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A Health Technology Assessment of the Strokefinder MD100

For Early Detection of Stroke and Traumatic Brain Injury in the Western Cape Healthcare System, South Africa

Degree project report in Biomedical Engineering

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Abstract

Stroke is the second leading cause of death worldwide, with particularly high prevalence in low- and middle-income countries (LMIC) such as South Africa. Traumatic Brain Injury (TBI) accounts for approximately six million deaths annually and is commonly caused by trauma, an especially significant issue in South Africa (SA), where rates of interpersonal violence and traffic accidents are notably high. The South African healthcare system consists of a private and a public sector. The private sector are profit-driven hospital groups, while the public sector is government-funded. The public system operates on a referral-based model, which is not well-suited to managing time-sensitive medical conditions such as stroke and TBI. This report presents a Health Technology Assessment (HTA) of the Strokefinder MD100 device developed by the Swedish company Medfield Diagnostics AB, within the context of the healthcare system in the Western Cape, South Africa. The HTA is based on an extensive literature review combined with semi-structured qualitative interviews conducted with relevant stakeholders. The findings support the final recommendations for optimal implementation sites of the MD100 with the main purpose of minimising time-to-treatment and thereby improve patient outcomes. With the identified healthcare needs in the Western Cape, the most appropriate implementation sites are identified to be in pre-hospital units, within both private and public healthcare sectors, or in level 1 hospital facilities lacking CT imaging capabilities within the public healthcare sector.

Keywords: Strokefinder MD100, HTA, Assessment, Western Cape South Africa, Triage, TBI, Medfield Diagnostics, Stoke, Truma, Healthcare.

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Ebba Alvaeus Tynnerstål, Alice Thornander
Gothenburg, June 2025

List of Acronyms

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

CDC	Community Day Centre
CHC	Community Health Center
CMS	Council of Medical Schemes
CT	Computed Tomography
CUR	Health Problem and Current Use of Technology
DALYs	Disability Adjusted Life Years
ED	Emergency Department
ECO	Costs and economic evaluation
EFF	Clinical Effectiveness
ETH	Ethical analysis
FAST	Face, Arm, Speech Test
GCS	Glasgow Coma Scale
HTA	Health Technology Assessment
IV r-tPA	Intravenous Recombinant Tissue Plasminogen Activator
LEG	Legal aspects
LMICs	Low- and Middle Income Countries
MRI	Magnetic Resonance Imaging
MWT	Microwave Technology
NHI	National Health Insurance
ORG	Organisational aspects
PMB	Prescribed Minimum Benefit
SA	South Africa
SAHPRA	South African Health Products Regulatory Authority
SAF	Safety
SATS	South African Triage Scale
SOC	Patients and Social aspects
SOP	Standard Operating Procedure
TBI	Traumatic Brain Injury
TEC	Description and technical characteristics of technology
QoL	Quality of Life
QALYs	Quality Adjusted Life Years
WC	Western Cape

WC EMS	Western Cape Emergency Medical Services
WHO	World Health Organization
WTP	Willingness-To-Pay

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Introduction

1.1 Background

The background introduces the medical conditions stroke and traumatic brain injury (TBI), along with an overview of current treatment and rehabilitation approaches. It also outlines the structure of the South African (SA) healthcare system in the Western Cape (WC) region, covering both the public and private sectors, as well as emergency medical services (EMS). In addition, the current standard operating procedures (SOPs) for stroke and TBI management in the WC healthcare system are presented.

1.1.1 Stroke

Stroke is a major global public health challenge and the second leading cause of death worldwide, accounting for an estimated 6 million deaths annually [1], [2]. While stroke affects populations globally, its burden is disproportionately higher in low- and middle-income countries (LMICs), including SA. Between 1990-2016, the number of stroke cases doubled in LMICs while it during the same period decreased by 42% in high-income countries [2]. With 70% of all stroke-related deaths and 87% of all stroke-related disabilities occurring in LMICs, stroke places as a significant socio-economic burden on society [2], [3].

Stroke is a neurological disorder in which blood flow in the brain is restricted [2]. It is an acute medical condition, as limited blood circulation progressively leads to oxygen deprivation, causing severe brain tissue damage if not treated promptly [4]. Time is a particularly important factor in this context. 1.9 million neurons and 13.8 billion synapses are lost every minute as a consequence of an untreated stroke which dramatically increases the risk of permanent brain damage, disability or in worst case death [5].

The symptoms of a stroke can vary and depends on both the severity and exact location [4]. As the brain is the central organ of the nervous system, the site of the stroke affects both what neurological functions that are impaired as well as to what extent [6]. Common symptoms of a stroke are numbness, weakness, speech and vision impairments as well as dizziness and difficulties with body coordination such as walking [7]. Often, only one side of the body is affected causing a one-sided

facial drop or paralysis [7].

Stroke risk factors are associated with both lifestyle and genetic influences, as well as pre-existing medical conditions [7], see Figure 1.1. In Africa, hypertension is the leading contributor of the stroke burden, followed by dyslipidaemia and obesity [8]. The World Health Organization (WHO) has estimated that the world's highest proportion of people with hypertension lives in sub-Saharan Africa, where SA is located [8], [9]. Additionally, the Human Immunodeficiency Virus (HIV) is another significant risk factor for stroke. Africa bears the highest global burden of HIV, with nearly 70% of the cases occurring in sub-Saharan Africa [8].

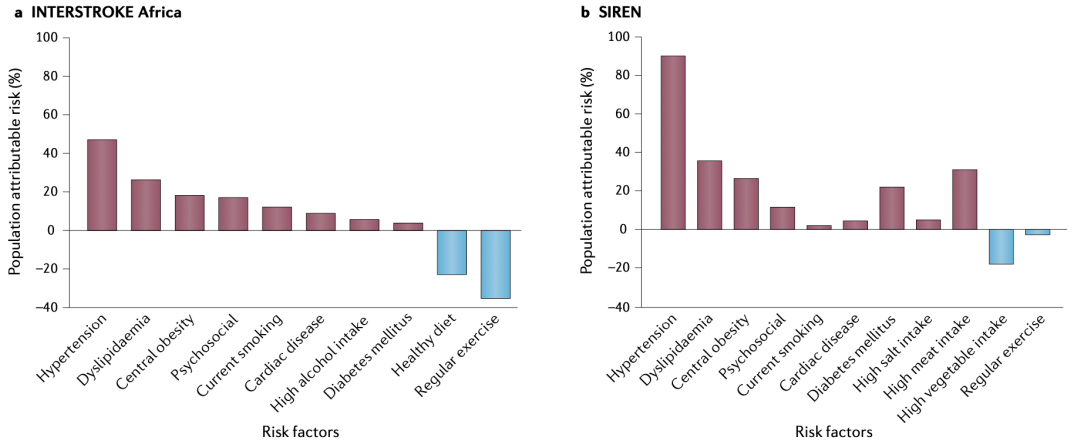

Figure 1.1: Associated risk factors of a stroke in Africa, based on two separate studies *INTERSTROKE Afrika* and *SIREN* [8].

There are two main categories of stroke, namely; ischaemic and haemorrhagic [2]. Globally, 80-85 % are ischaemic while the remaining 15-20 % are haemorrhagic, However, a study in SA showed a split of 60 % ischaemic and 40 % haemorrhagic, possibly due to the high rates of hypertension [10].

1.1.1.1 Ischaemic stroke

Ischaemic strokes occur when a blood vessel in the brain becomes blocked, commonly referred to as a blood clot [2]. Blood clots are often a result from gradual build-up of atherosclerosis inside the blood vessels, which over time narrows the vascular pathway and limits blood flow. There are two types of ischaemic strokes depending on its origin. If the blockage forms directly at the site of the occlusion, it is referred to as a thrombotic ischaemic stroke. A blood clot can also form in another part of the body and travel through the vascular system to the brain, where it becomes lodged. This type of stroke is called an embolic ischaemic stroke.

1.1.1.2 Haemorrhagic stroke

Haemorrhagic strokes are characterized by an intracranial brain bleeding, either caused from a ruptured blood vessel or a leaking blood vessel [2]. Typically, the

haemorrhage expand within 3–12 hours of onset, leading to a build-up of blood that increases intracranial pressure and restricts blood flow, resulting in progressive brain damage [11]. This type of stroke is generally associated with high morbidity and mortality due to the pressure exerted by accumulated blood on surrounding brain tissue [12], [13].

The symptoms of a haemorrhagic stroke are similar to those appearing in case of an ischaemic stroke, usually presented as severe headache, speech and vision difficulties as well as one-sided muscle weakness and facial palsy [12].

1.1.2 Stroke treatments

Treatment strategies for ischaemic and haemorrhagic strokes differ significantly. Management of haemorrhagic strokes typically involves supportive care, such as the administration of antihypertensive medications to control blood pressure or alternatively prescription of medication to promote clotting to stop the bleeding [11], [14]. In some cases, surgical interventions may also be considered for haemorrhagic strokes. Coil embolization is a minimally invasive procedure where small platinum coils are used to occlude the bleeding vessel by preventing further expansion. The coils are guided thorough the the blood vessels via a catheter to the site where there are deployed in order to minimize the free bleeding in the brain [15]. To relieve intracranial pressure caused by the accumulation of blood, another surgical intervention called decompressive craniotomy can be performed. This procedure alleviates the pressure resulting from cerebral edema induced by the bleeding [14].

In contrast, the two treatment procedures for ischaemic strokes are thrombolysis and thrombectomy. The eligibility for either treatment depends on the time from stroke onset, additional inclusion criteria, as well as the healthcare facility's capacity and access to necessary medical expertise.

1.1.2.1 Thrombolysis

Thrombolysis is a treatment that involves administering a drug to dissolve blood clots. This is typically done by injecting tissue plasminogen activator (tPA), a substance that breaks down fibrin which is the protein that holds the clot together [16]–[18].

Administering thrombolysis to patients with ischaemic stroke has been associated with a significant reduction in death and long-term disability, given that it is administrated within the therapeutic time-window of 4.5 hours from stroke onset [14], [17]. Outside the recommended time-frame, the risk of intracranial haemorrhage may outweigh the benefits as thrombolytic agents are not targeted medications, but has a degrading property of the entire fibrin matrix and not just the intended blood clot. Therefore, thrombolysis is not suitable for all patients, and should be avoided for patients with an active internal bleeding due to the elevated risk of haemorrhagic complications [17].

The greatest benefits of thrombolysis are observed when it is administered as early as possible [17], [18]. Patients who receive thrombolysis within 90 minutes of stroke onset experience nearly twice the benefit compared to those treated later [18]. Therefore, timely identification of stroke is crucial, yet often the reason patients are excluded from receiving thrombolytic therapy.

1.1.2.2 Thrombectomy

When obstruction occurs in the proximal cerebral arteries, known as a large vessel occlusion (LVO) which account for 1/3 of all ischaemic strokes [19], thrombolysis is often ineffective due to the extent of the blood clot [20]. Instead, a more effective approach is the mechanical thrombectomy, a procedure that involves the removal of the clot from a blood vessel under image guidance using endovascular devices [21]. The most common techniques for thrombectomy are catheter-based therapies, which utilize either a stent retriever or direct aspiration [14], [21]. Usually, a catheter is inserted via an artery at the groin and from there guided up to the neck and to the site of the blockage in the brain artery. The catheter works as a passage for the stent-retriever to reach the clot and manually remove it in order to restore blood flow.

Thrombectomy is compared to thrombolysis a more recent approved treatment for ischaemic stroke and has been proven to be both safe and effective at randomized controlled trials (RTCs), under the circumstances that the procedure is performed correctly [22]. Currently, the surgical procedure is mostly only performed by specialised surgeons such as interventional radiologist or interventional neurosurgeon [12]. The procedure is approved to be performed up to 24 hours after stroke onset [20], [23], although current evidence suggests that performing the procedure as early as possible yields better clinical outcomes [22].

1.1.3 Stroke rehabilitation

While cell death at the stroke core is irreversible, functional recovery is possible through neuroplasticity, which is the brain's ability to form new neural connections [24]. This process allows healthy brain regions to take over lost functions and is stimulated through targeted, task-specific exercises during rehabilitation [25]. Stroke rehabilitation typically includes physical therapy and strength training to restore mobility and aims to minimize the long-term effects of a stroke. Although recovery timelines vary between individuals, early intervention is crucial, as the most significant improvements usually occur within the first three to six months post-stroke [7].

1.1.4 Traumatic brain injury

TBI is major global health concern, accounting for approximately 6 million deaths annually [26]. It is defined as an acquired cerebral dysfunction resulting from an external force that inflicts trauma on the brain, often as a result from mechanical violence or compression injuries. As with stroke, the burden of TBI is disproportion-

ality high in LMICs, which also accounts for 90 % of the TBI-related deaths [27]. SA has one of highest TBI rates in the sub-Saharan Africa with intentional injuries almost seven times as high compared to global rates and road traffic accidents twice the global rates.

Similar to stroke, TBI is highly time-sensitive and accurate management is critical to prevent secondary brain injury and mitigate further neurological damage [28]. Secondary brain injuries refer to potential changes over time, sometimes even days after the actual point of injury. Secondary brain injury often results in increased intracranial pressure, which causes brain swelling that restricts blood flow and damages the brain tissue.

There are two main types of TBI: penetrating and non-penetrating injuries [28]. Penetrating TBIs are most often the result of interpersonal violence, where objects, such as bullets, pierce the skull and interferes with the brain tissue. Non-penetrating TBIs occur when an external force causes the brain to heavily move within the skull, causing a widespread trauma to the brain. Non-penetrating TBIs are commonly caused by falls, road traffic accidents and sports injuries.

Given the broad spectrum of different TBIs, symptoms also vary [28]. Common physical symptoms include severe headache, nausea, sudden seizures, pupil dilation and blurred vision. In some cases, clear fluid may drain from the nose or ears, indicating a more severe brain injury. In addition to the listed physical signs, neurological symptoms are similar to those observed in stroke patents, such as weakness and speech difficulties.

1.1.5 TBI treatments

TBI treatment typically involves one or more of three main approaches, medication, surgery and rehabilitation, depending on the injury's severity.

Medication plays a key role in managing TBI patients and there are a variety of drugs that may be prescribed based on the patient's specific needs [29]. Commonly, medications are used to reduce the accumulated fluid in brain tissue, which can otherwise increase intracranial pressure in the skull, putting patient at a significant risk of further damaging healthy brain tissue. In some cases, the free bleeding compresses blood vessels which puts patients at risk of seizures. To prevent this, anticonvulsants can be administered to reduce the likelihood of seizures and thereby minimize further damage.

Besides medication, surgical intervention is another important treatment alternative for particularly moderate to severe TBIs [29]. Surgery may be necessary to manually remove severely damaged brain tissue to relieve pressure and prevent further injury on surrounding healthy tissues.

In addition to acute medical and surgical treatments, rehabilitation therapies are considered as equally essential to improve long-term patient outcomes [29]. While

rehabilitation does not cure the TBI itself, it focuses on restoring lost brain function and improving quality of life (QoL). Recommended therapies aim to improve blood circulation and thereby oxygen delivery to the brain which helps reduce inflammation and supports patient recovery. Similar to stroke rehabilitation, these may include physical therapy, occupational therapy and speech therapy. Physical rehabilitation are specially important to help relieve muscle spasms and contractures which are common post-TBI symptoms.

1.1.6 South African Healthcare System

The healthcare in SA is divided into a public and a private healthcare sector. The public healthcare is funded by the government and used by 84% of the SA population, offering services that are either entirely free or available at subsidized rates [30]. The private healthcare sector is instead build upon those who afford to pay for their healthcare services via medical aid schemes and contributes for the remainder of 16% of the population. As stated, the majority of the population heavily rely on public healthcare. Still, almost 80% of the healthcare professionals work in the private sector, highlighting the significant resource disparity within the public healthcare system [31].

In May 2024, a major initiative to make healthcare more equitable and accessible became law in SA [32]. This initiative, known as the National Health Insurance (NHI) Act, represents SA's strategy to achieve universal health coverage through the establishment of a national insurance fund. Similar to other insurance models, all SA's citizens will routinely contribute to the NHI fund through taxes, and the government will use these funds to purchase healthcare services from both public and private providers. When healthcare services are needed, the NHI fund will cover the costs on behalf of the patient.

