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Planning a clinical trial for the Strokefinder MD100 in the Western Cape region

For diagnosing and triaging stroke and traumatic brain injuries in the Western Cape healthcare system, South Africa

Master's thesis in Biomedical Engineering

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CHALMERS UNIVERSITY OF TECHNOLOGY

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Abstract

Stroke and traumatic brain injury (TBI) represent major causes of mortality and long-term disability globally, with particularly high burden in low- and middle-income countries (LMIC), such as South Africa. The Strokefinder MD100 is a portable device intended for diagnosis and triage of stroke and TBI. This master's thesis aimed to investigate how clinical trials are conducted within the Western Cape (WC) healthcare system in order to develop a proposal for how, theoretically, a clinical study of the device could be designed and conducted in this context. The study was based on literature studies together with interviews with stakeholders from emergency medicine, neurology, trauma care, prehospital care, academia, and healthcare management in the Western Cape region. The findings suggested that a potential clinical trial could begin with a feasibility and validation study in a tertiary public hospital setting, where device findings are compared to confirmatory CT images as the gold standard, followed by a later phase, investigating possible effects on referral pathways and time-to-treatment within emergency medical services (EMS) and lower level healthcare facilities.

Keywords: Stroke, Traumatic Brain Injury, South Africa, Western Cape region, Clinical Trial, Healthcare, Clinical Study Design

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Sofia Börjesson Rintala, Tilde Kvarnström, Gothenburg, June 2026

List of Acronyms

Below is the list of acronyms that have been used throughout this thesis listed in alphabetical order:

3I-SS	3-item stroke scale
ALS	Advanced Life Support
APSS	Austrian Prehospital Stroke Scale
BLS	Basic Life Support
CPSS	Cincinnati Prehospital Stroke Scale
CRO	Clinical research organisation
CT	Computer tomography
DALY	Disability-adjusted life year
EMS	Emergency medical services
FDA	Food and Drug Administration
FAST	Face, Arms, Speech, Time
G-FAST	Gaze, Face, Arms, Speech, Time
GCS	Glasgow Coma Scale
HREC	Health Research Ethics Committee
HTA	Health technology assessment
ICER	Incremental cost-effectiveness ratio
ILS	Intermediate Life Support
INMB	Incremental net monetary benefit
LAPSS	Los Angeles Prehospital Stroke Screen
LMIC	Low- and middle-income country
MRI	Magnetic resonance imaging
NMB	Net monetary benefit
NIHSS	National Institutes of Health Stroke Scale
PI	Principal investigator
QALY	Quality-adjusted life year
SAHPRA	South African Health Products Regulatory Authority
SANCTR	South African National Clinical Trials Register

SATS	South African Triage Scale
TEWS	Triage Early Warning Score
TBI	Traumatic brain injury
UHC	Universal health coverage
WC	Western Cape
WTP	Willingness to pay

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1

Introduction

This chapter provides the theoretical and contextual background for the thesis and concludes by presenting the purpose, objectives and limitations of the study.

1.1 Background

This section provides the necessary theoretical and contextual background on stroke and traumatic brain injury in South Africa, including treatment and workflow principles, the organisation of healthcare in the Western Cape region, the Strokefinder MD100 and relevant economic concepts.

1.1.1 Stroke

A stroke is a medical emergency that can lead to permanent damage on the brain, long-term disability or even death [1]. It is one of the leading causes of death and disability worldwide, accounting for approximately 5.2 % of all mortalities worldwide [2]. Out of these 5.2 %, about 70 % of deaths and 87 % of stroke-related disabilities occur in low- and middle-income countries, and during the last years it has been a consistent increase in stroke incidence in the same countries [3].

The blood is responsible for transporting oxygen and nutrients to the brain cells, and a blockage of this can lead to brain injury. [4]. To what extent a person is affected by a stroke depends on what area of the brain the stroke has damaged and to what extent [5]. It can have consequences on crucial aspects of a human being such as how the person thinks, moves and behaves [5]. There are multiple different consequences from suffering a stroke, some possible consequences includes difficulty speaking, loss of hearing/vision/touch, seizures, problems with the language, memory or speech, muscle weakness and loss of strength [6]. Stroke can affect individuals of all ages and is associated with risk factors that can be modifiable or non-modifiable [5]. Although certain factors, such as age, can not be influenced, a substantial proportion of strokes are considered preventable through interventions of lifestyle and management of underlying risk factors [4]. Examples of modifiable risk factors include overweight and obesity, hypertension, elevated cholesterol levels, smoking, and excessive alcohol consumption [5].

There are two different types of stroke, ischaemic and haemorrhagic stroke, where both types stop blood from getting to areas of the brain but do so in different ways[5]. Stroke signs and symptoms are often similar for both types of stroke, but differ depending on what part of the brain is affected [6].

1.1.1.1 Ischaemic stroke

Ischaemic stroke is the most common type of stroke, and account for about 90 % of all strokes, and occurs when blood supply to the brain is blocked [1]. The blockage can occur due to different reasons, but is commonly due to a blood cloth blocking the supply [4]. The cloth standard forms in one of the large vessels that supplies blood to the brain or in the heart, and then travels up to a vessel in the brain. There are multiple reasons for an ischaemic stroke and some of the leading causes includes arteriosclerotic plaques of the cerebral vessels, cardiogenic cerebral infarction and lacunar infarcts from small vessel lesions [2]. Other causes include different heart conditions such as atrial fibrillation or damage to the heart, small blood vessles due to diseases or a dissection in a neck artery [4].

1.1.1.2 Haemorrhagic stroke

Haemorrhagic stroke is when a blood leak caused by a burst or broken vessel injuries the brain [7]. The leaked blood results in pressure in the brain and on the brain cells which can lead to damage [1]. There are two different types of haemorrhagic stroke, intracerebral or subarachnoid haemorrhage, and they differ based on where the bleeding is occurring[7]. An intracerebral haemorrhage is when an artery within the brain bursts or break leading to bleeding into the brain itself, whereas a subarachnoid haemorrhage is when the bleeding is occurring on the surface of the brain between layers of membranes that cover it. The main cause for haemorrhagic stroke is hypertension, where the high blood pressure breaks arteries within the brain. Other possible causes include cerebral amyloid angiopathy, blood-thinning medication, vascular malformations or aneurysm.

1.1.1.3 Stroke treatment

When a stroke is suspected the diagnosis is determined based on the patient's symptoms, medical history, physical examination and various diagnostic test results [8]. The purpose of the diagnosis is to identify the type of stroke, its underlying cause, and the affected region of the brain. Rapid testing is essential, as an earlier diagnosis enables faster initiation of the appropriate treatment. The choice of treatment depends on whether the stroke is ischemic or haemorrhagic and on the time elapsed since symptom onset [9]. While the specific diagnostic tests may vary due to resource availability and time, standard practice involves imaging of the cerebral blood vessels using computer tomography (CT) or magnetic resonance imaging (MRI), which provide

detailed brain images [8].

Treatment of ischemic stroke focuses on restoring blood flow to the brain [10]. This can be achieved through emergency intravenous medication, known as thrombolysis, or through a mechanical stent retriever procedure, referred to as thrombectomy. Thrombolysis is the most widely used treatment for ischemic stroke and has demonstrated clinical effectiveness when given within 4.5 hours of stroke onset [2]. The treatment works by recanalizing and reperfusing cerebral arteries using a thrombolytic agent. Thrombectomy is performed in cases involving large clots where thrombolytic drugs cannot completely dissolve the cloth [10]. The procedure is carried out using a catheter-based device that directly removes the clot and is commonly performed in combination with thrombolysis.

Treatment of haemorrhagic stroke focuses on controlling the bleeding and reducing the pressure in the brain [10]. The primary treatment options are medication and surgery [11]. The medication is administrated to enhance the body's natural clotting ability or to maintain the blood pressure within a safe range. Surgical intervention may be required to remove accumulated blood if intracranial pressure becomes excessively high.

Following emergency treatment, the patient requires close monitoring and undergoes individualized stroke care [10]. The objective of post-stroke care is to restore as much functional ability as possible and to enable the patient to regain independence in daily life. The type of care required depends on the extent and location of the brain damage, as impairments are closely related to the affected brain regions. The right side is commonly associated with motor control, while the left side is primarily related to language and speech.

1.1.1.4 Stroke in Africa

Historically, stroke has been relatively uncommon in Africa [12]. However, today the continent has some of the highest incidence of stroke burden in the world, with an incidence estimated to be two to three times higher than in Western Europe, and global statistics have identified a consistent increase in stroke in low- and middle income countries.

Since the year 2000, stroke has been the most common cause of death in South Africa after HIV/AIDS and coronary artery disease [2]. During the last two decades, the stroke burden has increased as the population has undergone a rapid epidemiological transition, including a rise in stroke risk factors and an increasingly aging population. The stroke incidence has been rising in sub-Saharan Africa, including South Africa, largely due to significant socioeconomic and epidemiological changes leading to non-communicable diseases and a growing elderly population [13]. Studies of stroke patients in South Africa have demonstrated a lower mean age at stroke onset compared to high- and upper-middle-income countries. Among the majority of

these patients, several modifiable risk factors have been identified, including hypertension and diabetes. Africa has the highest burden of hypertension worldwide, which is considered one of the most significant risk factors for stroke, as individuals with hypertension have a three- to four-fold increased risk of experiencing a stroke.

In recent decades, numerous initiatives have aimed to establish more stroke units across South Africa in order to improve the care of stroke patients [13]. At the same time, knowledge and awareness of stroke have increased across the continent. The improved understanding of risk factors has contributed to greater availability of information to the African population [12]. Despite these improvements, significant challenges remain. Limited affordability, accessibility and availability of essential neuroimaging services confines accurate stroke diagnostics in many African settings. Additional challenges include underdeveloped EMS, where emergency care faces regulatory and organisation difficulties, transportation delays, and poor ambulance availability. As a result, many individuals who suffer a stroke in South Africa have limited access to both acute stroke care and subsequent rehabilitation [13].

1.1.2 Traumatic brain injury

A traumatic brain injury refers to damage to the brain caused by an external force [14]. Such forces may arise from a blow to the head, a bump or jolt of the head, or external objects penetrating the skull and brain tissue. Each year an estimated 5.5 million individuals suffer severe TBIs worldwide, and according to the World Health Organization, approximately 90 % of TBI-related deaths occur in LMIC [15]. In these regions, the incidence is estimated to be 1.5 to 2.5 times higher than the global average [16]. Sub-Saharan Africa in particular has a large burden of this because TBIs frequently affects young people, leading to long-term disabilities which imposes large social and economic consequences [17].

TBIs can be categorized in multiple ways depending on the characteristics of the injury, looking at if the injury is penetrating or closed, primary or secondary, or focal or diffuse [17]. A penetrating TBI occurs when an object breaches the skull and directly damages brain tissue, for instance in the case of gunshot wounds or bone fragments [14]. In contrast, closed TBIs occur when external forces cause the brain to move within the skull without entering the skull. The distinction between primary and secondary injury relate to the timing of damage, primary injuries occur at the moment of impact, while secondary injuries develop over time as a consequence of physiological responses triggered by the initial trauma. Furthermore, focal injuries are localized to a specific brain region, whereas diffuse injuries affect larger areas of the brain. The severity of a TBI is classified according to the Glasgow Coma Scale (GCS), together with the duration of unconsciousness and the length of post-traumatic amnesia [17]. The consequences of TBI can range from temporary impairments to lifelong disability or death [14].

The cause of TBI differ depending on demographic, socioeconomic, and geographical factors [15]. In sub-Saharan Africa, the leading causes are road traffic accidents, assault and falls [17]. Falls are more frequently observed among children and elderly individuals, while traffic-related injuries and assaults are more common among young adults. Mortality associated with TBI is the highest in cases involving firearms, followed by road traffic incidents. A study conducted at Groote Schuur Hospital in Cape Town over a two-month period in 2022, including 522 patients with suspected TBI, identified blunt force trauma, sharp force trauma, and gunshot wounds as the most common causes [16].

