Design and Development of an Autoinjector Tracking Device to Integrate with Emergency Service

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Declaration

I, Qhamani Maqungu, declare that this thesis is composed of my original work, it contains no material previously published or written by another person except where due reference has been made in the text. This thesis is submitted to the University of Cape Town for the Master of Philosophy specialising in Financial Technology degree.

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Abstract

Anaphylaxis is a life-threatening allergic reaction that requires treatment by prompt injection of epinephrine typically via epinephrine autoinjectors (EAI). An immediate visit to the emergency room (ER) to avoid possible relapse is necessary. Studies have shown that the effectiveness of epinephrine decreases with the prolonged delay of injection after symptoms onset. Many patients get hospitalised or die due to delayed epinephrine injection or unavailability of the EAI devices when it is mostly needed. Some of the reasons for unavailability at the incident site is usually associated with patients forgetting to carry their EAI. Some patients hesitated to administer epinephrine, resulting to a relapse hours later and while some did not seek further monitoring from a trained clinician after administering epinephrine.

This study aimed at designing and developing an EAI tracking device to send reminder notifications to patients when they are located ten meters away from their EAI, and to alert emergency medical services (EMS) via SMS, containing location, when the patient is experiencing anaphylaxis. Using Impulse Biomedical's EAI *ZibiPen* device as a use case, a Bluetooth low energy (BLE) tracking device named GuardAin, was developed and linked to an Android mobile phone application.

A pilot case-based study aimed at validating the accuracy of the notification alert algorithm in three-dimensional directions was conducted at the Impulse Biomedical offices in the Western Cape. The test conditions were phone in hand and phone in pocket. The distance algorithm was validated using a t-test. The location accuracy from the emergency alert SMS was validated and compared to Google Maps.

A total of 80 notification alert tracking tests were conducted. Forty tests were conducted for the horizontal direction test resulting in the detection of ten meters with an average of 10.7 meters. Forty vertical tests resulted in poor detection of a ten-meter distance. However, consistency in detecting three meters was observed with an average of 3.3 meters. The 3.3 meters was the average floor height in the building. Eight locations were selected as the choice of emergency trigger locations. The emergency alert locations were accurately detected within a 50-meter radius.

The algorithm was found to be fairly accurate in detecting 10 meters and could serve as a reliable reminder for EAI adherence. However, walking pace determined how far past ten meters the notifications were sent. SMS emergency alerts were found useful to detect EAI usage and accurately relaying patient location to EMS and other emergency contacts. Future works include investigating the usability of the reminder system, and practicality of the emergency services alert system. Additionally, the tracking algorithm to be validated with different Android mobile devices.

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List of Abbreviations

APP	Application
BLE	Bluetooth Low Energy
BTS	Bluetooth Tracking System
OS	Operating System
EAI	Epinephrine Autoinjector
ECC	Emergency Call Centre
EMAS	Emergency Medical Alert System
EMS	Emergency Medical Services
ER	Emergency Room
FIA	Food-Induced Allergy
FR	Functional Requirements
HCP	Healthcare Professional
HSF	Health Science Faculty
HUI	Hardware User Interface
ICT	Information and Communication Technology
IDE	Integrated Development Environment
LMIC	Low- or Middle-Income Countries
NFR	Non-Functional Requirements
PIH	Phone in hand
PIP	Phone in pocket
PTSD	Post Traumatic Stress Disorder
PPS	Patient Portal System
RE	Requirements Engineering
RSSI	Received Signal Strength Indicator
SATS	South African Triage Scale
TFW	The Five Whys
UI	User Interface
UCT	University of Cape Town
UWB	Ultra-Wide Band
WAO	World Allergy Organisation

1. Chapter 1: Introduction & Background

1.1 Introduction

In recent years, there has been a growing interest in developing tracking devices to help monitor and improve patient outcomes. One area where tracking devices can be beneficial is administering medication via epinephrine autoinjector (EAI) devices, where adherence to the prescribed course of drugs is critical to achieving optimal therapeutic results. This research aims to present a new tracking device for autoinjectors, particularly reloadable injection devices used to treat anaphylaxis, to help these patients locate their EAI timely, improve adherence, and reduce the risk of adverse events.

The proposed tracker uses Bluetooth technology to communicate with a smartphone application (App). It provides emergency medical services (EMS) with alerts when a patient uses the EAI during an anaphylactic episode by sharing the patient's real-time location. Additionally, the tracker sends reminders when the patient is more than ten meters away. The device is compact and easily attached to autoinjectors via an innovative safety cap design. The importance of this research lies in its potential to improve EAI carrying adherence and patient outcomes for individuals with chronic conditions such as anaphylaxis or asthma. The device can help patients and carers better manage their health and reduce the risk of complications during severe allergic reactions by providing a more comprehensive way to track autoinjectors. Overall, this thesis aims to contribute to developing innovative solutions for improving medication management and patient outcomes.

1.2 Problem Description

Anaphylaxis is a rapid-onset allergic reaction that may cause death (Sheikh et al., 2009). It is an allergic reaction that can develop to its peak within five to 20 minutes (Frew, 2011; WAO, 2019). For this reason, it is considered to represent the most clinically severe reaction in the whole spectrum of allergic reactions (Turner et al., 2019).

The first line of treatment for the reaction is the injection of epinephrine via autoinjectors in community settings or intravenously in hospitals. Although epinephrine is the first-line treatment for anaphylaxis, delayed administration results in low efficacy of the medication, which is associated with high mortality rates (Prince et al., 2018). Epinephrine is most effective when it is promptly injected into the anterolateral aspect of the thigh (Mayo Clinic, 2023).

Studies found epinephrine to be ineffective when injected after 25 minutes of symptom onset, resulting in 46% of patients dying (Sampson et al., 1992). In another study of 124 anaphylactic patients who were administered epinephrine later than 15 minutes after severe respiratory symptoms, only 28% of the patients were resuscitated but later, on the same day, died because of

hypoxia (Pumphrey, 2000). Lack of improvement of symptoms has been attributed previously to delay in epinephrine injection and rapid reaction progression. Patients stand better chances of survival if they self-inject epinephrine within 10 minutes of the reaction (Enzan et al., 2020).

Given that injection time is crucial when counteracting an anaphylactic episode, patients must always carry EAI since at times allergen avoidance is impossible. However, it is an issue for patients always to have these devices with them, every day (Sheikh, 2012). One study found that the carrying rate of autoinjectors was as low as 10–44% (Jay et al., 2019). Another study by Brooks et al. on paediatric tertiary care found that half of the patients did not have their EAI at the time of reaction, leading to many hospitalisations (Brooks et al., 2017).

1.3 Project Rationale

An association between low carrying compliance of EAI and delayed self-administration can be explained as follows: If a patient experiences an anaphylactic episode and does not have their EAI at close reach, they can die because of delayed or no epinephrine injection. Even with anaphylaxis management guidelines available in public posters and online, patients tend to undermine the seriousness of not always having EAI. Most children do not have fundamental first aid measures like an anaphylaxis action plan, an EpiPen autoinjector, and someone willing and able to administer the device (Gold & Sainsbury, 2000). The absence of these resources may contribute to hospitalisations and fatalities when a patient is in an episode.

Therefore, more creative ways should be implemented to encourage them to have their autoinjectors. Knowledge and education about the risk of experiencing a severe reaction alone are insufficient to enforce adherence to anaphylaxis management, a more complex change is required, including a change in one's lifestyle (Gamboa-Antiñolo, 2020).

1.4 Significance of the Problem

The significance of this research lies in its contribution to clinical research for anaphylaxis management strategies. It provides a new solution that integrates a distance and emergency tracker with epinephrine autoinjector for patients suffering from anaphylaxis. With the widespread use of smart devices, the proposed solution represents a step towards creating a connected mHealth application.

It can potentially enhance epinephrine autoinjector-carrying compliance and significantly reduce the frequency of hospitalisations and fatalities resulting from delayed epinephrine injection during an anaphylactic episode. This, in turn, alleviates the burden on medical facilities, enabling them to

prioritise other emergency cases. Existing literature indicates that patients suffering from anaphylaxis experience a diminished quality of life (Lange, 2014). For example, Knibb RC et al. (2022) highlighted that patients with food-induced allergies were affected more on quality of life, than those with sting induced allergies due to their constant fear of experiencing an allergic reaction resulting in increased stress, anxiety and depression. The device has the potential to enhance their well-being by instilling a sense of security and confidence, knowing that their loved ones and emergency centres will respond swiftly in critical situations.

Given the modality of the proposed solution, this research can be further customised to other telemedicine and mHealth solutions such as smartwatches that can help in the early detection of anaphylaxis shocks.

1.5 Research Question

This research attempted to answer the following research questions:

Can a smart phone-based autoinjector with a distance tracker improve autoinjector carrying adherence through separation reminders, and can this tracker send an alert and relay patient location to emergency services when the autoinjector is used to ensure that patients receive the necessary treatment for anaphylaxis on time?

1.6 Study Aims and Objectives

This project aims to design, develop, and evaluate a smart phone-based tracker that encourages EAI carrying adherence and able to automatically send alerts to emergency services without user intervention. The aim of the project was achieved through the following objectives:

1. Design and develop a mobile phone-based tracker to alert patients to always carry their EAI.
2. Integrate the tracker with Impulse Biomedical's EAI *ZibiPen* to detect emergency usage and alert EMS.
3. Evaluate the smart device guided by mHealth software and hardware standards and evaluate the feasibility of the solution in the SA context.

1.7 Scope and Limitations of Study

This study focused only on the design, development, and evaluation of a prototype of the smart device capable of tracking a reloadable EAI compatible with the industry partner of this project, Impulse Biomedical, ZibiPen. A pilot case-based test and evaluation study was conducted, emphasising cases when the user is in possession of the phone and the autoinjector is within connection range. This assumption is essential, as tracking cannot be performed if neither of the devices is in the user's possession. It is assumed that the patient always utilises the mobile phone to

locate the tracker. The mobile application was designed and evaluated for only the Android operating system (OS). Given the perpetual real-world emergencies, the depth of the investigation of this study was limited to the equivalent of 90 MSc credits (minor dissertation), and not all real-world possibilities were investigated.

1.8 Thesis Outline

The dissertation comprehensively explores the research, design, testing, and outcomes related to the identified clinical problem as shown in Figure 1-1 below. Chapter 1 presents the current clinical problem, and Chapter 2 presents a literature review that focuses on disease pathology, the use of autoinjectors, and current anaphylaxis management strategies that address the pervasive adherence issue many patients face.

Chapter 3 presents the research methodologies adopted for this project. Building on the insights from Chapters 1 and 2, Chapter 4 details the formation of user requirements and technical specifications using the methods and frameworks defined in Chapter 3, leading to the development of the prototype. Chapter 5 presents the outcomes of the prototype development process, highlighting all the significant features of the system and a brief description of how it works.

Chapter 6 evaluates and presents the results and comprehensively assesses the device's capabilities and limitations. Finally, Chapter 7 concludes the preceding chapters and offers future research and development recommendations.

