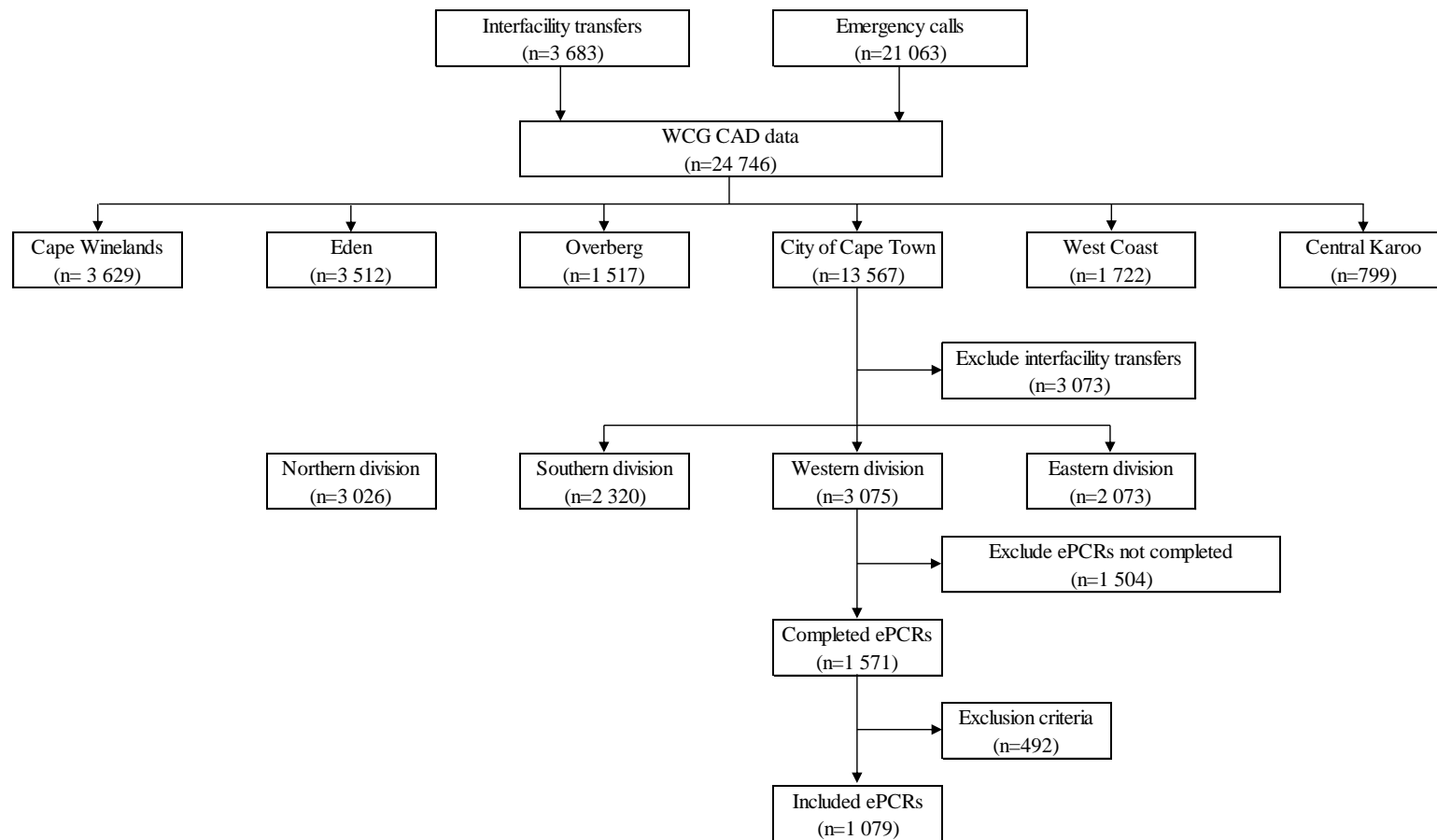
The complete dataset was subdivided as illustrated in Figure 1. Emergency calls originating in the Western division of the City of Cape Town (CoCT) (n=3 075) were selected for more detailed analyses. This sample was selected as this base serves both urban and rural areas, including high, middle- and low-income communities and thus may contribute to the

generalizability of the sample to the study population. CAD reference numbers were compared against the reference numbers of recorded electronic Patient Care Records (ePCR) in order to determine ePCR completion compliance amongst the practitioners in the subsample of data. Corresponding ePCRs for each of the CAD cases were extracted from the WCG EMS call centre database. All completed ePCRs from this sample underwent a clinical chart review. Of the 1571 completed ePCRs, 492 records did not meet the inclusion criteria and were thus excluded from analysis. Exclusion criteria were: ePCRs in which seizures and/or convulsions could not be verified (n=253), children less than 13 years of age (n=142), ePCRs indicating patients refusing treatment and/or transportation (n=77), ePCRs in which pregnancy was documented (n=11), ePCRs indicating patient dead on arrival (n=8), and double bookings of incident (n=1). All relevant information on the ePCRs was then captured onto an electronic spreadsheet. Information captured included on-scene clinical presentation, on-scene vitals, response times, and prehospital treatment provided. Standard descriptive statistical tests including frequency distributions, measures of central tendency (mean) and dispersion (standard deviations) were used to analyse and describe the subsample of patients.

The on-scene clinical presentation was sub-divided into one of three categories, namely general, post-ictal or active convulsions. The general convulsions category (n=561) was assigned to all patients in which a chief complaint of convulsions was recorded, but no further convulsions were witnessed during prehospital care. A working diagnosis of post-ictal (n=389) was assigned to all patients documenting a decreased level of consciousness, confusion or stating post-ictal. A working diagnosis of active convulsions (n=129) was assigned to all patients who were post-ictal on arrival, but a subsequent seizure was witnessed during prehospital care or to patients presenting with SE. Vital signs for respiratory rate (RR), heart rate (HR), blood pressure (BP), and peripheral capillary oxygen saturation (SpO<sub>2</sub>) were recorded as being performed on-scene if the vital signs were recorded during the time spent on scene, if the first vital sign of a set was recorded at the time of departure or if vitals were recorded within the first 20 minutes after arrival on scene in cases where the crew performed a rapid load and go. Additional vital signs (blood glucose levels, temperature and electrocardiogram) were included as on-scene if performed at any time during prehospital care. Incident times were recorded and analysed as dispatch duration (incident recorded until ambulance dispatched), response time (dispatch until arrival on scene) and on-scene time (arrival on scene until departure from scene).