However, the transformation of SA's healthcare system has only just begun, and it is expected to take many years to fully integrate the public and private sectors [32]. The ultimate goal of the NHI is to create a more efficient, fair and effective healthcare system that provides all SA citizens with the right to access high-quality affordable healthcare.

There is, as of today, not much collaboration between the public and private healthcare documented. However, it has been stated that all pre-hospital units, regardless of being private or public, is bound by law to take patients, regardless of possessing a medical aid scheme, to a hospital in case of injury [33]. In the cases where patients can not afford the private EMS, the government covers this cost [34].

1.1.6.1 Public Healthcare

The public healthcare services are divided into district, regional and tertiary hospitals as illustrated in Figure 1.2 [35]. Additionally, clinics, community health centres (CHC) and community day clinics (CDC), provides primary healthcare services supporting the pyramid-structure as well as emergency medical services (EMS).

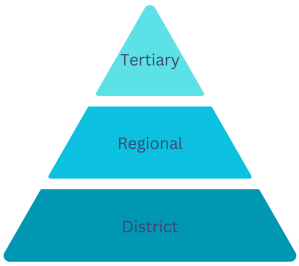

Figure 1.2: Hierarchy of public healthcare levels in SA with district at the bottom, followed by regional and tertiary at the top.

SA's healthcare system relies on patient referrals between hospital levels, as specialized care requires advanced facilities. However, this transfer process is time-consuming, costly and often inefficient with an estimated 20% of transfers classified as unnecessary [36]. Figure 1.3 illustrates the current SOP of referral pathways in the WC from lower level facilities to the two tertiary facilities Tygerberg hospital and Groote Schuur hospital. The clinics and district hospitals are distributed throughout both rural and urban areas of the province, while the tertiary care facilities are located in the urban center of Cape Town. This centralized healthcare structure often necessitates multiple referrals, and in some cases, patients may be transferred through as many as four different facilities before reaching the specialized care they require [33]. For time-critical medical conditions such as stroke and TBI, this structure is particularly challenging.

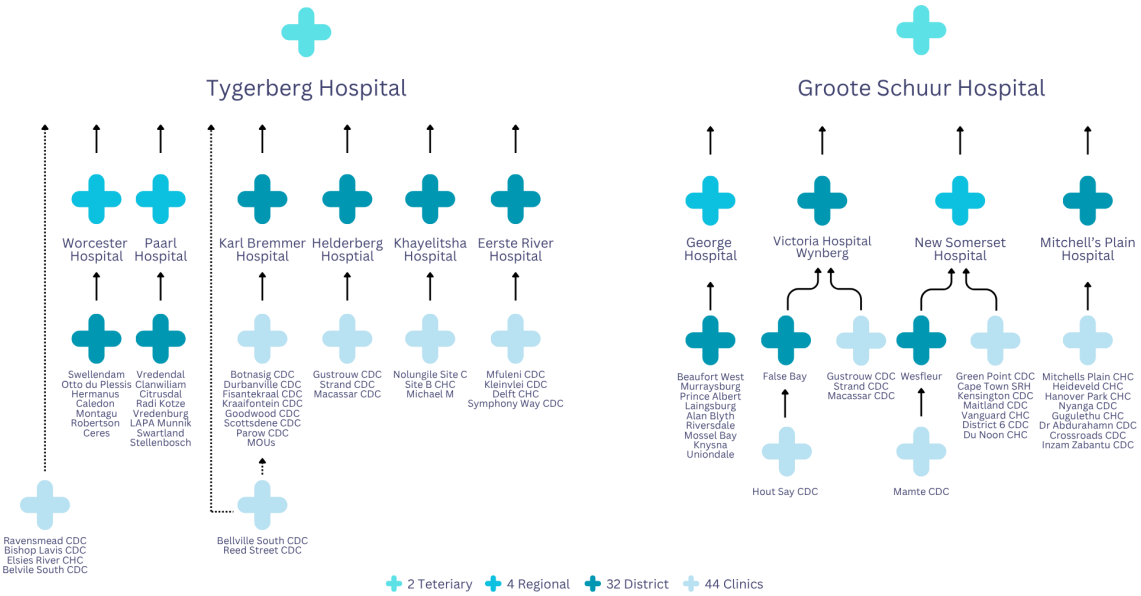

Figure 1.3: Overview of the general patient referral pathways between the hospital facilities in the WC.

Public healthcare can also be explained by the level of care the facilities offer. The clinics, that include both the CHCs and CDCs, offer primary healthcare services. These include maternal and child health, chronic disease management, HIV care, rehabilitative and therapeutic services. In some cases, limited emergency care [37].

District hospitals offer primary healthcare services on a 24-hour basis provided by generalist nurses, with four years of education and broader knowledge of basic nursing care, as well as clinical nurse practitioners who have advanced education in a specific area of healthcare and provide specialised care within that scope of practice[38], [39].The size of a district hospital varies between 50 to 600 beds. Common services include in-patient care and emergency care. Some district hospitals are also eligible to perform general surgery [37], [39]. If needed, the district hospitals may receive more specialised support from regional hospitals.

The regional hospitals, with 200 to 800 beds, are assigned with broader responsibilities as clearly defined in national regulations [39]. A regional hospital operates on a 24-hour basis and offers a range of healthcare services, including general surgery, internal medicine, as well as trauma and emergency care. Some extended services may be offered at regional hospitals but are typically limited to within provincial boundaries. The regional hospitals receive referrals from several district hospitals in the region and can in turn get support from tertiary hospitals.

The highest level of healthcare are the tertiary hospitals which offer specialized medical services and intensive care under the supervision of specialists [39]. Tertiary hospitals receive referrals from regional hospitals, and these referrals are not restricted to provincial boundaries. In WC there are in total two tertiary hospitals, Tygerberg hospital and Groote Schuur hospital. Both hospitals serve as university hospitals for Stellenbosch University and University of Cape Town respectively. As of today, Tygerberg and Groote Schuur are the only two public hospitals in the WC with the resources required to perform thrombolysis and thrombectomy as well as surgical intervention for treatment of TBI [34], [40].

Table 1.1 groups the different level of hospitals dependent on their accessibility and operation of CT-capabilities.

Table 1.1: Levels of healthcare facilities in the Western Cape

Level	Facility Description
Level 1	Clinics and district hospitals without CT capability
Level 2	District and regional hospitals with CT capability (typically operating 8a.m. to 4p.m. [34])
Level 3	Tertiary hospitals with CT capability 24/7

There are in total 32 district hospitals, 5 regional hospitals and 2 tertiary hospitals in the WC. Out of these, only 10 facilities are equipped with a CT [34]. Table 1.2 provides an overview of the hospitals equipped with CT scanners, patient referrals and the distances involved.

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

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]	-
Clanwiliam	District	No	Paarl [197 km]	-
Citrusdal	District	No	Paarl [144 km]	-
Radi 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]	-

1.1.6.2 Private Healthcare

Private healthcare is a voluntary service in SA, funded by medical aid schemes, which are commonly distributed with employment or can be bought privately [41]. There are approximately 8.9 million people in SA registered at one of 71 medical aid schemes across the country [41], [42]. There are multiple private hospital groups operating in the WC region of SA, where Mediclinic Southern Africa, Life Healthcare and Netcare are the leading ones [43], [44], [45]. Compared to public healthcare that operates on a provincial basis, private healthcare are offered via an entire hospital group that extends beyond provincial boundaries [46]. Members pay a monthly fee to their chosen medical aid scheme, which grants them access to private healthcare services in SA. The extent of coverage for these services depends on the specific medical aid plans [41]. All medical aid schemes are regulated by the national Council for Medical Schemes (CMS) to ensure compliance with Prescribed Minimum Benefits (PMBs) for their members, regardless of their medical aid plan [41].

1.1.6.3 Emergency Medical Services

Public EMS are a provincial function governed by the Provincial Departments of Health (PDoH), funded via the government [47]. In the WC province this is the Western Cape Emergency Medical Services (WC EMS). For private EMS, there are both privately owned companies and hospital groups that offer EMS, amongst those, ER24 is a part of the private hospital group Mediclinic Southern Africa [48]. ER24 units are staffed with paramedics and equipped with medication and medical equipment for advanced life support [48]. The collaboration between public and private healthcare in terms of pre-hospital services and units are somewhat limited [33].

The WCG EMS operate over 250 ambulances across the WC province of SA [49]. In SA specifically, the national recommendation is to have at least one ambulance per 10,000 citizens [50]. In the context of the WC's population with 7.2 million people, this would correspond to approximately 720 pre-hospital units [51]. Given that around 84 % of the WC population relies on public healthcare services, this gives a shortage of 350 units across the WC province. It has also been reported that many pre-hospital units are out of service [50]. A study from 2024 found that only 130 units operated in the WC, which represents to 52 % of the resources that should be functional [51], which highlights a significant shortfall. For private EMS operations in the WC, there is no information available on how many units that are available.

The WC government have reported that each public pre-hospital unit in WC is equipped with medication and medical equipment as well as two medical practitioners. It is stated that one or both of the practitioners in the EMS can perform basic life support (BLS), intermediate life support (ILS) and advanced life support (ALS) [49]. However, in a study from 2024 it was shown that the SA pre-hospital care providers knowledge about both BLS and ILS were lacking, especially the knowledge about Glasgow Coma Scale (GCS) which is a specifically critical evaluation

system used for triaging of stroke and TBI patients [50]. Besides pre-hospital care, the WCG EMS also perform inter-facility transfers of patients between different instances of the public healthcare in cases where the patient needs care that extend the capability of the current instance [49]. In an annual report from 2017/2018 it was concluded that approximately 1/3 of the WC EMS activity was dedicated to inter-facility transfers [52]. This further restricts the time allocated to handle primary medical responses, such as stroke and TBI.

1.1.6.4 Triage Scales

A definite diagnosis of stroke and TBI is confirmed by a neuroimaging service, either computed tomography (CT) or magnetic resonance imaging (MRI) [1]. These imaging methods not only confirm the presence of a stroke or TBI but also provide critical information about the exact location and the extent to which surrounding brain tissue has been affected.

The initial assessment of patients prior access of a neuroimaging service, is usually conducted using standardized triage scales, both in the pre-hospital setting and at the hospitals. Worldwide, commonly used scales for assessment of stroke in the pre-hospital settings are the 3-item stroke scale, the Austrian Prehospital Stroke Scale, the Cincinnati Prehospital Stroke Scale, the Los Angeles Stroke Screen and the Rapid Arterial Occlusion Evaluation scale [53]. All of the mentioned stroke assessment scales are highly based on clinicians interpretation of a patient's appearance and it has been reported that in 30 % of the pre-hospital cases, the stroke assessment scales are insufficient to adequately recognize stroke [53].

The most complete and detailed scoring system in-hospital settings is the National Institutes of Health Stroke Scale (NIHSS). This is a commonly used stroke scale which estimates the stroke severity based on 15 evaluating statements [53]. The assessment does not require neurology expertise, making it suitable as an initial evaluation tool at all hospital levels and contributing to its widespread use. To adapt the scale for use in the time-sensitive emergency setting, two modified versions have been developed, namely the modified NIHSS and the shortened NIHSS-EMS, which both are frequently used in the pre-hospital setting.

The specific stroke triage scales in SA are the South African Triage Scale (SATS), the Glasgow Coma Scale (GCS), and the Face-Arm-Speech-Time (FAST) test [54] [34]. Similarly, the initial assessment of a TBI patient is based on SATS and GCS [34]. For performance metrics of the individual assessment tools used, see tables 3.2 and 3.3.

South African Triage Scale

Triaging patients in SA pre-hospital and emergency centres (ECs) are done using SATS [55], [54]. The priority coding is divided into five different levels and managed accordingly; see Figure 1.4.

Priority COLOUR	Target time	Management
RED	IMMEDIATE	Take to the resuscitation room for **emergency** management
ORANGE	< 10 mins	Refer to majors for **very urgent** management
YELLOW	< 1 hour	Refer to majors for **urgent** management
GREEN	< 4 hours	Refer to designated area for non-urgent cases
BLUE	< 2 hours	Refer to doctor for certification

Figure 1.4: South African Triage Scale (SATS) chart showing priority levels and associated colour codes. Source: Emergency Medicine Society of South Africa (EMSSA), SATS Manual (2012). Shared under a CC BY-NC-SA 3.0 license [54]. No modifications were made.

The SATS follows a five step approach where the healthcare personnel begins with looking for emergency signs followed by looking for very urgent or urgent signs. Depending on the level of urgency, the next step is to measure the vital signs and calculate the Triage Early Warning Score. Finally , a triage priority level is assigned according to above [54]. The published manual also states that if the patient has any of the following emergency signs, a TEWS score does not need to be calculated in order to prioritize the patient as red; obstructed airway (not breathing), ongoing seizures, facial burns/inhalation, hypoglycaemia (glucose less than 3mmol/L) or cardiac arrest [54].

Glasgow Coma Scale

The GCS is particularly valuable for assessing patients with haemorrhagic stroke or TBI, and it is also applicable for comatose patients [53]. It is commonly used to perform neurological assessments at the hospital by evaluating the three key components: motor responsiveness, verbal performance and eye opening. Each component is assigned a specific score, which is then summed to yield a total score, as shown in Table 1.3 [56], [57].

Table 1.3: The different parameters of GCS and its respective score.

Motor function	Verbal Response	Eye response
Obey commands (6)	Oriented (5)	Spontaneous reaction (4)
Localising to pain (5)	Confused (4)	React to sound (3)
Normal flexion to pain (4)	Words (3)	React to pressure/pain (2)
Abnormal flexion to pain (3)	Sounds (2)	No eye opening (1)
Extension to pain (2)	No verbal response (1)	-
None (1)	-	-

The interpretation of the total scoring is divided into three different severity levels: a score between 13-15 is classified as a *minor head injury*, 9-12 is classified as a *moderate head injury* and ≤ 8 is classified as a *severe head injury or coma* [56].

The GCS is also incorporated into three more detailed neurological scoring systems; the World Federation of Neurological Surgeons (WFNS) scale, the ICH score and the Full Outline of UnResponsiveness (FOUR) score [53]. These scales build upon the GCS to provide a more comprehensive assessment tailored to specific clinical scenarios.

Face, Arm, Speech, Time - Test

The FAST assessment is an initial screening method used in the pre-hospital setting where the clinician evaluates the physical appearance of face drooping (F), arm weakness (A) and speech (S) difficulties [58]. The FAST test is designed to facilitate the early recognition of stroke symptoms and is widely applicable, both within healthcare and by the general public, due to its straightforward and easy-to-remember process. There are several modified versions of the FAST assessment [53]. The G-FAST test takes gaze deviation (G) into consideration while the BE-FAST version incorporates assessments of both balance (B) and eye (E) symptoms. Additionally, the FAST-ED scale includes eye deviation (ED) and signs of anosognosia or neglect, which is specially common for LVOs[53].

1.2 Purpose

Healthcare in SA faces significant challenges. The public sector, which serves the vast majority of the population, is severely under-resourced and overburdened, struggling to meet the growing demand for services. Shortages of financial and human resources and a high burden of disease place enormous pressure on healthcare providers and facilities.

Additionally, the current referral-based healthcare system introduces substantial delays in care, which are especially critical for time-sensitive conditions such as stroke and TBI. Consequently, timely diagnosis, effective treatment, and equitable access to care remain difficult to achieve, resulting in poorer patient outcomes and increased strain on healthcare services.

1.3 Goals

This project aims to evaluate the suitability of the Swedish medical innovation, Strokefinder MD100, in the WC public healthcare system, with a focus on its potential to shorten time-to-treatment for stroke and TBI patients. By examining current care pathways, the project will identify critical integration points where the MD100 could strengthen clinical decision-making and patient triage. Guided by the EUnetHTA Core Model, the assessment will ensure a structured and multidimensional evaluation of the device's clinical relevance and health system compatibility.

Based on the findings, the project will recommend suitable implementation sites to reach more timely and equitable access to care.