Treatment strategies and the possibility of recovery following TBI depend strongly on the extent and location of the brain injury [14]. CT is a crucial tool in the clinical evaluation and management of TBI patients [16], as it allows rapid identification of intracranial bleeding and changes in the patients neurological status [17]. A comprehensive analysis from 2021, which included 107 studies and where more than half originated from South Africa, reported that craniectomies was the most frequently used surgical treatment for TBI followed by burr hole procedures [18].

1.1.3 Strokefinder MD100

Strokefinder MD100 is a medical device intended for the diagnosis and triage of both TBI and stroke [19]. The portable device was developed by the former company Medifield Diagnostics. It is designed as a headrest that can be placed on an ambulance stretcher or a hospital bed and secured using a fastening mechanism that does not cause discomfort to the patient [20]. The device contains eight antennas arranged in four pairs. Three of the pairs are mounted on adjustable arms, while one pair is positioned at the base of the unit in contact with the back of the patient's head. Strokefinder MD100 operates using an AI-based algorithm trained to recognize stroke patterns. The measurement is initiated from a tablet computer that is wireless connected to the device [20]. Once activated, the measurement takes approximately two minutes to produce results. The output is objective and not influenced by patient characteristics such as age, sex or ethnicity. The device uses microwave technology and is considered harmless to both the patient and the operator. The version that received CE verification in 2022 demonstrated a sensitivity of 97 (95% confidence interval 0.80-1.0) and a specificity of 0.48 (95% confidence interval 0.35-0.60).

The operation of Strokefinder MD100 does not depend on advanced infrastructure, making it potentially suitable for use in low-resource settings, such as rural or peripheral metropolitan areas in the Western Cape region [19].

1.1.4 Health economy

Stroke care accounts for an estimated 3-4% of total healthcare expenditure in high-income countries, with the average lifetime cost per individual with ischemic stroke in the United States estimated at approximately 140 000 USD [21]. In contrast, there is limited evidence describing the economic impact of stroke in low- and middle-income countries. Data from rural South African setting indicate a substantially higher burden, with 1552 disability-adjusted life years lost per 100 000 person-years around double the estimates reported for high income countries during the same period. In this context, stroke related healthcare costs are estimated to account for 1.6-3% of total health expenditure. The overall economic burden extends beyond direct medical costs, as informal care and loss of productivity contribute significantly to the total societal cost [21].

To evaluate implementation of a medical device it is important to consider the health economy aspect. Disability-adjusted life years (DALY) are a commonly used metric for quantifying the burden of disease, injury and risk factors in populations. The concept is based on both economic and ethical considerations and provides a framework for comparing health outcomes across conditions. Another metric is Quality Adjusted Life Year (QALY), it is based on amount of days free from disability [22]. It is calculated by multiplying disability free days, x with the quality of life value, that is estimated by the patient. The quality of life value ranges from 0 to 1, where 0 corresponds to death and 1 to perfect health. Total QALY can be calculated by multiplying QALY with the number of patients n, the device is used on per year and the device lifetime [22].

$$\text{QALY} = \frac{x}{365} \times \text{quality of life value}$$

$$\text{Total QALY} = \text{QALY} \times \text{n} \times \text{device lifetime}$$

The incremental cost-effectiveness ratio (ICER) is calculated using the relationship between changes in costs and health outcomes [22]. In context, C represents the additional costs associated with an intervention, while B denotes the corresponding health benefit, typically expressed in QALYs. The parameter λ refers to the threshold value, the maximum willingness to pay (WTP) per QALY gained. The ICER therefore indicates the additional cost required to achieve one extra unit of health benefit. An intervention is considered economically favorable when the Incremental Net Monetary Benefit (INMB) is positive. The INMB framework combines both costs and health outcomes into single monetary measure, allowing for a direct assessment of value. It represents the net benefit of adopting a new intervention compared to an alternative, given a specified WTP threshold [22]. Here, NMB_{new} represents the net monetary benefit of the new intervention, while $\text{NMB}_{\text{alternative}}$ represents the net monetary benefit of the comparator or

existing standard of care.

$$\text{ICER} = \frac{\Delta C}{\Delta B} < \lambda$$

$$0 < \lambda \Delta B - \Delta C \quad \Rightarrow \quad \text{INMB} > 0$$

$$\text{INMB} = \text{NMB}_{\text{new}} - \text{NMB}_{\text{alternative}}$$

1.1.5 Healthcare in South Africa

The healthcare system in South Africa is a two-tiered healthcare system with one public and one private sector. The public sector is governmentally funded whereas the private sector is financed by medical aid schemes and individuals [23]. Around 80% of the South African population is served by public healthcare which is tax financed and suffers from underfunding, long waiting times and a lack of medical supplies. Private healthcare offers a wider range of services and higher standards, showing a clear resource imbalance between the sectors. It is estimated that less than 15% has access to private healthcare through being enrolled in a private voluntary insurance.

Since the 1994 South Africa has pursued universal health coverage (UCH) to address historical disparities and progressively improve all South Africans right to good quality healthcare. Fulfilling that is however challenging due to resource constraints [24]. If the UCH would be successfully implemented, national health insurance fund will provide common health benefits package, where services from both private and public healthcare sectors can be purchased, from one single payer.

1.1.5.1 Public healthcare

The public healthcare sector is organized into different categories of hospitals, namely district, regional and tertiary, as illustrated in figure 1.1. They are classified according to the level of care and service complexity as well as size [25] [26]. Generally, the first point of entry is often through primary healthcare facilities, also referred to as clinics. From there patients are transferred to either district, regional, tertiary, central or specialized hospitals.
There are small, medium and large district hospitals and they all serve defined populations within health districts and support primary healthcare facilities with services as in-patient, ambulatory health services and emergency health services. The small size district hospital has 50 to 150 beds, the medium size has 150 to 300 beds and the large size has 300 to 600 beds. Regional hospitals receives referrals from different district hospitals providing 24 hours healthcare services to a regional population, limited to boundaries between provinces. They have 200 to 800 beds. Tertiary hospitals has 400 to 800 beds and are not limited to provincial boundaries. Central

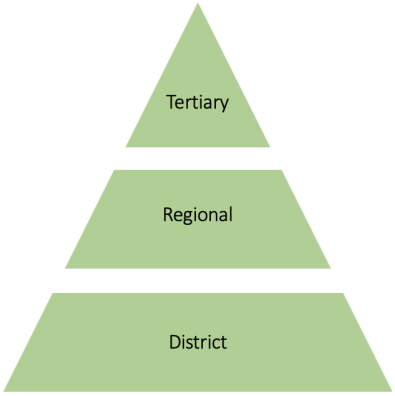

Figure 1.1: SA public healthcare hierarchy, with tertiary hospitals at the top followed by regional and district at the bottom

hospitals serves patients across provinces, providing tertiary hospital services, and in some cases provide national referral services that can include conducting research. Figure 1.2 illustrates the general referral pathway for patients in the Western Cape region [27]. In table 1.1 the CT capability of the different level hospitals are shown [28].

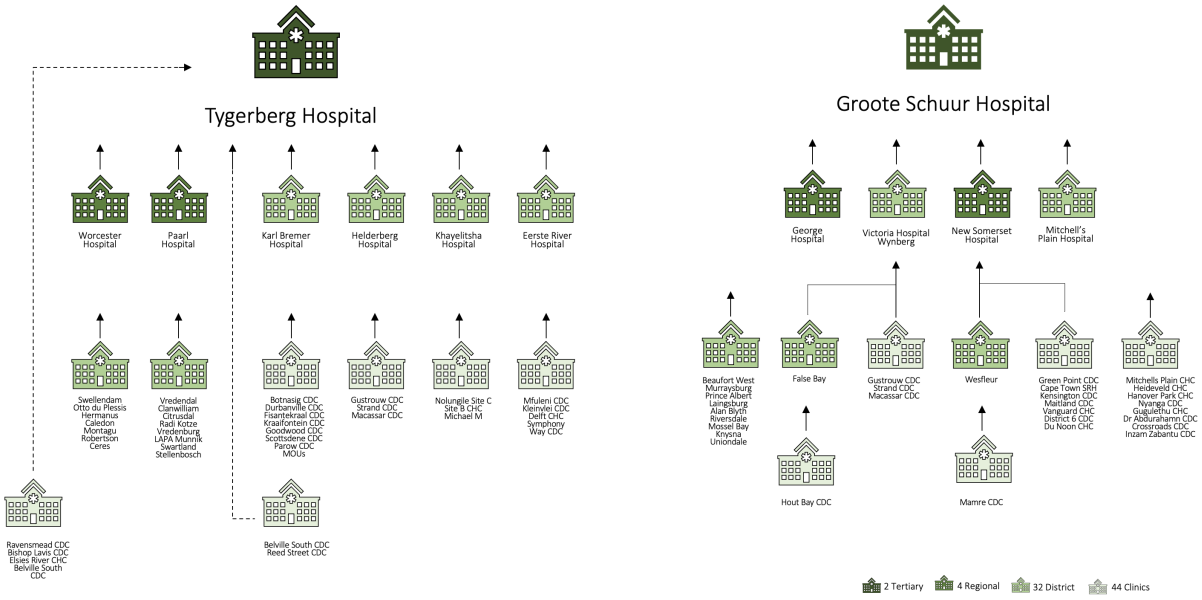

Figure 1.2: General patient referral pathway between hospitals in the Western Cape region

In table 1.2 an overview of hospitals in WC with their level, CT availability, and their referral distance is provided [28].

1.1.5.2 Private healthcare

The private healthcare sector is financed by medical aid schemes and individuals, offering a wider range of services with higher quality than the public sector [23]. It is estimated that the

Level	Facility Description
Level 1	Clinics and district hospitals without CT
Level 2	District and regional hospitals with CT (operating hours: 8 a.m. to 4 p.m. typically)
Level 3	Tertiary hospitals with CT capability 24/7

Table 1.1: Facility levels and CT availability

private sector has, on average, a 13-fold greater availability of CT and comparable imaging modalities than the public sector [29]. There are multiple different private healthcare providers in the Western Cape region including Mediclinic Southern Africa and Netcare [30][31]. It is estimated that about 28% of South African population access the private healthcare, among those a rather big segment are not insured, has a low income and pay for the services out of pocket. It is estimated that less than 15 % of the population has an enrollment in private voluntary health insurance [24].

1.1.5.3 Emergency medical services

There are both private and public emergency medical services and they are divided into provinces, funded by the government and governed by the Provincial Departments of Health [32]. They provide Basic Life Support (BLS), Intermediate Life Support (ILS), and Advanced Life Support (ALS) ambulance based emergency care throughout the provinces. In addition to prehospital clinical care, EMS is responsible for emergency medical response services [33].

The emergency care burden in Western Cape is substantial. More than one million patients present to emergency departments in the province annually, and approximately 40% of these patients arrive via ambulance transport [33]. Of the total emergency case load, roughly 40% consists of trauma related injuries, while the remaining 60% comprises medical cases, including surgical, paediatric, and obstetric emergencies.