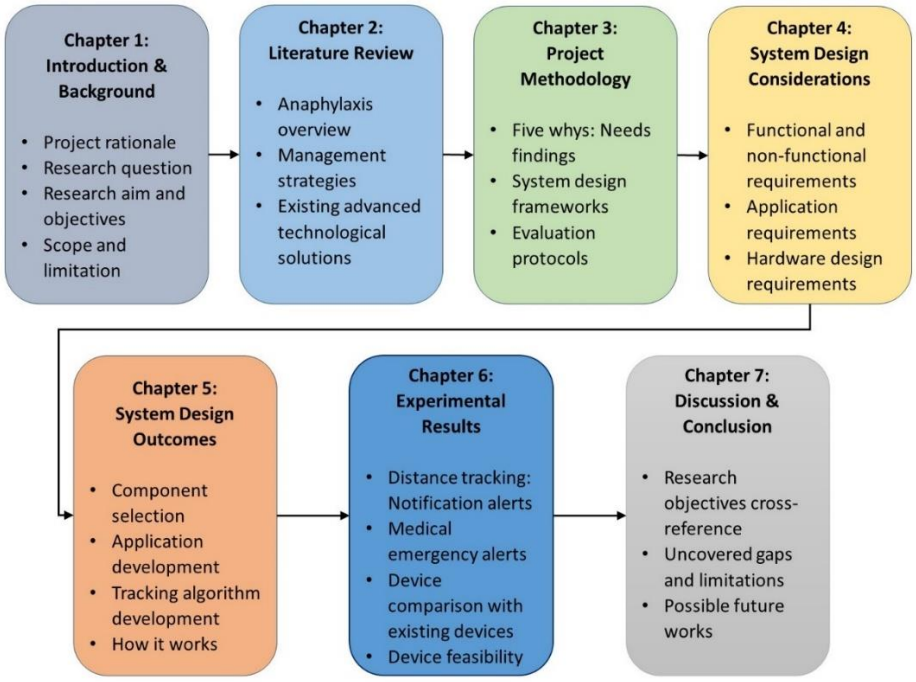

Figure 1-1: Flow chart showing the dissertation outline.

2. Chapter 2: Literature Review

This chapter explores an overview of anaphylaxis, focusing on management strategies to align with the research objectives. It further explores the existing solutions and discusses their limitations in the South African emergency medical context to formulate clinical needs.

2.1. Anaphylaxis Overview

2.1.1 Definition

Anaphylaxis is a life-threatening, systemic hypersensitivity reaction categorised by rapid onset and potentially life-threatening airway problems (Turner et al., 2019). The involvement of multiple organ systems makes the disease vitally dangerous. These include the respiratory, cardiac, and gastrointestinal systems, unlike other common allergies that typically involve only a single organ system (e.g., skin) (Dribin et al., 2022).

2.1.2 Pathogenesis

The mechanism of anaphylaxis typically involves IgE-mediated activation of mast cells and basophils (Peavy & Metcalfe, 2008). Mast cells are an integral part of white blood cells found in connective tissues in the body and are responsible for regulating vasodilation and vascular homeostasis (Krystel-Whittemore et al., 2016). When these cells are activated, the blood pressure drops, and patients suffer from dizziness and the onset of hypoxia. Cardiac arrest can result from shock due to peripheral vasodilatation and increased vascular permeability or from direct cardiac effects of anaphylactic mediators (Mali & Jambure, 2012).

2.1.3 Causes and Symptoms of Anaphylaxis

Typical causes of anaphylaxis include food containing specific ingredients, insect venoms, medications used perioperatively, natural rubber latex, and exercise (Sheikh et al., 2009). Symptoms can vary from mild (less severe) to severe reactions, as shown in Figure 2-1.

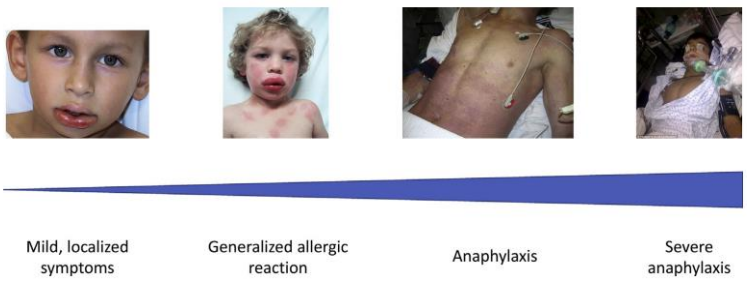

Figure 2-1 Anaphylaxis spectrum (Turner et al., 2019)

The severity of anaphylaxis is due to a compromise of at least two physiological systems; cardiovascular, respiratory, gastrointestinal, and integumentary (Cardona et al., 2020).
Most observed symptoms will include but are not limited to hives and skin rashes, hypotension, severe gastrointestinal pains, and respiratory collapse that may require a visit to the intensive care unit (ICU), as shown in Figure 2-1.

Patients suffering from anaphylactic shock have limited time to counteract the reaction. The time from ingesting a food allergen to the onset of food-induced allergy (FIA) symptoms is usually in the range of a few minutes. Teenagers are at greater risk, with the highest mortality rate from anaphylaxis due to peanut and tree nut allergies found between the ages of 15 and 24 (MacAdam et al., 2012). The onset of anaphylaxis to stings or injections is typically rapid, with an onset time of less than 40 minutes in 90% of cases (Rutkowski et al., 2012). A prompt response is of the essence, and medication availability at the scene plays a crucial role in avoiding severe consequences.

Symptoms in minors and young adults differ slightly from those in elderly individuals (Francuzik et al., 2021). For instance, adolescents and young adults were more likely to report generalised puritan urticaria, vomiting, and diarrhoea than elderly individuals who reported skin rash (Takazawa et al., 2017). The differences in the manifestation of symptoms between adults and adolescents often lead to physicians misdiagnosing other patients. Patients themselves may struggle to detect the creeping anaphylaxis shock on time which can result in fatal consequences or hospitalisation.

2.1.4 Epidemiology

Anaphylaxis cases are estimated to be between 1 and 761 per 100 000 persons per year (Cardona et al., 2020), with a steady mortality rate of less than 1% per annum (Paul et al., 2017). The global lifetime prevalence is about 5% (Cardona et al., 2020), and up to 2% of reactions are fatal (Ma et al., 2014). At least a third of South Africans will suffer from allergies, including anaphylaxis, during their lifetime, with 40% being adolescents (AFSA, 2023). While reactions can occur in any age group, they are most noted in the younger population (McLendon & Sternard, 2023). In the United States of America (USA) alone, it is estimated that about 29,000 severe food anaphylaxes occur each year (WAO,2019).

FIA is the most widely reported anaphylaxis trigger worldwide (220 million people). Most surveys indicate that food-induced reactions account for 30%–50% of cases, particularly peanuts, milk, and seafood, followed by insect stings in adults and children (Antonella & Antonella, 2012). The most reported FIA come from middle- and high-income regions like North America, Europe, Asia, and Australia (De Martinis et al., 2020). FIA in urban South African children is similar in comparison to other middle-income countries where rapid urbanisation and industrialisation occur (Botha et al.,

2019). These findings can be supported by a study conducted between 1992 and 2012 by (Takazawa et al., 2017), shown in Figure 2-2.

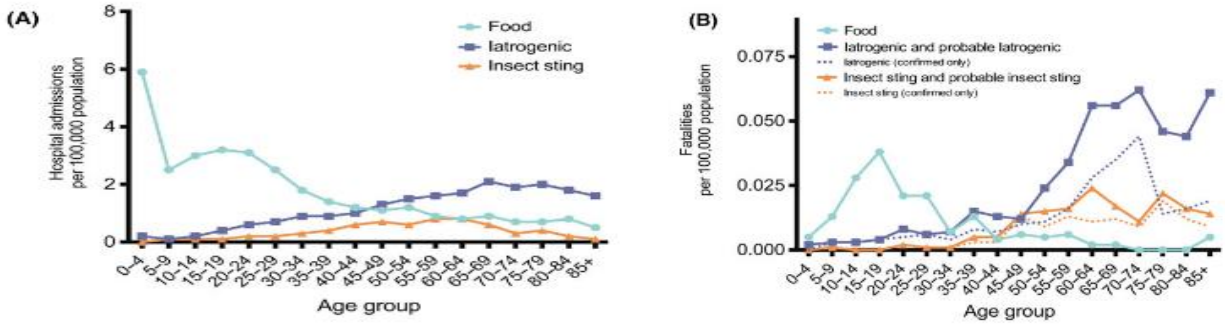

Figure 2-2: The Anaphylaxis trends conducted from 1992 until 2012 (Takazawa et al., 2017).

Following Iatronic induction, it has been observed that triggers in individuals below the age of 45 are commonly due to food, whereas for individuals above the age of 40 are more likely to be a result of stings.

2.1.5 Anaphylaxis Diagnosis

Identifying anaphylaxis poses challenges due to the broad spectrum of potential clinical presentations, and distinguishing between an allergic reaction and anaphylaxis is occasionally ambiguous (Jensen, 2007). The challenge in diagnosing anaphylaxis has led to instances of under-recognition and undertreatment in emergency departments (Fineman et al., 2015). For a response to be considered anaphylactic, it must meet a specific reaction criterion. The complexity of identifying the initial stages of anaphylaxis by clinicians makes it even more challenging for regular patients, leading to many hospitalisations for reactions. World Allergy Organisation (WAO) suggests that at least two criteria must be met for the clinical diagnosis of anaphylaxis. Table 2-1 summarises the clinical features adapted from WAO to identify severe allergic reactions.

Table 2-1: The diagnosis list for anaphylaxis (Cardona et al., 2020)

Clinical Feature	Including at least one of the following symptoms:
Acute onset of illness involving the skin, mucosal tissue, or both.	• Respiratory compromise. • Reduced blood pressure. • Severe gastrointestinal symptoms.
Acute onset of hypotension or, bronchospasm or, laryngeal involvement	• Hypotension is a systolic BP decrease greater than 30% from the person's baseline. • Bronchospasm, in this case would exclude the common lower respiratory symptoms. • And Laryngeal symptoms include vocal change, stridor, and odynophagia.

Table 2-1 checklist is consistent with the findings from emergency department studies of children, adolescents, and adults, and it has been demonstrated that the diagnostic criteria for anaphylaxis are accurate (Sicherer et al., 2017). Some reactions will initially not meet these criteria but will progressively worsen over time, and it is essential for patients to constantly check for these symptoms and consult a medical professional if they suspect an early reaction.

2.1.6 Anaphylaxis Treatment

Epinephrine and antihistamines are two well-proven medications for treating anaphylaxis clinically. Epinephrine reduces the body's allergic response, and antihistamines reduce respiratory system inflammation. The consensus in the literature suggests that epinephrine should be the first line of treatment (F. E. R. Simons et al., 2011). Additional professional medical assistance must follow immediately to assess the risks of relapse. (Levin, et al., 2015). For effective treatment, the medication must be applied on the anterolateral aspect of the thigh, and the patient must rest in a supine position (Doyle & McCutcheon, 2015).

Designated out-of-hospital EAI devices are often prescribed to patients by allergy specialists. These epinephrine autoinjector devices are the gold standard of treatment in community settings (Bodkin et al., 2013). They are easy to use and address most problems that traditional syringe and needle present for non-trained and non-clinical users. For patients using an EAI and weigh between 7.5 and 25 kg, the recommended dosage of epinephrine is 0.15 mg (Alvarez-Perea et al., 2017). Those who weigh over 25 kg should receive a dosage of 0.3 mg. (Muraro et al., 2014). Prompt injection of epinephrine after the realisation of symptom onset increases effectiveness. Patients may need to inject more than once, at 5- to 15-minute intervals, if the first shot is inadequate (Lieberman et al., 2015). Subsequent doses of epinephrine may be necessary for severe or rapidly progressing anaphylaxis or if the initial dose is ineffective due to a delayed injection, an inadequate dose, or an improper route of administration (K. J. Simons & Simons, 2010).

In certain cases of severe and rapid anaphylaxis without sufficient epinephrine dosage, the risk of collapse before reaching a medical centre is high, potentially leading to fatal consequences. A fast and effective way of treating the condition entails assuring medication availability and prompt response by medical emergency personnel at the patient's exact location. However, the ease of locating patients depends on many factors, including the patient's state of consciousness, the geographical location, and the availability of medical first responders at the time of the incidents.