1.4 Limitations

To ensure the feasibility of this project, certain limitations were necessary. Firstly, the assessment is geographically restricted to the WC province of SA. The scope includes both public and private healthcare sectors; however, the primary focus is on the public sector due to limited access and communication with stakeholders within the private sector. The assessment addresses both stroke and TBI. However, given that the MD100 is only CE-certified for stroke, this is our primary focus when performing HTA, but extends to TBI when appropriate. Due to the limited time-frame of the project and the current development status of the Strokefinder MD100, not all questions from the EUnetHTA Core Model could be fully addressed, see appendix B for specification. The helicopter emergency medical services are primarily responsible for longer transfers of acute patients to higher instances of care. Given the limited information about the helicopter emergency medical services in the WC, SA, this aspect of the healthcare will not be included in the discussions for the final recommendation of implementation sites. The discussions will also be based on that the standard operating procedures for patient referral pathways are followed, even though it has been stated that this is not always the case [40], [59].

2

Methods

This study employs a combination of an extensive literature review combined with qualitative interviews with relevant stakeholders. The following section outlines the specific methodologies respectively by detailing the process of sourcing and analysing the literature as well as describing the execution and analysis of the performed expert interviews.

2.1 Health Technology Assessment

Health technology assessment (HTA) is a systematic approach that evaluates health related technologies by applying a multidisciplinary approach that includes both direct and indirect aspects [60]. The process shall be transparent and accountable and by providing an evidence-based review of the technology, the HTA aims to support and serve stakeholders in the decision-making process of implementation of health technology [60]. The HTA aims to evaluate properties, effects and impacts of medical technologies [61] and is defined by WHO as follows:

"It is a multidisciplinary process to evaluate the social, economic, organizational and ethical issues of a health intervention or health technology. The main purpose of conducting an assessment is to inform a policy decision making." [61].

The European Network for Health Technology Assessment (EUnetHTA) has created a structured framework, EUnetHTA Core Model version 3.0 from 2016 [62]. This project is structured as per the EUnetHTA core model, focusing on properly answering each respective question via a comprehensive literature review combined with expert interviews.

2.1.1 Literature review process

The literature review focused on topics related to stroke and TBI, both in terms of epidemiology, prevalence, morbidity and mortality, therapeutics and rehabilitation in the specific area WC, SA. Other relevant areas where the Strokefinder MD100 and information regarding microwave technology (MWT). The used databases included Pubmed, Google Scholar and IEEE Xplore. Additional material was supplied by

professor Emeritus Mikael Persson, one of the founders of Medfield Diagnostics, as well as previous work by PhD student Tinashe A Chikunichawa at Stellenbosch University and M.Sc student Jean Paul Kulumba at Stellenbosch University.

2.1.2 Interview study methodology

To gain insights into the specific care of WC, SA, qualitative interviews were carried out through the 87 days in SA. In total, 12 interviews were held with participants selected based on their current or previous professional roles and relevant experience. The interviews were semi-structured to allow for open-ended responses and in-depth conversations, encouraging participants to share their perspectives on the topics discussed rather than providing short or single-sentence answers.

The interviews were conducted both in person and online, as outlined in Table 2.1, to accommodate the preferences of each interviewee. The duration of the interviews ranged from 45 to 150 minutes. Prior to each interview, all participants were informed of the study's purpose and gave their consent to participate voluntarily. Continuos notes were taken during the discussions. The data gathered from the interviews were transcribed and summarized to capture the key conclusions. These summaries were then sent to the respective interviewees for approval and possible correction. This process ensured that the information was accurately represented, minimizing misunderstandings or subjective interpretations, and instead focusing on preserving the integrity of the insights provided.

To form a comprehensive understanding of the healthcare system in relation to stroke and TBI care, and the implementation of medical technologies, interview participants were selected based on their expertise across multiple relevant domains, as outlined in Table 2.1. The diverse professional backgrounds were intentionally chosen to capture the perspectives of all stakeholders including real-world considerations such as regulatory frameworks, economic feasibility and market integration. This approach ensured the inclusion of both clinical and non-clinical viewpoints, providing a contextually grounded foundation for the study.

Table 2.1: List of interviewees, their roles, relevance, and meeting context

Name, Location & Date	Role	Relevance
Alan Bryer Groote Schuur Hospital, Cape Town 24.03.2025	Former Head of the Division of Neurology and Stroke Unit at Groote Schuur Hospital.	To understand current stroke management practices and SOPs of stroke at one of the tertiary facilities in WC, SA.
Daniel Youkee Groote Schuur Hospital, Cape Town 24.03.2025	Postdoctoral researcher with the Stroke group at the Neuroscience Institute and Emergency Medicine doctor at Groote Schuur Hospital, Cape Town.	Provided stroke insights in contexts without using CT-scanners.
Evan Herbst Online 08.04.2025	Director Public Health and Commercial Excellence with 25 years of experience within the South African healthcare market.	To provide perspective on medical technology device implementation and market access in SA.
Hendrick J Lategan Tygerberg Hospital, Cape Town 07.03.2025	Operational Head of the Trauma Unit at Tygerberg Hospital and Division of Emergency Medicine.	To understand current trauma triage processes at the tertiary facilities and gain insights of current patient flow pathways in WC, SA.
John Paul Kulumba Online 27.02.2025	Industrial Engineer, Macrologistics Data Analyst.	To explore integration possibilities and challenges of medical technology within the private healthcare sector.
Kathleen Bateman Groote Schuur Hospital, Cape Town 24.03.2025	Head of the Division of Neurology and Stroke Unit at Groote Schuur Hospital.	To understand current stroke management practices and SOPs of stroke at one of the tertiary facilities in WC, SA.
Mark Brand Online 01.04.2025	Managing Director at Brandtech Health Technology.	To gain industry perspective on implementation of medical technology in SA and regulatory aspects for the health system entry.
Mladen Poluta Online 21.04.2025	Health Technology Director at Southern Right HTM Consulting.	To understand procurement procedures and introduction of medical technology for both private and public healthcare in SA.
Naseef Abdullah Online 05.05.2025	Head of unit of the ambulance care, Western Cape Government.	To provide insights on current ambulance care in the WC and possible integration of the MD100 within this setting.
Sa'ad Lahri Tygerberg Hospital, Cape Town 30.04.2025	Head of division of Emergency Medicine at Tygerberg Hospital.	To understand current management of stroke and discuss clinical applicability of MD100 in the public healthcare of the WC region.
Sudesh Sivarasu University of Cape Town, Cape Town 31.03.2025	Leads the university's MedTech lab and Senior Lecturer in Biomedical Engineering.	To discuss local medical technology development processes with a focus on the regulatory context of SA.
Tinashe Chikunichawa Stellenbosch University, Stellenbosch 12.03.2025	PhD Student in Industrial Engineering, Stellenbosch University.	To discuss previous conclusions about the MD100 amongst healthcare professionals and discussing cost-effectiveness of the device in different contexts.

2.2 Health economy

The health economy aspect is a critical factor in the evaluation of medical technology implementation. In order to analyse this factor in the SA context, we have conducted health economic calculations.

The calculation of the Quality Adjusted Life Year (QALY) are derived from the amount of disability free days. In the equation, x is the number of disability free days and the utility value is a score between 0 (death) to 1 (perfect health).

$$\text{QALY} = \frac{x}{365} \cdot utility\ value \tag{2.1}$$

The total QALY gained can further be calculated, where n is the amount of patient the device is used on annually.

$$\text{Total QALY} = \text{QALY} \cdot lifetime\ of\ device \cdot n \tag{2.2}$$

The incremental cost-effective ratio (ICER) is derived by the following equation where C is the expected increase in costs, B is the benefit with respect to QALY and λ is the threshold value, i.e., the maximum per QALY which is the Willingness To Pay (WTP). ICER tells you how much extra cost is required to gain one additional unit of health benefit.

$$\text{ICER} = \Delta C/\Delta B < \lambda \tag{2.3}$$

Health economic is proved beneficial when the Incremental Net Monetary Benefit (INMB) is positive as explained in the following equation. INMB converts both costs and effects into a single monetary value and tells you the net value of switching to a new intervention, given a specific WTP threshold.

$$\begin{aligned} \text{if:} \quad & 0 < \lambda \cdot \Delta B - \Delta C \\ \text{then:} \quad & \text{INMB} > 0 \end{aligned} \tag{2.4}$$

$$INMB = NMB_{now} - NMB_{comparator} \tag{2.5}$$

3

Results

This section presents the findings from our research, answering the questions from the EUnetHTA Core Model version 3.0 from 2016 for the Medfield Diagnostics device Strokefinder MD100 in SA. The chosen issues are directly taken from the EUnetHTA and specified in the table for each of the domains. The excluded issues, their respective ID, domain and the reason for exclusion is specified in appendix B.

3.1 Health problem and current use of technology

Understanding the health context in which the MD100 is intended to operate is essential for assessing its potential value. This domain provides an overview of the current management of stroke and TBI in the WC, SA. It also discusses the burden of these conditions, the role the MD100 is intended to play in their management and the device's current regulatory status.

Target population

The following issues and their corresponding IDs, from the EUnetHTA Core Model, aims to address the target population.

ID	Issue
A0007	What is the target population in this assessment?
A0023	How many people belong to this target population?
A0002	What is the health condition falling under the scope of this assessment?
A0003	What are the known risk factors for the health condition?
A0004	What is the natural course of the health condition?
A0005	What are the symptoms or health condition for the patient?

Stroke is a significant public health concern in SA with approximately 75 000 identified cases a year [63]. It is the second leading cause of death in SA, and contributing to an estimated 25,000 deaths annually [1], [63]. The natural course of untreated stroke can result in significant neurological impairments or in some cases death, risks that increases if diagnosis and intervention are delayed [6]. Symptoms and associated risk factors are specified in section 1.1.1. The largest risk factor, hypertension,

is a known consequence of both alcohol and substance abuse, which both are considerable public health challenges in SA [64]. The other associated risk factor, HIV, has a 20% prevalence in SA with close to 8 million diagnosed cases [1], [65].

SA has one of the highest rates of TBI globally, with an estimated 89,000 cases reported annually, likely excluding a substantial number of unreported cases [66]. The significant burden of trauma is a national concern in SA, with rural areas being particularly affected [67]. The majority of trauma patients in SA are due to interpersonal violence [33], with national rates reaching up to seven times the global average [68]. Studies link the high prevalence of trauma to factors such as unemployment, alcohol abuse, and gang-related activity [69]. These issues are especially prominent in poorer neighbourhoods and townships, where elevated crime and violence rates contribute to the socio-economic burden. TBI often results in long-term neurological and physiological impairments, placing additional strain on individuals, families, and the healthcare system [68].

Target condition

The next topic in this domain is the target condition, where the following issues will be addressed.

ID	Issue
A0006	What are the consequences of the health condition for the society?
A0009	What aspects of the consequences/burden of disease are targeted by the technology?

Permanent disabilities resulting from a stroke or TBI can significantly reduce a patient's quality of life (QoL) and impose a considerable burden on healthcare systems due to the long-term demand for medical care and rehabilitation resources [26]. In fact, stroke is among the top ten leading causes of disability in SA, accounting for approximately 95,000 years lived with disability nationwide [70]. The post-stroke outcomes are influenced by multiple factors, including the type, severity, and location of the stroke, as well as the timing and accessibility of medical intervention. Survivors frequently require multidisciplinary rehabilitation to regain physiological functions, still around 40% of surviving stroke-patients have to live with other severe permanent impairments [7].

Stroke is also associated with substantial direct healthcare costs. A previous study estimated these costs to include expenditures related to hospitalisation, medication, physiotherapy, speech therapy and outpatient care services [71]. Over a five-year period, the total direct cost was estimated at R7.3 trillion. The mean medication cost per patient during this time was approximately R65,700. These findings illustrate the substantial economic burden that stroke care imposes on the healthcare system and society at large.

The MD100 has the potential to reduce time-to-treatment by enabling earlier identification of suspected stroke cases. In line with the "time-is-brain" principle [72],

earlier diagnosis and initiation of appropriate treatment are associated with improved clinical outcomes and a higher likelihood of functional recovery. Enhanced recovery increases the potential for patients to regain independence and return to work, thereby contributing to gains in quality-adjusted life years (QALYs) [72]. From a societal perspective, this may lead to reduced long-term rehabilitation needs and associated healthcare costs, delivering both clinical and economic benefits. Linked evidence from a study performed showed no difference in cumulative healthcare costs when earlier thrombectomy where performed on acute ischeamic stroke patients [72]. This, since the total cost for healthcare were spread out across the longer life-time of the patient when earlier treatment were given [72].

Current management of the condition

Next, current management of the condition stroke and TBI are adressed by answering the following issues from the topic.

ID	Issue
A0018	What are the other typical or common alternatives to the current technology?
A0024	How is the health condition currently diagnosed according to published guidelines and in practice?
A0025	How is the health condition currently managed according to published guidelines and in practice?

Currently, no technology exists to assist in stroke triage outside the hospital setting; clinicians must rely solely on their clinical judgment guided by standard assessment scales as presented in Section 1.1.6.4. The MD100 is not intended to replace these scales neither hospital-based neuroimaging (CT or MRI), but rather to complement these in early decision-making.

Groote Schuur hospital has an on-call stroke physician who assists in prioritizing potential stroke patients for the CT-scanner [40], [59]. Stroke patients at Groote Schuur hospital can either be admitted to the dedicated stroke unit or to the emergency department (ED) depending on capacity [40], [59]. Groote Schuur Hospital administers thrombolysis within the 4.5-hour window and thrombectomy within the 7-hour window, provided that patients meet the eligibility criteria. In total 35-40 thrombolysis per year are administered at Groote Schuur and an unknown number of thrombectomies, primarily due to the fact that the patients reach the stroke unit outside of the time window for treatment. At the other public tertiary hospital Tygerberg, 120 thrombolysis are administered and 48 thrombectomies are performed annually [34], also a limited number as a consequence of the strict time-window [34], [40], [59].

The Standard operating procedures (SOPs) for trauma cases in the public WC is for the EMS to take the patient to the nearest ED to perform an initial stabilisation before further referral. Those who then require specialised care will after the initial

stabilisation be referred to a tertiary facility for further interventions [33]. However, SOPs are not always strictly followed, resulting in the transfer of non-stabilized patients to tertiary facilities which places an additional strain on already overburdened tertiary hospitals [33].

Utilisation

The following section addresses the aspect of utilisation by examining the issues outlined.

ID	Issue
A0001	For which health conditions and populations, and for what purposes is the technology used?
A0011	How much are the technologies utilised?
A0012	What kind of variations in use are there across countries/regions/settings?
G0009	Who decides which people are eligible for the technology and on what basis?
F0001	Is the technology a new, innovative mode of care, an add-on to or modification of a standard mode of care or replacement of a standard mode of care?

The MD100 is a novel and innovative technology designed to serve as an add-on to existing modes of care and treatment protocols with intended use as a triage support tool for suspected stroke and TBI. The technology does not, at current state, possess the ability to differentiate between the two types of stroke, ischaemic or haemorrhagic. The studies involving the MD100 are listed in the Table 3.1.

Table 3.1: Overview of the clinical trials involving Medfield Diagnostics Strokefinder MD100 and its current status.

Clinical Trial	**Trial ID**	**Country**	**Status**
Study to Evaluate Performance, Usability, Safety of Microwave Technology When Collecting Data From Patients With Stroke	NCT02266459	Sweden	Completed 2015
Detecting Chronic Subdural Hematoma With Microwave Technology	NCT02282228	Sweden	Completed 2016
Clinical Evaluation of a Microwave-Based Device for Detection of Traumatic Intracranial Hemorrhage	NCT02291261	Sweden	Completed 2017
Detecting Traumatic Intracranial Hemorrhage With Microwave Technology	NCT02728908	Sweden	Completed 2019
Detecting Stroke at the Emergency Department by a Point of Care Device: A Multicenter Feasibility Study	N/A	Greece	Completed 2024
NSW Ambulance First in the World to Trial New Stroke Care Technology	N/A	Australia	Completed 2024
Microwave Imaging in NeuroTrauma	NCT05960279	England	Unknown
Detecting Traumatic Intracranial Hemorrhage With Microwaves and Biomarkers	NCT04666766	Sweden	Unknown
Evaluating Use of Microwave Technology to Differentiate Hemorrhagic Stroke From Infarction in the Acute Phase	NCT02490306	Sweden	Unknown
Mobile Microwave-based Diagnosis and Monitoring of Stroke (MODS)	NCT04257149	Norway	Unknown

In the public sector of WC, the eligibility of medical technology is determined by the National Department of Health (NDoH) [73]. The public hospitals are simply requesting the technology they need via a basic list. For the academic institutions, such as Tygerberg and Groote Schuur, the list is forwarded to their respective committee inside the hospital unit, whereas other public hospitals in the WC submit the list to a provincial committee. This procedure is done on provincial level as each of

the provinces in SA operates independently, meaning that nation-wide adoption of medical technology requires approval and integration into the healthcare system of each separate province [74].