Response times is critical in EMS settings, in rural or out of town areas of the Western Cape, average response times approach the national benchmark of 40 minutes, with approximately 60% of responses occurring within this target [33]. Although, there is a lot of variability and individual cases can deviate a lot from the mean. This is highlighting the challenges in achieving equitable and timely emergency response across geographically diverse areas of the province. Internationally, a common cited benchmark for ambulance provision is one ambulance per 50 000 population [32]. In contrast, South Africa's national norm is one ambulance per 10 000 people, adjusted according to socioeconomic and geographic distribution. Despite this high ambition, no province has achieved this national norm. In addition to resource limitations, workforce preparedness presents further challenges. A review of emergency care providers' knowledge, attitudes, and practices suggests deficiencies, particularly among basic and interme-

Hospital	Level	CT	Referral [distance]	Referral [distance]
Tygerberg	Tertiary	Yes	-	-
Worcester	Regional	Yes	-	Tygerberg [96 km]
Paarl	Regional	Yes	-	Tygerberg [47 km]
Karl Bremer	District	Yes	-	Tygerberg [4.6 km]
Helderberg	District	No	Tygerberg [41 km]	-
Khayelitsha	District	Yes	-	Tygerberg [27 km]
Eerste River	District	No	Tygerberg [22 km]	-
Swellendam	District	No	Worcester [111 km]	-
Otto du Plessis	District	No	Worcester [151 km]	-
Hermanus	District	No	Worcester [119 km]	-
Caledon	District	No	Worcester [90 km]	-
Montagu	District	No	Worcester [73 km]	-
Robertson	District	No	Worcester [47 km]	-
Ceres	District	No	Worcester [55 km]	-
Vredendal	District	No	Paarl [270 km]	-
Clanwilliam	District	No	Paarl [197 km]	-
Citrusdal	District	No	Paarl [144 km]	-
Radii Kotze	District	No	Paarl [109 km]	-
Vredenburg	District	No	Paarl [143 km]	-
LAPA Munnik	District	No	Paarl [88 km]	-
Swartland	District	No	Paarl [45 km]	-
Stellenbosch	District	No	Paarl [35 km]	-
Groote Schuur	Tertiary	Yes	-	-
George	Regional	Yes	-	Groote Schuur [429 km]
New Somerset	Regional	Yes	-	Groote Schuur [8.8 km]
Mowbray Maternity	Regional	No	Groote Schuur [2.6 km]	-
Victoria Wynberg	District	Yes	-	Groote Schuur [10.7 km]
Mitchell's Plain	District	Yes	-	Groote Schuur [22.5 km]
Beaufort West	District	No	George [235 km]	-
Murraysburg	District	No	George [395 km]	-
Prince Albert	District	No	George [167 km]	-
Laingsburg	District	No	George [228 km]	-
Alan Blyth	District	No	George [158 km]	-
Riversdale	District	No	George [134 km]	-
Mossel Bay	District	No	George [53 km]	-
Knysna	District	No	George [63 km]	-
Uniondale	District	No	George [110 km]	-
False Bay	District	No	Victoria Wynberg [20 km]	-
Wesfleur	District	No	New Somerset [55 km]	-

Table 1.2: Table of all hospitals in the WC region, including availability of CT, level and referral distances

diate life support practitioners [32]. Reported gaps include insufficient familiarity with the GCS and limitations in triage competence.

Operational risks further complicates the EMS delivery. The Western Cape Department of health and wellness has reported multiple incidents in which EMS teams were targeted by violent criminals [34]. Most attacks did not result in severe physical injury. However, they disrupted essential healthcare services to vulnerable populations and caused distress among staff.

1.1.5.4 Triage scales

The primary way to confirm diagnosis of stroke and TBI is by neuroimaging services, like MRI or CT [13]. These methods also have the ability to provide information about the exact location and and what surrounding brain tissue has been affected by the stroke or TBI.

To obtain good patient outcomes when the blood supply returns to the brain after ischemia, accurate and rapid identification of of stroke is required [35]. Public awareness, emergency prehospital, as well as hospital care is crucial for better clinical outcomes. Identification and quantification of stroke can be possible using triage scales but they have their limitations. In 30% of cases, in prehospital setting, stroke is not adequately recognized. Some triage scales used in in prehospital settings have been developed to recognize large vessel occlusion strokes, similar to stroke recognition, but still 20% of the large vessel occlusion strokes remain unrecognized.

Face, Arms, Speech, Time (FAST) test is the most commonly used triage scale in prehospital settings for stroke [35]. The scale is considered very useful for strokes in the anterior circulation, but commonly misses over 70% of patients with strokes in the posterior circulation. For stroke screening, Gaze, Face, Arms, Speech, Time (G-FAST) test is a useful tool, which is similar to FAST but gaze is also included. To better diagnose strokes in the posterior circulation, assessment of symptoms regarding balance (B) and eye (E) is added to FAST, known as BE-FAST. FAST-ED is another modification of FAST, which includes anosognosia/neglect and eye deviation, this scale predicts higher value for strokes that might be related to large vessel occlusion and candidates for thrombectomy. Common triage scales used for acute stroke are the 3-item stroke scale (3I-SS), the Austrian Prehospital Stroke Scale (APSS), the Cincinnati Prehospital Stroke Scale (CPSS) and the Los Angeles Prehospital Stroke Screen (LAPSS). Among those acute stroke scales, used to confirm diagnosis LAPSS is the one with highest sensitivity and specificity.

In hospital settings, The National Institutes of Health Stroke Scale (NIHSS) is adopted broadly and is a stroke and impairment severity scale [35]. To estimate and measure the severity of stroke, it uses 15 evaluating segments in points, where the maximum is 42 points. It can predict neurological short term and long term outcomes and be performed quickly by trained healthcare providers that are not experts in neurology. The main limitations are that it does not evaluate

cranial nerves in detail, for patients with cerebellar or brainstem infraction, disease is often underestimated, discrete neurological deficits might be missed. Reflection of the stroke severity of each cerebral hemisphere is not always accurate, for patients with cognitive dysfunction, the score is the least reliable. The scale does not always reflect clinical changes from repeated examinations and an abnormality in NIHSS can not refute or support for a stroke diagnosis. There are versions of NIHSS that are suitable for prehospital settings, most promising versions are, the shortened NIHSS and the modified NIHSS-EMS.

The Glasgow Coma Scale is useful in traumatic brain injury and haemorrhagic stroke patients as well as in the evaluation of comatose patients. The three clinical parameters assessed are eye opening, verbal response, and motor response [35] [36]. Levels of responsiveness of the 3 parameters are scored 1-5, where 1 is no response and up to 4 (eye-opening response), 5 (verbal response) and 6 (motor response). The total score ranges from the lowest 3 to the highest 15. This total score is a sum of the scores and individual elements. The total score should not be used if any of the components of the GCS scale is not testable as well as denoted as "not testable". For acute traumatic brain injury the total GCS score is commonly classified as mild if GCS 13-15, moderate if GCS 9-12 and severe if GCS 3-8 [36].

The South African Triage Scale (SATS) is a five-level system used to assess patient acuity, or severity of illness, used for both stroke and TBI [37] [38]. The triage category is determined through a combination of clinical discriminators, such as presenting symptoms, mechanism of injury, and reported pain and a physiological scoring system, the Triage Early Warning Score (TEWS). In addition, the system permits senior healthcare providers to override the assigned acuity level when necessary. This ensures that clinical judgment can compensate for potential missclassification and serves as an additional safety mechanism. The final triage categories are colour-coded as red for emergency, orange for very urgent, yellow for urgent, green for routine and blue for deceased.

1.2 Purpose

The purpose of this master's thesis is to investigate how clinical trials are conducted in the Western Cape region of South Africa in order to develop a proposal for how a future clinical study of the Strokefinder MD100, could be designed and conducted in this context. This includes identifying key factors such as relevant stakeholders, suitable study sites, practical considerations for device placement, time-related aspects, attitudes towards such a study, and potential challenges that may influence its future implementation.

1.3 Goals

The goal of this thesis is to develop an understanding of stroke, traumatic brain injury, and the healthcare system in the Western Cape region of South Africa. Furthermore, the thesis aims to investigate how clinical trials are conducted in this context, including their structure, regulatory processes, stakeholder involvement, and common challenges and pitfalls associated with their implementation. Another objective is to identify relevant stakeholders for a potential clinical study of the Strokefinder MD100 in the WC context, thereby also gaining insights into practical challenges related to conducting such studies.

This is achieved through a literature review and interviews with relevant stakeholders, conducted in the WC region. Based on these findings, the thesis aims to develop a proposal for a future clinical trial of the Strokefinder MD100 could be designed in this context.

1.4 Limitations

The scope of this thesis is defined by several limitations. As the study is part of a larger research project, building on a previously performed health technology assessment and conducted in parallel with another master's thesis focusing on implementation, it was important to ensure that the work did not overlap with related studies. Most limitations were defined at the beginning of the project, while some were added during the field study due to limited availability of data and stakeholders.

The geographical scope of this thesis is limited to the WC region of SA. Although some healthcare-related data is only available at a national level, the analysis and discussion are focused on the WC healthcare system. Data collection through interviews was primarily conducted at selected public hospitals, including Tygerberg Hospital and Groote Schuur Hospital, providing insight into the healthcare system and clinical workflow. Due to the absence of a national stroke or traumatic brain injury registry, patient-related data included in the study is based on information obtained through interviews rather than comprehensive national datasets. Furthermore, the final proposal is not limited to one version of the Strokefinder MD100 device, based on the project developments and practical considerations during the field study.

An additional limitation is that the group will not write a complete protocol for a clinical study, but rather investigating what should be included in such a protocol.

Finally, the data collection was constrained to a three-month field study period in SA, which limited the number of interviews that could be conducted.

2

Method

This section describes the methodology used in this thesis. The study combines a literature review and empirical data collection in the form of interviews and field observations conducted in the Western Cape region of South Africa. A literature study was conducted to establish a theoretical foundation and served as preparatory work for the field study. The empirical part of the study consisted of interviews with relevant stakeholders and observations conducted on site. Finally, all collected data was analysed in order to address the thesis research questions.

2.1 Literature study

The literature study focused on stroke and traumatic brain injuries, including their prevalence and epidemiology in the WC region of SA. In addition, relevant clinical trials for medical devices, applicable guidelines and regulations, and literature on the Strokefinder MD100 and it's underlaying microwave-based diagnostic technology were reviewed. The primary databases used for the literature search were PubMed, Google Scholar, and Scopus. The review was further supplemented with materials provided by interviewees and Professor Mikael Persson. Previous work conducted by Master's students Ebba Alvaeus Tynnerstål and Alice Thornander at Chalmers University of Technology, as well as PhD student Tinasche A. Chikunichawa at Stellenbosch University, was also included and critically examined. All sources were evaluated using a critical approach, with particular attention given to biases. Special consideration was taken when reviewing data supplied from the private sector in order to minimize the risk of bias. In 2025, a health technology assessment was conducted in the WC region, SA, evaluating the Strokefinder MD100 [39]. The project was guided by the EUnetHTA Core Model and focused on identifying potential implementation sites, evaluating the health economic viability and assessing the potential future role of the Strokefinder.

The HTA resulted in three main conclusions, First, implementation was considered most beneficial in prehospital settings and level 1 healthcare facilities that currently lack diagnostic capabilities [39]. Second, the device was found to be economically viable in the South African context, primarily due to its potential to significantly reduce time to treatment for stroke patients. This reduction could improve patient outcomes while also generating societal cost savings. Fi-

nally, the HTA concluded that a clinical trial is necessary to support further implementation of the device in the SA context, in order to demonstrate clinical effectiveness and validate its impact on patient outcomes. The present thesis primarily focuses on addressing this need.

2.2 Preparations for South Africa

Preparations for the field study included meetings with supervisor Mikael Persson to plan and structure the data collection process. These discussions involved identifying relevant interview participants, obtaining contact information and reviewing their professional backgrounds to assess the type of information and insights they could contribute to the project. Ethical considerations were also addressed in advance, including how such considerations might differ in this setting compared to the Swedish healthcare context. A substantial part of the literature review was conducted prior to the field study, focusing on topics such as stroke, stroke treatment and TBI, as well as the structure of the healthcare system in SA and the WC region.

2.3 Interviews

The field study consisted of 21 interviews conducted with 18 different relevant stakeholders in the WC region in SA. A majority of the interviews were carried out in collaboration with two other master's students who, during the same time period, were conducting their thesis work in SA involving the Strokefinder MD100 with a focus on implementation at the Department of Industrial Engineering at Chalmers University of Technology. Each interview lasted 60 to 90 minutes and was divided into two parts, the first addressing aspects related to clinical trials and the second focusing on implementation. This structure allowed both groups to gather relevant information for their respective studies. The interviews were conducted over a period of three months, from mid-February to mid-May 2026. Most interviews took place on site at various locations in and around Cape Town, and a small number were conducted digitally at the request of the interviewee.