In addition, this study excluded all ePCRs in which pregnancy could be identified as these patients commonly convulse as a result of eclampsia and thus warrant different pharmacological agents. The authors recognize that early trimester pregnancy might have been missed by practitioners. However, eclampsia is commonly associated with the second and third trimester of pregnancy, and it could therefore be assumed that any seizures occurring prior to that had a different mechanism, thus warranting similar pharmacological agents. All children less than 13 years of age were excluded due to the high incidence of febrile convulsions amongst this population of patients.<sup>[10]</sup>

Approval for this study was obtained from both the Human Research Ethics Committee of the University of Cape Town (HREC ref: 753/2018; R014/2017) and the WCG EMS (NHRD Ref: WC\_201811\_026).



**Figure 2. Western Cape Government Computer Aided Dispatch data collection and analysis process**

*CAD: Computer aided dispatch; ePCRs: electronic patient care record; WCG: Western Cape Government*

## **Results**

A total of 24 746 cases were recorded in the WC during the study period including both emergency (n=21 063) and IFT (n=3 683) calls. Demographic information for all cases with a chief complaint of seizures and/or convulsions are displayed in Table 1. The results showed that emergency calls accounted for 85% of recorded calls, with 64% (n=15 815) of calls occurring during dayshifts (07h00 – 19h00). Males accounted for 59% (n=14 061) of the incidents where sex was recorded in the CAD data. The most common age groups requiring prehospital EMS were children < 13 years of age (18.1%, and the 31 – 40 year (16.2% and 41 – 50 year (15.1% age groups.

**Table 1. Western Cape Government Computer Aided Dispatch population demographics**

<i>Variables</i>	<i>Cape Winelands</i> (n=3 629)	<i>Central Karoo</i> (n=799)	<i>City of Cape Town</i> (n=13 567)	<i>Eden</i> (n=3 512)	<i>Overberg</i> (n=1 517)	<i>West Coast</i> (n=1 722)	<i>Total</i> (n=24 746)
<b>Sex</b>							
Male	2 056 (56.7)	417 (52.2)	7 804 (57.5)	1 984 (56.5)	848 (55.9)	952 (55.3)	14 061 (56.8)
Female	1 279 (35.2)	337 (42.2)	4 883 (36.0)	1 203 (34.3)	558 (36.8)	631 (36.6)	8 891 (35.9)
<b>Total</b>							22 952
<b>Age group (years)</b>							
< 13	613 (16.9)	104 (13.0)	2 613 (19.3)	612 (17.4)	242 (16.0)	298 (17.3)	4 482 (18.1)
13 – 20	245 (6.8)	78 (9.8)	872 (6.4)	226 (6.4)	119 (7.8)	147 (8.5)	1 687 (6.8)
21 – 30	473 (13.0)	114 (14.3)	2 038 (15.0)	470 (13.4)	284 (18.7)	220 (12.8)	3 599 (14.5)
31 – 40	524 (14.4)	163 (20.4)	2 252 (16.6)	568 (16.2)	260 (17.1)	244 (14.2)	4 011 (16.2)
41 – 50	585 (16.1)	150 (18.8)	1 997 (14.7)	518 (14.7)	225 (14.8)	258 (15.0)	3 733 (15.1)
51 – 60	494 (13.6)	91 (11.4)	1 619 (11.9)	412 (11.7)	167 (11.0)	218 (12.7)	3 001 (12.1)
61 – 70	302 (8.3)	38 (4.8)	803 (5.9)	221 (6.3)	74 (4.9)	90 (5.2)	1 528 (6.2)
71 – 80	115 (3.2)	15 (1.9)	322 (2.4)	80 (2.3)	54 (3.6)	46 (2.7)	632 (2.6)
> 80	36 (1.0)	5 (0.6)	156 (1.1)	36 (1.0)	16 (1.1)	17 (1.0)	266 (1.1)
<b>Total</b>							22 939
<b>Type of call</b>							
Emergency	3 459 (95.3)	783 (98.0)	10 494 (77.3)	3 310 (94.2)	1 380 (91.0)	1 637 (95.1)	21 063 (85.1)
Interfacility transfer	170 (4.7)	16 (2.0)	3 073 (22.7)	202 (5.8)	137 (9.0)	85 (4.9)	3 683 (14.9)
<b>Total</b>							24 746
<b>Incident time</b>							
Day shift	2 238 (61.7)	527 (66.0)	8 493 (62.6)	2 554 (72.7)	894 (58.9)	1 109 (64.4)	15 815 (63.9)
Night shift	1 391 (38.3)	272 (34.0)	5 074 (37.4)	958 (27.3)	623 (41.1)	613 (35.6)	8 931 (36.1)
<b>Total</b>							24 746

*Values are presented as counts and proportions of column totals in parentheses.*

Emergency calls from the CoCT were distributed amongst divisions according to municipal boundaries, as indicated in Figure 1. The ePCRs were completed in 51% (n=1 571) of all cases managed by Western division practitioners. The commonest reasons for not completing ePCRs were calls cancelled as an ambulance was no longer required on scene (n=432), cancelled by the dispatcher prior to dispatching an ambulance (n=377), patient refused treatment and/or transportation (n=165), and no patient located (n=109). A total of 239 cases were identified in which patients were treated and transported to an emergency care facility, but no ePCR was completed. For the cases with a corresponding completed ePCR (n=1 079), basic demographic information is displayed in Table 2. A known past medical history of epilepsy was documented in 66% (n=716), with 22% (n=155) of these documenting default on antiepileptic drugs. Male patients accounted for 66% (n=716), the mean age attended to was 44 ( $\pm$  16) years, with the majority of calls being in the 31 – 40 years (24.1%) and 41 – 50 (20.8%) year age groups. Call frequency rates showed a steady increase from midnight till early morning, peaking at late morning and then steadily dropping again from midday till midnight.