The provincial committee consists of experts with insights and great knowledge about the respective facilities that they are overseeing [73]. The list follows a three-phase assessment. The first phase involves an initial screening, where only technologies that meet basic approval criteria proceed to the second phase of the evaluation cycle. The exact criteria for this are still uncertain. The second phase involves a comprehensive evaluation and review of technical specifications and clinical relevance. Finally, the third phase consists of an economic assessment that analyses cost-effectiveness and financial feasibility, which often is the reason why requested technology are declined.

Once medical technology has passed the three-phase assessment and thereby been approved for funding, its implementation within a hospital setting is typically overseen by the head of the unit, also the person writing the request. The head of unit is also responsible for updating and adapting the SOPs to incorporate the new technology into clinical workflows [33]. It has been emphasized that modifying established procedures among healthcare professionals requires a high level of trust within the clinical team. The hospital's hierarchical structure, which is grounded in mutual respect and professional trust, plays a key role in facilitating a smooth transition. As a result, when changes are introduced to a department these are generally accepted and well-integrated by the healthcare staff [33].

In the private healthcare sector, decisions regarding the eligibility and funding of medical technologies are made by individual medical schemes and their respective administrators. Supporting this process are the Health Policy Units (HPUs) and Clinical Policy Units (CPUs), which are responsible for conducting the HTAs [46]. HTA play a crucial role in the private healthcare sector as it is used when evaluating the clinical effectiveness and cost-efficiency of new technologies, helping to determine whether a technology should be included in the medical aid scheme's list of covered services. The process operates under the oversight of the CMS, which is a statutory regulatory body that supervises medical schemes to ensure that the CMS ensures that schemes comply with relevant legislation, particularly the Medical Schemes Act, and that they uphold members' rights and access to appropriate healthcare services [75].

Regulatory status

The last topic in this domain addresses the regulatory status and adressess the following issues.

ID	Issue
A0020	For which indications has the technology received marketing authorisation or CE-marking?
A0022	Who manufactures the product?

In June 2022, the MD100 received CE certification under the Medical Device Regulation (EU) 2017/745 as a Class IIa medical device for the detection of stroke. According to the manufacturer, the device is intended to function as a decision-support tool to assist in the clinical evaluation and triage of suspected intracranial injuries in acute care settings. The MD100 is developed and manufactured by Medfield Diagnostics AB, a company founded and headquartered in Gothenburg, Sweden. As of June 2024, the company has declared bankruptcy and is currently undergoing reconstruction proceedings.

3.2 Description and technical characteristics of technology

This HTA domain is centred on the MD100 device in the SA context. To fully understand its potential value, it is essential to first understand the technology itself. This domain provides a brief overview of the device's features and training required to support its effective use in a clinical setting.

Features of technology

The first topic in this domain examines the specific features of the technology, answering the following issues.

ID	Issue
B0001	What is the technology and the comparator(s)?
B0002	What is the claimed benefit of the technology in relation to the comparators?
B0003	What is the phase of development and implementation of the technology and the comparator(s)
B0004	Who determines the technology and the comparators and in what context and level of care are they provided?
B0018	Are reference values or cut-off points clearly established?

The MD100, Figure 3.1, utilizes microwave technology (MWT) combined with artificial intelligence (AI) to assist in the triage of potential stroke patients. MWT have been a developing area of research for almost three decades [76]. MWT is a low-cost and non-invasive method, free from ionizing radiation [77].

Figure 3.1: Strokefinder™ MD100 sourced from Medfield Diagnostics [78]

MWT builds upon the existence of different dielectric contrast in human tissues [76]. The difference in dielectric properties of healthy brain tissues and non-healthy brain tissues, including blood and edemas provides the basis of the MWT [77]. The relative permittivity, also known as the dielectric constant, is a material parameter that is important for the wave propagation through the tissue [79]. In the case of a haemorrhagic stroke, the accumulation of blood can be detected due to the difference in relative permittivity between blood and brain tissues [77]. In the case of an ischaemic stroke, the detection relies on that the restricted blood flow to brain tissue causes oxygen deprivation which changes in the dielectric properties of the affected areas through edema formation.

The MD100 is portable and designed to fit around the patient's head, enclosing only the outer portion of the skull without covering the face, and used when the patient lies flat on the back [78]. It operates via eight applicators where low-power electromagnetic waves within a specific frequency range are transmitted through the patient's head [77], [78]. For a complete measurement, each applicator acts both as a transmitter and a receiver. The applicators pressure around the skull are manually adjusted with a handle for a correct position on the head. Additionally, the device incorporates a sensor designed to reduce variability in head positioning by ensuring that consistent pressure is applied, regardless of individual head size. The scanning process takes two minutes, where AI analyses the backscattered, reflected and transmitted microwaves to detect possible abnormalities that signalizes a stroke. As a result, "stroke" or "no stroke" is displayed on the connecting touch screen tablet which communicates with the MD100 via Bluetooth [78].

In contrast to current triage assessment scales, which rely on clinical observations and subjective evaluation of the patient, the MD100 provides results based on an AI-driven analysis of objectively collected signal data from the MWT. However, as the device requires direct contact with the skull, it is not applicable in all scenarios such as in cases when the skull is deformed or compromised due to penetrating trauma [78].

Investments and tools required to use the technology

The next topic address issues in regards to investments and tools required to use the technology.

ID	Issue
B0007	What material investments are needed to use the technology?
B0008	What kind of special premises are needed to use the technology and the comparator(s)?
B0009	What equipment and supplies are needed to use the technology and the comparator?
B0010	What kind of data/records and/or registry is needed to monitor the use of the technology and the comparator?

The full system comprises the MD100 device itself, an associated touchscreen tablet and the backpack in which the entire system is safely stored and easily transported. As the system is powered by a rechargeable battery, it requires access to electricity for charging prior to use. The entire system weighs 6 kg, and with complementary single-use hygiene covers required for each patient, it operates independently and only requiring routine maintenance of the system. Given that the system utilizes AI-based algorithms, periodic maintenance in the form of software updates may be necessary to ensure optimal performance and reliability of the system.

The current triage assessment scales as presented in Section 1.1.6.4, does not require any supplies or equipment.

Training and information needed to use the technology

The last topic in this domain addresses issues regarding training and information needed to use the technology.

ID	Issue
B0012	What kind of requirements in terms of qualification and quality assurance processes are needed for the use or maintenance of the technology?
B0013	What kinds of skills and training characteristics and information are needed for the personnel/caregivers using this technology?
B0015	What information about the technology should be provided outside the target group and to the general public?

Ensuring the quality, safety and effectiveness of a medical technology in accordance with SA's regulatory requirements is a shared responsibility between hospitals, healthcare professionals and manufacturers [73]. One important quality assurance mechanism is to gain acceptance within the local context, meaning that new medical devices must be validated within SA and not solely rely on international performance data. While this serves as a critical safeguard to ensure suitability and reliability in

local contexts, it also adds an additional layer of complexity when introducing new technologies to the SA market. Integrating a device is not merely a matter of distribution, strict protocols must be followed to ensure it is used as intended and delivers on its promised performance. This process includes post-market surveillance, which is overseen by the South African Health Products Regulatory Authority (SAHPRA).

The MD100 is intended for use by trained healthcare professionals, but its intuitive design and automated signal analysis significantly reduce the operational skill requirements. Unlike current triaging scales, which require clinical expertise to interpret and draw conclusions based on the patients behaviour, the output when using MD100 is straightforward, "stroke" or "no stroke". As a result, no advanced skills or experience are necessary to operate the MD100 besides the ability to determine when its use is appropriate. Consequently, the estimated training required, to operate the device and understand the patient-technology interface, is approximately 12 hours [80].

When introducing new medical technology, it is important to minimize concerns amongst the general public. Therefore, relevant information to share about the MD100 is that it is a radiation-free triage support device that aims to shorten time-to-treatment and thereby improve patient outcomes.

3.3 Safety

When implementing the MD100, it is critical to assess the safety aspects for both patients and healthcare professionals to ensure that the benefits outweighs potential harm. This addresses safety considerations from multiple perspectives and outlines relevant safety management practices.

Patient safety

The first topic in this domain addresses patient safety according to the following issues.

ID	Issue
C0008	How safe is the technology in relation to the comparator(s)?
C0002	Are the harms related to dosage or frequency of applying the technology?
C0004	How does the frequency or severity of harms change over time or in different settings?
C0005	What are the susceptible patient groups that are more likely to be harmed through the use of the technology?
C0006	What are the consequences of false positives, false negatives, and incidental findings generated by using the technology from the viewpoint of patient safety?
C0007	Are the technology and comparator(s) associated with user-dependent harms?

Since the MD100 is CE-certified, it complies with the European Union's directive on Electromagnetic Compatibility (EMC), Directive 2014/30/EU. The directive's essential meaning is *"to ensure the electromagnetic compatibility of electrical and electronic equipment"* [81]. It outlines requirements which equipment must fulfil to avoid interference with other equipment. The MD100 does therefore meet the requirements for emission limits, immunity levels, conformity assessment procedures, labelling and documentation. In the European Union, there is another directive, namely Directive 2013/35/EU for Electromagnetic fields (EMF). This directive is stated to be the *"minimum health and safety requirements regarding the exposure of workers to the risks arising from electromagnetic fields"* [82] and aims to ensure that a risk assessment of the EMF is performed at the workplace ensuring the safety of the workers [82]. Since MD100 operates via MWT and complies with the Directive 2014/30/EU, the EMF is ensured through risk analysis and user instructions, as safety information is provided to ensure that Directive 2013/35/EU will be met.

The current AI-based algorithm in the MD100 have been trained to demonstrate the highest point of sensitivity on the ROC-curve at 97%, corresponding to a specificity of 48% for stroke detection [80]. With a larger amount of training data, it is a reasonable to assume that the model's performance will improve over time, reaching a higher sensitivity and specificity [83]. This is because algorithms require substantial data to fully converge and reach optimal performance, making them dependent on more extensive datasets. With a high sensitivity, nearly all true stroke cases are correctly identified, with only approximately 3% of stroke cases missed, supporting the device's safety in identifying potential stroke patients. However, the low specificity suggests a high rate of false positives, meaning that nearly half of the non-stroke patients are incorrectly classified as having a stroke. While this over-triage does not pose a direct safety risk to the patient, it may lead to unnecessary resource utilization and potential delays in care for other conditions. Nonetheless, from a safety perspective, the high sensitivity ensures that stroke patients are unlikely to go undetected when applying the MD100.

The same reasoning goes for TBI where the sensitivity is shown to be 100% and the specificity is 75% for subdural hematomas [84].

For reference, the performance metrics of the MD100 can be compared to the current triage assessment scales. As shown in Sections 3.2 and 3.3, the MD100 demonstrates higher sensitivity, suggesting improved patient safety when used in clinical decision-making.

Occupational safety

The next topic examines the MD100 in regards to occupational safety by answering the issue specified below.

ID	Issue
C0020	What kind of occupational harms can occur when using the technology?

The MWT used in the MD100 operates within a frequency range of 500 MHz to 1.1 GHz, which is within the limits defined by the device's CE certification [76]. Importantly, there is no evidence suggesting harmful electromagnetic exposure to the device operator. For context, standard mobile phones operate at even higher frequencies, typically between 700 MHz and 2.6 GHz, depending on the network generation (2G to 4G) [85] This highlights that the MD100 uses lower-frequency microwaves and does not puts either the clinician or the patient at risk during usage of the technology.

Environmental safety

Additionally, environmental safety considerations associated with the technology are addressed in the following section.

ID	Issue
C0040	What kind of risks for public and environment may occur when using the technology?

During operation, the MD100 does not emit or require any harmful substances or chemicals, making it safe for both users and the environment. Unlike imaging technologies that may rely on contrast agents or radioactive tracers, the MD100 operates without consumables that require special handling or disposal.

Like all battery-driven electronic medical equipment, MD100 must be disposed in accordance with electronic waste regulations at the end of its life cycle. There are no evidence that the device pose any unusual environmental risks beyond those of standard medical electronics. Similarly, the single-use hygienic covers should be recycled or disposed of according to local medical waste guidelines.

In addition, CE certification ensures that all materials in contact with the patient are biocompatible and non-toxic, making it suitable for clinical use.

Safety risk management

The final topic in the safety domain focuses on safety risk management and examines the issues below.

ID	Issue
C0062	How can one reduce safety risks for patients (including technology-, user-, and patient-dependent aspects)?
C0063	How can one reduce safety risks for professionals (including technology-, user-, and patient-dependent aspects)?
C0064	How can one reduce safety risks for the environment (including technology-, user-, and patient-dependent aspects)?

The primary safety considerations for the patient in regards to the MD100 relates to

its software maintenance as well as proper use. The MD100 is intended to support triage and clinical decision-making rather than to provide a definitive diagnosis. This distinction is crucial for healthcare professionals to understand in order to ensure that the use of the device does not compromise patient safety. Therefore, it is important the MD100 is used in accordance with its CE-certification and the specified intended use. Additionally, maintaining up-to-date software is vital to ensure the AI algorithm remains accurate and effective, thereby minimizing risks associated with outdated or malfunctioning.

Safety considerations for healthcare professionals include the need for appropriate training to ensure correct use of the device. Proper handling techniques may reduce the risk of strain or injury during repeated use, particularly in high-volume settings such as emergency care or ambulance services.

3.4 Clinical Effectiveness

Evaluating the clinical effectiveness of the MD100 is a crucial step in assessing its potential impact on patient outcomes. This domain explores how future implementation within the WC healthcare system may influence patient management and contribute to improved clinical decision-making of stroke and TBI cases.

Mortality and morbidity

The two first topics in this domain investigates issues related to mortality and morbidity as listed below.

ID	Issue
D0001	What is the expected beneficial effect on the technology on mortality?
D0026	How does the technology modify the effectiveness of subsequent interventions?

Early detection of stroke and TBI has the potential to significantly reduce the time-to-treatment. By assisting in triage and complementing current assessment scales, MD100 may facilitate earlier treatment. Evidence shows that earlier treatment improves patient outcomes by minimizing long-term disabilities, reducing rehabilitation time and increasing survival rates [86], [87]. However, earlier recognition alone does not guarantee earlier treatment which is what the concept of "time is brain" refers to [72]. Improved patient outcomes ultimately depend on whether patients receive appropriate care within the critical treatment windows[87]. In this context, the MD100 serves as a crucial tool in facilitating timely access to care but for the treatment aspect, it requires healthcare facilities to have the necessary resources and capacity to deliver timely and effective treatment. As of today, there are no direct clinical evidence demonstrating the impact of the MD100 on mortality rates. However, since faster treatment is strongly associated with improved outcomes, the MD100 - if it successfully enables earlier intervention - may indirectly contribute

to reduced mortality [87], [88]. Nonetheless, further studies are needed to establish this direct link.

Function

The function of the technology is addressed by examining the following issues.

ID	Issue
D0011	What is the effect of the technology on patient's body functions?
D0014	What is the effect of the technology on work ability?
D0015	What is the effect of the technology on return to previous living conditions?
D0016	How does the use of the technology affect activities of daily living?