2.3.1 Selection of interview participants

The selection of interview participants was based on identifying stakeholders with relevant knowledge. An initial list of potential interviewees was provided by the supervisor, consisting of individuals who had been interviewed in a master thesis conducted within the same project the previous year. The list was reviewed and relevant individuals were identified by looking into the field of expertise of each person. Areas considered relevant for the thesis mainly included the healthcare system, stroke, TBI and clinical trials. Initial contact with the selected individuals was made by the thesis supervisor, and if the person agreed to being contacted by the students, the students reached out to schedule interviews. In addition to the individuals on the initial list,

further stakeholders were identified through research of relevant projects in the Western Cape region. The group also had the opportunity to contact PhD students at the department of Industrial Engineering at Stellenbosch University. During each interview, participants were asked whether they could recommend other relevant stakeholders, enabling additional participants to be identified throughout the field study.

A complete overview of the interview participants, including their roles is provided in Table 2.1.

Table 2.1: Overview of interview participants

Name	**Role**	**Date**	**Location**	**Relevance**
Georgia Channon	PhD student at industrial engineering, Stellenbosch University	2026-03-02	Digitally	To gain understanding for SA specific challenges in bringing medical technology concepts to market access and discuss earlier conducted case study of the Strokefinder MD100
Mladen Poluta	Director, Southern Right HTM Consulting	2026-03-03	Digitally	To understand how medical technology can be introduced on the SA market and gain insights into the regulatory process
Sa'ad Lahri	Associate Professor and Head of Emergency Medicine	2026-04-03	Stellenbosch University	To understand organizational aspects of the SA healthcare system, stroke treatment and referral pathways
Daniel Youkee	Emergency Medicine doctor and Postdoctoral researcher at the Neuroscience Institute at Groote Schuur Hospital in Cape Town	2026-03-05	Groote Schuur Hospital, Cape Town	To gain insights about stroke care and related challenges

Name	Role	Date	Location	Relevance
Sudesh Sivarasu	Professor in Biomedical Engineering and Director of UCT's Biomedical Engineering Research Centre	2026-03-09	University of Cape Town	To discuss implementation of medical technology in the SA context and main challenges
Hendrick Lategan	Specialist Surgeon - Trauma and Emergency Medicine	2026-03-09, 2026-03-13 and 2026-04-01	Tygerberg Hospital	To understand TBI current TBI workflow, discuss clinical trials and potential implementation sites of the Strokefinder
Kerstin Hall	Biomedical engineer and Product Manager at Impulse Biomedical	2026-03-10	Impulse Biomedical office, Cape Town	To discuss different pathways for clinical trials learn about Impulse biomedicals' experiences in clinical trials
Robyn Holgate	ER24 Chief Medical Officer and Mediclinic Emergency Medicine Manager	2026-03-11	Mediclinic, Stellenbosch	Gain insights about stroke workflows, challenges and discuss clinical trials within the private healthcare sector
Willem Stassen	Associate Professor of Emergency Medicine at University of Cape Town, Deputy Director: WHO Collaborating Centre for Integrated Clinical Care	2026-03-12	Digitally	Gain insights into clinical trials in the SA context and discuss related regulatory challenges
Doctors at Tygerberg trauma unit		2026-03-02	Tygerberg Hospital	Gain insights about TBI workflows and attitudes towards clinical trials from ground staff perspective

Name	Role	Date	Location	Relevance
Tinashe Chikunichawa	PhD in Industrial Engineering at Stellenbosch University	2026-03-18	Digitally	To discuss previous findings about implementation of the Strokefinder in the SA setting
Martin Nieuwoudt	Professor at Northwestern University and Stellenbosch University, 20 years of experience in Biomedical Engineering, Epidemiology, research methods and grant writing	2026-03-27, 2026-04-30	Digitally	To gain insights into clinical trial designs, protocol writing and discuss potential trial designs for the Strokefinder in the SA context
Pamela Naidoo	CEO at Heart and Stroke Foundation South Africa	2026-04-15	Heart and Stroke Foundation office, Cape Town	To gain insights into challenges and preventative work related to stroke from a non-profit organisations' perspective
Alan Bryer	Former Head of the Division of Neurology and Stroke Unit at Groote Schuur Hospital	2026-04-16	Groote Schuur Hospital	To understand the stroke workflow at Groote Schuur and discuss previous clinical trials and propositions for a potential Strokefinder trial at this site
Clint Hendrikse	Associate Professor and Head of Division at Emergency Medicine, University of Cape Town	2026-04-20	Groote Schuur Hospital	To understand EMS workflows and referral pathways, discuss potential implementation sites and clinical trial suggestions for the Strokefinder

Name	Role	Date	Location	Relevance
Mark Brand	Owner and Manager of BRANDTECH Health Technology Consulting	2026-04-21	Somerset West	To gain insights on implementation of medical devices in SA from an industry perspective
Cliff Lowan	PhD in biomedical/industrial engineering at University of Stellenbosch	2026-03-02	Stellenbosch University	Discuss regulations related to clinical trials and implementation of medical technology on the SA market
Lerato Jessica Moseme	MSc Medicine Candidate, Ethics Lab at University of Cape Town	2026-04-23	Digitally	Discuss findings from her thesis titled: "Roadmap for Clinical Investigations in South Africa: Facilitating Market Access for Locally Manufactured Medical Devices"

2.3.2 Interview technique

The interview technique, including question formulations and the structure of interaction during interviews, was developed iteratively throughout the study. The approach was continuously refined, with the most significant changes occurring between the first three interviews. As non of the group members had extensive prior experience conducting interviews, the process began with two practice interviews with PhD students at the Department of Industrial Engineering at the University of Stellenbosch. This provided valuable training and helped improve the interview approach.

The first interview following the practice session was conducted with Mladen Poluta. Prior to this interview, background research was carried out to better understand his area of expertise and to develop relevant questions. The questions were then reviewed by the thesis supervisor and revised based on feedback. They were also compared with those written by the other student group to avoid overlap. This procedure was applied consistently before all interviews. During the interview with Mladen Poluta, it became clear that the prepared questions were too specific. As a result, the approach was adjusted for following interviews. Broader, more flexible questions were developed based on each participant's professional background and area of expertise. Alternative questions were also prepared for cases where participants had limited knowledge of

clinical trials. During the first week doing interviews, it became apparent that many participants lacked in-depth knowledge and experience with clinical trials, which further reinforced the need to adapt the approach. Consequently, the group developed a more flexible way of working during the interview, where the interviews could be adjusted dynamically based on the participant's responses. The final set of questions for each interview was tailored to the participant as well as the timing of the interview and the context. In the initial phase, additional general questions were included regarding the healthcare system and the workflows in the WC region in order to get a broader understanding of the background and the context. At the end of each interview, participants were asked whether they could recommend other relevant stakeholders for the study, which contributed to the identification of additional participants throughout the field work.

2.3.3 Interview procedure

In the early stages of the field study, it was important to clearly communicate to all participants that the interviews were conducted solely for the purpose of collecting data for the master's thesis, and not on behalf of any company or external organisation. This clarification became necessary after some participants requested information regarding ethical approval and related documentation.

Whenever possible, interviews were conducted on site at the participant's workplaces. This was preferred because it was considered to improve the quality of the interviews and help build trust between the researchers and participants. The majority of the interviews took place in person in and around Cape Town. During the interviews both group members were present and actively participated asking questions. The responsibility for taking notes was alternated between the two members from interview to interview. Almost all interviews were audio recorded, after obtaining consent from the participants, in order to ensure accurate and reliable use of the collected information during the analysis phase.

2.4 Observations

During the field study, observations of the acute trauma unit at Tygerberg hospital, Cape Town was conducted. The first observation took place on a Monday morning, corresponding to the peak period of the week with the highest patient load, in order to better understand workflows and waiting times for the CT scan. A second observation was conducted on a Wednesday morning, when the patient load was considerably lower. This allowed for an assessment of where the Strokefinder could be practically implemented within the unit in the event that a pilot study was to be conducted at this site.

2.5 Data analysis

The data collected from interviews were critically reviewed and weighted based on the participants' backgrounds, expertise, and potential biases related to their affiliations within the healthcare sector. Consideration was also given to their prior knowledge about the Strokefinder MD100 before the interview, as well as how effectively information was communicated and questions or statements were addressed during the interviews. Ongoing discussions with supervisor Mikael Persson were held to support this evaluation process. Where possible, materials gathered from the interviews were continuously cross-checked against relevant research articles to further substantiate the findings presented in the results and to minimize potential bias.

3

Results

In this section the results from the literature review as well as interviewees perspective on healthcare system factors to the clinical trials will be presented. General frameworks guidelines and principals for how clinical trials are conducted in SA, context specific challenges and an economic evaluation will be described.

3.1 Healthcare system factors related to the clinical trials

When planning a clinical trial in South Africa, several healthcare system factors need to be taken into consideration. This section presents factors identified during the field study that may influence the feasibility and conducting of a clinical trial in the Western Cape context.

3.1.1 Stroke and TBI workflows

To investigate possible implementation sites for new medical devices, it is important to understand current care workflows. In the following section it is described what a patients journey from falling ill in stroke or TBI to treatment in the WC region can look like according to interviews.

Access to emergency care in South Africa varies considerably between the public and private sectors, influencing patient pathways in both stroke and TBI. In many settings, patients are transported to healthcare facilities by private means rather than by ambulance services, partly due to limited trust in public emergency medical services. When ambulances are utilized, ambulance personnel assess patients on scene and apply prehospital triaging tools [40].

Upon arrival at the emergency centre, patients undergo further clinical evaluation, and a CT scan is typically requested to confirm diagnosis to accurately distinguish between ischemic and haemorrhagic stroke [40]. In the private sector, CT imaging is generally available without significant delay, enabling rapid diagnostic clarification and treatment decisions. In contrast, access to CT imaging in the public sector may be restricted. Patients presenting outside of CT available hours may require transfer to tertiary hospitals for imaging, potentially introducing delays in diagnosis and treatment [40]. Geographic factors further influence access, as patients

in rural areas may face long transport distances to tertiary centres, as opposed to patients in more urban settings, where facilities are located in closer proximity.

According to interviews conducted with personnel involved with the private sector, within emergency centres, some facilities prioritize suspected stroke patients for immediate imaging, bypassing standard waiting processes to minimize delays [41]. Thrombolysis can be administered in appropriately equipped centres, including smaller hospitals with adequate training and CT capabilities.

A significant challenge that remains for stroke healthcare despite these workflows is delay in patient presentation [40] [41]. A retrospective study conducted at the University of Cape Town found that the median time from symptom onset to hospital arrival was approximately 24 hours on weekday, with slightly shorter times observed over weekends [21]. Most patients developed symptoms at home and those requiring admission generally presented earlier than those discharged from the emergency centre.

For TBI, patient management is largely determined by injury severity. Mild TBI cases can be handled at community health centres or district hospitals, while more severe injuries are directed to higher level facilities [28] [27]. In some cases, patients are first stabilized at the nearest facility before being referred to tertiary care. In TBI triage decisions, evaluation using the Glasgow Coma Scale along with consideration of injury mechanism and severity is often used [27].

3.1.2 Attitude towards research and trials

When considering the implementation of new technology, and consequently the execution of clinical trials, the attitude and level of engagement among those involved are crucial factors. This applies both to decision-makers at managerial levels and to frontline staff who are expected to adapt their daily routines and working practices. Several interview participants emphasized that change is generally received positively when it is well motivated and clearly communicated. A recurring point was the importance of ensuring that those affected by the change are able to see its value, which in this case related to improved patient outcomes and reduced time from symptom onset to diagnosis. It also became evident that perspectives differed depending on whether the interviewees had managerial roles or worked directly in clinical practice, where the effects of the change are felt directly in daily work.

Participants in higher managerial positions described change as something that is usually accepted as long as the purpose is clearly understood [28]. Furthermore, the existence of a well-established regulatory framework in South Africa was considered to contribute to acceptance, as initiatives that have been formally approved by regulatory bodies are generally not

questioned [42].