**Table 2. Demographic characteristics of the Western division subsample**

Variable	n (%)
<b>Sex:</b>	
Male	716 (66)
Female	363 (34)
<b>Total</b>	<b>1 079 (100)</b>
<b>Age</b>	
13 – 20	68 (6.3)
21 - 30	175 (16.2)
31 - 40	260 (24.1)
41 - 50	224 (20.8)
51 - 60	210 (19.5)
61 - 70	77 (7.1)
71 - 80	42 (3.9)
> 80	23 (2.1)
<b>Total</b>	<b>1 079 (100)</b>
<b>Incident times</b>	
00h00 – 03h59	91 (8.4)
04h00 – 07h59	126 (11.7)
08h00 – 11h59	277 (25.7)
12h00 – 15h59	255 (23.6)
16h00 – 19h59	195 (18.1)
20h00 – 23h59	135 (12.5)
<b>Total</b>	<b>1 079 (100)</b>

On-scene clinical presentation analysis indicated that 52% (n=561) of patients presented in the general convulsions category, 36% (n=389) presented in the post-ictal state and 12% (n=129) of patients presented with active convulsions. Of the 1 079 cases, 11% (n=122) were excluded as none of the vitals recorded met the on-scene vital sign criteria, thus leaving 957 cases for on-scene vital signs analysis. Of these cases, excluding ECGs, a mean of 11% of cases had missing on-scene vitals. On-scene and other vital signs recorded are displayed in Table 3 below. The SpO2 recording was missing in 42% (n=402) of cases, with 14.2% (n=79) documenting a SpO2 < 95%. Further analysis showed that patients whom presented with active convulsions (n=129), had missing SpO2 recordings in 42% (n=54) of cases and a documented SpO2 < 95% in 16% (n=20) of cases. A HR > 100 b/min was documented in 36.2% (n=342) of cases. Thirty-six per cent (n=309) of patients presented with a blood glucose level of smaller than 5 mmol/L, or greater than 8 mmol/L.

**Table 3. Recorded on-scene vital signs**

<b>Vital sign</b>	<b>Field completion rate (%)</b>	<b>Mean (±SD)</b>	<b>Proportion of total n (%)</b>	
<b>Respiratory rate</b> (b/min)	99.6	18 (7)	< 12 5 (0.5)	> 20 138 (14)
<b>Pulse oxygen saturation</b> (% SpO <sub>2</sub> )	58.0	N/A	< 95 79 (14.2)	95 -100 476 (85.8)
<b>Heart rate</b> (b/min)	98.9	94 (36)	< 50 1 (0.1)	> 100 342 (36.2)
<b>Systolic blood pressure</b> (mmHg)	97.6		< 90 3 (0.3)	> 200 11 (1.2)
<b>Blood glucose levels</b> (mmol/L)	79.3	N/A	< 5.0 128 (15.0)	> 8.0 181 (21.1)
<b>Temperature</b> (°C)	99.7	N/A	< 35 15 (1.4)	> 38 17 (1.6)
<b>Electrocardiogram</b>	9.5	N/A	N/A	N/A

SD: Standard deviation

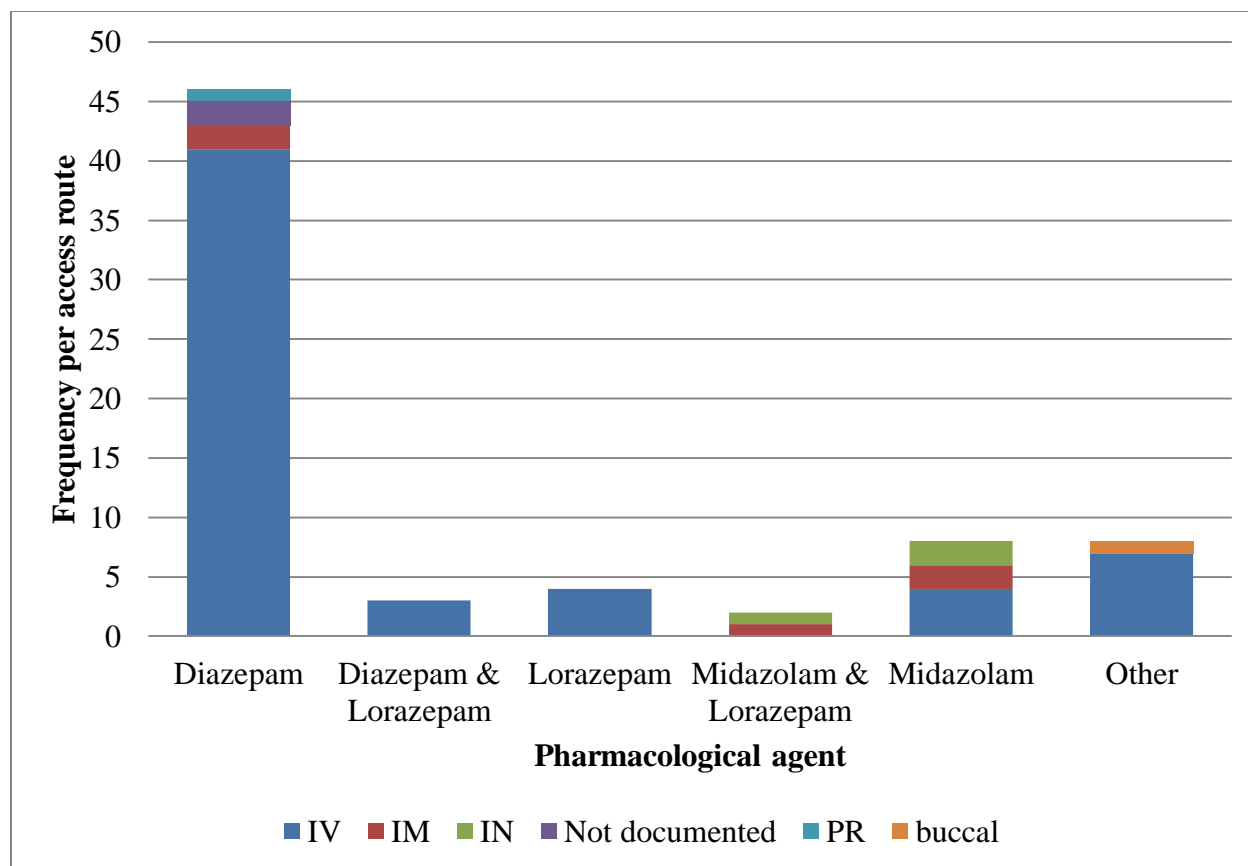
Of the 1 079 cases, two cases were excluded for response time analysis due to missing arrival at scene times and 18 cases were excluded for on-scene time analysis due to missing depart scene times. The mean dispatch time was calculated as 20 ( $\pm 36$ ) minutes, with 29% (n=311) of calls exceeding the mean dispatch time. The mean response time was 14 ( $\pm 10$ ) minutes and the mean on-scene time was 25 ( $\pm 13$ ) minutes.

Prehospital management was recorded under airway, breathing, circulation and pharmacological sections. Management interventions performed are displayed in Table 4. Supplemental oxygen was administered in 20% (n=218) of all cases with the most common device being the venturi face mask (71%). Further supplemental oxygen analysis was performed in patients presenting with a SpO<sub>2</sub> < 95%. Of the 79 patients with a documented SpO<sub>2</sub> < 95%, supplemental oxygen was only provided to 51% (n=40) of patients. A total of 30% (n=319) of patients had successful IV access placement, 3% (n=32) had documented failed IV access and normal saline was the most common (n=238) IV administration fluid.