The technology does not directly have an effect on the patient's body functions. Indirect evidence however, suggests that earlier intervention of stroke and TBI may facilitate improved patient outcomes. With the assumption that the MD100 would support in triage, contributing to a faster diagnosis and thereby earlier treatment, it would reduce the extent of brain tissue damage and thus decrease rehabilitation and likely improve patient outcomes. This includes a higher probability of functional recovery, increased ability to return to work and a greater chance of returning previous living conditions.

Health-related quality of life

In order to investigate the health-related quality of life, the following issues are adressed in this section.

ID	Issue
D0013	What is the effect of the technology on disease-specific quality of life?
D0030	Does the knowledge of the test result affect the patient's non-health-related quality of life

Previous studies estimate that every 10-minute reduction in time-to-treatment for stroke results in an average gain of 39 days of disability-free life [72]. As discussed under *mortality and morbidity*, the MD100 may support earlier identification of stroke, which in turn could enable earlier treatment. Under the assumption that earlier identification leads to earlier treatment, the MD100 may therefore be indirectly associated with improved QoL, as earlier treatment is linked to better clinical outcomes [86], [88]. However, it is important to note that no direct evidence currently demonstrates this specific linkage.

Test-treatment chain

The test-treatment chain topic answer the following issue.

ID	Issue
D0024	Is there an effective treatment for the condition the test is detecting?

The main treatments for stroke are outlined and described in Section 1.1.2. However, the effectiveness of these treatments is limited by narrow therapeutic time windows, which restrict the number of patients eligible for intervention. For example, at Tygerberg Hospital, patients who arrive outside the 4.5-hour window for thrombolysis are not prioritized for a CT scan, as the opportunity for thrombolytic therapy has already passed [34]. In some cases, patients may not receive CT imaging at all. Instead, a clinical assessment by a physician confirms a stroke, after which the patient is referred directly to rehabilitation without any technology-based diagnostic evaluation.

Similar, treatment decisions for TBI are highly dependent on the location and severity of the hemorrhage and the identified options are detailed in Section 1.1.5.

Test accuracy

The next topic addresses the test accuracy and contains the following issues.

ID	Issue
D1001	What is the accuracy of the test against the reference standard?
D1002	How does the test compare to other optional tests in terms of accuracy measures?
D1003	What is the reference standard and how likely does it classify the target condition correctly?
D1004	What are the requirements for accuracy in the context the technology will be used?
D1006	Does the test reliably rule in or rule out the target condition?
D1007	How does the test accuracy vary in different settings?
D1008	What is known about the intra- and interobserver variation in test interpretation?
D1019	Is there evidence that the replacing test is more specific or safer than the previous one?

An article was published in 2024 showing that the sensitivity and specificity of GCS for TBI for moderate to severe brain injury (GCS score ≤ 12) was 83.1% and 93.1% respectively [89]. For stroke, another study was performed in 2018 where GCS was compared to Glasgow Coma Scale motor component (GCS-M), also known as the Simplified Motor Score (SMS). Sensitivity and specificity of the SMS was compared during different times and for different localisation of haemorrhage in the brain.

Depending on these different factors, the sensitivity for GCS-M varied from 66.7 % for when death occurred after 72h from haemorrhage in the left hemisphere to 100 % when death occurred after 0h in the right hemisphere. The corresponding specificities for these scenarios were 82.4 % and 85.7 % [90].

In 2021, a study was done on the performance of SATS in the Western Cape Government Emergency Medical Services (WCG EMS) [91]. For trauma, 28.8 % of patients were under-triaged corresponding to a sensitivity of 71.2 % and 13.7% were over-triaged corresponding to a specificity of 86.3% [91]. No performance metrics could be found on the SATS used on stroke patients. Tables 3.2 and 3.3 shows an overview of the tools and their corresponding specificities and sensitivities.

Tool	**Sensitivity**	**Specificity**	**Setting**	**Intended use**	**Reference**
FAST	77% *	60% *	Pre-hospital	Initial identification	[92]
GCS-M	66.7%–100% **	82.7%–85.7% **	Pre-hospital In-hospital	Triage	[90]
SATS	N/A	N/A	Pre-hospital In-hospital	Triage	-

Table 3.2: Sensitivity and specificity of triage tools for stroke.
* For acute ischaemic stroke.
** Dependent on time of stroke onset and localisation of the haemorrhage.

For stroke detection, MD100 has demonstrated a sensitivity of 97% and a specificity of 48% [93]. Compared to other triage tools, the MD100 exhibits high sensitivity, which is critical for both the initial identification and appropriate triage of patients with suspected stroke. While the GCS-M has reported a sensitivity of up to 100 %, it is important to note that this figure, as previously discussed, refers to a case where the patient died within 0 hours, limiting its generalisability.

Although the specificity of the MD100 is currently lower than that of the other tools assessed, this limitation must be balanced against its high sensitivity. A lower specificity implies an increased risk of over-triage, potentially leading to greater strain on healthcare resources. On the other hand, the benefit of a high sensitivity is that it minimizes the risk of missed stroke cases, which is a critical consideration in stroke care management.

Additionally, the MD100 is not supposed to replace the triage assessment scales currently used. It should instead act as a complement, which in combination could increase both the current total sensitivity and specificity of triaging stroke and TBI.

Tool	Sensitivity	Specificity	Setting	Intended use	Reference
GCS	83.1% *	93.1% *	Pre-hospital In-hospital	Triage	[89]
SATS	71.2%	86.3%	Pre-hospital In-hospital	Triage	[91]

Table 3.3: Sensitivity and specificity of triage tools for trauma
* For GCS score ≤ 12 in prehospital setting

For the detection of chronic subdural haematomas, MD100 demonstrated a sensitivity of 100 % and a specificity of 75% [84]. In this context, the MD100 showed the highest sensitivity among the triage tools evaluated for TBI, indicating strong potential for accurate identification of affected patients.

While the specificity of the MD100 remains lower than that of some existing tools, this should be interpreted in light of its superior sensitivity. The trade-off between sensitivity and specificity is particularly relevant in emergency and pre-hospital settings, where the risk of under-triage may have severe clinical consequences. Thus, the higher sensitivity of the MD100 may justify its relatively lower specificity, especially in scenarios where early detection is critical to patient outcomes.

The potential impact on the accuracy across different clinical settings has not yet been thoroughly investigated. A local clinical trial is therefore required to validate the performance of the device within the specific healthcare context and ensure compliance with local conditions and practices [46], [73].

Change-in management

The last topic in regards to the clinical effectiveness domain answers the listed issues in regards to the change-in management.

ID	Issue
D0010	How does the technology modify the need for hospitalisation?
D0020	Does the use of the test lead to improved detection of the condition?
D0021	How does use of the test change physicians' management decisions?
D0022	Does the test detect other potential health conditions that can impact the subsequent management decisions?

The MD100 is expected to contribute to reduced time-to-treatment, which may also shorten the need for in-hospital care during rehabilitation. When used in pre-hospital settings, the device can support clinical decision-making and potentially allow certain facilities to be bypassed, thereby reducing the burden on lower-level hospitals and optimizing patient flow within the healthcare system. However, this

may concurrently place additional demand on higher-level facilities, which must be considered in system integration.

The high sensitivity of the MD100 is particularly advantageous when compared to existing triage assessment scales, as it demonstrates the highest sensitivity 3.2, 3.3, indicating a reduced risk of missed positive cases. This suggests that the use of MD100 may enhance the detection of positive patients, contributing to improved clinical decision-making. As of today, the MD100 can only differentiate between "stroke" or "no-stroke" but MWT has proven potential for a wider medical usage which potentially could make it applicable in other areas in the future [94]. However, this is up for further investigation.

3.5 Cost and economic evaluation

Another critical factor to consider particularly given that implementation is being assessed in a LMIC context, is the economic evaluation of the technology. This domain examines the associated costs and resource utilization, while also exploring variations and uncertainties that may influence the overall cost-effectiveness of the MD100.

Examination of costs and resource utilisation

First, the examination of costs and resource utilisation are examinated by answering the issues below.

ID	Issue
E0006	What are the estimated differences in costs and outcomes between the technology and its comparator(s)
E0001	What types of resources are used when delivering the assessed technology and its comparators (resource-use identification)?
E0002	What amounts of resources are used when delivering the assessed technology and its comparators (resource-use measurement)?
E0009	What were the measured and/or estimated costs of the assessed technology and its comparator(s) (resource-use valuation)?
D0023	How does the technology modify the need for other technologies and use of resources?
G0007	What are the likely budget impacts of implementing the technologies being compared?

In contrast to current triage tools, the use of the MD100 requires a substantial initial investment. The cost per device has been estimated to €90,000 (R1,850,000) and the total procurement cost depends on the number of devices acquired. For the purpose of illustrating the number of devices that may need to be adopted at each level of care, Table 3.4 shows the total number of units or facilities at each level.

Table 3.4: Number of facilities for each suggested implementation site and the purpose of the MD100 in each instance.

Number of Devices	Implementation Sites	Purpose
250 [49]	Public EMS (prehospital units)	Identify and transport potential stroke patients directly to treatment-capable facilities
75 [33]	Level 1 facilities	Triage patients to determine stroke likelihood before referral
8 [33]	Level 2 facilities	Prioritize suspected stroke patients in the CT queue or use when CT scan is not operational
2 [33]	Level 3 facilities	Prioritize suspected stroke patients in the CT queue

The fixed cost of the device includes the MD100 system itself, the cost of training healthcare professionals in operating the device as well as the cost of integrating the device into existing health systems. The variable cost of the device includes the single-use hygiene covers, software updates and maintenance of the device, electricity for charging it and potential training refreshes of healthcare professionals.

The MD100 does not require extra staffing beyond already existing personnel as healthcare workers currently responsible for patient assessment and triage will be trained to operate the device. However, the use of MD100 could potentially increase the demand for confirmatory CT-scans and thereby place additional strain on resources at the hospitals.

Regarding healthcare costs for the patient, a previous study showed that the cumulative costs remained the same for the patients who received treatment compared to the ones who did not [72]. The healthcare costs are rather dispersed throughout the life-time, ultimately resulting in the same total costs but with a higher QoL for the patients who received treatment faster [72].

Measurement and estimation of outcomes

Next, measurement and estimation of outcomes of the technology are analysed via the issue below.

ID	Issue
E0005	What is (are) the measured and/or estimated health-related outcome(s) of the assessed technology and its comparator(s) (outcome identification, measurement and valuation)?

For stroke, every minute counts. From a study performed on stroke patients suffering LVOs, for every minute reduction in time to receiving a thrombectomy resulted in 1.3 days of additional disability-free life [95]. This shows that even the slightest

reduction in time-to-treatment, results in a gain to be found for the patients. With QALYs gained, patients are additionally able to work and by this contribute to society, which has a positive social impact.

Another study showed that every 10-minute reduction in time-to-treatment corresponds to an average gain of 39 days of disability-free life as well as an INMB of approximately $10,500 [72]. Both studies draw the conclusion that every minute reduction in time-to-treatment adds to the patient outcomes as well as the economical societal impact [72], [95].

Appendix A illustrates the amount of time that must be saved over the entire lifetime of the MD100 for the application to be considered economically viable. The calculation includes estimated values, or numbers sourced from relevant literature. Here, the previously mentioned study provides a positive INMB for 10 minutes savings in time-to-treatment [72]. The results clearly demonstrate that even a small time saving can result in a substantial benefit in terms of health outcome for the patient. Assuming a device lifetime of 10 years, the calculations show that a total of 100 minutes saved during the life time of the system makes the system health economically viable. This suggests that the willingness to pay (WTP) threshold may not be a limiting factor, given the significant benefit generated when saving time-to-treatment. However, it is important to note that the WTP must align with the cost of the device.

Assuming that all 75,000 stroke patients in SA experience a 10-minute reduction in time-to-treatment, the maximum cost per QALY is estimated as in Appendix A. This results in an approximate annual saving of $724,500,000 for the SA healthcare (see Appendix A). Such a substantial figure highlights the potential benefit of even a small reduction in treatment delay. However, it is important to recognize that, under current conditions, very few patients reach medical facilities in time to receive treatment, largely due to structural challenges within the healthcare system. Nevertheless, considering the previous discussions and the positive INMB, it can be reasonably assumed that even small reductions in time-to-treatment would provide significant value within the current system.

The time-factor is just as important for TBIs where access to timely care is associated with lower rates of morbidity and mortality [28]. Additionally, earlier triage that initiate faster care may also initiating rehabilitation earlier. This has furthermore been proven associated with improved patient outcomes. Studies suggests that earlier rehabilitation improves overall physical recovery and cognitive function while shortening the overall rehabilitation time and thus reducing its associated costs [96], [97].

Characterising heterogeneity and uncertainty

The following two topics, characterising heterogeneity and characterising uncertainty, explore the following issues.

ID	Issue
E0011	To what extent can differences in costs, outcomes, or 'cost-effectiveness' be explained by variations between any subgroups using the technology and its comparator(s)?
E0010	What are the uncertainties surrounding the costs and economic evaluation(s) of the technology and its comparator(s)?

The cost-effectiveness should be evaluated in respect to the possible options of implementation sites. When more frequently used, the cost per usage is lower and thereby the device is considered to be more cost-effective. However, more research should be conducted in regards to the amount of time that, in practice, can be saved per patient to be able to draw a conclusion regarding the cost-effectiveness of the MD100 at different implementation sites in the healthcare system.

There are also several uncertainties in the economic evaluation. First, it is important to acknowledge that the calculations in Appendix A are based on a study involving thrombectomy in patients with acute ischaemic stroke [72]. The gain in disability-free days from earlier intervention in this specific patient group may not directly translate to other types of stroke patients. Additional limitations in the calculations include assumptions about the device's cost and its operational lifetime, both of which remain unconfirmed at this stage. Another key assumption is that all 75,000 annual stroke patients in SA would benefit from the device and in average experience a 10-minute reduction in time-to-treatment. This is uncertain, given the currently low proportion of patients who receive timely treatment. Nevertheless, the purpose of the calculation is to illustrate the potential and demonstrate the substantial value that could be generated under optimal conditions. It highlights the possible upper bound of cost-effectiveness in terms of QALYs, even under generous assumptions.

3.6 Ethical analysis

Ethical considerations are essential when evaluating the implementation of medical technologies. This domain explores the ethical implications of the MD100, addressing both the ethical dimensions of the technology itself and the potential ethical consequences its implementation may have on the WC healthcare system as a whole.

Benefit-harm balance

The first topic in this domain address issues regarding the benefit-harm balance.

ID	Issue
F0010	What are the known and estimated benefits and harms for patients when implementing or not implementing the technology?
F0011	What are the benefits and harms of the technology for relatives, other patients, organisations, commercial entities, society etc.?
F0104	Are there any ethical obstacles for evidence generation regarding the benefits and harms of the intervention?

The technology demonstrates a high level of sensitivity, offering a clear benefit by reducing the number of missed stroke patients to just 3% and missing no patients with traumatic brain injury (TBI). However, this benefit must be weighed against the downside of additional CT scans being performed without clinical necessity given the lower specificities of 75% for TBI and 48% for stroke.

On the negative side false positives, resulting from a low specificity, may potentially delay the diagnosis and treatment for other patients with time-sensitive medical conditions.

Given the concept of "time is brain" in combination with the economical aspects presented in section 3.5 it can be estimated, under the current assumptions, that the benefit-harm balance is positive. Given that more patients would be within the time-window for treatment, there is a very large benefit with implementation of the MD100. The harm can therefore be assumed to be outweighed by the potential benefit.

Autonomy

The next topic investigates the autonomy, and the following issues is addressed.

ID	Issue
F0005	Is the technology used for individuals that are especially vulnerable?
F0004	Does the implementation or use of the technology affect the patient's capability and possibility to exercise autonomy?
F0006	Is there a need for any specific interventions or supportive actions concerning information in order to respect patient autonomy when the technology is used?
F0007	Does the implementation or withdrawal of the technology challenge or change professional values, ethics or traditional roles?

Traditional triage assessment scales for stroke and TBI rely heavily on clinical judgment and subjective evaluations by healthcare professionals. In contrast, MD100 offers an objective binary result where all patients, regardless of social factors such as gender, race, or age, are assessed equally. Moreover, relying solely on clinical assessments introduces the risk of cognitive biases, which have been shown to influence triage decisions [98]. Implementing structured tools like the MD100 can help

reduce cognitive biases, improve triage accuracy, and promote more consistent and fair decision-making. Both increased objectivity and bias reduction in patient triage are essential factors in ensuring equitable access to care.