2.1.7 Anaphylaxis Risk Factors and Long-Term Effects

Existing respiratory diseases increase the risk of anaphylaxis in patients. Adolescents and young adults are the most susceptible age groups(Grabenhenrich et al., 2016). In younger patients, peanut

allergy is the risk factor for severe anaphylaxis (Worm et al., 2013). Patients will likely be at a higher risk for anaphylaxis if they have a disease that impedes their ability to recognise allergen triggers or symptoms, including eye and auditory impairment, developmental delay, and neurological disease (Simons, 2010). Multiple studies have demonstrated that inadequate management of allergic asthma is a significant risk factor for life-threatening anaphylaxis (Worm et al., 2013). Asthma is a prevalent respiratory disease among South Africans, affecting a substantial proportion of the population with a lifetime prevalence of 34% (Baard et al., 2020). This poses a considerable risk of anaphylaxis for those living with the condition.

A food allergy can significantly impact one's quality of life and reduce performance in conducting daily activities. Children with food allergies express anxiety about potential allergen exposure (Boden & Wesley Burks, 2011). Due to the inability to foresee the severity of future reactions based on past responses, patients with food allergies and their families fear that subsequent exposure may be fatal (Herbert et al., 2021). Anaphylaxis can be avoided by avoiding identified food allergens, but accidental exposures continue (Boden & Wesley Burks, 2011). Psychological changes occur in patients, including stress and post-traumatic disorder (PTSD), as they live in fear of accidental exposure for the next episode. Mental health issues have been associated with adult patients who had previously experienced a reaction (Knibb et al., 2023).

2.1.8 Chronic Management

Chronic management of anaphylaxis involves a comprehensive approach to minimise the risk of future allergic reactions and effectively respond in an emergency. This section discusses some strategies typically suggested for individuals who have experienced an anaphylactic episode before.

2.1.8.1 Identification and avoidance of triggers

Once patients have identified the triggers, they must strictly avoid them and carefully read food labels. Allergy specialists can identify anaphylaxis triggers and provide information on potential cross-reacting agents and safe alternatives, particularly in cases of drug hypersensitivity (Alvarez-Perea et al., 2017). It is also essential to educate oneself and others about potential sources of exposure. With all the precautionary measures one can take to avoid identified food allergens, many patients continue experiencing accidental exposures through indirect contact (Boden & Wesley Burks, 2011). These burdens on the patient, and their quality of life can be reduced.

The problem of trigger avoidance has resulted in implementing technological solutions that patients may use to further detect allergens in their food products. These smart solutions use existing and innovative solutions to identify allergens, whether in food or geographical location. For targeted users, these devices would be an extra accessory to an allergy-mitigation process they already

possess. Users must carry the allergy test device, an EAI, and a written emergency allergy plan, in either a bracelet or medical ID card.

2.1.8.2 Medication management

Individuals at risk of anaphylaxis may be offered preventive drugs such as antihistamines or corticosteroids in some situations to assist in minimising the severity of an allergic reaction or prevent it from occurring (George M. Goodman, 2020). They are often prescribed as long-term therapy for severe conditions when patients' quality of life is affected. In certain instances, immunomodulatory and/or etiological therapies, insect venom immunotherapy, and food oral immunotherapy may be offered (Alvarez-Perea et al., 2017).

Oral immunotherapy costs can exponentially rise given the requirements of trained healthcare professionals, clinical facilities needed and the availability of specialised physicians to provide these at home (Brozek et al., 2022), as with other therapy procedures. For long-term financially sustainable means, most patients have no choice but to use traditional and technological solutions to mitigate the risk by remembering to carry an epinephrine autoinjector, practice allergen avoidance, and memorise a personalised emergency action plan to prepare for the worst.

2.1.8.3 Emergency action plan

A patient's emergency action plan is often developed with the guidance of a healthcare professional. The plan includes detailed instructions on how to recognise the symptoms of anaphylaxis, when and how to administer self-injectable epinephrine, and when to seek immediate medical assistance (Alvarez-Perea et al., 2017). It is also dependent on the type of autoinjector device a patient owns. It will include instructions on how to use a particular EAI device and what physical positions a patient must rest on for maximum efficiency. A section of a generalised emergency plan adapted from the Australian Society of clinical immunology and Allergy (ASCIA) can be seen in appendix A.

Typically, this plan is communicated to the individual's family, carers, and other pertinent individuals, to provide support and educate the patient about these steps. Most traditional anaphylaxis emergency plans are written on paper, however, with improved technology, now these are accessible on digital platforms.

Individuals are strongly recommended to visit an emergency room, with at least an 8- to 24-hour observation period, to ensure biphasic anaphylaxis does not occur (Oya et al., 2014). Biphasic anaphylaxis is defined as the recurrence of anaphylaxis hours after recovery of the initial symptoms, with no further exposure to the trigger (Sampson et al., 2006). Since biphasic anaphylaxis often occurs, trained clinical staff should strictly monitor patients in a medical centre (Alvarez-Perea et al.,

2017). The amount of monitoring will vary from case to case, depending on the severity of the symptoms.

2.1.8.4 Education and support

Individuals and their families dealing with anaphylaxis can benefit from seeking education and support from healthcare professionals, patient support groups, or online communities. Support can include valuable information, resources, and emotional support to help manage the condition. Compelling evidence in the literature suggests there are benefits of education and support in decreasing mortality (Turner et al., 2017).

Patients should be taught to review their action plans and avoid potential triggers that could increase their risk of severe anaphylaxis (Simons et al., 2015). Such information can be accessed online, positively contributing to anaphylaxis long-term management. Studies suggest that the usage of the Internet and mobile applications could play a key role in future anaphylaxis management and education (González-de-Olano & Botella-Padilla, 2017).

2.2 Smartphone Intervention in Healthcare (mHealth)

South Africa is one of the biggest smartphone adopters in Sub-Saharan Africa (SSA), with a significant increase from 60% in 2015 to 90% of the population in 2020 (ICASA,2020) using the technology. This growth enables easy adoption of mHealth within the country and other low and -middle-income regions in SSA. mHealth can take many forms, with SMS and phone calls being the most widespread adoption because of the relatively low cost and rapid delivery (Rohman et al., 2015; Chung et al., 2015). With increasing access to internet data, many people use mobile applications throughout their daily lives, encouraging mHealth popularity.

2.2.1 mHealth

Mobile health (mHealth) refers to delivering healthcare services and information via mobile devices, such as smartphones and tablets, to improve health (WHO,2023). mHealth interventions can be used to improve health outcomes in a variety of ways, including as stated by WHO:

1. **Monitoring and tracking health data:** mHealth devices can be used to collect and track data on a variety of health metrics, such as blood pressure, weight, and blood sugar levels. This data can be used to monitor health status and identify trends over time.
2. **Providing education and support:** mHealth interventions can provide education and support to patients and their caregivers without direct contact. This can include information on health conditions, self-management strategies, coping mechanisms over synchronous video calls with trained clinicians, and access to pre-recorded videos and texts.

3. **Delivering interventions:** mHealth interventions can be used to deliver interventions, such as cognitive-behavioural therapy or behavioural modification programs. These interventions can be used to improve health outcomes by changing patient behaviour.
4. **Emergency Medical Service applications:** mHealth can improve EMS's response time to locate patients in critical health conditions. This can be done by sharing the user's location, health state at the time and user relatives' information.

The South African government is supportive of mHealth initiatives. In 2015, the government launched a mHealth strategy outlining the government's vision for using mHealth in the country (Department of Health, 2015). The mHealth strategy has highlighted various priorities, including managing chronic diseases, maternal and child health, and disease surveillance. The future of mHealth in South Africa is bright. The country has several factors conducive to the growth of mHealth, including a high mobile phone penetration rate and a supportive government. The use of mHealth services has the potential to aid in connecting a functional network infrastructure with a well-operating prehospital system (Griswold & Rubiano, 2022). Some information and communication technologies (ICT) used to support, educate, or provide EMS data are discussed below.

2.2.1.1 SMS Intervention

SMS is a short message of up to 160 characters between two or more phones (Toorani & Beheshti, 2010). Most users today use it asynchronously as a communication method to relay important or reminder messages. SMS can broadcast a message to more than one recipient simultaneously. Research on SMS in health care services has been focused on two main areas: behaviour change interventions and reminders (or alerts) (Schwebel & Larimer, 2018). A study published in the Journal of the American Medical Association (AMA) found that a text message reminder system increased medication adherence by 25%. Another study published in the Journal of Clinical Oncology found that a smartphone app increased medication adherence by 30%.

Although the technology has shown success in medication adherence reminders through SMS reminders, epinephrine is not a medication that needs to be taken regularly. It is only intended for emergencies. However, the technology can be used in emergencies. As it is quick, it can relay important information about the health situation when a direct call cannot be made to EMS upon arrival. Kumar and Rahman's study examined using SMS features on mobile phones for a wireless health recording and alert system for elderly individuals or athletes (Kumar & Rahman, 2006). The system included a sensor, base, and server unit. Users could send an emergency SMS, and caregivers receive alerts based on sensor data.

2.2.1.2 Phone calls Intervention

Phone calls are a mobile telecommunication component that allows real-time communication between two or more users. Like SMS, phone calls are used for disease management, medication adherence reminders and behaviour change in low- or middle-income countries (LMIC). A direct call reminder system for supporting patient's adherence to treatment regimens was also presented by (Kunutsor et al., 2010). Phone calls are a traditional and mainly used communication for contacting EMS during a life-threatening situation. The tradition has been adopted so the call taker from the emergency call centres (ECC) can assess the seriousness of the caller's condition and triage, accordingly, significantly reducing the risk of death at the scene (Wu et al., 2012). However, the national emergency number for SA directs a caller to an automated call receiver and can add time to response time.

All emergency numbers are free of charge. However, the main concern of EMS contact is the process of looking up for the emergency number, while one is fighting for their life. In worst cases, patients may collapse before finding the emergency number on their cell phones. Another common issue in emergency calls is mishearing the patient's location (Alshehri et al., 2020a). EMS can be dispatched to an incorrect location which can cause massive delays in attending the patient as found in the research by Alshehri et al. This motivated the creation of a faster and more accurate method to contact EMS through Internet of Things (IoT) solutions.

2.2.1.3 IoT Intervention in Healthcare

IoT describes the wireless interconnection of multiple physical objects and devices to collect, store, and perform data exchange among them without the need for human to computer interaction (Li et al., 2024). The use of modern communication protocols and storage architectures, including Bluetooth Low Energy (BLE), Wi-Fi, and cloud storage, allows seamless communication of electronic devices over the Internet. In healthcare, these devices are used to promote patient outcomes through remote and onsite monitoring (Alshammari et al., 2023). Cloud storage allows for reliable storage, management, and representation of the data collected on the IoT device by making use of the Internet.

The collected data needs to be transmitted to cloud-based servers for storage and analysis. This is achieved using the Hypertext Transfer Protocol (HTTP). HTTP offers a standardised and reliable mechanism for data exchange, ensuring secure transmission between devices and cloud servers. (IETF, 2018). A layer of organised structure and meaning to the data involves the Application

Programming Interface (API), which acts as an intermediary between IoT devices and cloud applications. They use HTTP methods (GET, POST, PUT, DELETE) to perform specific operations on the data stored on the cloud. The advancement of portable computers like smartphones has allowed the exchange of data through the Internet to happen at every moment without the need for one to be in fixed on one computer location.

2.2.1.4 Mobile Health Apps for Medical Emergencies

Unlike phone calls and SMSs, mobile health application requires a smartphone with internet access as shown in Table 2-2 as stated by (Jensen, 2007). Mobile health applications are constantly growing and will soon be the first entry into a healthcare system. Mobile health apps are specifically aimed at helping people with their own health and wellness management (Roncero et al., 2020). The utilization of mobile applications can assist in the sharing of vital information among healthcare providers during a potential medical emergency.

Table 2-2: Minimum requirements for a mobile device to enrol as an mHealth device (Jensen, 2007).