Pharmacological agents were administered in 7% (n=71) of patients. Of the 71 patients in whom medication was administered, 89% (n=63) received at least one of the benzodiazepines. The most common pharmacological agent administered was diazepam (n=49), with 89% (n=41) of this agent being administered via the IV administration route. The mean dosages administered per agent were 7.7mg ( $\pm 3$ ) for diazepam, 4.4mg ( $\pm 2$ ) for lorazepam and 9.2mg ( $\pm 5$ ) for midazolam. Pharmacological agent administration per administration route is as displayed in Figure 2.

**Table 4. Prehospital management performed in sample**

	<b>Proportion of cases n (%)</b>	<b>Intervention specifications</b>	<b>n (%)</b>
<b>Airway</b>	318 (29.5)	Lateral decubitus position	309 (28.6)
		Oropharyngeal suctioning	3 (0.3)
		Endotracheal intubation	3 (0.3)
		Oropharyngeal airway	2 (0.2)
		Head-tilt chin-lift	1 (0.1)
<b>Breathing</b>	218 (20.2)	Nasal cannula	12 (6.0)
		Venturi face mask	154 (71.0)
		Non-rebreather face mask	26 (12.0)
		Bag valve mask with reservoir	4 (2.0)
		Device not specified	22 (10.0)
<b>Circulation</b>	319 (30.0)	Normal Saline	238 (75.0)
		Lactated Ringers	17 (5.0)
		Saline lock/J-loop	27 (8.0)
		Access not specified	37 (12.0)
<b>Pharmacological</b>	71 (6.6)	Diazepam	46 (65.0)
		Midazolam	8 (11.0)
		Lorazepam	4 (6.0)
		50% Dextrose + Lorazepam	3 (4.0)
		Midazolam + Lorazepam	2 (3.0)
		Other agents	8 (11.0)



**Figure 3. Administration route frequency per pharmacological agents administered**

*IV: Intravenous; IM: Intramuscular; IN: Intranasal; PR: Per rectum*

## Discussion

The first important finding of this study was that the mean dispatch time was 20 ( $\pm 36$ ) minutes with 29% of calls exceeding the mean. There are no previously published studies directly evaluating dispatch times amongst this population of patients. The organisation in which this study was performed adheres to national standards with regards to response interval targets.<sup>[15]</sup> Response intervals however combine dispatch and response times, thus making it difficult to find specific data on dispatch times alone.<sup>[16]</sup> The national standards warrant a P1 urban response interval of < 15 minutes and a P1 rural response interval < 40 minutes.<sup>[15]</sup> It is evident from the current results that response intervals were already exceeded prior to dispatching an emergency vehicle. The WC Department of Health Annual Report 2017-2018 indicated that P1 targets were

only met in 59.5% of urban P1s and 79.3% of rural P1s.<sup>[15]</sup> This finding raises concern as response intervals are used as a key performance indicator in most EMS systems and forms an important indicator of healthcare system quality.<sup>[16]</sup> Furthermore, studies suggest that the patient's prognosis and responsiveness to treatment decreases inversely with the duration of seizures.<sup>[17]</sup> One article suggested that seizures with a duration of more than 30 minutes might have a mortality rate as high as 19%, depending on the total duration, aetiology and age of the patient.<sup>[17]</sup> The Global Burden of Disease Epilepsy Collaborator group indicated that SA was amongst the countries with the highest epilepsy related deaths documented in 2016.<sup>[18]</sup> Thus, the delay in dispatch times directly affects response times and may thus how quickly this population of life-threatening patients receive access to health care.

The second key finding of this study was that a large percentage of ePCRs had missing on-scene vitals. Of the sample (N=1 079), 11% (n=122) of cases had to be excluded from initial on-scene vital signs analysis as none of the recorded vital signs met the on-scene vital sign criteria. Of the remaining cases (n=957), the mean percentage in missing vital signs were calculated at 11% ( $\pm 34\%$ ). International literature has documented missing vital signs amongst 23% of total records reviewed.<sup>[4]</sup> It is difficult to speculate as to why practitioners didn't record on-scene vitals. One speculation is that practitioners might have recorded it during the on-scene period, but only entered it into the ePCR at a later stage and/or not documenting the actual times of vital sign recordings. The recording of initial on-scene vitals forms a critical step in determining the patient's clinical baseline. Studies have indicated that seizures often result in autonomic changes, giving rise to either sympathetic or parasympathetic manifestation, both of which can be life-threatening.<sup>[8]</sup> Furthermore, practitioners may miss easily rectified common underlying causes of seizures such hypo- or hyperglycaemia.<sup>[10]</sup>

The study results further indicated that only 51% (n=40) of patients with a SpO<sub>2</sub> < 95% received some form of supplemental oxygen. No studies could be found directly documenting the frequency amongst which supplement oxygen was provided to patients with a SpO<sub>2</sub> < 95% amongst this population of patients. A study performed by DeLorenzo et al. indicated the causes of mortality amongst status epilepticus patients to be 21% due to anoxia (n=71), 16% due to hypoxia (n=53) and 10% due to cerebrovascular disease (n=33).<sup>[19]</sup> Due to the pathophysiology of seizures, it is typical of patients to present with a brief period of respiratory depression and

thus hypoventilation during or immediately following seizures.<sup>[8,13,20]</sup> Although the value of supplemental oxygen remains uncertain and no evidence could be found showing improved patient outcomes, emergency care experts have discussed this at length. The evidence suggests that supplemental oxygen should initially be administered at 15L/min in actively seizing patients, thereafter it should be titrated, starting with a nasal cannula device, to achieve a SpO<sub>2</sub> between 94% and 98%.<sup>[11,13]</sup> Ictal hypoxemia has been documented to occur in up to 35% of patients.<sup>[11,13]</sup> Due to the correlation between SpO<sub>2</sub> and tissue perfusion, supplemental oxygen administration and returning SpO<sub>2</sub> levels to within normal limits are crucial, especially amongst patients experiencing seizures.