When adding technologies such as the MD100 in the setting, the decision to use the device ultimately lies with the healthcare professional, who must assess its appropriateness in different scenarios. As the device is non-invasive and poses no physical risk to the patient, its use on even unconscious patients can generally be justified in emergency settings, provided it does not delay necessary diagnostics or treatment. Still, clear and accessible communication about the device's strengths and limitations is crucial in order to respect patient autonomy.

Justice and equity

The next topic addresses issues regarding justice and equity.

ID	Issue
F0012	How does implementation or withdrawal of the technology affect the distribution of health care resources?
F0013	How are technologies with similar ethical issues treated in healthcare system?
H0012	Are there factors that could prevent a group or person from gaining access to the technology?

The allocation of resources to public healthcare is determined at the provincial level [73]. Given the constraints of a limited budget, resource allocation decisions must be guided by robust clinical evidence. Therefore, studies that demonstrate the MD100's impact are essential to justify its prioritization over other medical equipment and represent a critical step toward its potential integration into the SA healthcare system [46], [99].

There is no technology that could be compared to the MD100, making it difficult to find similarities and differences in regards to ethical issues.

The accessibility of the MD100 heavily relies on the implementation sites and could potentially introduce inequalities in the aspect of its accessibility for the SA citizens. However, such disparities reflect broader structural characteristics of the healthcare system rather than limitations inherent to the MD100 itself. Nonetheless, this contextual factor is important to acknowledge when discussing implementation in regards to ethical considerations.

Legislation

The last topic in the ethical domain address issues related to legislation. The MD100 has the potential to strengthen the right to equitable healthcare by providing an objective triage support with higher sensitivity compared to currently used triage assessment scales.

ID	Issue
F0014	Does the implementation or use of the technology affect the realisation of basic human rights?
F0016	Can the use of the technology pose ethical challenges that have not been considered in the existing legislations and regulations?

3.7 Organisational aspects

The organisational aspects provides an overview of the WC healthcare system and its key stakeholders to offer a comprehensive understanding of how the system functions. It outlines the current healthcare delivery processes related to stroke and TBI management, the structure of the regional health system and how factors such as management practices and organisational culture may influence the deployment of medical devices like the MD100.

Health delivery process

The first topic in this domain answers issues related to the health delivery process.

ID	Issue
G0001	How does the technology affect the current work processes?
G0100	What kind of patient/participant flow is associated with the new technology?
G0002	What kind of involvement has to be mobilized for patients/participants and important others and/or caregivers?
G0003	What kind of process ensures proper education and training of staff?
G0004	What kind of co-operation and communication of activities have to be mobilised?

The current workflows within the public healthcare system are strongly shaped by the established referral structure, as illustrated in Figure 1.3. The integration of the MD100 into the SA healthcare system has the potential to alter clinical processes with the aim of reducing time-to-treatment. The specific impact of its implementation will depend on the point of integration within the healthcare pathway and may vary across different settings.

If MD100 is implemented in the WC EMS, it could potentially enable the assessment of identification of stroke already during transport. This may lead to a revision of SOPs, allowing for direct transport to tertiary facilities for confirmatory imaging and treatment, rather than to the nearest facility with only CT capabilities and no treatment options [34], [40], [59]. Such a change could reduce time-to-treatment and thereby increase the likelihood of shortened rehabilitation and improved patient outcomes.

At clinics or district hospitals without CT imaging capacity, the MD100 could support in earlier identification and prompt direct inter-hospital transfers to tertiary facilities with treatment capabilities, bypassing intermediate steps in the referral chain and thereby saving time. This applies for patients arriving to level 1 facilities with private transport, under the assumption that WC EMS SOPs are transferring potential stroke-patients to facilities with CT-capability directly.

Within tertiary facilities, the MD100 could be used to triage patients awaiting neuroimaging, prioritizing those with suspected stroke for access to CT scans. The device may also assist in identifying patients presenting with mild or atypical symptoms that might otherwise go undetected.

In the context of TBI, patients in high-acuity situations are typically transported to the nearest facility for initial stabilization. In cases involving poly-trauma where the presence of intracranial injury is uncertain, the MD100 may support triage decisions by distinguishing patients requiring urgent transfer from those who can be stabilized at lower levels of care.

According to current EMS SOPs, suspected stroke patients should be taken to the nearest hospital with CT capabilities, typically a level 2 facility [34]. The first level of care for patients who self-refer is level 1 facilities, where the SOP is an intermediate transferral to a level 2 facility for a confirmatory CT scan [40]. However, interview data suggest that physicians at level 1 facilities sometimes deviate from this protocol and advise patients who are still within the treatment window to go directly to a level 3 facility where treatment is provided [40]. It should however be noted that a patient can choose to go to whatever instance they want [40].

Patients who are using private transport and go directly to the tertiary hospital, Groote Schuur, are those who most often arrive within the treatment window compared to using EMS service [40] which argues for delays in the care pathway for stroke patients using WC EMS. Here, several stages have been identified: delayed EMS pick-up, delays in obtaining a confirmatory CT scan at a level 2 facility, delays in inter-hospital transfers to a level 3 facility, and delays in accessing a CT scan at the level 3 facility. These cumulative delays suggest that the time-to-treatment is significantly prolonged, restricting the 4.5h time-window.

Similar delays have been associated in the transportation of TBI patients; delays in arrival at the initial facility, in-hospital delays, delays in inter-hospital transfers, delays in accessing CT imaging and delays in surgical intervention [100]. Delays for TBI patients may be even more pronounced than for stroke patients, as EMS SOPs mandate transport to the nearest ED for stabilization and not a CT-capable facility as in the stroke-case. As a result, TBI patients may be transferred through two different facilities before reaching a level 3 hospital where intervention is possible.

Based on the delays identified for both stroke and TBI, we have identified four key healthcare contexts where the MD100 could be implemented (see Table 3.5).

Table 3.5: Identified locations in the public healthcare system for potential adoption of the MD100.

Identified Location	Purpose
Pre-hospital units	As a triage tool to determine which level of hospital the patient should be taken to.
Level 1 facilities	To expedite inter-hospital transfers to a level 3 facility.
Level 2 facilities	To avoid unnecessary CT scans and expedite patients to a level 3 facility.
Level 3 facilities	To triage patients in the queue for the CT scan.

Depending on the location, different processes must be established to ensure appropriate education and training of healthcare staff. As discussed in Section 1.1.6.3, reports indicate that EMS personnel in SA may have limited knowledge of the GCS. This suggests that additional training may be necessary to ensure EMS personnel can operate the MD100 device safely and effectively. In contrast, this may be less of an issue at level 1, 2, and 3 facilities, where healthcare staff are generally more familiar with operating medical technology.

Structure of healthcare system

The next topic in this domain address issues related to the structure of the healthcare system and its impact on the technology.

ID	Issue
G0005	How do de-centralisation or centralisation requirements influence the implementation of the technology?
G0101	What are the processes ensuring access to the new technology for patients/participants?

Centralised implementation, such as deployment at tertiary or regional facilities equipped with CT scanners, may offer logistical and operational advantages. As outlined in the previous section, such settings typically have personnel who are used to operating advanced medical technologies. Consequently, with minimal training, these users may be able to adopt the device effectively given their current experience. Furthermore, higher patient volumes at these facilities, may increase the utilization of the device, thus improving its cost-effectiveness through economies of scale.

In contrast, decentralised implementation, such as in the WC EMS and facilities without CT access, may generate greater clinical value as no existing technologies are currently available to facilitate triage in this context. Integration of MD100 in these settings could support earlier identification of stroke and TBI, enabling revised SOPs that allow for direct transfer of patients to facilities capable of definitive

treatment. This could significantly reduce time-to-treatment and potentially improve clinical outcomes. However, decentralised deployment may presents notable challenges. EMS personnel as well as staff at lower-level facilities may be less familiar with using medical technologies, necessitating more extensive training to ensure correct and reliable use. Additionally, patient volumes at these sites are likely to be lower, which may reduce the cost-effectiveness of the technology in these settings.

In the public healthcare sector, decisions regarding the acquisition of new medical technologies are governed by the Western Cape Department of Health and Wellness (WCDHW), in coordination with the National Treasury [46], [73]. Procurement processes are typically initiated based on identified clinical needs, budgetary constraints, and alignment with provincial health priorities. Once a medical technology has passed the 3-phase assessment, it is then approved for clinical use within the facility.

In the private healthcare sector, SOPs related to technology adoption are not publicly available and therefore cannot be assessed within the scope of this HTA. As a result, the potential influence of centralisation or decentralisation requirements on the implementation of the technology in the private sector remains uncertain.

Management

The following issue discusses management problems and opportunities associated with the technology.

ID	Issue
G0008	What management problems and opportunities are attached to the technology?

As previously noted, the procurement of medical technologies in the public sector of WC constitutes a financial decision within a resource-constrained environment. The allocation of funds to one product may directly influence the availability or prioritization of other technologies, stating the need of careful consideration of the cost evaluation of the MD100 [73]. Once a product is made available within a facility, it must be formally integrated into the relevant SOPs to ensure its appropriate use [33].

Culture

The final topic in the organisational domain address issues cultural aspects in regards to the technology.

ID	Issue
G0010	How is the technology accepted?
G0011	How are the other interest groups taken into account in the planning/implementation of the technology?

Acceptance of a new technology is strongly related to having a dedicated local supporter of the product, commonly referred to as a "*champion*" [40], [46], [59], [73], [99]. This person is an external part who advocates for the product and initiates a clinical trial and therefore, having a local champion for the MD100 is crucial in getting a technology accepted [40], [46], [59], [73], [99].

Internal process of SOPs modification is facilitated by mutual trust and professional respect within the team [33]. It was also emphasized extensive clinical experience are crucial factors for the successful implementation of updated protocols. This trust-based culture facilitates the smooth implementation of new SOPs as junior doctors rely on the expertise and decisions of their senior counterparts [33]. Another important contributing factor is the accountability, as the head of the unit takes responsibility if any issue would arise from following an updated procedure [33].

3.8 Patients and social aspects

This domain explores the broader societal and individual perspectives, examining how the implementation of the MD100 may influence various social groups and the potential societal impact of the device.

Patients perspectives

The first topic in this domain discusses patients perspectives based on the following presented issues.

ID	Issue
H0200	What are the experiences of living with the condition?
H0100	What expectations and wishes do patients have regard to the technology and what do they expect to gain from the technology?
H0002	What is the burden on care-givers?

Patients suffering from post-stroke conditions or TBI are likely to experience both physical and mental complications. Common side effects include one-sided paralysis, language impairments, slurred or slow speech, difficulty swallowing, seizures, and cognitive deficits [6]. These symptoms often result in patients requiring assistance with activities of daily living, being unable to work, leading to loss of income, and experiencing mental distress due to the loss of independence [6]. Additionally, studies show that patients who have experienced a stroke are up to four times more likely to have a second stroke [101].

Recovery is a complex and highly individualized process, and full recovery is by no means guaranteed. The overall goal of the rehabilitation is to mitigate the degree of disability the patient experience post-stroke [102]. Early initiation of rehabilitation has been proven highly valuable in order to prevent secondary complications and reduce mortality. Post-stroke rehabilitation when addressing multiple disciplines,

has been shown to improve the overall QoL of stroke-survivors. In contrast, when rehabilitation is limited or delayed, it has been linked with prolonged disabilities such as motor impairment, reduced mobility as well as increased dependency on the caregivers.

As patients may require assistance with basic activities of daily living and often need substantial rehabilitation to regain essential functions, which increases both societal and financial demands [102].

The delays currently identified in the SA referral system not only affect time-to-treatment but also have a significant impact on time-to-rehabilitation. Since timely rehabilitation has been proven crucial for improving QoL, the same reasoning about the MD100's potential to reduce time delays also applies to the rehabilitation process benefiting both society and patient outcomes.

Social group aspects

Besides patient perspectives, social group aspects are another important area and this section addresses the following issues related to the topic.

ID	Issue
H0201	Are there groups of patients who currently don't have good access to available therapies?
H0012	Are there factors that could precent a group or person from gaining access to the technology?

The strict therapeutic time-window for the interventions, such as thrombolysis and thrombectomy, significantly limits their accessibility for patients. This implies that patients residing in areas outside the central urban region of the WC, where the two hospitals providing therapies are located, face substantially longer travel distances, and thereby travel times, which further narrows the already limited time-window for treatment. As a result, geographical disparities may limit patients' access to treatment therapies by delaying their ability to receive care within the required time frame. The MD100 has the potential to identify stroke earlier by supporting clinical judgement even in the pre-hospital setting. Earlier identification may facilitate bypassing intermediate hospital facilities and by so saving time and shorten time-to-treatment. Thereby, the MD100 may facilitate treatment to a broader patient group under the circumstance that earlier intervention also leads to treatment.

In the private healthcare setting, budgetary constraints may be less of a priority [46], [73]. However, disparities in access to care and the potential for unequal treatment remain important ethical concerns to be further investigated.

Communication aspects

The last topic in this domain investigates communication aspects in regards to the technology according to the issues below.

ID	Issue
H0202	How are treatment-choices explained to patients?
H0203	What specific issues need to be communicated to patients to improve adherence?

For both stroke and TBI, the choice between the different treatment options is highly dependent on the time elapsed from onset as well as the type of stroke and its severity. If treatment is relevant, the specific method depends on several factors as well as the condition of the patient. This decision is determined by the physician's assessment. Though the patient is not often involved in the choice of treatment it is important to keep the patient well informed about a potential procedure that is about to take place in order to have consent.

3.9 Legal aspects

Legal considerations are a vital part of evaluating the implementation of new medical technologies. This domain outlines the key legal aspects relevant to the use of the MD100, including patient autonomy, privacy and the right to equitable access to healthcare. It also discusses the ethical and legal frameworks surrounding medical device authorization in the WC setting, safety standards as well as market regulations. Understanding these elements is essential to ensure that the deployment of the MD100 aligns with both SA laws and ethical medical practice.

Privacy of the patient

The first topic is related to the privacy of the patient and answers the following listed issues.

ID	Issue
I0007	Is there a possibility that the use of the technology produces additional information that is not directly related to the current care of the patient and may violate their right to respect for privacy?
I0008	What do laws/binding rules require with regard to informing relatives about the results?
I0009	What do laws/binding rules require with regard to appropriate measures for securing patient data and how should this be addressed when implementing the technology?

The collection and storage of patient data in SA is governed by the law called Protection of Personal Information Act (POPIA) [103]. When implementing MD100, it is essential to ensure compliance with POPIA such that the technology meets the legal requirements in regards to patient autonomy and privacy.

The MD100 does not reveal any additional health information, other than the "stoke" or "no-stroke" assessment. However, the medical results still fall under SA regulations in the aspects of patient confidentiality and thereby are healthcare providers not eligible to disclose any of the information to third parties without consent.

Equality in healthcare

The next topic is associated with equality in healthcare according to the issue below.

ID	Issue
I0011	What do laws/binding rules require with regard to appropriate processes or resources which would guarantee equal access to the technology?

The South African Human Right Comission (SAHRC) is an independent institution formed to protect human rights in SA [104], [105]. According to section 27 of the Constitution, all citizens should have the right to access healthcare services. In this context, the MD100 and the extent to which it will be accessible to all citizens largely depends on the locations where it is implemented.

Ethical aspects

This topic address issues related to ethical aspect for the legal aspects domain.

ID	Issue
F0014	Does the implementation or use of the technology affect the realisation of basic human rights?
F0016	Can the use of the technology pose ethical challenges that have not yet been considered in the existing legislations and regulations?

As stated by SAHRC, all SA citizens have the right to access healthcare services. The portable design of MD100 makes the device suitable for deployment in underserved or remote areas which might facilitate triaging of patients already at pre-hospital or lower-level care facilities.

Authorization and safety

Another important aspects is authorization and safety for the technology which this part examines based on the following issues.