Devices	**Capability**
Smartphone, Tablet	Video camera Web browser GPS (global positioning system) 3G+ internet access Mobile operating "platform" (such as iOS, Android) Ability to download and manage applications VoIP (Voice over Internet Protocol) Sufficient Storage

Cloud computing is the core of mobile health applications nowadays. The exchange of data such as GPS location, medical files, and media has facilitated the development of quicker emergency alerts and thereby providing an efficient method in contacting EMS. Application include iER, which is an application that contains all emergency response departments and can be contacted by a simple tap of the button. Panic buttons have also been implemented to aid in the fast response of EMS.

2.2.2 Reminder Systems for Adherence

Numerous studies have demonstrated the positive impact of reminder systems on medication adherence. The literature reveals that several reminder systems, including mobile apps, text

messaging, phone calls, electronic pillboxes, and wearable devices, have improved adherence rates across patient populations and medical conditions (Griffiths et al., 2012). According to the transtheoretical model, reminders can help with behaviour change (Prochaska et al., 1994). Another advantage of using reminders is improving of your prospective memory, which is the ability to remember to complete a task in the future (Guynn et al., 1998; McDaniel et al., 2004). SMS reminders demonstrated excellent promise towards automated support mechanism.

Unlike traditional reminder methods, cloud and local smartphone notifications can be implemented to support adherence to medication intake. This method is cheaper and gives the user more control than every other reminder method, and it is adopted almost in every application nowadays. While reminder systems show promise, widespread implementation and adoption challenges exist. Some barriers include technology literacy, access to mobile devices, cost considerations, privacy concerns, and the potential for reminder fatigue (Gromisch et al., 2021).

2.3 Management Approaches Improved

Significant solutions have been developed to aid in anaphylaxis management, including simple medical IDs, allergen test devices, and therapeutic devices. This section will explore improved management approaches for chronic anaphylaxis management.

2.3.1 Medical ID devices

Anaphylaxis medical ID is a tag that relays information about a patient's medical emergency contacts and allergen identification. These tags include bracelets, medical cards, wrist bands, etc. Now smart versions of the devices are available on the market. These bracelets and cards usually have the type of allergen, the severity of the allergy, and the patient's doctor's name and family contact details. In the event of anaphylaxis, emergency personnel can use this information to treat the wearer quickly and safely. Typical examples of these devices are shown in Figure 2-3. Although patients are recommended to carry these allergy identification devices, they must always have their prescribed epinephrine autoinjector on them.

Figure 2-3: Emergency Bracelet, Card, and wristband (Mediband, 2023).

A more sophisticated approach towards smart devices is employed to improve the simple medical ID devices. Digital devices can contain much more information on a small electronic board than a traditional ID card or bracelet.

2.3.2 Allergen test kits

These smart devices were developed to mitigate the risk of accidental exposure by using a test sample of food. Within a few minutes, the devices can determine whether the sample contains a specific allergen. An example will include Allergy Amulet, shown in Figure 2-4, a pocket device that uses chemical reactions to identify possible allergens based on a food sample. It comprises two parts: a sampler, a cartridge to which the food is placed, and a tester; an electrochemical device that uses sensors and sends results to the patient. The device alerts the patient within a few seconds with the results, via a mobile application or on the tester. The device tests for peanuts, soy, and gluten via this four-step process:

1. Insert food on the sampler, and close twist to crush.
2. Engage the sampler with the tester device and start the testing process.
3. Results will be reported on the mobile application or the tester device.
4. Dispose of the sampler and use a new one for another test.

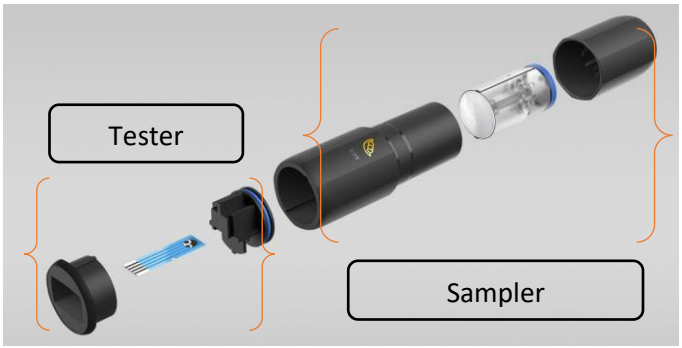

Figure 2-4: Allergy Amulet. A food allergen test device (Allergy Amulet, 2023).

One drawback of the solution is the possibility of getting a sample that is allergy free, and the device tests it negative. Companies that produce such devices always state that these devices are not a complete replacement for avoidance but are to be used as an added security measure.

Another technology aimed at addressing food-induced allergy is using smartphone scanners to detect allergens. There are over 1300 mobile applications related to the identification of food ingredients (Mandracchia et al., 2020). The process involves using a phone camera to scan a package barcode and report if there is a possible allergen on the food product based on a predefined comparison list. The mobile applications rely on the packaging information but do not consider potential cross-contamination during packing and transportation. An example of the application is

Soosee (Soosee: Quickly Scan Ingredient Labels., 2023.), which can scan up to 15 European languages and convert them to English.

One of the triggers of anaphylaxis is insect stings and exercises. Thus far, the best solution is to avoid wearing bright clothes and wear long sleeve shirts and pants during summer, and no other technological intervention has been developed at the time of writing, according to the author's knowledge. Exercise anaphylaxis is often induced because of changes in mucosal tissue osmolality which can result in basophil histamine secretion (Peter N Huynh et al., 2022). The best strategy is to avoid extensive exercise and have an EAI on hand to prepare for unexpected stings.

2.3.3 Epinephrine Autoinjectors

Autoinjectors are intended for individuals lacking formal medical training in using conventional hypodermic and needle devices. They are popular and have been used for a variety of purposes, including stress relief, diabetes, anaphylaxis, and diseases of the nervous system. EAIs administer a measured dose of adrenaline (epinephrine) through the skin. It is only available to patients diagnosed with anaphylaxis by an allergist (Regent & Johnson, 2020). Approximately four million patients have reportedly been prescribed these devices worldwide (Kränke et al., 2011), and they must be carried everywhere since reactions are unpredicted. For possible biphasic reactions, it is advised that patients carry two EAI doses of at least 0.3 mg each. Research on anaphylaxis has encouraged the development of enhanced designs to address obstacles identified in the literature. Even though most available autoinjectors are solely mechanical devices, they have served as a crucial function in managing anaphylactic reactions.

Autoinjectors currently include at least four components. A safety mechanism, an activation mechanism, medication in a cartridge, a needle, and a safety cap (cover). EAIs ensure that the needle is only exposed during the device usage, in which case, the patient must remove the safety mechanism before injecting themselves. The additional step may delay the device's use, but it addresses accidental pricks on undesignated anatomical regions that pose a greater danger to the patient (Kränke et al., 2011).

Figure 2-5 below depicts a simplified, block-shaped autoinjector with the arrow pointed towards the needle side. All existing EAI are limited to single use due to the need for sterilisation after one or two doses. Depending on the manufacturer's design, the safety mechanism and safety closure may or may not be present simultaneously. But at least, one must be present.

Figure 2-5: A simple autoinjector building block [left] and different EAI brands [right] (Brown et al., 2020).

Several brands of EAI are available, including EpiPen, Auvi-Q, Adrenaclick, and Symjepi, and all have advantages and disadvantages based on the design shape and sizes, dosage amount and cost-effectiveness. A common and popular design is a cylindrical housing with better ergonomics than other square and rectangular injectors, shown in Figure 2-5.

2.3.3.1 Availability

EAI are available in about 63 countries, and SA is one of them (Tanno & Demoly, 2020). Availability is based on factors including cost, evidence of the value of epinephrine and evidence about having an anaphylaxis reaction in a particular region. Most of these regions are high-income countries, as seen in Figure 2-6, as the cost influences adoption.

Figure 2-6: Autoinjector availability in the world (Tanno & Demoly, 2020)

SA is an emerging EAI market, with fewer adoptions of existing design because most existing EAIs were not designed for LMIC, with the lowest market share due to weak healthcare infrastructures. Without this medication for immediate injection during an anaphylactic reaction, the risk of progression to a severe episode and mortality increases (Tanno et al., 2017).

EAI users have ongoing issues with their devices that may require a complete design change of the EAIs. Some of the problems include incorrect self-administration techniques, incorrect route of administration, and needle-stick injuries, which have resulted in low carriage compliance (Frew,

2011). It is easy to forget the EAI when it is not used regularly. However, accidental exposure to allergens can happen at any time. Having two autoinjectors, one at home and one at work, alleviates the burden of remembering to carry EAI, especially for kids; However, this is not the ideal solution because people usually visit more than two locations in their ordinary lives. It would be impractical to have an autoinjector already placed everywhere one goes, including restaurants, beaches, and the homes of acquaintances.

2.3.3.2 Factors Affecting Autoinjector Carrying Compliance

A study found that one of the top reasons for not always having an EAI is that patients feel redundancy in carrying the EAI at all times because they never need to use it (Portnoy et al., 2019). Meanwhile, in the USA, most fatal cases are associated with the absence of EAI at the time when needed (MacAdam et al., 2012). This behaviour leads to patients forgetting the need for carrying EAI even to places of high-risk exposure. Another consideration highlights the design size of EAI, which discourages the carriage. However, the scope of this research is based on management strategies for an EAI design that has tackled the size issue. Training users on the correct administration procedure has improved the chances of having an EAI readily available.

2.4 Carrying Adherence: Existing Devices

This section discusses the current solutions for providing effective emergency action plans and general management. Important things to remember for an anaphylaxis emergency episode include:

1. Having an EAI at hand and being able to identify early symptoms.
2. Following the correct injection sequence (remove the safety mechanism, apply on the thigh, and hold it for at least three seconds).
3. Remembering to alert EMS first before alerting family members.
4. When calling for EMS, a patient must explain their health situation and know their location.
5. Lying down in a supine position until the patient feels better.

2.4.1 Epi-Trak

Epi-Trek is a mobile application designed to promote adherence to EAIs among patients. It leverages location-based alerts delivered through a mobile device to prompt patients to carry their EAIs. The application employs a system that combines Global Positioning System (GPS) and Wi-Fi technologies to achieve location tracking. The user manually adds places they wish to have reminders set on, as shown in Figure 2-7 below.

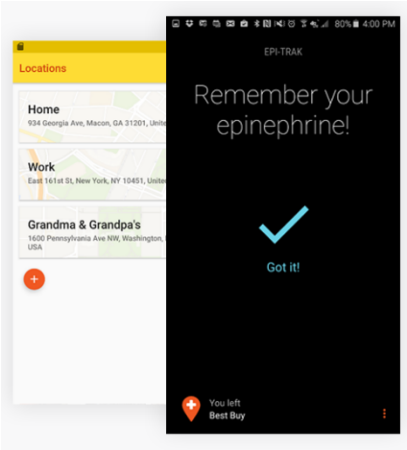

Figure 2-7: Epi-Track mobile application (Epi-Trak, 2023).

Once a location is set within the EPI-TRAK application, the app will send a reminder each time the patient leaves that location through a distinctive alert tone on the phone. If one has their EAI, then they dismiss the alarm. Some notable improvements that can be made on the application include:

1. All locations must be known beforehand for the application to remember to send alerts to the mobile application.
2. Most triggers happen outside and instantly. A user might need to remember the device at a different location than the one registered on the app, and when they do get a reminder, they will struggle to trace it back quickly.

Much improvement can be made to address the apparent limitations. Epi reminder, discussed below, is one of the technologies that further developed the technology.

2.4.2 Epi-Reminder

The Epi-Reminder tracker is a USA-based trackable attachment tag. It is wrapped around an EAI with a string to accommodate different autoinjector devices. The tag connects with a mobile application that constantly sends notifications whenever the device is left behind. The following are the key features of the tracker:

1. The mobile application allows the creation of different user profiles with different privileges, namely, admin, caregiver, and observer.
2. The admin is usually the patient if they own a phone or the parents if they are minor. Notification reminders are received by all users and are always notified when they are away from the device.