In contrast, interviews with trauma staff working at the trauma unit at Tygerberg Hospital provided a more detailed picture of the practical challenges associated with change [43]. These participants emphasized that implementing a new initiative, such as a clinical trial, does not only affect one individual but requires adjustments throughout the entire system. They highlighted the necessity of having clear guidelines and structured training, rather than decisions introduced from higher management without sufficient practical support. According to these participants attitude in the hospital was described as: "things have been running like this for 20 years, why must we do this new thing". One reason for this resistance was explained as the already heavy workload experienced by frontline staff, and that changes often are perceived as adding to this workload rather than making daily work more efficient.

At the same time, the staff at the Tygerberg trauma unit emphasized that openness to change exists when the value of change is evident, both in terms of practical workflow improvements and patient benefits. Achieving this often requires obtaining genuine buy-in from staff at the operational level and ensuring that they feel ownership of the change, rather than experiencing it as an imposed decision. It was also pointed out that initiatives originating in high-income contexts often fail when introduced without sufficient adaptation to the local context and its specific challenges [43].

3.1.3 Perspectives on desired stroke and TBI care pathway

Interviews with different stakeholders across the South African healthcare system suggested several areas for improvement in the organisation and delivery of stroke and TBI care. These perspectives consistently highlighted the need for strengthening prehospital systems, improving access to advances diagnostics and treatment and expanding specialized care infrastructure.

A recurring subject was the importance of enhancing early detection and prehospital management. Participants emphasized the need for improved general knowledge about stroke symptoms, alongside with better training and support for emergency call handlers and paramedics to facilitate early recognition and prioritisation of suspected stroke cases [42] [44]. Pre-notification systems, whereby ambulance services alert receiving facilities in advance, were identified in the private sector as an important component of an optimized care pathway and were suggested as a standardized intervention on a national level [41]. Strengthening emergency transport systems, including enabling early intervention during transit, was also viewed as essential to reducing delays and improving outcomes [42] [44].

Access to diagnostic imaging and acute interventions emerged as another key priority. Stake-

holders in the private sector highlighted the potential value of innovations such as mobile CT units, although these were acknowledged to be resource intensive [41]. More broadly in both public and private sector, the need to expand the access to reperfusion therapies, including both thrombolysis and thrombectomy, which are currently limited by resource and infrastructure constraints [41] [45]. While some participants expressed optimism regarding gradual improvements in access to these treatments over time, it was also noted that disparities compared to high-income settings are likely to persist due to differences in resources and system capacity [45].

The development of dedicated stroke units was frequently proposed as a central strategy to improve patient outcomes. Such units, including designated stroke beds and specialized care teams, were seen as possible factor to improve continuity of care [41]. Given resource limitation, it was suggested that initial implementation should prioritize high volume urban centres, supported by well-defines referral pathways from less resourced facilities [41]. In the context of TBI, it was highlighted that CT scanners specifically dedicated to trauma to reduce waiting times would contribute to improving efficiency and patient management [27].

Finally, the importance of economic considerations in shaping future care models was highlighted by interviewees. This included the need for more robust data on the cost of stroke at both the health system and societal levels, to better inform resource allocation and policy decisions [44]. Overall, participants highlighted that improvements in stroke and TBI care would require coordinated investment across multiple levels of the healthcare system, including prevention, prehospital care , acute treatment and rehabilitation.

3.2 Conducting trials in South Africa

To develop a proposal for a future clinical trial of the Strokefinder MD100, several aspects related to the conduct of clinical trials in South Africa must be considered. This section presents key findings from the field study regarding regulatory processes, study design, sponsorship, healthcare sector characteristics, and potential study sites.

3.2.1 Regualtory process for clinical trials

The regulatory process for a clinical trial in South Africa differs depending on previous testing and possible implementations of the medical device, including if the device has been CE-marked in Europe or approved by the Food and Drug Administration (FDA) in the US [46]. If the device has been approved by the FDA or CE-marked, the process can be considered fairly straight forward in South Africa and the key thing that needs to be demonstrated during testing is safety an cost efficacy in the SA context. It can be considered standard to bring the device to Europe or the US before initiating trials in SA, and companies are often encouraged to do so first [47].

No matter the previous marking the device will need to get ethics clearance and clinical trial approval since the trial will be engaging with human participants [48]. For these clearances a clinical trial protocol will need to be written which is a very detailed description of the trial going into details regarding what will happen to the patient, how the trial will be performed and similar information. The company or organisation behind the medical device takes ownership over the protocol, but it can be written as a collaborative process between an external Clinical Research Organisation (CRO) and the device company, depending on sponsors and resources. Once the trial protocol has been approved it has to get ethical approval from an ethics board and approval from South African Health Products Regulatory Authority (SAPHRA) before the trial can initiated. How the ethics clearance is one depends on the research facility, for example if doing it through an university they commonly manage the ethics. Looking at a protocol application from the Health Research Ethics Committee (HREC) at Stellenbosch University, over 20 different appendices needs to be added when submitting an ethics application [49]. Some of the things included here includes research protocol, consent an assent forms, letter of authorization from institution such as hospital or clinic, budget, and a description of the recruitment process and consent process proposed for the local site. Other than application the clinical trial needs to be registered in the South African National Clinical Trials Register (SANCTR) [50].

Another aspect highlighted during interviews was that the regulatory requirements may differ depending on whether the device is considered substantially equivalent to an already approved device, commonly referred to as a predicate device [50]. Interview participants described that if a medical device is based on similar principles and has a comparable intended function to an already approved device, previous evidence may potentially be used to support the regulatory application process. In such cases, regulators might request supplementary laboratory validation or technical testing to demonstrate substantial equivalence before allowing progression to later trial phases. If the intended use of the device changes substantially, or if the modification is considered significant, additional early-phase clinical testing may be required before further clinical trials can be initiated [50]. The interviewees also emphasized that although the general principles that govern clinical trials are generally well established, the exact regulatory pathway remains highly based on context and is often evaluated based on specific cases by the regulatory authorities [50].

3.2.1.1 Frameworks guiding clinical trials

There are different frameworks a clinical trial needs to comply with. A very central document is the "South African Good Clinical Practice: Clinical Trial Guidelines"-document, which is a document from the Department of Health in South Africa. The document includes detailed guidelines that promotes good practice when conducting clinical trials in the country [51]. It is mandated to comply with these guidelines according to the National Health Act No.61, the

medicines and relate substance act, and the national research ethics guidelines. This documents covers information about investigators, ethics committees, manufacturers, sponsors, authorities and trial participants. The guidelines apply to both academic and contract clinical research with the intention of applying to all stages of health product development, in whole or in part or general biomedical research.

The guidelines goes in detail and focus on the designing, planning, management, conducting and regulation of clinical trials, where the term clinical trials is not specifically related to a certain type of trial but rather all types including complementary medicine, traditional medicines, surgical procedures, medical devices, cell therapy and imaging technology.

3.2.2 Sponsors

According to SAHPRA, a sponsor is defined as the individual or organisation responsible for the initiation, management, and financing of a clinical trial [51]. The sponsor may consist of a pharmaceutical company, academic institution, principal investigator, (PI), funding body, or another organisation responsible to oversee the study. SAHPRA guidelines further state that clinical trials may be conducted either with or without an external sponsor. In cases where no formal sponsor is involved, responsibility for the functions related to the sponsor must be defined by the study protocol. The guidelines additionally describe that sponsors may delegate certain operational responsibilities to CROs, although oversight responsibilities remain with the sponsor and applicant [51]

Interview participants discussed clinical trial models supported by both hospitals and CROs [50]. One interviewee suggested that studies sponsored by hospitals may reduce overall study costs, as existing hospital personnel and infrastructure can potentially support parts of the trial processes [50]. In contrast, trials supported by CROs were described as potentially involving higher costs, but with the perceived advantage of dedicated research infrastructure and quality assurance processes. Participants suggested that selection of sponsorship model may therefore depend on the specific circumstances, available resources, and requirements of the proposed study [50].

3.2.3 Clinical trials in private versus public healthcare sectors

During interviews, participants suggested that the private sector may in some cases be more cautious regarding experimental interventions and emerging technologies, with a preference for approaches that are already supported by established evidence [40]. This was discussed in relation to the perceived risks associated with clinical trials, particularly during earlier stages of evaluation [40].

Differences in patient volume were also highlighted. According to interviewees, lower patient numbers in the private sector may prolong recruitment periods and make it more difficult to achieve sample sizes with statistical power in shorter periods of time **robyn** [40]. In contrast, participants noted that hospitals in the public sector generally manage larger patient volumes, which may facilitate faster enrollment in clinical studies [40].

At the same time, several practical and advantages related to resources were identified [40]. Interviewees suggested that patients in the private sector may in some cases present earlier and move more rapidly through diagnostic and treatment workflows due to the availability of greater resources [40]. Certain specialized interventions and infrastructure were also described as more readily available in private healthcare settings, which could make these environments a suitable option for potential EMS clinical studies [40].

Participants further indicated that the public healthcare sector integration with academic and research institutions may be stronger [40]. Investigators in public hospitals were described as holding university affiliations and having established access to academic research infrastructure, including institutional ethics committees [40]. In contrast, interviewees mentioned that studies in the private sector may commonly require collaboration private ethics review services or external universities [40] [41].

Important considerations mentioned in the public sector were resource allocation and workflow integration [40]. Interviewees noted that clinical studies may require dedicated externally funded personnel, such as research nurses, in order to not interfere with routine clinical operations [40]. It was suggested participation in clinical trials should not alter prioritisation of standard clinical resources, such as access to CT scan, for patients outside of the study [40].

Regarding the conduct of clinical trials within private healthcare institutions, one participant described that phase three studies are performed more commonly than earlier phase studies [41]. It was mentioned that often regulatory approvals and ethical documentation would generally have to be established before implementation at hospital level [41]. It was suggested that the private sector may not provide comprehensive clinical trial infrastructure in house throughout the study process, requiring external coordination and preparation prior to initiation of study [41]. Additionally, it was discussed that financial and administrative considerations related to trial participation in private healthcare environments might be required before enrollment can occur [41].

3.2.4 Study design

Clinical trials are typically divided into several phases, where each phase is designed to address specific research objectives and clinical questions [52] [53]. These phases can include phase 0, phase 1, phase 2, phase 3, phase 4. Phase 0 and phase 2 are generally considered exploratory phases, phase 1 focuses primarily on safety and is therefore regarded as a non-therapeutic phase, while phase 3 serves as the therapeutic confirmatory phase. Phase 4 is conducted after regulatory approval and is mainly concerned with post-marketing surveillance and long-term monitoring of treatment effects.

Clinical research designs can broadly be divided into observational (non-interventional) and experimental (interventional) studies [52]. Observational studies may either include comparator groups, such as in cohort or case-control studies, or be purely descriptive without a comparison group. Experimental studies, on the other hand, may be randomised or non-randomised. Several different clinical trial designs exist within experimental research [52].

Cohort studies are a form of observational study design in a defines group of individuals is followed over time based on criteria established by the researcher [54]. In prospective cohort studies, participants are enrolled before the outcome has occurred, and the investigator classifies them according to exposure status before monitoring outcomes over time. Relevant baseline variables are collected throughout the the study period. In retrospective cohort studies, both exposure and outcome data are obtained from existing records, meaning that the outcomes have already occurred at the time of analysis [54].

One interview participant proposed a two phased study design for evaluation of the Strokefinder in the WC healthcare setting [50]. The suggested initial phase involved a feasibility and validation study conducted in a tertiary hospital environment, including patients presenting with suspected acute stroke or TBI within 24 hours of symptoms onset. In this proposed design, patients would first undergo the standard triage procedures, such as GCS or SATS assessment, followed by examination with the Strokefinder device prior to confirmatory CT scan. The CT results would serve as a reference standard for evaluation of the diagnostic performance of the device, including sensitivity and specificity within the WC population [50].