The most common pharmacological benzodiazepine that was administered was found to be diazepam (69%) which was administered via the IV route in 89% (n=41) of cases. The results of this study were not in accordance with the best evidence-based practice suggested within the literature.<sup>[13,21]</sup> Studies have shown that IM midazolam should be preferred to IV diazepam due to its superior first-dose seizure suppression, alternative administration routes, shorter onset of action, and ease of storage when compared to diazepam.<sup>[13]</sup> The RAMPART trial compared different routes of administration with the time intervals to administration and cessation of seizures and found that the IV route had shortened intervals to cessation of seizures whereas the IM group had shorted times to medication administration.<sup>[13]</sup> The NICE guidelines also suggest that IM midazolam should be considered as the first-line prehospital medication and route of administration in patients without an *in situ* IV line.<sup>[21]</sup> The latter no longer recommend that IV or rectal diazepam be considered as the initial medication and routes of administration for patients presenting with status epilepticus.<sup>[21]</sup> It is speculated that practitioners still prefer diazepam to midazolam due to out-dated protocols and due to the perceived fewer adverse effects when compared to midazolam. It is ethically important for practitioners to keep up to date with best evidence based practice recommendation and the described recommendation may decrease the need for IV access placement in the actively convulsing patients, thus limiting the occurrence of needle stick injuries.

Lastly, with regards to the demographic characteristics, the mean patient age was 44 years with the majority of patients falling into the 31 – 40 years (42.1%) and 41 – 50 year (20.8%) age groups. Nair et al. observed a bimodal age distribution amongst their population with the

majority of incidents occurring within the first year of life and in the population aged 60 years and above.<sup>[12]</sup> Contrary to this, Dickson et al. determined that their cohort consisted of more calls originating in the younger compared to the older population, with the majority of calls originating in patients aged 16 to 49 years.<sup>[4]</sup> Our results also indicated that male patients accounted for 66% (n=716) of all patients attended to, which is in agreement with previous reports.<sup>[4,12,22,23]</sup> Our call frequency rates showed a steady increase from midnight till early morning, peaking in the late morning and then steadily dropping again from midday till midnight. The results agreed with Dickson et al. who also reported that call frequency rates peaked during late morning hours.<sup>[4]</sup> We speculate that the observed peak in frequency might be associated with the duration of time required for AEDs to reach therapeutic concentrations after oral ingestion. Oral AEDs reach therapeutic levels after 2.04 – 2.35 hours post oral ingestion.<sup>[24]</sup>

### **Strengths and limitations**

The ePCR system is a relatively new patient information capturing system implemented within the public sector of the WC. As a result, some cases may have been missed due to information being manually captured on paper-based patient report forms. Moreover, the WC also has multiple competing private emergency care services. As a result, this study was not able to draw any robust conclusions regarding the total incidence or prevalence of convulsion in the prehospital emergency care setting. However, to our knowledge, this is the first recorded study describing this population of patients presenting to prehospital emergency care practitioners within South Africa. The information provided in this study will assist in providing fundamental information on which future research and epidemiological studies can build.

### **Conclusion**

Dispatch times directly contribute to response intervals and thus subsequently the duration of time taken to attend to patients with this time-sensitive life-threatening condition. Due to the high epilepsy related mortality rate in SA, more emphasis should be placed on reducing dispatch times for these emergencies.<sup>[18]</sup> Future investigations should focus on investigating the reasons for the delays in dispatch and response times.

The recording of on-scene vitals forms a crucial step in determining the patient's clinical baseline status, and neglecting to do so may lead to the failure to recognise easily rectified underlying causes of seizures, such as hypo- or hyperglycaemia. In addition, supplemental oxygen was only provided to half of patients with a documented SpO<sub>2</sub> of < 95%. Effective prehospital management plays an important part in the overall continuum of patient care, as this is often the first point of access to healthcare. Studies have shown that anoxia (21%) and hypoxia (16%) are common causes of mortality amongst patients with SE.<sup>[19]</sup> Emphasis should be placed on the importance of recording on-scene vitals and providing supplemental oxygen to patients presenting with decreased oxygen saturation.

Lastly, recorded pharmacological agent administration practices are not in accordance with best evidence based practice recommendations.<sup>[13,21]</sup> The literature has shown IM midazolam to be the superior first-line benzodiazepine, especially in patients without an *in situ* IV line, within the prehospital emergency care setting.<sup>[13,21]</sup> It is thus recommended that future training efforts should emphasise evidence based practice recommendations in managing these patients.

### **Conflict of interests**

The authors have no conflicts of interest to declare.

### **Data sharing statement**

Data for this study was formally requested via the National Health Research Database following ethical approval. Should other researchers be interested in the data used within this study, the same formal application process could be followed.

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**PART C: APPENDICES**

## **APPENDIX 1: Instructions for authors**

### **South African Medical Journal: Instructions for Authors**

The journal selected for publication is the South African Medical Journal (SAMJ), as this journal primarily publishes research impacting clinical care within the African continent. The authors of this article believe that the results and recommendations of this study are particularly applicable to African audience.

**Instruction for Authors can be found at the following link:**

<http://www.samj.org.za/index.php/samj/about/submissions#authorGuidelines>

## **APPENDIX 2: Research Protocol**

### **A descriptive study of patients presenting with a chief complaint of seizures to the prehospital emergency care practitioner of the Western Cape**

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**This study is in partial fulfilment of the requirements for a Masters in Philosophy:  
Clinical Emergency Care**


## **Declaration**

I, Beatrix Hendrina Bester, hereby declare that the work on which this thesis is based is my original work (except where acknowledgments indicate otherwise) and that neither the whole work nor any part of it has been, is being, or is to be submitted for another degree in this or any other university.

I authorize the University to reproduce for the purpose of research either the whole or any portion of the contents in any manner whatsoever.

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10. Where I have used the words of others, I have indicated this by the use of quotation marks.
11. I have referenced all quotations and properly acknowledged other ideas borrowed from others.
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14. I am attaching the summary of the Turnitin match overview (when required to do so).

Signature: 

Date: \_\_\_\_22 May 2018\_\_\_\_

## **A descriptive study of patients presenting with seizures to the prehospital emergency care practitioner in the Western Cape.**

### **Background**

Seizures and status epilepticus (SE) are time-sensitive and potentially life-threatening conditions. They account for approximately 1% of all emergencies seen in emergency centres and are a common complaint attended to by prehospital emergency care practitioners (1,2). Diagnosing seizures remains a challenge in both the in-hospital and prehospital emergency care settings (35).

Seizures are broadly defined as a sudden onset of change in behaviour which may be characterized by an alteration in the patient's sensory perception or motor activity (2). As a result of this broad definition, one of the first challenges practitioners face is distinguishing true seizures from other mimicking conditions such as syncope and migraines (2). To complicate matters even more, seizures can further be categorized as unprovoked, acute symptomatic secondary to an acute insult, febrile or psychogenic with epilepsy which usually refers to the occurrence of two or more unprovoked seizures (1). SE is defined as any prolonged activity of more than five minutes, or the presence of multiple seizure episodes without returning to baseline between episodes (36).