As Medfield Diagnostics is currently in bankruptcy, the CE-certification is not at present time active. However, as the MD100 was previously granted a CE certification as a Class IIb medical device, it indicates that it complied with the European regulation on the safety and performance of medical devices (MDR 2017/745).

ID	Issue
I0015	What authorisations and register listings does the technology have?
I0017	What do laws/binding rules require with regard to the safety of the technology and how should this be addressed when implementing the technology?

The MD100 has an intended use as a triage support tool, designed to assist healthcare professionals in their assessment of patients. As such, it should be implemented as an adjunction to, not a replacement for, clinical judgment. When implementing the MD100, it is important to consider the specific context of the implementation site to ensure the device is appropriately adapted to that setting. This is essential for achieving a smooth integration into existing healthcare workflows and aligning with the practices of healthcare professionals.

Regulation of the market

Finally, the regulation of the market is investigated based on the following issues.

ID	Issue
I0023	What kind of legal price control mechanisms are there that are relevant to the technology?
I0024	What kind of regulation exists for the acquisition and use of the technology?
I0025	What legal restrictions are there for marketing the technology to the patients?
I0026	What should be known about the legal issues in cases of new technologies where the current legislation is not directly applicable?
I0037	Are there relevant concerns about conflicts of interest regarding the preparation of binding rules and their implementation?

The International Statistical Classification of Diseases and Related Health Problems - Tenth Revision (ICD-10), developed by WHO is a system which classifies diseases and health conditions using codes [106]. The system is used in SA and was adopted by the National Health Information System of SA (NHISSA). Currently, it is a part of the health information strategy of the NDoH and used in both the private and public healthcare sector.

National Pharmaceutical Product Index (NAPPI) are specific codes that are used in SA as a unique identifier for healthcare products [107]. These are mainly used by the private healthcare sector and to bill medical schemes. In turn, medical scheme programs uses tariff codes which describes what interventions were performed on a patient [108]. Each of the tariff codes has an associated cost that specifies the cost of a specific service or operation. NDoH determines the tariffs of the medical aid scheme and can change annually.

The South African Health Products Regulatory Authority (SAPHRA) is the national regulatory body in SA, a part of the NDoH, which aims to ensure that health products meet the standards of quality, safety, efficiency and performance [109]. SAHPRA follows the constitution, the National Health Act, 2003 (Act No. 61 of 2003), the Medicines and Related Substances Act, 1965 (Act No. 101 of 1965) and other relevant legislation, regulations and policies. Responsibilities include regulations of health products and clinical trials as well as licensing of suppliers medical devices. Additionally, SAHPRA provides guidelines for the classification of medical devices with the latest update from March 2024 [110]. In SA there are four classification levels for medical devices; A, B, C and D 3.6.

Classification	**Level of Risk**
Class A	Low Risk
Class B	Low-Moderate Risk
Class C	Moderate-High Risk
Class D	High Risk – where risk relates to the patient or to public health

Table 3.6: Classification risk according to guidelines from SAHPRA [110]

The classification of a medical device is based on a set of rules; [110].

a) Manufacturer's or distributor's intended use of the device or IVD.

b) Level of risk to patients, users and other persons.

c) Degree of invasiveness in the human body.

d) Duration of use and exposure.

Initially, the manufacturer determines the classification of the medical device; however, the SAPHRA has the authority to override this classification if deemed necessary as regulatory requirements vary depending on the classification [110]. For any medical technology to enter the SA market, SAHPRA approval is required to ensure compliance with relevant quality management systems (QMS) and regulatory standards [111]. The QMS should align with ISO 13485 and is mandatory to obtain a license from SAHPRA [112].

As of today, SAPHRA are lacking both capacity and expertise to independently validate new medical technologies above class A [99]. In those cases, the medical devices must first obtain international certification, CE or FDA, prior to applying for SAHPRA approval to enter the SA healthcare market. This adds an additional layer of complexity for local companies seeking to enter the SA healthcare market, as obtaining certification from abroad, Europe (CE) or US (FDA), which is a highly costly process. These financial and regulatory barriers may limit the development and accessibility of new medical devices within SA.

Manufacturers, importers and distributors of the medical device must obtain appropriate licenses as per SAPHRA regulations [46], [73], [74]. To distribute an international product such as the MD100 in SA, the developer company Medfield Diagnostics must partner with a locally based and registered distributor, alternative locally register the company in SA in which the same regulations apply. The company has meets two key requirements: holding a distributor license issued by SAPHRA and maintaining a certified QMS that follows the ISO13485 standards. Both the manufacturer and local distributor must be certified as per the international standard for QMS specific to medical devices namely the ISO 13485. Once these conditions are met, the local company can in turn distribute the MD100 into clinical use by supplying it to hospitals.

4

Discussion

The discussion provides a critical reflection on the findings of the HTA of the MD100 within the WC healthcare system, highlighting key limitations and contextual factors that may influence its implementation. Drawing from the assessment, potential deployment sites are discussed in relation to the time-sensitive nature of stroke and TBI, as well as the current healthcare infrastructure in the region. Lastly, the section presents a future outlook, emphasizing the importance of conducting a local clinical trial and outlining how such a study could be applied in the WC healthcare setting.

4.1 Clinical study

For a future implementation, there is a clear need for locally conducted clinical trials. These trials are essential to demonstrate that the MD100 aligns with current clinical workflows and that the MD100 does not hinder the work of healthcare professionals, but rather supports the healthcare system by functioning effectively as triage supporting device. The trials should evaluate the device's performance on the local population where environmental and other contextual differences may influence its effectiveness and usability compared to results from previous studies conducted in other countries. An aspect of this could be derived from what was mentioned in section 1.1.6.3, that it has been stated that WC ambulance personnel were reported to be lacking knowledge in critical evaluation scales. Adding a medical technology could potentially support the triage for these healthcare workers, provided that adequate training on its effective use is delivered and well-received.

The SA referral system is not always strictly adhered to in practice [33], [40]. As a result, initiating a clinical study within the EMS setting may not be an optimal starting point, as it could lead to inconsistencies and misrepresentative outcomes due to structural challenges in the healthcare system. Conducting the first initial clinical trial at a tertiary facility may offer a more controlled environment, allowing the study to focus on demonstrating the device's clinical value and compatibility with the current healthcare system. After such a trial, an additional clinical trial may be conducted in the pre-hospital setting as this is one of the identified suggestions of implementation sites.

Before initiating a clinical trial in any setting, identifying a local *champion* willing to evaluate the MD100 is of utmost importance. Local support is essential, as no trial can be successfully conducted without it and ideally, the initiative of a clinical trial should be driven by the *champion* themselves. This key individual should be a well-respected professional within their field, preferably with expertise in stroke or trauma care. They may come from either the public or private sector but would ideally have strong connections within both to ensure widespread market reach.

Given the reasons outlined above, the first step will be to initiate a clinical trial, led by a local champion, at one of the two tertiary facilities: Tygerberg or Groote Schuur Hospital. These institutions possess the necessary medical expertise, experience in conducting clinical trials, and resources to support such an initiative.

The primary objective of the trial will be to assess the feasibility of deploying the MD100 device within the SA healthcare setting, specifically in an ED environment. The device will be used on all patients presenting to the ED with suspected stroke or TBI, with diagnoses subsequently confirmed via CT scan. This approach will allow for the evaluation of the device's performance in the target population and its usability by healthcare professionals.

Additional parameters of interest may include: The proportion of patients arriving via private transport versus ambulance, time from symptom onset to ED arrival and the number of stroke and TBI cases missed during initial assessment. These variables will require further investigation to determine their relevance and feasibility for inclusion in the study.

Following the initial trial, the results will help identify the most suitable site for broader clinical implementation. A follow-up study should then be conducted at this site, focusing on the device's usability and clinical value in real-world settings. The aim will be to generate robust evidence to support the justification for widespread adoption in similar healthcare environments.

4.2 Suggestion of future implementation sites

Building on the findings of the HTA analysis, this section presents the proposed implementation sites for the MD100 within the WC healthcare sector in SA, covering both public and private settings.

4.2.1 Public healthcare

The public healthcare system in SA faces numerous challenges, particularly regarding resource allocation, high patient load and economic constraints. The following section discusses the possible implementation sites of the MD100 in the public healthcare of WC and presents our view on the optimal implementation sites.

Pre-hospital care

Deploying the MD100 in the pre-hospital setting may facilitate triaging of patients by supporting clinical decision-making with an objective technology. This can potentially reduce time-to-treatment, by enabling EMS to bypass level 2 facilities, which have CT capabilities but cannot provide definitive treatment, and transport patients directly to level 3 facilities eligible to provide both diagnosis and treatment at the same facility. As seen in figure 4.1 the intermediate stop at a level 2 can potentially, with the MD100, be bypassed if a stroke is detected in the ambulance unit which in turn would yield in a great time saving.

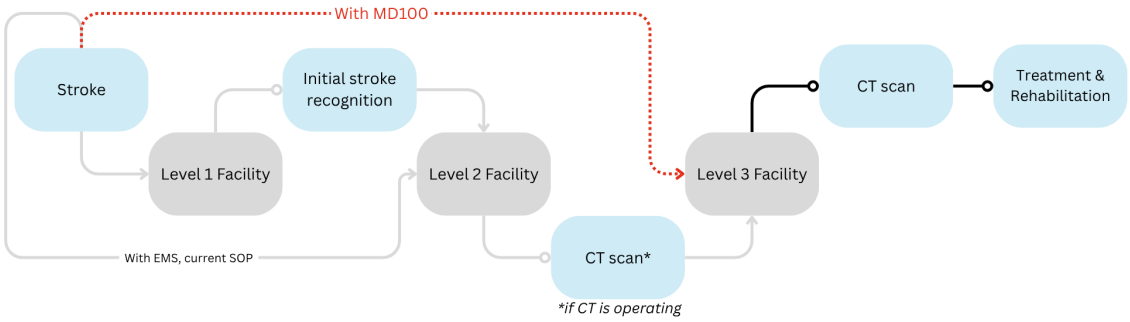

Figure 4.1: The current patient referral system of stroke and the possible implementation site of the MD100 in the pre-hospital care.

Implementing a MD100 in all 250 ambulances would require a quite large initial investment. For a LMIC, one can assume that this corresponds to a considerable part of the allocated healthcare budget. Therefore, implementing the device in a subset of pre-hospital units in the WC may be a more sustainable alternative when considering budgetary constraints. However, this raises the question of which specific units that should be equipped. Such selective deployment may pose an ethical concern, as access to the device would vary between ambulance units, potentially resulting in unequal access to the technology. However, this inequality stems from the broader structure of the SA healthcare system, where specialized care is highly centralized in urban areas. As a result, access to advanced medical technologies is inherently uneven, reflecting systemic disparities rather than being a direct consequence of choice of implementation sites for the MD100. Identifying specific high-priority areas may be an optimal strategy. For instance, areas where stroke are more prominent, where trauma burden is very high or where there is a long distance between the hospital instances. This would however require further investigation. Utilizing the device in the pre-hospital setting may limit its overall impact, as the frequency with

which EMS encounters stroke and TBI patients remains a key factor that influences the health economic viability of deploying the MD100 in this context.

Level 1 facilities

Another investigated implementation site are level 1 facilities which are the facilities that do not possess CT capability. Similar to the pre-hospital setting, an implementation of the MD100 at level 1 facilities may improve time-to-treatment by enabling bypassing of level 2 facilities that are not equipped to provide definitive treatment as illustrated in figure 4.2. As shown in Table 1.2, the distance from district hospitals to the nearest facility with CT capabilities can be as far as 395 km. In such cases, an intermediate stop at a level 2 facility without treatment capabilities is both time-consuming and unnecessary, restricting the time-window for treatment and potentially worsening patient outcomes.

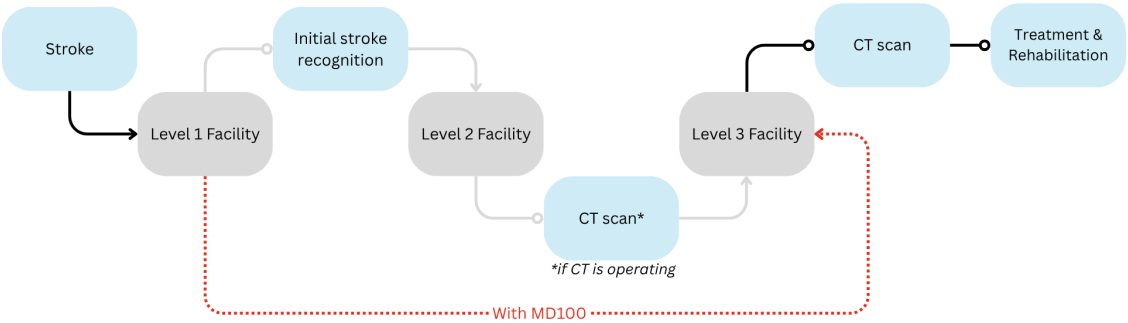

Figure 4.2: The current patient referral system of stroke and the possible implementation site of the MD100 at the level 1 facility.

A distinction between deploying the MD100 at a level 1 facility versus in a pre-hospital setting lies in the patient reach. Installing the device at a facility may enhance the accessibility of the triaging support for a broader patient population by including patients not transported by EMS. This setup may extends its patient reach. However, the proportion of patients who self-refer versus those arriving via EMS remains unknown. Therefore, further investigation is needed to determine where, between level 1 facilities and EMS units, the MD100 could have the greatest impact and reach the highest number of patients.

Implementing the MD100 in all level 1 facilities (in total 75 facilities) would result in a lower investment compared to full-scale deployment across all pre-hospital units. However, given that it is still a large cost, it may be necessary to prioritise

certain facilities due to budgetary constraints similar to the prioritisation within the pre-hospital units. One potential strategy could involve prioritising those located furthest from tertiary facilities, in order to maximise time savings and clinical impact. This prioritisation approach, however, requires further investigation.

Level 2 facilities

Level 2 facilities, which include regional and district hospitals equipped with CT scanners, face challenges due to limited CT availability, typically restricted due to limited resources, resulting in the operating time frame of 8 a.m – 4 p.m and not a 24/7 hour access as in tertiary hospitals. During hours when CT access is unavailable, the impact of the MD100 aligns closely with its potential use in level 1 facilities as it could support clinical decision-making by helping identify patients who require urgent referral to tertiary hospitals. The required investment of this option is lower than implementing the MD100 in all level 1 facilities, since there are only 8 level 2 facilities in total. It should however be noted that this option might provide a lower clinical value as level 2 facilitates already possess CT-scans and additionally have greater expertise and resources compared to pre-hospital units and level 1 facilities, which might decrease the need of the MD100 as a triage tool in that particular setting. On the other hand, the level 2 facility could use the MD100 to directly identify stroke-patient, without delays of CT-scanning at the level 2 facility which is the current SOP. This could reduce the time-to-treatment as CT-identified stroke-patients at the level 2 facility requires transfer to a level 3 facility to get treatment.

Level 3 facilities

Implementing the MD100 at level 3 facilities, equipped with CT scanners, could assist in prioritising patients awaiting neuroimaging. Using the MD100 in combination with existing clinical assessment scales offers an additional tool that supports clinical decision-making and has the potential to facilitate for clinicians in the prioritisation of patients for the CT scan. However, as of today, deploying the MD100 for prioritisation in CT queues may not represent the most effective use of the technology as patients at level 3 facilities often already are outside of the critical time-window for treatment at this stage of the care [40]. As a result, deploying MD100 at this point may not significantly alter treatment access.

4.2.2 Private healthcare

Under the assumption that stroke represents a global healthcare burden and is a time-critical medical emergency, we infer that private healthcare providers in the WC also need to reduce time-to-treatment. This suggests that the MD100 could have utility within the private sector as well. However, the optimal point of integration cannot yet be determined, as uncertainties regarding the organizational structure and referral pathways remain.