Further the interview suggested that, after a successful validation in the first phase, that the study could potentially progress to a second phase focusing on evaluation of the devices' effect on the transport pathways and patient flow [50]. This phase was described as a possible cluster-randomized study involving selected EMS units and lower-level healthcare facilities in the WC region. One proposed study arm would involve using the Strokefinder device to support direct transfer to suspected stroke patients to tertiary stroke centres, while the comparator arm would

follow existing standard operating procedures involving transport to the nearest facility with CT availability for initial stabilisation and imaging [50].

The proposed study design was described as being structured to evaluate the Strokefinder in the WC context, accounting for limitations and delays identified during previous HTA assessment processes [50]. Within this proposed framework, patients assessed with the Strokefinder in combination with standard clinical care were considered the experimental group, whereas patients managed according to existing standard operating procedures, including GCS, SATS and FAST, constituted the control group. The suggested primary endpoint was reduction in overall time to treatment, including thrombolysis or thrombectomy when applicable. Additional proposed outcomes was evaluation included measures such as door to CT time, defined as the interval between hospital arrival and initiation of confirmatory neuro imaging [50].

3.2.5 Stakeholders and roles in clinical trials

During the interviews, participants were asked to describe which stakeholders and roles would be important in the design and implementation of a clinical trial for the proposed technology, as well as key considerations related to coordination and governance.

Across interviews, the importance of a dedicated champion was repeatedly highlighted [55] [46]. This role was described as a key driver for implementation and was often associated with an individual with strong influence within the frontline team as well as within the public healthcare sector, for example a head of department or senior clinician with established links to the Department of Health. The champion was also described as someone capable of facilitating engagement across departments and ensuring sustained institutional support for the trial [55] [46].

A necessary role for clinical trial execution is a principal investigator, (PI), who would carry overall responsibility for the study design, ethical compliance, and regulatory applications [50]. It was also suggested that clinical investigators would be required at participating sites, depending on the selected facilities and level of implementation. The PI was further described as a central figure in coordinating both ethical approval and regulatory submissions, including engagement with ethics committees and regulatory authorities [50].

Data management was highlighted as as another critical component of the trial structure. Participants emphasized the need for a dedicated person with the role to analyse data and responsible for consistency in analytical approaches, given that different analysts may otherwise produce varying interpretations of the same dataset. In larger trials, this role could involve oversight of additional analysts, but with clear responsibility for final analytical decisions remaining cen-

tralised [50].

In terms of operational implementation, interviewees also highlighted that champions may differ depending on the care setting. In prehospital environments, experienced paramedics were described as potential key drivers of implementation, whereas in hospital settings leadership was more commonly associated with senior medical staff and departments heads. Thus, it was noted that that nursing staff often play crucial roles as practical on-the-ground champions due to their continuous presence in clinical workflows and their ability to facilitate sustained implementation in routine care [42].

3.2.6 Possible use cases and implementation sites

Several interviewees discussed potential applications of the Strokefinder MD100 within the prehospital stroke pathway, particularly in relation to destination triage and referral decisions [56] [42] [40]. Participants suggested that the device could potentially support EMS personnel in determining the most appropriate receiving facility for patients with suspected stroke. A scan result that is stroke positive could be a possible indicator for direct transfer to a stroke capable centre or a facility with CT availability [56] [40]. Some interviewees further suggested that, if versions of the Strokefinder were capable of distinguishing between ischemic and haemorrhagic stroke, this information could potentially influence referral decisions regarding facilities with thrombectomy availability [40].

Several participants highlighted the prehospital environment as a potentially valuable implementation setting for the technology [56] [43] [42] [41] [40]. Potential challenges associated with implementation in current EMS systems could include the limited ambulance availability and inconsistencies in referral pathways [43]. Participants noted that these factors could influence how the technology would ultimately be integrated into clinical workflows [43] [41].

At the district and regional hospital level, a possible "rule out" application of the Strokefinder was suggested, particularly in settings where CT is not available in evenings or weekends [56]. Proposals that negative scan results in clinically stable patients could potentially reduce unnecessary overnight transfers to tertiary hospitals and instead allow observation at lower-level facilities until formal imaging becomes available [56]. This potential use case was discussed primarily in relation to hospitals with limited imaging access after hours [27] [40].

Another potential use case for the device could be used in patient prioritization while awaiting CT imaging or treatment [27] [56]. During discussions it was highlighted that the Strokefinder version capable of differentiating subtypes of stroke could be particularly important when it comes to potentially making decisions in emergency departments, leading to earlier treatment

[40].

During discussions of potential applications of the device for TBI, participants suggested that the system could be used as a screening tool for mild to moderate head injuries in order to identify patients at lower risk of intracranial bleeding [27]. In such cases clinically stable patients could potentially undergo neurological observation instead of immediate CT scanning, while the CT could be reserved for patients who are in greater immediate need. Interviewees described this as particularly relevant in settings with high patient volumes and constrained imaging resources [27].

Lower-level hospitals and healthcare facilities in rural areas were also identified as possible implementation sites, particularly in settings with limited CT access or specialist stroke services [42] [41] [40].

3.2.7 Possible clinical study sites

Several interviewees discussed the potential role of diagnostic accuracy and feasibility studies as initial steps in the clinical evaluation of the proposed technology [42] [40] [50]. Participants suggested that early studies would likely involve comparisons between device findings and CT imaging as the reference standard [42] [40]. Emergency departments were frequently described as suitable study environments, since patients undergoing CT scans could potentially also be assessed using the Stokefinder device without substantially altering existing clinical workflows [40].

Interviewees further suggested that prospective study designs would likely be preferable for evaluation of the clinical performance of the system [50]. Participants emphasized the importance of patient selection strategies, randomisation approaches and assessment of feasibility prior to implementation in larger clinical trials [50] [42]. Feasibility studies were described as important for assessing whether the device can be integrated into routine clinical settings and workflows before evaluating the potential effect on referral pathways or patient outcomes [42].

Academic and tertiary hospitals were commonly identified as potential sites for clinical studies, due to the large patient volumes, established stroke workflows and 24 hour access to CT imaging [45] [41] [40]. Stroke units and academic centres, such as Groote Schuur in the WC region were specially highlighted as potential environments for stroke related early phase studies [45] [41]. Participants noted that sufficient patient volumes would likely be necessary in order to achieve adequate statistical power and assess diagnostic performance reliably [41] [27].

For TBI applications, the acute trauma unit at Tygerberg Hospital was proposed as a potential

pilot site [27]. Interviewees described that the unit receives a broad spectrum of TBIs, including GCS mild, moderate, and severe cases, partly because of limited CT availability at surrounding hospitals after hours and during weekends. It was suggested that initial pilot studies could focus on mild TBI and compare device findings with CT results over a defined data collection period [27]. Based on the patient flow at the acute trauma unit, it was suggested that approximately three to six months could potentially be used to have recruited at a minimum 300 patients in the defined category and reach statistical power to be able to assess feasibility before progressing to larger scale investigations [27].

Prehospital clinical studies were also discussed as a possible application area for the future [40] [41]. Participants noted that EMS systems in the WC region could potentially be suitable collaborators for such clinical studies, although it is acknowledged that prehospital clinical trials may involve logistical and ethical complexities [41].

Several interviewees highlighted the administrative and practical requirements that are associated with the conducting of clinical trials in this context. These included the need for dedicated staff, allocated workspace, potential collaboration with institutions, processes for ethical approval, and engagement with provincial health authorities [27] [45] [50].

3.3 Possible challenges

Although several opportunities for conducting a clinical trial of the Strokefinder MD100 were identified, the interviews also highlighted a number of potential challenges. This section presents organisational, resource-related, ethical, and regulatory considerations that may affect the planning and conduct of a clinical trial in the Western Cape context.

3.3.1 Organisational and resource-related challenges

Interviewees described organisational and logistical barriers that could potentially affect implementation of clinical trials within the South African healthcare system [46] [27] [40] [55]. Participants suggested that identifying motivated collaborators, departments or champions can be challenging and important for initiating and sustaining a study [46]. It was also suggested that interest in participation could depend on whether healthcare facilities perceive a direct clinical benefit or sufficient financial support associated with the project [55].

Resource limitations were repeatedly mentioned as a potential challenge, particularly within the public sector [40] [27] [55]. Interviewees noted that clinical trials may require dedicated staff members for data collection and device operation, rather than relying on already burdened clinical personnel [40]. Questions were also raised regarding staffing during overnight hours and

how device related procedures could be integrated into existing workflows without interfering with routine patient care [27]. One participant additionally suggested that financial constraints within the public sector may complicate implementation if additional funding or incentives are not available [55].

Participants further described clinical trials as administratively demanding and resource intensive [40]. Potential challenges discussed included deviation in protocols, screening failures, extensive documentation requirements and need for additional personnel and clinical trial infrastructure [40]. The importance of defining realistic study aims and avoiding overly ambitious trial designs during early stages of development [50].

3.3.2 Ethical and regulatory consierations

Interviewees identified several regulatory and ethical considerations related to conducting clinical trials EMS and prehospital settings [40] [47] [50]. Participants suggested that regulatory pathways for medical devices in higher risk classes may currently be insufficiently defined, potentially creating uncertainty regarding approval procedures and clinical validation requirements [47]. Both institutional registration and regulatory body approval were described as necessary processes that may substantially prolong study initiation timelines [47].

Challenges associated with conducting prehospital research under existing regulatory frameworks were discussed [40]. An issue described was that current regulations may assume that investigational interventions are administrated by medical doctors, which may not align with prehospital environments where paramedics or other emergency care providers would likely operate the device. Further it was noted that definitions of clinical trial sites may be difficult to apply in prehospital settings, where patient inclusion and intervention can occur across multiple unpredictable locations [40].

It was additionally suggested that implementation within the public sector would likely require not only from provincial health authorities, but also from local departmental leadership and healthcare professionals directly involved in patient management [50]. It was noted that implementation strategies initiated from the top-down may encounter resistance if local stakeholders are not actively engaged in the process [50].

3.3.3 Delayed consent and post-trial access

The issue of delayed consent in EMS research was specifically discussed by interview participants [40]. It was suggested that patients experiencing acute stroke or TBI may not always have the capacity to provide fully informed concent during the emergency phase of care [40]. As a result, participants described delayed consent models as potentially necessary for EMS

clinical trials, where consent procedures are conducted after initial stabilisation rather than at the moment of enrollment [40]. Interviewees further noted that emergency clinical trials remain relatively uncommon in SA, which may contribute to uncertainty among ethics committees and regulatory bodies regarding how such concent models should be applied [40].

Post-trial access was identified as an important ethical consideration [40]. Participants suggested that if a device demonstrates clinical benefit during testing, consideration should be given to whether SA public healthcare system would realistically be able to access or afford the technology after study completion [40]. Interviewees described concerns regarding situations where research is conducted within SA, but the long-term benefits primarily become available in higher income settings [40]. Potential approaches discussed included contractual agreements, subsidisation models, or other mechanisms aimed at ensuring future accessibility of successful technologies within the local healthcare system [40].

3.4 Economic evalutation

Implementation of new medical technologies requires evaluation of both clinical benefits and economic consequences. Cost-effectiveness analyses are commonly used to assess whether the additional costs of an intervention are justified by the health benefits it provides. One commonly used measure is the quality-adjusted life year, which combines both the length and quality of life gained from an intervention. By comparing the costs of a new technology with the expected health benefits, economic evaluations can support decisions regarding whether an intervention provides sufficient value for the healthcare system.

Implementation of the Strokefinder MD100 would require an initial financial investment compared with currently used clinical triage tools, which are primarily based based on clinical assessment scales and do not involve dedicated diagnostic hardware. Assuming an estimated device cost of €90 000 per unit, the total implementation cost would depend on the number of devices acquired and deployed within the healthcare system. The estimated costs associated with the device include not only hardware acquisition, but also training of healthcare systems, but also training of healthcare personnel, integration into existing clinical workflows and healthcare systems, and ongoing operational expenses. Potential recurring costs may include single-use hygiene covers, software updates, maintenance, charging and electricity use, as well as periodic refresher training for healthcare professionals. The estimated cost of €90 000 represents an assumed acquisition cost and may differ from the actual implementation cost in the SA healthcare system. Therefore, the following economic calculations should be interpreted as scenario-based estimates rather than precise predictions of implementation costs.