Seizures often result in autonomic changes resulting in cardiovascular, respiratory, pupillary and urinary manifestations (4). Studies have suggested that sympathetic responses predominate during most types of seizures and commonly result in increased heart rates, tachypnoea, hypertension, mydriasis and diaphoresis (4). However, patients may present with ictal parasympathetic activity or with an inhibited sympathetic response, during which they may present with increased salivation and gastric acid secretions, miosis, bradycardia and hypotension (4). As a result of the latter, the recording of baseline vital signs forms a critically important part of prehospital emergency care in patients presenting with or suspected of having seizures.

The three biochemical abnormalities most commonly associated with seizures are hypo- or hyperglycaemia and hyponatremia (20). Currently, no data could be found regarding the measurement of blood glucose levels in this population in the Western Cape (WC) prehospital environment. Early and aggressive IV treatment with a first-line medication of benzodiazepines

has been shown to be beneficial (2). Recently, the Rapid Anticonvulsant Medication Prior to Arrival Trial (RAMPART) suggested that early intramuscular administration of Midazolam is superior to alternative administration routes and administration of benzodiazepines in the management of SE (2). However, there is limited data describing current patterns of first-line treatment for these patients in the South African setting.

It has been estimated that up to 2.4% of seizure patients in developed countries gain access to the healthcare system through prehospital emergency medical care services (3). It has also been estimated in the state of Ohio that calls involving suspected seizures account for up to five per cent (5%) of all emergency calls attended to by emergency medical services (EMS) (37).

All South African prehospital healthcare practitioners are required by law to register with the Health Professions Council of South Africa and should follow the protocols as published by the Professional Board of Emergency Care (38). Practitioners are registered according to their scope of practice and include Basic Ambulance Assistants (BAA), Ambulance Emergency Assistants (AEA), Emergency Care Technicians (ECT), paramedics registered as Ambulance Emergency Technicians (ANT) as well as practitioners registered as Emergency Care Practitioners (ECP). With respect to the management of seizures and SE, the BAA scope of practice includes the administration of oxygen, whereas the AEA protocol includes oxygen administration as well as the capability of establishing intravenous (IV) access. Pharmacological management using benzodiazepines is limited to the ECT, ANT and ECP scopes of practice.

As seizures are considered to be a time-sensitive and potentially life-threatening condition, prehospital emergency services are under pressure to meet rapid response time targets. As a result, these complaints are usually considered as Priority one calls which warrant a response with lights and sirens, urgent identification of the condition and aggressive prehospital management (5).

## **Motivation**

Currently, there appears to be a gap in our knowledge with regards to this population of patients within the WC. International research has determined that seizures are one of the most common calls attended to by EMS personnel, however, currently, there is no evidence describing the

number of seizure complaints attended to by prehospital emergency care services within the WC. Information provided from this research could aid in identifying the impact which this population of patients has upon the total call rate of prehospital emergency care services within the Western Cape Government (WCG).

Furthermore, no evidence could be found describing this population of patients within our local context. Demographic information describing this population of patients with regards to age, geographical location, and sex could aid in identifying whether we need to adjust current training practices and potentially suggest a reallocation of resources.

As seizures are considered to be a true medical emergency, the time from onset of seizures till the first encounter with appropriate medical assistance should be minimized. The results of this study will provide us with information regarding the average time intervals spent on each of the stages during prehospital emergency care response and whether there is a need to further prioritize response and on-scene times.

Seizures have been documented to alter the autonomic nervous system's function with regards to the parasympathetic, sympathetic and adrenal medullary systems during the ictal, postictal and interictal stages (4). Studies have suggested that seizure-induced cardiovascular dysfunction, postictal autonomic depressed respiratory reflexes, may contribute to unexplained death in patients suffering from epilepsy (4). As a result of the latter, recording of vital signs and the appropriate subsequent management of alterations in baseline vital signs are critically important. Currently, we have no evidence to suggest which vital signs and clinical presentations are recorded during the prehospital emergency care interaction with this population of patients, nor the subsequent treatment being provided. The result of this study will be able to identify the current data that is recorded by WC prehospital emergency care practitioners and thus could aid us in identifying training and management needs.

Lastly, the results of this study may aid in determining relevant ePCR data fields that were missed during prehospital management and could possibly suggest mandatory fields that have to be captured in this population of patients in the future.

## **Research question**

What are the demographics, clinical presentations and current management patterns of patients presenting with a chief complaint of seizures to the prehospital emergency care practitioner in the WC?

## **Aim and objectives**

This retrospective, descriptive study aims to describe the population of patients who present with a chief complaint of seizures to the prehospital EMS in the WC province of South Africa.

The specific objectives of this study are to:

1. Describe the demographics of patients presenting with a chief complaint of seizures/convulsions in the WC
2. Describe the on-scene clinical presentation of a subsample of these patients
3. Describe the prehospital emergency care provided to these patients
4. Describe the prehospital emergency care response with regards to the incident, dispatch, response, on-scene and overall mission times

## **Study Methodology**

### Study design

This study will be performed using a retrospective, descriptive analysis of clinical and administrative documents.

### Study setting and population

The study will be performed in the prehospital emergency care setting of the Western Cape Government (WCG) EMS. The study will include all electronic Computer Aided Dispatch (CAD) data of calls, including emergencies and inter-facility transfers (IFT) with an identified chief complaint listed as seizures or convulsions, for the specified time period. Furthermore, electronic patient care report (ePCR) forms of patients who presented to the prehospital

emergency care practitioners with a complaint indicating seizures will be included for sub analysis.

#### Data collection, management, and analysis

Data will be collected using a consecutive sampling method from the EMS dispatch centre of the WCG located in Bellville in the WC. We will request deidentified CAD data for all emergency and IFT calls, registered with a chief complaint of seizures/convulsions for the period 1 August 2017 till 31 July 2018. This data will be used to determine epidemiological and demographic information regarding this population of patients. From unpublished reports, we have estimated the number of CAD recoded seizure/convulsion cases to be approximately 25 400 for the WC during the study period.