3. Caretakers, such as babysitters, will receive notifications when they are "handed off to" within the app, and have their location visible to the admin. However, they would not receive notifications when they are not responsible for the EpiPen.

The observer role is usually assigned to parents of teenagers. Observers receive the same notifications as the admins, but do not receive any notifications related to the medication's proximity. The device uses Bluetooth technology to perform tracking and uses cloud notifications to send the same notification to connected users. Additionally, it contains a temperature sensor to ensure the device is kept under nominal conditions. Figure 2-8 shows the white tag (Epi-Reminder) wrapped around two EpiPen devices.

The device uses a CR2032 coin cell battery. These are generally available at regular stores and pharmacies. It must be run in the background, with a notification banner on the device notification bank. One of the issues is that the notification can be accidentally closed, and the tracking would be discontinued.

Figure 2-8: Epi reminder device and mobile application (EpiReminder, 2023).

The solution, however, has solved the issue of patients not always carrying their EAI. Additionally, it has provided a platform to create a community that safeguards the patient, ensures carrying compliance, and ensures the patient does not keep an expired EAI. However, there are essential considerations that still need to be addressed. Knowing the patient's GPS location, knowing when it is an emergency and alerting relevant members. The current product relies on a caregiver supplying such information.

Given that the tag is wrapped around the EAI, it is highly possible that it would fall off and still reports proximity. There is no way of ensuring it is permanently, at least for the lifetime of the EAI, attached to the device.

2.4.3 Veta Smart Case

Veta Smart Case is one of the innovative smart solutions developed for the EpiPen autoinjector. It covers almost all the limitations of the preceding devices. It consists of hardware and mobile software components that are cloud-connected and enable people with anaphylaxis and their families to manage their condition effectively and support one other in the case of an allergic response. Figure 2-9 below shows the Veta case, which houses one EpiPen. A case to simultaneously house two EAIs is also now available.

The device monitors medication expiry dates and when users replace their auto-injectors and send alerts via signals on the case. Extreme temperature monitoring is done using a built-in thermometer to ensure controlled conditions are maintained. When users access their auto-injectors from the Veta case, The case automatically notifies a pre-selected group of family and friends, enabling them to utilize GPS information of the patient to redirect an ambulance to the location.

Once users have accessed the upper section of the case and activated the alarm, the Veta device waits for a few minutes before prompting users to confirm their consciousness and functionality. If users are unable to do so, the device will emit an audible alert to notify bystanders of the medical emergency. Veta allows users who travel abroad to report issues using the local language. The Veta Smart Case has several valuable features:

- **Removal Alerts** inform the user's support circle when the auto-injector is removed.
- **Separation Alerts** notify the user when the auto-injector is left behind.
- **FindMe Locator** quickly and easily locates misplaced auto-injectors using a map and smart case activation.
- **Temperature Monitor** alerts the user when the auto-injector's temperature exceeds the specified range.
- **Expiry Watch** warns about approaching expiry dates that may compromise the epinephrine's integrity.
- **The Support Circles** feature enables individuals and families to stay connected and provide comfort and assistance during an allergic reaction to support someone with anaphylaxis.

The Veta smart case mobile application is currently unavailable in Southern Africa, and a case can costs about R600.00 (US $29.00) on Amazon in 2023 (*Amazon.Com*, 2023). When the device is in use, the mobile application alerts do not reach the emergency contacts unless the application is actively open. This is an essential consideration, as patient supporters need to get instant alerts when the patient is at risk of an episode.

Figure 2-9: Veta smart Case, containing an EpiPen (Aterica Digital Health, 2019).

Additionally, given the choice of design, an added extra step is required when patients use an EAI during an emergency episode. The user must open the case before triggering the safety mechanism on the EAI. It has been studied that patients panic when in an emergency and tend to make more mistakes when triggering the safety mechanisms. A more advanced approach is required to minimise and improve the solution. One that directly alerts the patient's family when the user operates the EAI. Another EAI smart case called AnApphylaxis aims to close that gap.

2.4.4 AnApphylaxis

Like Veta, Anaphylaxis features removal alerts, separation alerts, temperature monitors, and an expiry tracker using Bluetooth technology. In addition, when the device is triggered, it directly alerts the emergency contacts and possible EMS. There is limited information on how it contacts the EMS and patient emergency list on the company website (Adan Medical Innovation, 2023) and the device location at the time of trigger. An important feature is the device's ability to detect close-by hospitals when the cap is opened. It also plays a video demonstrating to the user how to properly use the EAI, together with the patient's medical information for EMS preparation.

The solution covered most of the issues addressed in the emergency management plan for anaphylaxis. However, training on what and how to say it effectively to EMS when giving them a call remains unsolved. Patients are often under-triaged because of how they describe their conditions to the emergency call centres (Alshehri et al., 2020a). Again, the case trigger adds more steps for the patient to get to the injection phase. Despite being less apparent, locating an EAI timely is a crucial step in the disease management. A Bluetooth connection range can be 10 to about 80 meters according to the Bluetooth Group official website. It's crucial to note that being connected does not necessarily imply proximity to the device, a critical consideration in the development of Bluetooth-based tracking systems.

2.4.5 Ypsomate SmartPilot

Ypsomate SmartPilot is an additional housing smart device that adds on a traditional Ypsomate autoinjector. It is developed by a Swiss company YpsoMed.

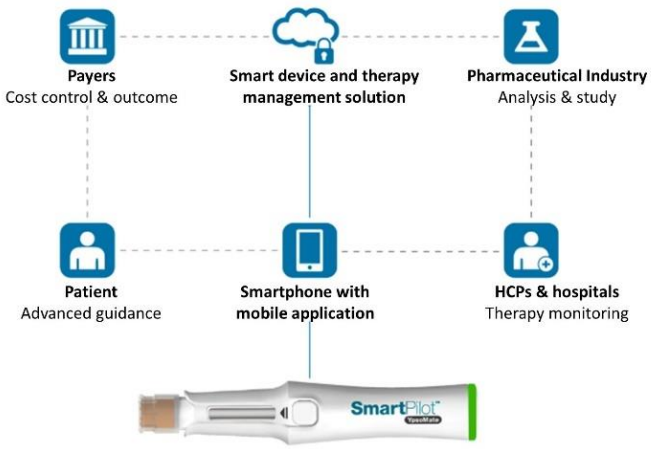

Figure 2-10: SmartPilot autoinjector ecosystem (Ypsomed, 2023).

The device's intended purpose is for correct injection adherence, training, and support of patients and for most research studies. SmartPilot is part of a healthcare ecosystem connecting pharmaceuticals, patients and HCPs, as shown in Figure 2-10.

The system tracks and monitors autoinjector usage with features like adherence monitoring, guidance, and wireless transmission of injection success. Patients receive visual and audible feedback during injection with the SmartPilot and can access complementary information on a mobile app. The system reduces medication errors and integrates easily into existing systems by using sensors that detected whether injection is a success.

In summary, the device improves the correct usage of EAI by incorporating sensors detecting the activation time, checking whether the injection is a success or not and the expiry date. But it doesn't address tracking EAI location and alerting a support group when the injection is unsuccessful. It is notably a great solution for creating an ecosystem of HCPs, payers, and pharmaceuticals. This should be the initial direction to developing a system to look at the patient and consider other directly related stakeholders to provide an effective long-term anaphylaxis management plan.

2.5 South Africa's Emergency Medical Service (EMS) System

EMS are directly linked to anaphylaxis management strategies. They serve to attend to a patient in need of emergency care. EMS is a "comprehensive system that provides personnel, facilities, and equipment for the effective, coordinated, and timely delivery of health and safety services to victims

of sudden illness or injury" (Moore, 2009). WHO regards EMS as an essential part of an effective healthcare facility for life-threatening injuries or illnesses (Al-Shaqsi, 2010). South Africa has one of the few completely developed EMSs in Africa. It employs the South African Triage Scale (SATS) to assign emergency resources to patients (Naidoo, 2011). Triage is the classification of patients according to the severity of their clinical care needs (Alshehri et al., 2020b). The classification ranges from P1 to P4, with P1 representing the most urgent situation and P4 representing the least. The categories are established to ensure that patients requiring essential care receive higher priority than patients with non-urgent cases.

SA comprises both private and public EMS, but most people use public EMS (Hardcastle et al., 2013). With just over 300 ambulances available in the country, the correct triage process must be followed to allocate resources to patients that need the service most. To allocate EMS, two main centres are involved in this process. Namely, the Emergency Communication Centres (ECC) which receives inquiries and determine triage, and the Emergency Medical Centres (EMC) dispatches ambulances based on the information provided by the ECC (Alshehri et al., 2020a). Like most other nations, South Africa uses the telephone (112 for the public) to request emergency medical personnel. The private EMS have different emergency numbers and a possible patient portal system (PPS), for example a hospital like system employed in all Netcare hospitals in South Africa called *myNetcare Online*.

In public hospitals' EMS, triage timing works as follows: 90% of high-priority (P1) occurrences in urban areas should be addressed within 15 minutes, and all other incidents should be handled within 60 minutes (Stein et al., 2015). That is when ECC receives a call and the time the ambulance gets to the scene. The dispatch process commences when an ECC call-taker answers an incoming call. Call takers categorise the call into a complaints list after obtaining demographic information, location, and symptoms through questioning (Alshehri et al., 2020a). To be correctly understood, the caller must speak calmly and distinctly. The triage scale will then determine the priority level by the caller taker. The prioritized call is subsequently relayed to a dispatcher terminal on the computer. Dispatchers can then filter various categories such as priority and choose a vehicle on a dispatch console before forwarding the call to EMS personnel for a response via computer or radio.

Non-P1 cases can be as long as an hour, even more in townships and remote rural areas. Studies assessing the criteria for being assigned the P1 triage scale on the Western Cape EMS found the criteria in Table 2-3 below to be common.

Table 2-3: Common complaints recorded by Western Cape EMS in SA between 2016 and 2017 (Alshehri et al., 2020b).

Dispatch Complaint	Percent (%)
Non-Cardiac Pain	16.88
Respiratory Complaints	9.71
Abdominal Complaints	5.92
Vomiting and Diarrheal	5.44
Unresponsive Patient	2.97
Other	59.08

About 40% of the complaints received were the best description of severe anaphylaxis symptoms. According to the study, all these cases were attended to within the expected timeframe of 15-20 min. However, misusing these complaints may strain the EMS system and put the patients needing the service at risk. Anaphylaxis episodes are not always severe and fall under P1 triage. Some cases take up to 6 hours before severe reaction kicks in. This would give patients enough time to make alternative medical emergency plans should the symptoms fall under triage P2 and P3. A study conducted about triage for anaphylaxis patients found that lower acuity levels (P3 or P4) were more likely to be assigned to adult and paediatric patients with skin-related main concerns (Chiang et al., 2021). This can lead to delayed epinephrine injection in patients who do not have an EAI on hand when they experience anaphylaxis.

Anaphylaxis patients must be prepared beforehand and anticipate the possible triage scale based on their symptoms, as this is how the real EMS system works in SA. One study found that one of the reasons for the low carriage of EAI was that the participants were confident that EMS would provide appropriate care should they need it, given that they were travelling in urban areas (Money et al., 2013). By understanding the EMS system, we can better develop potentially practical solutions and teach the patient more about the importance of having an autoinjector, as this project focused on designing a smart tracking system to integrate with an existing EMS.