The Strokefinder is not expected to require additional clinical staffing, as proposed implemen-

tation model involves training already existing healthcare personnel responsible for triage and patient assessment to operate the device. This assumption depends on successful integration of the device into existing workflows, and additional operational requirements may introduce costs not captured in the current model.

Previous studies evaluating stroke treatment pathways have demonstrated that earlier treatment of acute stroke may provide substantial clinical and economic benefits. One study investigation endovascular treatment for large vessel occlusion stroke reported that each minute reduction in treatment delay was associated with a median gain of approximately 1.3 disability-free days, while cumulative healthcare costs over a five-year period remained relatively unchanged [57]. The same study estimated a net monetary benefit (NMB) increase of €309 every minute earlier endovascular treatment [57]. These findings originate from healthcare systems with different resources and treatment pathways compared to SA. A reduction in time-to-treatment may not necessarily translate into improved outcomes if access to imaging, thrombolysis, thrombectomy, or specialist care remains limited.

Similarly, another study found that every 10-minute reduction in treatment delay resulted in an average gain of 39 disability-free life days [58]. Although lifetime healthcare costs remained comparable between earlier and later treatment groups, earlier intervention was associated with improved health outcomes and increased net monetary benefit from both healthcare and societal perspectives [58]. These meaningful economic and clinical benefits, even in situations where total long-term healthcare expenditures remain relatively stable.

Timely management is also important in TBI, where faster access to appropriate care has been associated with reduced morbidity and mortality[59]. Earlier triage and diagnosis may potentially enable more rapid initiation of both acute treatment and rehabilitation services. Previous studies have shown that earlier rehabilitation following TBIs is associated with improved physical recovery, better cognitive outcomes, and shorter overall rehabilitation duration, which may additionally contribute to reduced rehabilitation-related costs [60] [61].

The following calculations are simplified estimates based on published data from high-income healthcare settings. The transferability of these economic benefits to the WC healthcare context remains uncertain, including the WTP for improved stroke outcomes.

- Assumed cost per device: €90 000
- Assumed lifetime of the Strokefinder: 6 years
- Assumed number of measurements per device per year: 500 patients (scenario assumption)
- Total expected measurements during device lifetime: 3 000 patients (500 patients/year × 6 years)
- Estimated cost per patient measurement: $34.76/patient (€90 000 converted to $104 267

/ 3 000 measurements)

- Assumed time reduction per patient: 10 minutes (based on US-based estimates from literature) [58]
- Estimated QALY gain associated with a 10-minute reduction in treatment delay: 0.107 QALYs (39 disability-free days/365, assuming disability-free days approximate full health utility), derived from literature [58]
- Willingness-to-pay threshold (λ): $3 015 per QALY [62]

It has been estimated reported that reductions in time-to-treatment of approximately 10 minutes are associated with minimal changes in overall healthcare costs (ΔC), while resulting in substantial health gains (ΔB) [58]. Under these assumptions, the estimated net monetary benefit can be calculated to evaluate whether the expected health benefit justifies the additional cost of implementation. In order to relate device cost to expected economic benefit, the device price of €90 000 is converted to $ 104 267.

The economic evaluation was performed on a per-patient basis. The cost of implementing the Strokefinder was distributed across the expected number of measurements during the lifetime of the device. Assuming a device lifetime of 6 years and 500 measurements per year, the total number of expected measurements is estimated as:

$$6 \cdot 500 \ = 3000 \text{ measurements}$$

The estimated cost per patient measurement is therefore:

$$\frac{\$104\ 267}{\$3000} = \$34.76 \text{ per patient}$$

The net monetary benefit was estimated by converting the expected QALY gain into monetary value using the WTP threshold and subtracting the additional cost per patient associated with the implementation of the Strokefinder.

$$\text{NMB} = (3015 \text{ x } 0.107) - 34.76 = \$287.85 \text{ per patient}$$

A positive NMB suggests that, under the stated assumptions, the expected health benefits outweigh the additional costs per patient, including potential cost-effectiveness of the intervention. This estimated economic value should be interpreted as a theoretical scenario rather than the expected financial benefit of implementation in SA. Actual outcomes will depend on local healthcare capacity, treatment availability, and whether saved time can be converted into improved patient outcomes.

3.4.1 Proposal of clinical study site and design

Information gathered during the literature study and interviews suggest that a possible clinical trial for the device, regardless of intended use, could preferably be conducted within the

public healthcare sector with a university or academic hospital acting as sponsor. The public sector was considered suitable due to the larger patient volumes and the established integration with academic and research environments. By conducting the study through a hospital-based or university-affiliated structure, costs may potentially be reduced through the use of existing personnel and infrastructure . The proposed primary aim of the study should initially be to demonstrate that the Strokefinder MD100 can be integrated into the intended healthcare context without disrupting existing workflows or increasing the burden on healthcare staff, and thereafter to evaluate whether the device contributes to systematic reductions in time from symptom onset to diagnosis and treatment.

To achieve this, a two-phased study design is considered appropriate. The initial phase would involve a feasibility and validation study conducted in a tertiary hospital environment, including patients presenting with suspected acute stroke or TBI within 2 hours of symptom onset. During this phase, patients would undergo standard triage procedures followed by examination with the Strokefinder MD100 prior to confirmatory CT imaging. The CT results would then serve as the reference standard for evaluation of the diagnostic performance of the device, including measures such as sensitivity and specificity. For TBI applications, the trauma unit at Tygerberg Hospital was identifies as a suitable site due to the high patient volumes and broad spectrum of TBI cases. For stroke-related applications Groote Schuur Hospital was highlighted due to its established stroke pathways and 24-hour access to CT imaging. Following successful feasibility and validation testing, the study could progress to a second phase focusing on evaluation of systematic time savings associated with implementation of the device. In this phase, patients assessed using the Strokefinder MD100 could be compared with patients managed according to existing clinical pathways and triage systems. This phase could potentially involve selecting EMS units and lower-level healthcare facilities within the Western Cape region, although no specific units were identified during the study.

4

Discussion

In this discussion, several potential applications and implementation context for the Strokefinder MD100 are considered in relation to how a clinical study should be designed. During the conducted interviews it was mentioned, as described in the results, that the device has a possible value in multiple settings, including different stages for both stroke and TBI. For stroke care, suggested possible applications included usage in the prehospital pathway to support destination triage and referral decisions, assisting emergency staff when deciding where to transport the patient. Additionally, supporting prioritization of patients while awaiting CT imaging or treatment at hospital level. For TBI care, the system was described as potentially useful as a screening tool with the aim of identifying patients at lower risk of intracranial bleeding. As these different applications address distinct clinical needs and could be evaluated in different settings, the discussion presents several alternative proposals for how a clinical trial of the Strokefinder MD100 could be designed.

4.1 Key considerations for clinical trial design

When discussing how a clinical trial for the Strokefinder MD100 should be designed in the Western Cape context, several aspects must be considered, including the study design, sponsorship model, participant inclusion, consent procedures, an most importantly, the intended outcome of the study. Defining the primary objective of the trial was considered crucial, as this determines both the study structure and what outcomes should be evaluated. During the field study, several interview participants emphasized that successful implementation of a clinical trial requires motivated collaborators and engaged staff. It was repeatedly highlighted that healthcare staff need to understand both the purpose of the study and the potential value of the technology in order to support the implementation. In this context, the main perceived value was related to improved patient outcomes and reduced time from symptom onset to diagnosis and treatment. Based on mentioned factors, it could be argued that the clinical trial should be divided into different phases, where each phase addresses a specific research objective.

One important practical aspect of the study design concerns sponsorship. According to SAHPRA guidelines, clinical trials in South Africa can be conducted either with or without an external

sponsor, provided that the responsibilities normally assigned to a sponsor are clearly defined within the study protocol. Both sponsorship models were discussed during the interviews and were considered to have both advantages and disadvantages. Hospital-sponsored studies may potentially, reduce overall study costs by utilizing already existing personnel and infrastructure within the healthcare system. In contrast, studies involving external sponsors or CROs may involve higher costs, but could provide advantages in terms of dedicated research infrastructure, quality assurance processes, and administrative support. The most appropriate sponsorship model would therefore likely depend on the available resources, study requirements, and practical circumstances surrounding the trial.

4.1.1 Proposed clinical study design

When considering the structure of the clinical trial, it was regarded as important that each included phase addresses a clearly defined clinical question. Throughout the interviews, a relatively consistent view was seen regarding how a study of the Strokefinder MD100 should preferably be conducted. Participants emphasized the importance of initially demonstrating that the device can function within the existing healthcare context without disrupting established workflows or placing additional burden on healthcare staff. Furthermore, it was considered important to generate local data regarding diagnostic performance, including sensitivity and specificity within the Western Cape population. Once feasibility and validation have been established, the study could progress towards evaluating more system-related outcomes, such as whether implementation of the device contributes to reduced time from stroke onset to treatment.

Several different clinical study designs were considered relevant when discussing how the trial should be structured. Clinical studies can generally be divided into observational and experimental designs, with experimental studies further including multiple possible trial structures and designs. Since the Strokefinder MD100 actively interacts with the patient and is intended to support clinical decision-making, the proposed trial would be considered interventional in nature. Due to the characteristics of the intended patient population, certain aspects of the study design were also relatively predefined. Patients include in the study would present with suspected stroke of traumatic brain injury in acute settings, making it difficult to establish predefined cohorts followed over time in the same way as in many other clinical studies. Instead, the experimental group would consist of patients assessed using the Strokefinder MD100 in combination with standard clinical care.

Another important consideration concerns the consent procedure. Since patients presenting with acute stroke or TBI may have impaired consciousness or reduced decision-making capacity during the emergency phase, delayed consent models were considered necessary for this type of study. Such an approach would allow inclusion during the acute phase of care while informed

consent could instead be obtained after initial stabilization.

Based on discussions with interview participants experienced in clinical trial planning, a two-phase study emerged as a particularly suitable approach for this context. In the initial phase, the focus would be on feasibility and validation within an existing clinical workflow. Patients would first undergo standard triage and assessment procedures before being examined using the Strokefinder MD100 prior to confirmatory CT imaging. The CT results would then serve as the reference standard for evaluation of the diagnostic performance of the device. Conducting the study in this way would make it possible to evaluate whether the technology can be integrated into routine clinical practice without significantly disrupting existing workflows or delaying standard patient management. This phase would also generate local validation data regarding the performance of the device in the Western Cape context.

Following successful feasibility and validation testing, the study could potentially progress to a second phase focusing on system-related outcomes and transport pathways. In this phase, patients assessed using the Strokefinder MD100 could be compared with patients managed according to standard clinical pathways and existing triage systems. The purpose of this phase would primarily be to evaluate whether implementation of the device contributes to reduced time to diagnosis and treatment. One important advantage of such a phased approach is that it reduces the risk of destining an overly ambitious trial at an early stage, which was highlighted during several interviews as a common challenge in clinical research within the South African healthcare system.

Dividing the clinical evaluation into several phases could also provide advantages from a regulatory perspective. If future versions or applications of the device are considered sufficiently similar to previously evaluated intended uses, earlier validation data may potentially support later regulatory applications and reduce the need for repeating all early-stage investigations.

Based on the findings from the field study, endpoints related to integration into the healthcare system and reduction in treatment delays were considered particularly important in the proposed clinical trial. Additional outcomes that may be relevant for future studies include measures such as door-to-CT time, defined as the time interval between hospital arrival time and confirmatory imaging. Meaning how much time can be saved if the Strokefinder is used to make patient referral decisions.

Based on the TBI patient flow at the acute trauma unit at Tygerberg Hospital in Cape Town, it was suggested that approximately three to six months could potentially be used to have recruited at a minimum 300 patients in the defined category and reach statistical power to be able to assess feasibility before progressing to larger scale investigations.