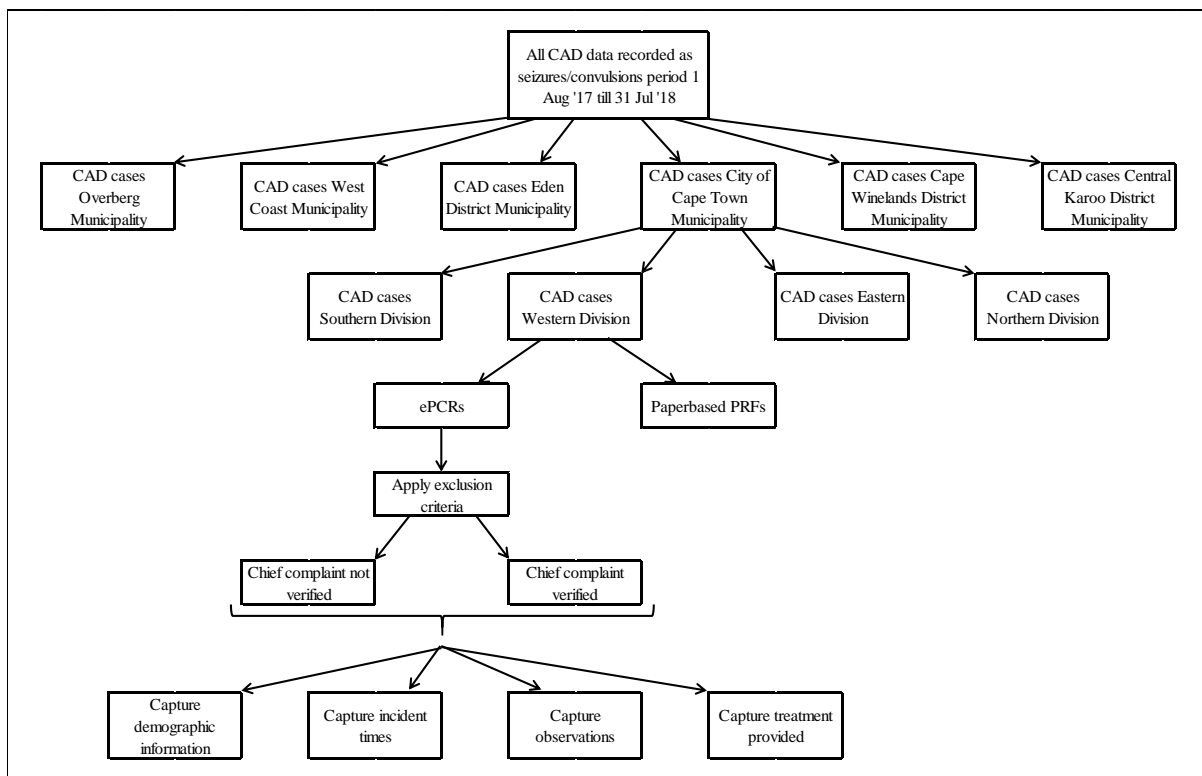
Due to the large number of cases, a sample of the CAD data will be used for clinical analysis. From unpublished quality control data, we know that ePCR completion compliance is the highest amongst practitioners working at the Western Division of the City of Cape Town EMS. The sample for clinical analysis will therefore be identified using CAD data from the Western Division in the City of Cape Town. CAD reference numbers will be compared against the reference numbers of recorded ePCRs in order to determine ePCR completion compliance. All completed ePCRs from the Western Division will be identified and the exclusion criteria applied where after the remaining cases will be included for clinical analysis. The Western Division serves both urban and rural areas, including high-, middle- and low income communities and thus may contribute to the generalizability of the sample to the entire study population.

All identified ePCR forms completed by practitioners stationed at the Western Division for one calendar year period, 1 August 2017 till 31 July 2018, will then be evaluated and captured onto the data collection sheet. A one calendar year period will allow for the inclusion and consideration of seasonal and weather variations. The researcher will then evaluate all ePCRs necessary fields and capture the relevant information. Furthermore, all sections allowing practitioners to enter free text will be evaluated in order to identify whether information captured by practitioners verified an incident complaint of seizures/convulsions. As completion of the working diagnosis field on the ePCR only became compulsory in February 2018 the additional

notes and progress notes fields will also be evaluated for information indicating verification of the complaint. Following the latter, the inclusion and exclusion criteria indicated below will be applied.

Data from all the eligible ePCRs will then be captured onto an electronic data collection spreadsheet in Microsoft Excel and used for statistical analysis (Appendix 1).

Data will be analysed using standard descriptive statistics and interpreted to address the study objectives.



**Figure 4. Representation of the 2017 ILAE Classifications of seizures**

### **Inclusion criteria**

All ePCRs identified from the CAD database with a chief complaint documented as seizures/convulsion.

All ePCRs completed by WCG prehospital emergency care practitioners serving Western Division under the City of Cape Town Municipality boundary.

All ePCRs completed during the period 1 August 2018 till 31 July 2018.

### **Exclusion criteria**

All ePCRs indicating a CAD chief complaint of seizures/convulsions in children less than 13 years of age will be excluded due to the high incidence of febrile seizure in this population of patients (20). Febrile seizures are considered the most common first-time onset seizure in childhood with an approximate single incidence rate of four per cent amongst children younger than five years of age (39). Although these children are commonly transported by EMS to ECs, febrile seizures are most often found to be benign, self-terminating and seldom requires specific medical interventions (39).

All ePCRs indicating a CAD chief complaint of seizures/convulsions in which the entered free text areas or current medical history indicates that the patient is pregnant, and thus subsequently may be suffering from pregnancy-related seizures. Seizure activity during pregnancy is usually assumed to be eclampsia, and thus managed accordingly, until proven otherwise (40). As a result of the latter, the management of seizure activity during pregnancy may differ significantly from seizures due to other aetiologies and thus will be excluded from the subsample for clinical analysis.

All ePCRs indicating a CAD chief complaint of seizures/convulsions where the patient refused treatment and/or transportation to a medical facility and a refusal triage transport slip number can be identified.

All ePCRs from the interfacility transfer group with an incident type of seizures and/or convulsions will be excluded as this may result in duplication of data entries.

### **Ethical considerations**

The primary researcher will apply for ethics approval from the University of Cape Town's (UCT) Human Research Ethics Committee (UCT HREC) prior to conducting this research. The WCG EMS call centre registry which includes the CAD and ePCR records has been successfully registered with UCT HREC (R014/2017). The researcher will also apply for facility approval

from the WCG EMS' director in order to gain access to medical treatment fields completed on eligible ePCRs.

Data from the included ePCRs will be allocated according to their individual incident numbers only and thus no personal details of patients or practitioners will be identified in order to keep personal information confidential in order minimize the risk of group harm. Incident numbers will be captured on the data collection tool in order to prevent duplication of data capturing. Only data points identified in Appendix 1 will be extracted from eligible ePCRs and captured onto the data collection tool for analysis.

All data required from the ePCRs will be captured by the primary researcher onto a password protected data collection tool on a password protected computer. Printed ePCRs will be kept in a locked cupboard in a secure building at the WCG EMS offices in Bellville until all data could be captured onto the data collection tool by the end of the suggested data collection timeframe. Once data collection has been completed, all printed copies will be destroyed in a secure manner by means of shredding. Electronic copies of ePCRs will be kept in a secure, locked cupboard on a password-protected hard drive at the EMS Building in Bellville.