2.5.1 Private Sector

The private sector comprises three big hospital organisations: Netcare, Life Healthcare, and Mediclinic. The hospitals use the SATS system to allocate emergency resources; however, response time is shorter than public healthcare. Netcare's EMS is by far the most technologically advanced compared to the rest of the groups. However, they all have similar response times. To access the services, a user must register on the hospital's database beforehand. Similarly, to the public sector,

Mediclinic and Life Healthcare operate via call centres to respond to emergencies. Here are a few things that a caller would need when requesting care in Life Healthcare and Mediclinic Hospitals:

1. Once connected to the ECC, the caller states their name and phone number.
2. The caller describes the emergency.
3. For easy locating, the caller provides information about the exact location, including physical address and landmarks.
4. The caller stays on the line with the call taker to help while the patient waits for the EMS team to arrive at the scene.

Following the call, an ambulance is directed to the location based on the concluded triage scale. Depending on which category a patient falls in, they would be allocated a regular ambulance or a helicopter for life-threatening cases.

Netcare has an advanced EMS that uses mHealth and Telehealth to manage emergency care better (Netcare, 2023). In addition to the regular emergency call, Netcare uses SMSs to communicate with the caller to speed up the process as shown in Figure 2-11. They allow their emergency responders to get an accurate GPS location using google maps services.

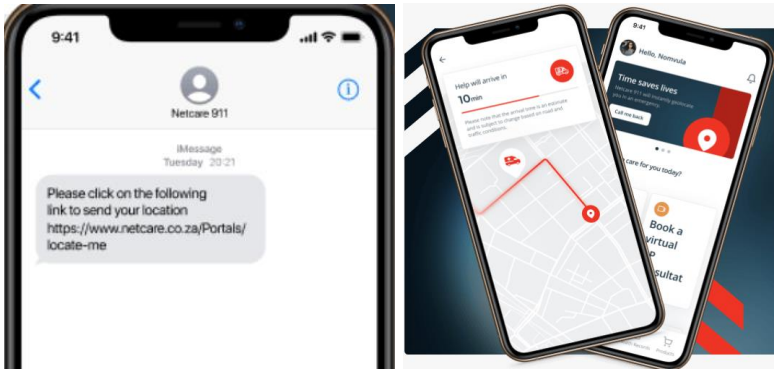

Figure 2-11: Netcare emergency mobile (application (Netcare 911, 2023).

Patients with a smartphone can download the Netcare mobile application to track the ambulance. The ambulances are equipped with IoT medical devices that constantly send patient-on-transit vitals to the doctor using online servers (Netcare 911, 2023). This excellent technology would benefit patients suffering from anaphylaxis when experiencing an episode.

Private healthcare is expensive; only about 18% of South African residents use these facilities regularly (Mayosi & Benatar, 2014). A solution exclusively designed to integrate with private healthcare would only cater for a fraction of the South African population.

2.6 Summary

The literature review analysed the current challenges of anaphylaxis, its management and existing solutions. It was discovered that anaphylaxis can be a life-threatening condition that requires immediate action. Although the current management strategies are effective for many patients, a common problem is that patients don't always have their autoinjectors with them, which puts them at risk of hospitalization or even death. Efforts have been made to explore technological solutions to improve management plans, such as incorporating mHealth applications. Several solutions were discussed, along with their limitations, and the possibility of using a reminder system to prompt patients to always carry their EAI. A summary of the findings from these devices is shown on Table 2-4. The review also examined existing solutions that address this issue and their potential application to South African EMS. However, these solutions cannot be directly applied to South African EMS, so further exploration is needed to identify the gap and formulate user requirements for developing a suitable anaphylaxis EMS application for South African context to ensure patients always carry EAI.

Table 2-4: A summary of existing tracking devices to improve carrying adherence.

Device	mHealth application	Wireless technology	Availability in SA	EMS connected	EAI connected	Tracking Ability	Distance algorithm	GAP
Allergy Amulet	Optional	Bluetooth	Y	N	N	N	N	Cannot alert emergency contacts
Epi-Trak	Y	N	N	N	N	GPS (Global Positioning System) based	N	Does not perform short range tracking
Epi-Reminder	Y	Bluetooth	N	N	Y	BLE (Bluetooth Low Energy) based	N	It is not connected to EMS
Veta Smart Case	Y	Bluetooth	N	Y	Y	BLE based	N	Does not provide a “find my device” feature
AnApphylaxis	Y	Bluetooth	N	Y	Y	BLE based	N	Unaccounted long-distance connection between BLE devices.
Ypsomate SmartPilot	Y	Bluetooth	N	N	Y	N	N	Costly and does not provide reminder alerts to carry EAI.

3. Chapter 3: Research Methodology

3.1 Methodology Overview

This chapter presents the methodology used to conduct the research study. It follows applied research methodology: research and development based on pilot case studies. As shown in Figure 3-1, the study was divided into three sections: The user requirements formation through background research, the design and development of the proposed system, and the system's evaluation.

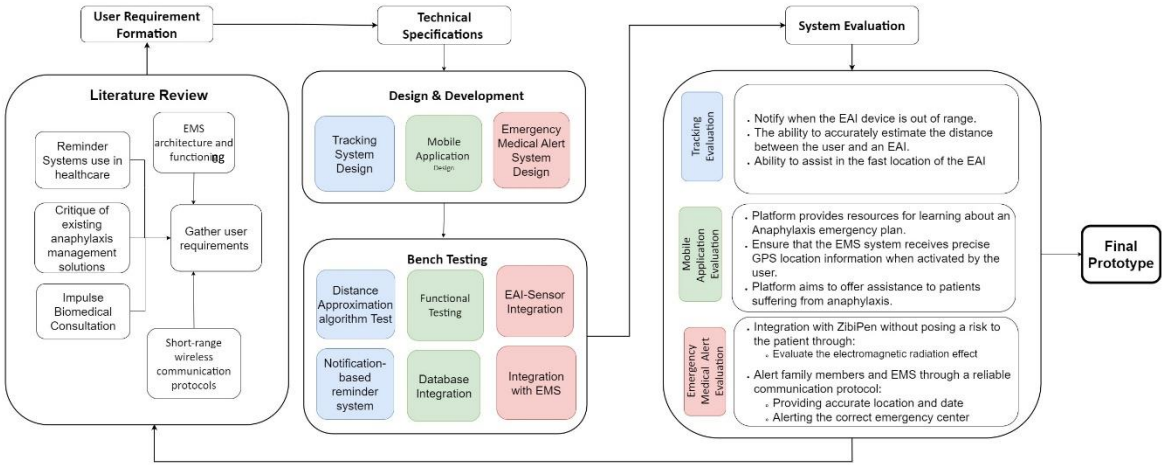

Figure 3-1: Research Methodology Overview

3.2 Needs Identification

The first stage of the project is to gather correct user needs. User requirements are crucial information for developing new solutions or enhancing existing designs, therefore an accurate understanding of end-user requirement information is the key to providing reliable design decisions for the designers to optimise their design of resources. A qualitative literature review and stakeholder insights approach was adopted in which the key primary needs were identified. Secondary needs were also identified.

Requirements engineering (RE) was utilised to identify user needs that are technically feasible. According to INCOSE 2011, user requirements are a set of requirements a system needs to provide services needed by users and stakeholders in an established environment. Good requirements include but are not limited to complete, unambiguous, feasible, traceable to the source and correctly derived instructions (INCOSE, 2022). Nowadays, methods like design thinking, or user centred design are favoured because of the need to understand end-user needs. However, these methods require actual users to be in the design problem identification, solution development and

solution evaluation. This project had limited access to anaphylaxis patients, however, a second opinion from Impulse Biomedical had been used as a guide.

A combination of "The Five Whys" and "Use Cases" methods were used instead, to gather user needs. *The Five Whys* method addresses the possible root cause of a problem a typical user is facing by asking *why* five times and getting responses (CMS, 2024). This method was used in conjunction with the literature review process, and research-based needs were developed. The *Use Case* method is based on creating scenarios that provide value to a system user (Iqbal et al., 2020). The use case diagram visualises interactions between a direct solution user and other related stakeholders. From reviewing existing market products and documenting reviews on such products by the actual users, use cases were created.

3.3 System Design

The engineering design and development followed a modified v-model shown in Figure 3-2 below. A traditional V-model follows a sequential pathway starting from system requirements at the top and going down to design and implementation at the bottom while documenting testing protocols simultaneously for each stage. As much as this method is great, it poses a great disadvantage when the designer does not incorporate a user-centred design on each stage, i.e., having a user to provide feedback to enforce user need. As mentioned in section 3.2, good identification of user needs results in a system that is right for the user. Therefore, a modified V-Model was developed that greatly emphasises developing the right system.

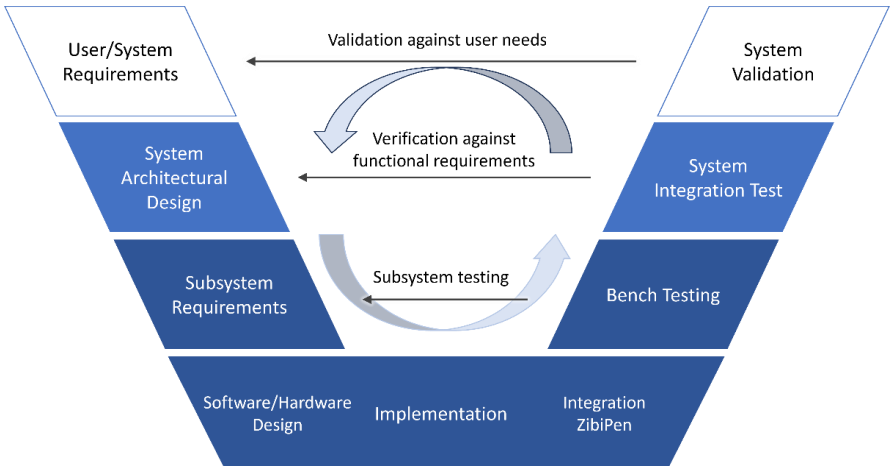

Figure 3-2: V-model framework followed to design and develop the proposed system.

This model uses the iterative behaviour between each lower-level component of the system before making a full system validation. A three-loop iteration was implemented where each system was tested and redesigned to meet technical specifications. The validation protocols were only developed after the completion of such a system.

3.3.1 Mobile Application Design

The mobile application's design utilised the three-layered architecture containing presentation, Business, and Data layers (IBM,2023), shown in Figure 3-3. The presentation layer is the layer that is responsible for displaying the data to the user; in this case, it would be the user interface design. The business layer exposes application data to the user interface (UI) from the data layer. The business layer is where the logic and the controllers of the applications reside. A data layer manages data through storage, manipulation, and reformatting.

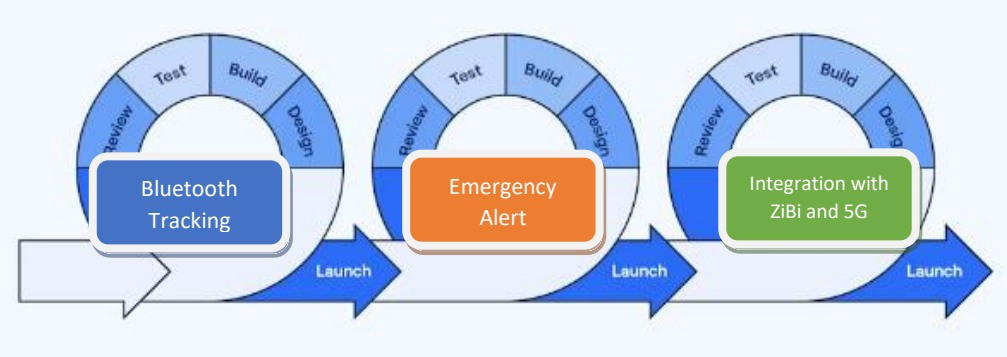

Figure 3-3: Agile Methodology

Each layer and the mobile application development followed agile methodology to ensure effective development. The agile methodology in Figure 3-3 uses smaller objectives (sprints) that allows a more manageable project schedule. This methodology is standard in most mobile application designs that would eventually scale bigger. Three subsystems of the smart device were developed guided by the three components on the mobile application to provide a complete operational mobile-based anaphylaxis management action plan.