4.1.2 Suggested clinical study sites

A central question when discussing a possible clinical trial of the Strokefinder MD100 is suitable study sites to perform the trial at. Based on the interviews conducted during the field study, several aspects were identifies as important in this process, including differences between the public and private healthcare sectors, patient volumes, access to research infrastructure, workflow integration and the intended future implementation area of the device. The findings further suggested that the most suitable setting for an initial clinical trial may not be in the same setting as the most suitable implementation.

When comparing the public and private healthcare sectors both advantages and disadvantages were identified. The private healthcare sector was described as having greater access to resources, leading to patients presenting earlier and a more rapid patient flow throughout diagnostics and treatment, which could be considered beneficial in stroke-related applications where time is a critical element. However, several interview participants described the private sector as more cautions regarding experimental interventions and emerging technologies, which may complicate the initiation of clinical trials. In addition it was highlighted that the private sector might lack full availability of established in-house research infrastructure, potentially requiring more involvement of external coordinator or CROs during the study process.

The public healthcare sector was instead identified as potentially more suitable for early phase clinical studies. One major reason for this was the substantially larger patient volumes at public tertiary hospitals, which may facilitate faster requirement and improve the possibility of achieving sufficient statistical power within a reasonable time frame. Furthermore, public academic hospitals were described as having stronger integration with universities and established research environments, including access to institutional ethics committees and clinical research infrastructure. Although the public sector is often characterized by resource limitations and heavy clinical workloads, the combination of patient volume, existing stroke workflows and academic collaboration may make tertiary public hospitals more feasible environments for an initial validation and feasibility study.

During the field study a clear distinction emerged between potential implementation sites and suitable sites for conducting the first clinical trial. Several interviewees highlighted the prehospital stroke pathway as one of the most relevant future implementation areas for the Strokefinder MD100, particularly in relation to destination triage and referral decisions. In such settings, the device could potentially support EMS personnel in identifying patients requiring urgent transfers to facilities with CT imaging or thrombectomy capability. Despite this potential value, the

prehospital setting may currently be difficult to use for an initial clinical trial in the Western Cape context. Several practical, ethical and regulatory barriers related to conducting the trial in a prehospital setting were identified during the interviews. One challenge that was discussed was that existing regulatory frameworks may assume that investigational interventions are administrated by medical doctors, whereas a prehospital study would likely rely on paramedics or emergency care personnel operating the device. Additional challenges include the non-specified location of prehospital care, where patient interventions may occur across multiple unpredictable locations rather within a controlled hospital environment. Furthermore, patient recruitment in a prehospital setting may be slower and more logistically demanding, which could potentially prolong the study period and complicate the data collection. Taken together, these factors suggested that although prehospital implementation may be a highly relevant application of the technology, it may not represent the most feasible environment for an initial validation study.

Instead, the interviews indicated that an early-phase clinical trial may be suitable to be conducted in a tertiary hospital environment. Several participants specifically highlighted academic stroke centres such as Groote Schuur Hospital in Cape Town due to the large patient volumes, established stroke pathways, and 24-hour access to CT-imaging. Such a setting would comparison between device findings and CT imaging without altering the existing workflows. A hospital-based feasibility and validation study could therefore represent a more realistic first step before progressing towards more complex implementation studies in prehospital environments in the future.

4.1.3 Human and organisational factors influencing trial feasibility

In addition to organisational and logistical factors, the interviews also highlighted the importance of staff engagement and local ownership during implementation of new technologies and clinical trials. Regardless of the selected study site, successful implementation was described as highly related and dependent on whether staff members understand the purpose and potential value of the project. Several interview participants emphasized that changes introduced without clear motivation or practical support may face resistance, particularly in environments with high workload and limited resources. Interestingly, despite the demanding conditions within the public healthcare sector, staff members at Tygerberg Hospital trauma unit were generally positive towards the possibility of participating in a clinical trial, provided that the staff felt involved in the process and understood the potential clinical value of the medical device. This suggests that staff engagement and perceived clinical relevance may be as important as infrastructure and resources when selecting future study sites for the clinical trial.

4.2 Limitations

Several limitations should be considered when interpreting the findings of this study. First, the number of conducted interviews was relatively limited, and although participants represented multiple perspectives within the WC healthcare system, additional interviews and broader data collection could potentially have provided a wider range of insights regarding implementation challenges, workflow integration, and clinical needs. Recruitment of relevant stakeholders was also challenging, particularly due to the limited availability and demanding schedules of clinicians, healthcare managers, and emergency care personnel.

The field study was conducted over a relatively short period of approximately three months. A longer study period could potentially have enabled more extensive stakeholder engagement, additional site visits, and deeper analysis of clinical workflows and referral pathways. Furthermore, a larger proportion of interviews were conducted within the public healthcare sector compared with the private sector, which may have influenced the perspectives and priorities reflected in the results. Additionally, a clinical study protocol is not written in this project.

Another limitation is that many interview participants had academic or research-related backgrounds. Although this provided valuable expertise regarding clinical trials and implementation strategies, inclusion of a broader range of professions and operational healthcare staff may have contributed additional practical perspectives regarding implementation, the conducting of clinical trials and effects of resource constraints.

Geographically, the study primarily focused on stakeholders located in Cape Town and surrounding urban areas. Since the WC covers large rural regions with substantially different healthcare infrastructure and access conditions, the findings may not fully reflect challenges present in more remote settings.

As master's students conducting this project, there is also an inherent limitation in the group members level of clinical, regulatory and technical knowledge regarding all aspects of the device and healthcare system. This may have influenced the ability to fully address technical questions, concerns, or implementation-related uncertainties raised during interviews, and may also have affected the interpretation of certain healthcare processes and stakeholder perspectives.

Another limitation was the relatively limited availability of detailed local data regarding patient flows, referral pathways, imaging utilization, and the economic burden of stroke and TBI within the WC context. Difficulties in obtaining such data from both public and private sectors complicated the development of more detailed implementation models and clinical trial proposals.

In addition, stakeholders from different professional backgrounds often expressed differing opinions regarding optimal implementation sites, study designs, and clinical use cases for the proposed technology. While these differing perspectives provided valuable insight into the complexity of the healthcare system, they also made it challenging to determine which priorities or recommendations should be emphasized most strongly in the proposed implementation strategies.

Finally, although substantial evidence exists regarding the burden of stroke and TBI globally, the availability of stroke and TBI data from the WC region remained limited. This complicates the ability to fully quantify the local clinical and economic need for implementation of the proposed technology within the regional healthcare system.

4.3 Health economy

The economic estimates presented in the economic evaluation should be interpreted as simplified, scenario-based calculations rather than a complete health economic evaluation. Several assumptions were made regarding device cost, device lifetime, number of patients treated, and achievable reductions in time-to-treatment. The analysis is based on a WTP threshold applied to QALYs, while clinical effect estimates are derived from previously published studies conducted in high-income healthcare settings. The extent to which these findings can be directly transferred to the SA healthcare context remains uncertain.

The estimated economic benefit reduced treatment delays is dependent on whether earlier triage using the Strokefinder would actually translate into faster access to CT imaging, thrombolysis, thrombectomy, or rehabilitation services. Interviews conducted in this study suggested that delayed access to imaging, interfacility transfer requirements, and limited after-hours CT availability may cause bottlenecks within parts of the public healthcare sector. Consequently, the potential value of the device may depend not only on diagnostic performance, but also on the surrounding healthcare infrastructure and referral pathways.

Another important aspect is that implementation of the device could potentially increase demand for confirmatory CT imaging, particularly if the device is used as an additional triage tool rather than as a replacement for imaging. While earlier identification of stroke patients may improve prioritization and reduce delays for some patients, it may simultaneously increase pressure on already resource-constrained imaging services. The balance between these effects remains unclear and would likely need to be evaluated prospectively after implementation. A potential effect could also be that more pressure is applied on the government to invest in more CT scans.

The potential societal benefits associated with reduced disability may be particularly relevant in the SA setting, where stroke frequently affects economically active populations and where access to long-term rehabilitation and social support may be limited. Earlier treatment could therefore potentially influence not only direct healthcare costs, but also caregiver burden, productivity loss, and long-term dependency. These indirect potential societal costs were not included in the calculations.

4.4 Ethical considerations

One of the most prominent ethical aspects identified throughout this study relates to the substantial inequalities that exist within the SA healthcare system. Multiple interviews highlighted that the large differences in access to imaging, ambulance availability, and stroke treatment pathways between public and private sectors, as well as between urban and rural settings. These disparities raise important ethical questions regarding who would realistically benefit from implementation of advanced diagnostic technologies such as the Strokefinder. It is likely that the device has the potential to improve care for patients in more vulnerable rural areas but there is a risk that populations in richer urban areas with less resource constraints benefit the most from the device depending on where it is implemented

A potential ethical concern is that implementation of new technologies may unintentionally benefit healthcare environments and populations that are already more well resourced compared to other environments and populations in the region. Facilities with existing access to CT imaging, stroke units, thrombechtomy services, and structured referral pathways may be more capable of integrating and utilizing the device effectively, while settings with less resources continue to face the the same systematic barriers regardless of additional support. There is therefore a risk that technological implementation could contribute to widening existing inequalities if deployment strategies are not specifically designed to address these challenges.

Geographical conditions within the WC constitute an important ethical consideration. Long transport distances, rural infrastructure limitations, and variable ambulance availability as well as limited knowledge about stroke symptoms, may strongly influence whether earlier stroke detection can realistically translate to earlier treatment. In several interviews, ambulance shortages and prolonged transport times were described as a major constraints within EMS care pathways. In this context, improved diagnostic capability alone may not necessarily improve outcomes unless accompanied by sufficient transport capacity and access to care at hospital facilities.

Another important consideration relates to the broader challenge of introducing technologies that has been developed in high income healthcare contexts into low- and middle-income healthcare

contexts. Throughout the interviews, participants repeatedly emphasized the importance of understanding the local healthcare context before proposing technological solutions. Several stakeholders highlighted that implementation strategies cannot simply replicate workflows from other contexts, but instead need to account for local referral structures, workforce limitations, limited imaging availability, infrastructure constraints, and financial realities.

5

Conclusion

This thesis investigated how clinical trials can be conducted within the healthcare system of the Western Cape region in South Africa, including relevant stakeholders, suitable study sites, practical considerations, attitude towards clinical research and potential challenges. The purpose was to develop a theoretical proposal for how a clinical trial of the Strokefinder MD100 could be designed within this specific context. This was achieved through a combination of literature review, field observations, and interviews with relevant stakeholders conducted on site. Through this process, sufficient information was gathered to allow the group to formulate a proposal for a possible future clinical trial design adapted to the Western Cape healthcare setting.

Based on the findings of this thesis, a clinical trial of the Strokefinder MD100 appears most feasible within the public healthcare sector in the Western Cape region. The combination of high patient volumes, established clinical pathways, and integration with academic research environments provides favorable conditions for conducting an early-stage clinical evaluation. The findings further suggest that a phased study design may be the most appropriate approach. An initial feasibility and validation phase conducted in a tertiary hospital setting could establish the diagnostic performance of the device and assess its compatibility with existing clinical workflows. If successful, this could be followed by a second phase evaluating whether the use of the device contributes to reduced delays in diagnosis and treatment within the stroke and TBI care pathways. Such an approach would allow both the practical feasibility and the potential clinical value of the technology to be evaluated before larger-scale implementation is considered.

The present study highlighted that successful implementation of clinical research in this context depends not only on technical performance, but also on staff engagement, workflow integration, realistic study design, and adaption to the local healthcare environment. In particular, the importance of motivated collaborators, local ownership, and clear communication with involved healthcare personnel emerged as central factors influencing the feasibility of the proposed clinical trial.

Overall, the findings of this thesis suggests that a clinical trial of the Strokefinder MD100 in the Western Cape region appears feasible, provided that the study is carefully adapted to the local healthcare context and introduced through a two-phased clinical study approach.

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