As private healthcare facilities operate as businesses, there is a degree of competition

among them driven by the fact that patients ultimately fund their own care via medical aid schemes. This competition may motivate providers to adopt technologies that enhance the quality and efficiency of their provided services. In SA, both public and private healthcare facilities can receive specific certifications that signals high-quality care to the public. Though the credibility of these certifications is sometimes debated [59], such recognitions can enhance a facility's reputation and in turn, its patient appeal. On that note, private hospital groups may be more inclined to adopt innovative technologies that may offer a strategic advantage to stay at the forefront of care, with the goal to ultimately enhance patient appeal. Unlike in the public sector, where limited funding often poses a major barrier of adapting medical technologies [73], financial constraints are generally less pronounced in the private healthcare sector. Therefore private hospital groups may also become adopters of the MD100, given that strong clinical evidence demonstrates its effectiveness and cost-efficiency that argues for long-term sustainable investment [46]. However, this is still up for investigation.

4.3 Health economy

The economic evaluation presented in Appendix A and Section 3.5 outlines a simplified case to demonstrate the potential cost-effectiveness of the device. It is important to note that the study used to derive key parameters, such as the INMB, relies on the assumption that patients actually receive treatment and faster as well. However, in SA, the majority of patients are currently excluded from receiving treatment particularly due to the existing time constraints related to their arrival outside the treatment-window. In the health economic evaluation we have assumed that more patients would, with the implementation of the MD100, be able to be within the time-window for treatment when arriving at the stroke unit. There is currently no information available regarding after how long time patients arrives to the tertiary facilities after stroke onset which makes this assumption difficult to prove in the current state.

This factor should be kept in mind when interpreting the calculated annual cost savings of $724,500,000. This figure is calculated under the assumption of a a 10-minute saving in time-to-treatment for all of the 75,000 stroke-patients annually in SA. However, this estimate is likely to be significantly overstated, as not all patients will experience a full 10-minute time saving, and not all patients will ultimately receive treatment. Some patients might have a significantly larger time saving than 10 minutes and reach the tertiary facility within the time-window while some patients might receive any beneficial time saving. An example is when a patient gets a stroke during their sleep resulting in that they are already outside of the time-window for treatment when they wake up, in these cases the MD100 might not facilitate any additional benefit. While patients having a stroke during the day and are far from a tertiary facility can be scanned directly with the MD100 and be escalated to the tertiary facility to receive treatment.

The WTP must align with the clinical value and benefit that the MD100 can deliver. Demonstrating this clinical value, particularly the time savings that could be achieved with implementation, should therefore be a key focus of future research. As presented in Appendix A, even a very small improvement in time-savings per patient (e.g., 10 patients each saving just one minute would yield threshold for cost-effectiveness during a 10-year lifetime of the device), clearly demonstrate that MD100 can generate meaningful clinical benefit on patient outcomes. This is especially relevant in the SA context, where significant time savings may be possible within the current patient referral pathways. The main aspects of the economic modelling is that even a small amount of time saved is enough to justify the devices benefit and that the WTP is not the most important aspect to consider but rather the clinical value will have.

4.4 Limitations

Several uncertainties are associated with this project, including methodological limitations. For example, interviewees expressed differing perspectives on certain issues and with more time, additional data could have been gathered and analysed, capturing an even broader range of insights.

As the MD100 is a new and innovative technology, there is limited availability of existing data on its performance within the SA context. This lack of context-specific evidence poses challenges for a comprehensive assessment of its long-term clinical value. Consequently, the analysis performed relies primarily on linked and indirect evidence. Under the assumption that the MD100 can facilitate time-to-treatment, it has the potential to generate significant value. Given the current constraints and delays in the SA healthcare system, the MD100 could play an important role in improving outcomes by enabling more timely intervention.

Another limitation was the availability of information regarding the private healthcare sector. Since the private healthcare is profitable, current SOPs and statistical numbers within the healthcare concern was not public figures and neither willingly disclosed. Interviews focusing on the private healthcare sector were limited, primarily due to the difficulty in accessing relevant stakeholders. As a result, no first-hand interviews with individuals directly involved in the private healthcare system could be conducted. Instead, insights were gathered through second-hand discussions with individuals who have indirect involvement or knowledge of private healthcare operations. As a result, this limited the HTA in regards to the applicability of the MD100 in the private healthcare sector.

Another important topic that emerged from the interviews was the difference in opinions among the various stakeholders. Each interviewee, drawing on their expertise in their respective fields, expressed differing views on both the device itself and the most appropriate site for its implementation.

In regards to the findings from the HTA there are many limitations for cost estima-

tions and cost-effectiveness. This aspect will be important in the process of adopting the MD100 in the SA healthcare given their budget constraints. In order to perform a justified estimation of the economical aspects, it must be performed a local clinical study in order to collect evidence which will assist in proving clinical value of the device in that particular setting.

4.4.1 Future outlook

As of today, very few stroke patients receive thrombolysis or thrombectomy treatment in WC, SA. The current referral system and management of the conditions significantly limits access to treatment by further narrowing this critical time-window. Thrombolysis is administered at both Tygerberg and Groote Schuur, in accordance with international guidelines recommending administration within 4.5 hours of stroke onset. Thrombectomy is like thrombolysis, only performed at Tygerberg and Groote Schuur but up to 7 hours after stroke onset. However, the international recommendation makes thrombectomy applicable up to 24 hours after stroke onset, but given the lack of advanced imaging capabilities and resources it is not currently followed in WC. Given this, current focus should be on minimising the time it takes for patients to reach the stroke units to hopefully arrive within the current time-window for treatment.

The device's primary clinical value lies in its ability to reduce time-to-treatment. Given the urgency associated with these neurological emergencies, it is essential to identify the points within the SA healthcare referral system where MD100 implementation would yield the greatest time savings. Based on the HTA, we have identified the two most suitable implementation sites for the MD100 within the public healthcare system. First, in the pre-hospital units where the MD100 could be used to bypass lower-level facilities lacking treatment capabilities and directly transport patients to tertiary hospitals. Second, deployment at level 1 facilities to enable early triage and facilitate timely referral to higher-level facilities with treatment capacity, again avoiding unnecessary intermediate stops. Strategically prioritizing implementation in these contexts may maximize the clinical and economic value of the device while working within the constraints of the SA healthcare system.

5

Conclusion

In conclusion, this project focused on conducting a HTA of the Strokefinder MD100 for the early detection of stroke and TBI in the WC of SA. Guided by the EUnetHTA Core Model, we evaluate the health economic viability of the MD100, identify potential implementation sites and provide a forward-looking perspective on its future role.

Based on the assessment, three main conclusions can be drawn:

Firstly, one of the most significant identified challenges in the WC, SA, is that stroke and TBI patients often do not arrive within the therapeutic time-window thus restricting their access of treatment. This issue is largely attributed to the structure of the referral system, which is characterized by overburdened hospitals and, the often, long transfer distances between healthcare facilities. To address this, efforts should be focused on reducing these delays, particularly by minimising referral times to increase the likelihood that patients arrive within the time-window of treatment. Therefore, implementation should, as of today, focus on locations lacking diagnostic capability, such as pre-hospital units and level 1 healthcare facilities without access to CT imaging in order to target the sites associated with the longest delays. With a triage support tool such as the MD100, these intermediate stops can be avoided by directly transfer patients to tertiary facilities with primary goal to meet the time-window for treatment.

Secondly, the high incidence rate of stroke in SA combined with the limited availability of specialised care, particularly in rural and underserved areas, the MD100 offers a way to extend technology-based triage capabilities. By so, enabling earlier triage optimizes resource use. With the expected time savings resulting from MD100 implementation, the device is considered economically viable in the SA context, primarily driven by its potential to significantly reduce time-to-treatment for stroke patients. With the linked evidence that a 10 minute reduction in time-to-treatment corresponds to an average gain of 39 days of disability free life as well as an estimated cost saving of $10,500, the MD100 demonstrates strong potential to deliver both clinical and economic value in stroke care management by addressing the critical time-factor. Even small reductions in time-to-treatment, such as one minute, have been shown to result in meaningful improvements in patient outcomes, including both the increased disability-free days and the reduced long-term care needs.

Again, implying both clinical improvement and economic societal savings.

Lastly, a clinical trial is needed to demonstrate the device's clinical effectiveness and validate its impact on patient outcomes in the SA context. After conducting the HTA, points of delays in the healthcare referral system have been identified. However, the actual amount of time savings that are associated with usage of MD100 is yet to be confirmed. An initial step would be to conduct a trial in a controlled hospital environment, which possess enough resources and capabilities to prove its clinical value in the SA setting. However, as the broader goal is to improve stroke care pathways in SA to shorten time-to-treatment, the MD100 aims to address points in the healthcare system where time savings are most critical.

Distance is time. Time is brain.

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A

Appendix 1

The following appendix shows the calculations for ICER, QALY gained and INMB with the following assumptions and values.

Parameter	**Assumption**
Cost of one device	€ 90,000
Number of stroke cases per year in SA	75,000
Disability free days for 10 minutes saved	39 days [72]
INMB for 10 minutes saved	$ 10,500 [72]
Max cost per QALY (λ)	$ 100,000 [72]
Cost (C)	Negligible

$$\text{ICER} = \frac{\Delta C}{\Delta B} < \lambda \tag{A.1}$$

It has been estimated little to no changes in the total costs (Δ C) of the healthcare when saving 10 minutes on time-to-treatment [72], resulting in a small ICER and proven large benefit (Δ B).

Given that λ is estimated to $ 100,000 by [72] this shows:

$$ICER < \lambda \tag{A.2}$$

€ 90,000 converts to $ 102,318 and if we assume the INMB for 10 minutes saved is $ 10,500 [72]:

$$\frac{\$102,318}{\$10,500} = 9,74\ years \approx 10\ years \tag{A.3}$$

This means that the lifetime of the device should be 10 years to be assumed as the health economic viable. It is reasonable to believe that the device life-time would be 10 years. If we assume that the device saves 10 minutes per year.

$$10\ years \cdot 10\ min\ saved = 100\,\text{min} \tag{A.4}$$

100 minutes are needed to be saved during the entire lifetime of MD100 to reach INMB that corresponds to the instrument cost.

To illustrate cost-effectiveness in simplified terms, the total minutes saved during the lifetime of MD100 can be distributed, if the device enables 10 patients to receive treatment 1 minute earlier per year, under the entire period of ten years, it would meet the threshold for cost-effectiveness across its expected lifespan.

Disability-free days in relation to 10 minutes of time-savings

A 10-minute reduction in time-to-treatment results in an average gain of 39 disability-free days per patient [72]. If this time reduction could be achieved for all stroke cases in SA, the total number of disability-free days gained per year can be estimated as follows:

$$\text{Total disability free days saved annually} = 39 \cdot 75,000 = 2,925,000 \tag{A.5}$$

Cost savings in relation to 10 minutes of time-savings

Similarly, a 10-minute reduction in time-to-treatment results in an average saving of $ 10,500 per patinet [72]. If this time reduction could be achieved for all stroke cases in SA, the total cost savings can be estimated as follows:

$$\lambda = 10,500 \cdot 75,000 = \$724,500,000 \tag{A.6}$$

B

Appendix 2

The following table lists all the issues that are not addressed from the EUnetHTA CM.

Domain/Topic	ID	Issue	Reason for exclusion
CUR/Regulatory Status	A0021	What is the reimbursement status of the technology?	Not yet in the stage where a conclusion can be drawn.
SAF/Safety Risk Management	B0010	What kind of data/records and/or registry is needed to monitor the use of the technology and the comparator?	N/A
EFF/Morbidity	D0005	How does the technology affect symptoms and findings (severity, frequency) of the disease or health condition?	N/A
EFF/Morbidity	D0032	How does the test-treatment intervention modify the magnitude and frequency of morbidity?	N/A
EFF/Morbidity	D0006	How does the technology affect progression (or recurrence) of the disease or health condition?	Not applicable
EFF/Health-related Quality of life	D0012	What is the effect of the technology on generic health-related quality of life?	N/A
EFF/Patient satisfaction	D0017	Were patients satisfied with the technology?	Not yet in the stage where a conclusion can be drawn.
EFF/Test accuracy	D1005	What is the optimal threshold value in this context?	Not yet in the stage where a conclusion can be drawn.

Domain/Topic	ID	Issue	Reason for exclusion
ECO/Validity of the model(s)	E0013	What methodological assumptions were made in relation to the technology and its comparator(s)?	Not yet in the stage where a conclusion can be drawn.
ECO/Validity of the model(s)	E0012	To what extent can estimates of costs, outcomes or economic evaluation(s) be considered as providing descriptions of the technology and its comparator(s)?	Not yet in the stage where a conclusion can be drawn.
ETH/Benefit-harm balance	F0003	Are there any other hidden or unintended consequences of the technology and its applications for patients, relatives, other patients, organisations, commercial entities, society etc.?	Not yet in the stage where a conclusion can be drawn.
ETH/Respect for persons	F0008	Does the implementation or use of the technology affect human dignity?	N/A
ETH/Respect for persons	F0009	Does the implementation or use of the technology affect the patient's moral, religious or cultural integrity?	N/A
ETH/Respect for persons	F0101	Does the technology invade the sphere of privacy of the patient/user?	N/A
ORG/Health delivery process	G0012	In what way is the quality assurance and monitoring system of the new technology organised?	N/A
ORG/Process-related costs	G0006	What are the costs of processes related to acquisition and setting up the new technology?	Can not be concluded in the current stage.
SOC/Patient's perspectives	H0006	How do patients perceive the technology under assessment?	N/A
LEG/Autonomy of the patien	I0002	What kind of legal requirement are there for providing appropriate information to the user or patient and how should this be addressed when implementing the technology?	N/A
LEG/Equality in health care	I0012	What are the consequences of various EU level and national regulations to the equal access to the technology?	N/A
LEG/Ownership and liability	I0019	What should be known about the intellectual property rights and potential licensing fees?	Not yet in the stage where a conclusion can be drawn.

Domain/Topic	**ID**	**Issue**	**Reason for exclusion**
LEG/Ownership and liability	I0021	What should be known about the legal or binding rules regarding the width, depth and length of the manufacturing guarantee?	Not yet in the stage where a conclusion can be drawn.

C

Appendix 3

Summary of key thoughts from interviews

The interviews included subjective thoughts about the implementation of new technology and regulatory requirements. Experience about the stroke and trauma care was also discussed.

During all interviews, the participants were united regarding the fact that a *champion* were crucial for a successful implementation of a new medical device on the SA market. However, who this individual would be was different when discussing it with different stakeholders. Some suggested that this person should be from academia [74] and some suggested that a respected healthcare professional, such as the head of unit, would be the most appropriate champion [33], [40]. However, there was an agreement that a champion should be a highly respected individual within their field and possessing a significant amount of influence.

A lot of information regarding both stroke and trauma care gave insights into current SOPs for the different conditions at Tygerberg and Groote Schuur hospitals [33], [40], [59]. The exact SOPs for care at the facilities were however not able to be shared since these are not public documents. For attitude towards new technology, it was emphasized that the primary focus should be on the benefits for the healthcare professionals, as they are the direct users of the technology [99]. For CT access, it was stated that patients were only prioritised in the queue to a CT-scan when they are inside the time-window for treatment [34]. If they are outside time-window and possess major risk factors for stroke, they might not receive a confirmatory CT due to limited resources [34].

For procurement of new medical devices there are a time-consuming procedure that includes to getting the technology approved and after that have the appropriate evidence for justifying implementation in the SA healthcare system. The system is highly built upon the benefits that the technology brings to the healthcare [46], [73], [99]. The hospitals in the WC SA can requests technology and medical consumables through a "wish list" which they put together [73]. The lists are then sent to either an internal committee or the provincial committee which consists of experts [73]. The respective committee's then performs a three phase assessment process; initial approval, comprehensive evaluation and finally an economic assessment [73].

Approval for introduction on the SA market were discussed in regards to SAHPRA's role,

it was stated that since the device holds a CE-certification, this process will be streamlined [99]. Proving the device value, as an international company trying to introduce a medical device on the SA market, is also an aspect which must be considered to be able to perform a clinical trial [99].

Discussions were also held about optimal implementation strategies of the Strokefinder MD100 in regards to regulatory aspects [46]. The structure of the private healthcare sector were also discussed including the function of medical aid schemes and the actors involved in the private sector. Additionally, aspects of the private healthcare procurement of medical devices were discussed.

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