3.4 System Verification and Evaluation

The evaluation process is an essential and critical measure for project completion. A verification and validation test for the system were performed.

3.4.1 Verification Testing

Bench testing was performed in the medical devices lab at the University of Cape Town, where each sub-system was tested against design specifications. Test 1 explored the robustness of the cap removal detector, when the cap is removed and placed back, and removed again. Test 2 explored the integration with ZibiPen and its effect on the operation of the EAI.

3.4.2 System Validation

All three subsystems were validated using similar research published and relevant standards. Additionally, the overall system was evaluated to assess the feasibility of the solution in the South African context.

System 1: Distance Algorithm (Distance estimator): A three-dimensional test field was set up in an indoor and outdoor controlled environment following the method used by Guiliano et al. 2020, to validate an indoor asset tracking for museums using BLE beacons. The indoor environment was conducted at the UCT Biomedical Engineering Division Anatomy building and Impulse Biomedical offices, and the outdoor was conducted at the UCT Health Science Faculty (HSF). The results were analysed quantitively looking at distance accuracy, and conversion error.

System 2: Reminder Notifications Tracking: Case-based protocol to test the functional performance of the system was implemented. Frequency of the notification, and performance on different ringer profiles (general, vibrate, and silent, including "do-not-disturb" mode) was analysed.

System 3: Emergency Alert Capability

A testing protocol guided by ISO 14971:2019 (risk management), Medic Alert Foundation of South Africa and the U.S Department of Homeland Security emergency alert technology guide was utilised. The system was ranked against necessary features that comply with emergency alert guides. An overall comparison with other existing devices was conducted. The import medical emergency alert requirements from MedicAlert relevant to Anaphylaxis are:

- Disclosure of all medication and dosages.
- Emergency contacts.
- Allergy nature and history.
- Use a personal identification number for easy extraction of medical history.

ISO 14971 requires the fulfilment of a checklist that mitigates potential risk for the system or the user. The checklist was used in the application of alerting EMS (for potential false alarms), detecting when one of the devices has turned off, and detecting the correct geographical location. The standard framework is as follows:

- **Risk analysis and evaluation:** How can the identified risk cause harm to the user (s)?
- **Risk control or mitigation:** Measures taken to reduce or eliminate the risk.

Risk management overview: Possible risk(s) left behind and what can be concluded after taking the risk control and mitigation.

4. Chapter 4: System Design

This section explains the design of both the tracking and the mobile application. Firstly, an overview of the medical emergency ecosystem in SA's public healthcare is shown in Figure 4-1. This overview helps to understand the design choices made on the proposed solution. The requirements, design considerations and conceptual model are then presented.

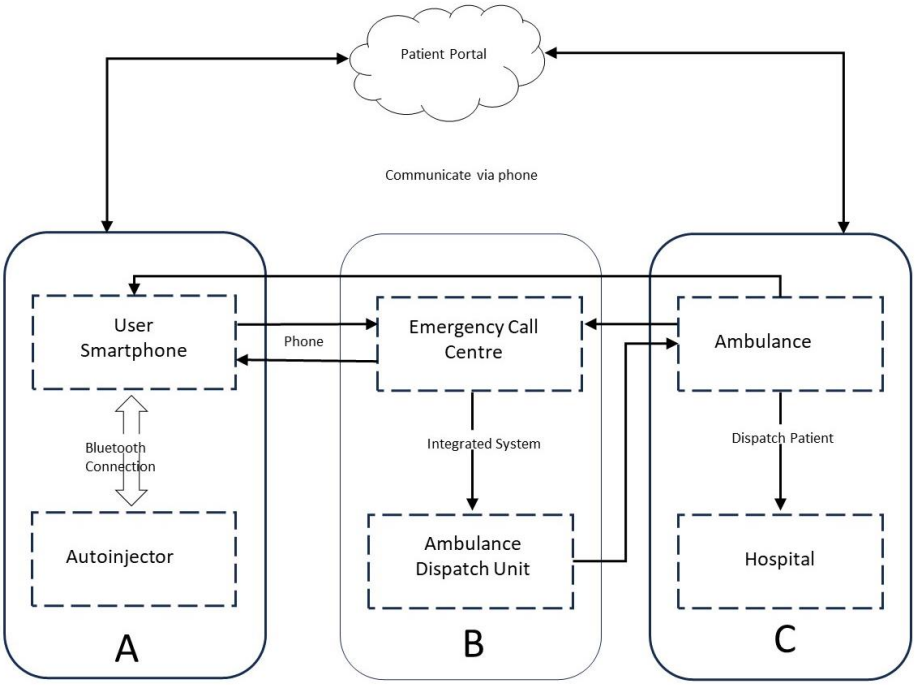

Figure 4-1: An overview of integration of the smart tracker with South Africa's EMS.

This research focuses on fully designing the components that makeup system A. However, other related systems like the ECC, the EMS, and a digital patient portal system were simulated, guided by literature and literature review of existing EMS systems. The aim was to simulate the behaviour of the real emergency system for testing purposes since using the real EMS system is considered unethical for prototype testing.

System A comprises the user, EAI, and the mobile application that works together to provide effective tracking and emergency alerts. This system is responsible for tracking EAI and recording patient demographics information, emergency contacts data, and smartphone data. This system also includes training via digital platforms in the mobile application and is the only system that the user will be in direct contact with.

System B is the ECC, the first entry when a patient is having an emergency episode. It uses an identifier to request health information from the patient portal system, which is sent to EMS, and

system C, when the user's system confirms a real emergency. System B and C are outside the scope of the project and was not developed but it is mentioned to make the reader understand the overall emergency triage flow.

4.1 User Needs

Using the RE approach, user needs, or the root problem were extracted from literature and stakeholders by applying *The Five Whys (TFW)* approach. Further, the findings from the TFW were then translated into functional and non-functional features, functionality, and use cases of the proposed solution.

Table 4-1: User requirements formation.

Literature Findings	**ID**	**User Requirement**
Anaphylaxis is rapid and requires prompt action from the patient.	UR1	Patients need a way to have access to rapid emergency medical services.
Most anaphylaxis incidences happen in common areas that another patient had previously identified.	UR2	A way to identify hotspot areas beforehand and make patients aware to prepare better.
Having access to a personalised anaphylaxis emergency plan is crucial.	UR3	A way to access the emergency plan at anytime and anywhere.
EAI are to be always carried by patients.	UR4	Patients need a reliable reminder to always carry their EAI with them.
Recognising early symptoms can help get medical assistance on time and avoid hospitalisation.	UR5	A need for a learning environment that teaches about early symptoms detection.
Delayed epinephrine injection can cause fatal consequences.	UR6	A way to ensure that epinephrine is injected promptly and immediately after realising symptoms.
Medical IDs are essential for giving the brief medical condition of a patient at a scene.	UR7	A way to store medical history and hand it to EMS during an episode.
Support groups may improve the quality of life for people suffering from anaphylaxis.	UR8	A way to make next-of-kin aware when a patient requires their help and support.
Knowing exactly what to say to EMS increases the chances of being attended quickly.	UR9	A way to prepare patients to describe their health condition during an emergency with minimal time.

EMS services need to know the exact location to better service the patient.	UR10	A way to share their accurate location with the EMS as quickly as possible.

4.2 Functional Requirements

Functional requirements (FRs) define the minimum requirements a system must be able to do, to perform a functional concern (Glinz, 2007). Combining the user requirements with the *Five Whys* framework, the functionals requires were derived and are presented in Table 4-2.

Table 4-2: Functional requirement derived from user requirements.

ID	Functional Requirements
FR1	Secure permanent connection with the EAI
FR2	Ability to detect separation with EAI
FR3	System to predict physical distance between EAI and tracker
FR4	Detection of the use of the EAI
FR5	Automatically alert EMS and emergency contacts when a patient uses the EAI
FR6	Relay of the correct location of the patient

According to El-Attar and J. Miller (2007), use case modelling is often used to drive the design phases of an interactive system because it is very simple to use to effectively describe the functional requirements of a system (El-Attar and J. Miller, 2007). A use case diagram comprises use cases (depicted as ovals) and actors, summarizing the interaction between actors and use cases, as well as the relationships among the use cases. The use case diagram shown in Figure 4-2 summarises the core FRs identified for the tracker.

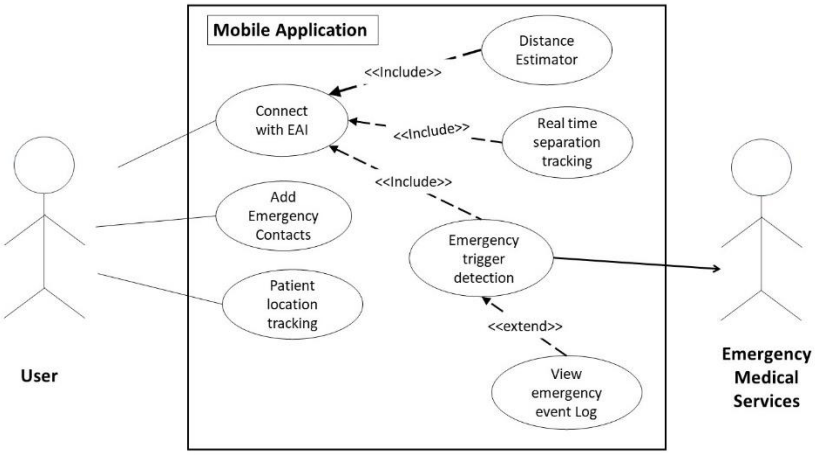

Figure 4-2: Use case diagram for the proposed tracker.

4.3 Non-functional Requirements

Non-functional requirements (NFRs) pertain to the performance quality or constraints of a solution space that exceed the essentials needed to fulfil the core (functional) requirements. (Glinz, 2007). Non-functional requirements for the tracking system are listed in Table 4-3 below.

Table 4-3: Non-functional requirements to consider for practicality.

Design Constraints:	**Description:**
Portability	The device must not constrain a user to only one location to perform its core functions.
Availability	The success of the solution relies on its availability to a majority of its intended userbase. As shown in literature, one of the major factors infringing the adoption of EAI was the increased cost (Regent & Johnson, 2020).
Modularity	A modular design avoids having to redesign a parent device. This project focuses on the design of the tracker and not EAI device.
Design and Implementation	This consideration includes size, the communication technology of choice, and the wireless technology chosen.

4.4 System Design Considerations

4.4.1 Hardware Component Design

The proposed system was divided into subsystems namely Bluetooth Tracking System (BTS), Emergency Medical Alert System (EMAS), and Hardware User Interface (HUI) shown in Figure 4-3.

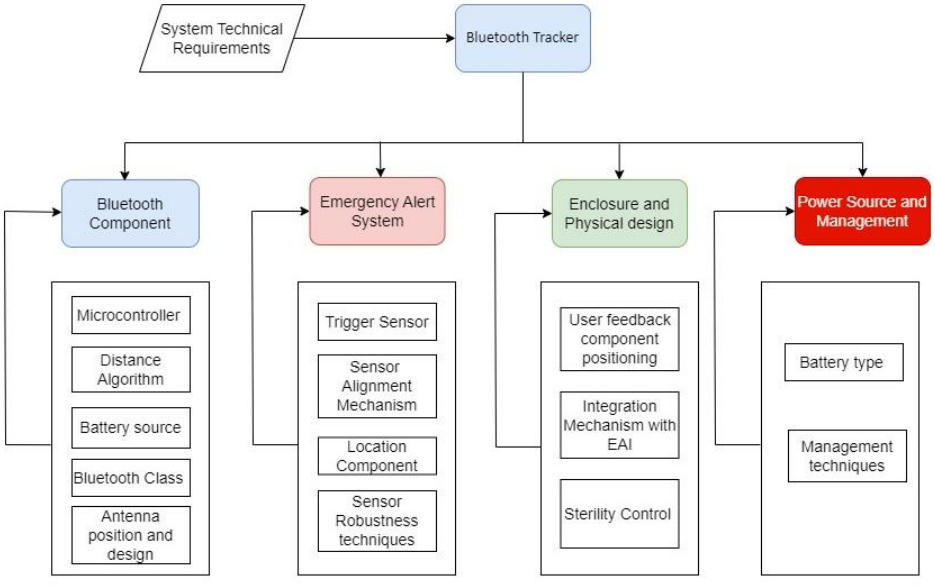

Figure 4-3: Subsystems Requirements breakdown.