The study poses a minimal risk as it will use a retrospective descriptive study design, reporting on what information was captured on the ePCR database. Further, the risk for harm will also be minimized by ensuring confidentiality and anonymity by not reporting on any identifying information of neither the attending practitioners nor the patients included in this study.

The potential benefits of this study include providing us with fundamental demographic information on this population of patients specific to the WC context. Furthermore, this may identify criteria on which future training programs need to focus. The results of this study will also assist in quantifying the number of cases attended to by prehospital emergency care practitioners of the WCG which may aid in resource allocation, identifying future training and research needs and form a basis on which other research can be based.

## **Timeframe**

- Submission of a full research proposal and data collection tool to UCT’s Emergency Medicine Divisional Research Committee by May 2018.
- Proposal submission to the UCT HREC for approval by October 2018.
- Submission of facility approval to WCG Emergency Medical Care Services ethics committee by November 2018.
- Submission of all necessary documentation submitted to UCT’s Post graduate office (PGO) by November 2018.
- Data collection and analysis from November till January 2018.
- The write-up of the final results from January till February 2018.
- Submission of D8 forms to PGO by end of January 2018.
- Final submission by March 2018.

**Budget**

A layout of the estimated expenditures are indicated below (Table 1) and will be funded by the researcher.

**Table 5. Estimated expenditure**

<i>Expenditure:</i>	<i>Estimated cost:</i>	<i>Total cost:</i>
<i>Paper (1000 pages)</i>	R 300.00	
<i>Printing (600 pages at R2.00/page)</i>	R1 200.00	
<i>Calls and Internet data</i>	R1 000.00	
<i>Traveling cost to and from WCG EMS dispatch centre for data collection</i>	R1 000.00	.....
		R3 500.00

**Limitations**

The researchers acknowledge that the ePCR system is a relatively new patient information capturing system implemented in the government sector of the WC. As a result, some cases may be missed due to information being manually captured on paper-based patient report forms. Moreover, the WC also has multiple competing private emergency care services. As a result, this study will not be able to draw any conclusions regarding the incidence or prevalence of seizures in the prehospital emergency care setting.

The researcher acknowledges that some of the ePCR information fields may be incomplete or missing. This study will report on the fields with missing data, however, due to the study design will not be able to address specific reasons as to why certain fields were not completed as a qualitative study design would be required in order to answer these questions.

As a result of the challenges faced with diagnosing complaints or a history of seizures as true neurogenic seizures, the researchers acknowledge that some patients may be misdiagnosed. As a result, the study will not be able to verify the accuracy of the documented prehospital diagnosis but will rely solely on the working diagnosis as stated by the prehospital emergency care practitioner and thus report on information collected from these ePCRs.

Paediatric patients will be excluded from this study due to their high incidence of febrile seizures (20).

Although drug doses administered will be documented, this study will not be able to determine whether the appropriate doses of Benzodiazepines were administered, as the estimated weight of the patient is currently not a compulsory field on the ePCR.

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## APPENDIX 3: Human Research Ethics Committee Approval Letter



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



Room E53-46 Old Main Building  
Groote Schuur Hospital  
Observatory 7931  
Telephone: (011) 406 6631  
Email: [phurella.thomas@uct.ac.za](mailto:phurella.thomas@uct.ac.za)  
Website: [www.health.uct.ac.za/fhs/research/humanethics/form](http://www.health.uct.ac.za/fhs/research/humanethics/form)

22 November 2018

**HREC REF: 753/2018**

**Dr Coleen Saunders**  
Emergency Medicine  
F51, OMB

Dear Dr Saunders

**PROJECT TITLE: A DESCRIPTIVE STUDY OF PATIENTS PRESENTING WITH SEIZURES TO THE PREHOSPITAL EMERGENCY CARE PRACTITIONER IN THE WESTERN CAPE (MPHIL Candidate - Ms B Bester)**

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

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 November 2019.**

Please submit a progress form, using the standardised Annual Report Form 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](http://www.health.uct.ac.za/fhs/research/humanethics/forms))

**Please quote the HREC REF in all your correspondence.**

Please note that the ongoing clinical 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.

**The HREC acknowledge that the student, Beatrix Bester will also be involved in this study.**

*Yours sincerely*

Signature Removed

**PROFESSOR M. BLOCKMAN**  
**CHAIRPERSON, FHS HUMAN RESEARCH ETHICS COMMITTEE**  
Federal Wide Assurance Number: FWA00001637,  
Institutional Review Board (IRB) number: IRB00001938

HREC 753/2018

This serves to confirm that the University of Cape Town Human Research Ethics Committee complies to the Ethics Standards for Clinical Research with a new drug in patients, based on the Medical Research Council (MRC-SA), Food and Drug Administration (FDA-USA), International Convention on Harmonisation Good Clinical Practice (ICH GCP), South African Good Clinical Practice Guidelines (DoH 2006), based on the Association of the British Pharmaceutical Industry Guidelines (ABPI), and Declaration of Helsinki (2013) guidelines.

The Human Research Ethics Committee granting this approval is in compliance with the ICH Harmonised Tripartite Guidelines E6: Note for Guidance on Good Clinical Practice (CPMP/ICH/135/95) and FDA Code Federal Regulation Part 50, 56 and 312.

## APPENDIX 4: Western Cape Government Emergency Medical Services Approval Letter



DIRECTORATE: **EMERGENCY MEDICAL SERVICES**

ENQUIRIES: **Dr Shaheem de Vries**

📧 shaheem.devries@pgwc.gov.za

☎: +27 21 508 4523

**Attention: Ms. B. Bester**

**RE: A DESCRIPTIVE STUDY OF PATIENTS PRESENTING WITH SEIZURES TO THE PREHOSPITAL EMERGENCY CARE PRACTITIONER IN THE WESTERN CAPE**

Dear Ms. Bester,

Your request on the above matter refers.

Thank you for the request to conduct research within the Western Cape Government Emergency Medical Services. Your proposal has been evaluated by the Emergency Medicine Division Research Committee and has been recommended for approval by this office.

**I am therefore pleased to inform you that such approval is hereby granted.**

I wish you well in your endeavor and trust that you will keep this office and its department informed of your findings when these become available. I am so looking forward to the insights that your research will afford us.

Yours sincerely

Signature Removed

**Dr Shaheem de Vries**

Head: Emergency Medical Services  
Western Cape Government Health

**Date:** 22<sup>nd</sup> December 2018