4.4.1.1 Bluetooth Tracking System (BTS)

A module to provide wireless real-time tracking that is located on the EAI was needed. Bluetooth was chosen over Wi-Fi and Ultra-Wide Band (UWB) tracking technologies for the following reasons. UWB became available only from 2019 in Apple devices, and only in 2023 in Android (Samsung) devices. Only a few users have access to the technology. Similarly, Wi-Fi requires built infrastructure, and poses a great limitation in outdoor areas.

Bluetooth Overview

Bluetooth is categorised into two short-range communication groups: Bluetooth Classic and Bluetooth Low Energy (BLE). Both technologies work at frequencies between 2.402- 2.480GHz, divided into 79 1MHz channels, with a median frequency of 2.4GHz (BSIG, 2023). The median frequency is commonly shared with other wireless technologies, including Wi-Fi, wireless baby monitors, and microwave ovens. For this reason, Bluetooth experiences much interference when these signals exist in the same space. However, Bluetooth uses a frequency hopping mechanism to identify a free, uninterrupted channel to operate if the other 78 channels are occupied.

BLE offers a very low power operation through a standardised communication protocol, shorter transmission times, and reduced duty cycle (BSIG, 2024). This design allows BLE devices to be a preferred choice for portable, and wearable wireless applications. The communication protocol for BLE includes:

- **Advertising:** Peripheral devices such as sensors advertise to central devices.
- **Scanning & Connection:** A central device actively searches for advertising peripherals to initiate a connection request. A secure communication will be established once connected.
- **Service Discovery:** Once connected, the central device can discover the services offered by the peripheral using a standardized protocol called the Generic Attribute Profile (GATT).
- **Data exchange:** The services exchange the data between the devices through objects called characteristics which are handled by the Attribute Protocol (ATT). These objects can either read or write to another BLE device of different type or class.

The type of Bluetooth refers to the version of Bluetooth or the design architecture the technology follows. Bluetooth class refers to the connectivity range of the Bluetooth module. The typical ranges with their associated classes are tabulated below. Each class and type have its advantages, but notably; the more powerful the module is, the higher the connection range and the more power it consumes when transmitting the data. Table 4-4 shows different available Bluetooth classes and their associated connection range.

Table 4-4: Bluetooth device classification.

Bluetooth Class	Maximum Power	Operating Range
Class 1	100 mW (20dB)	100 meters
Class 2	2.5 mW (5dB)	10 meters
Class 3	1 mW (0dB)	1 meter

Two or more class 1 Bluetooth devices must communicate to achieve maximum range. The device with the lower class determines the connection range. Modern smartphone devices contain Bluetooth classic architecture, as opposed to BLE. However, BLE devices can communicate seamlessly with Bluetooth classic devices. For this application, a Bluetooth 4.0 or higher, notably Bluetooth Low Energy (BLE) module with a class 2 rating, was needed to ensure an extended range of up to ten meters within a line of sight. The module operates at unlicensed 2.4 GHz to comply with local radio frequency usage standards.

Bluetooth is the essential part of the system responsible for providing a communication pathway between EAI and the user and is provided by the BTS. This system interfaces with the EAS as well, and it considered the following design requirements:

- **Bluetooth Range:** Ability to track reliably over a range for a typical standard big room (office or house) without losing connection.
- **Component size:** The size of the module must be as small as possible to ensure it reduces bulkiness to the EAI device. Size is one of the factors influencing the carrying rate of EAI devices (Macadam, C et at., 2012).
- **Power source:** The power source must allow the system to be portable since the tracking is on a constantly moving object.
- **Distance estimator:** A robust algorithm that can minimise the interference effects from other radio signals.

A variety of off-the-shelf BLE components are available on the market; therefore, this component was not developed from circuit design principles. Rapid prototyping was adopted. South Africa's electronics supplies like DigiKey SA, Takealot, Communica SA, and RS Components were vendors of choice.

4.4.1.2 Emergency Alert System (EAS)

The emergency alert system is responsible for sensing the use of the EAI and reporting to EMS. This uses the BTS system to transmit data from the trigger sensor to the mobile application. The design considerations of this system included:

- **Attachment mechanism:** The system's design must not introduce an extra trigger step when the EAI is used during an emergency.
- **Sensor type:** The sensor should be low-power, affordable and not obstruct the regular operation of the EAI.
- **Robustness:** The system must be robust enough to avoid giving accidental (false) triggers that state the user is in a medical emergency when there is not. This includes differentiating between false positives and false negative triggers.
- **Location:** The system must be able to tell the patient's location at the time of the EAI trigger or intention to use.

4.4.1.3 Hardware User Interface

The user interface serves as the point of human-computer interaction and communication in the device. The design considerations were as follows:

- **Integration with existing EAI -** The enclosure should be designed to be compatible with ZibiPen and must not exceed double the size of the ZibiPen body.
- **Easy to use -** Feedback components should be user-friendly and easily understandable by users.
- **Sterility -** It is essential to ensure that the tracker's point of contact with the ZibiPen does not interfere with the sterile component, including the needle and medication.

The enclosure of the device was 3D printed in the UCT Medical Devices Design Lab using the following technologies:

- SolidWorks Student Edition as the CAD tool.
- Cura V5.1.1 was used as the 3D printer slicing tool.
- Ender V3 3D printing machine was used with a PLA 0.3 millimetres (mm) filament to manufacture all plastic components. An infill of 20% and a layer height of 0.2 mm were used for printing setting.

4.4.2 Mobile Application Design

The programming framework utilised for the project is Flutter. This framework was chosen for easy integration and compatibility for iOS and Android smartphone users. The advantage of using Flutter over native code, java, is the rapid prototyping capability that can be achieved compared to native programming language. Android Studio was used as the integrated development environment (IDE) because of its ability to provide a smartphone emulator. The emulator facilitates testing the application functionality and performance on different smartphone architectures.

Communication Protocols

The mobile application uses local notifications to remind patients to carry the EAI. SMS was used to communicate with emergency medical services, and cloud messaging was used to communicate with healthcare centres. Phone call protocol was used to communicate with emergency call centres and high-priority local notifications were used to remind the user when the separation between the user and the EAI was detected. All these communication protocols were implemented to operate automatically without user intervention.

The mobile application was developed using a UCT computer with the following specifications.

- Brand: Proline
- Processor: 12th Gen Intel(R) Core (TM) i7-12700 2.10 GHz
- Installed RAM: 16,0 GB (15,7 GB usable)
- Storage: 500 GB
- System type: 64-bit operating system, x64-based processor

4.4.3 Database Integration and Network Considerations

The data storage for the mobile application is the Google Firebase database. This system is essential in storing patient data and event records and liaising with ECC and EMS. The design considerations of this system were therefore:

- **Communication protocol -** Conform with HTTP internet protocol using a standard internet data format protocol Java Script Object Notation (JSON) format.
- **Programming language -** A programming language that allows easy integration with the Django-based (Python) telemedicine testbed.
- **Smartphone -** A mobile phone with 5G network protocol compatible with the UCT 5G network testbed.
- **Network Services -** A cloud-based SMS service must be present to allow communication of emergency alerts via servers.

5. Chapter 5: System Design Outcomes

This chapter discusses the implementation of the tracker hardware and software components. The source code of the mobile application and Arduino can be found in Appendix C.

5.1 System Architecture

Figure 5-1 shows a high-level system architectural interaction of all tracker components.

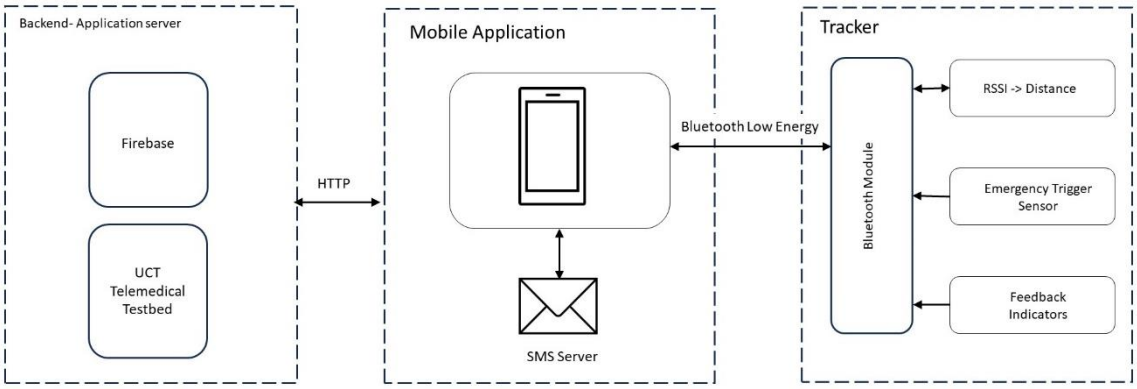

Figure 5-1: Architectural diagram for technologies used to develop GuardAin.

The main components of the architecture include:

- **Mobile Application -** This part of a user interface developed with Flutter framework with dynamic features:
    - **Automated emergency voice –** Activated when an emergency trigger is detected. It used the speaker of the mobile phone.
    - **Direct voice call –** A direct call, without the user interaction, is activated when the AEV has finished playing.
- **Backend Application Server –** The applications responsible for running tasks over the internet. This includes:
    - **SMS server:** Manages emergency SMS delivery.
    - **Firebase-** Stores data like patient data, and emergency events.
    - **5G Telemedicine Testbed –** Provides redundant database.
- **Tracker –** This is the component that consist of the hardware processes that are relayed to the mobile phone via BLE module:
    - **Distance estimator -** Calculates distance based on RSSI values received from the mobile phone by the tracker.

- **Emergency trigger sensor –** Utilises logic HIGH/LOW value to detect when the safety cap of the EAI is removed.
- **Feedback Indicator –** An LED indicating an emergency in darker environment.

5.2 Permission Handler

Many of the functional requirements of the mobile application operate without user awareness. To comply with ISO/IEC 27701, a permission handler class was developed to handle all permissions needed for the operation of the mobile application. All the permissions required are listed in Table 5-1. If the permission is not granted, the application will not work efficiently.

Table 5-1: List of permission necessary for the operation of the GuardAin tracker.

Permission	Minimum conditions	Reason
1. LOCATION	Always	The application always uses the location to track the EAI and the patient.
2. BLUETOOTH	Always	The EAI always communicates via Bluetooth.
3. READ AND WRITE SMS	Always	The application broadcasts a message to family and emergency services during an emergency.
4. PHONE CALL	Always	Application may require calling EMS when the user is in an emergency automatically.
5. READ CONTACTS	While using the app or always	Use the mobile application to add existing contacts from the phonebook.
6. SEND NOTIFICATIONS	Always	Always sends notifications to remind patients when the EAI is not detected near the user.
7. MUSIC AND AUDIO	While using the app	For learning and support pages. Videos require audio access.

5.3 GuardAin Tracker

Technologies that were utilised in the implementation of the smart tracker are discussed below. Functionality was the primary focus. Additional factors that were key to selection and design, were integrability and compatibility, cost, manufacturing, and market feasibility.

5.3.1 Bluetooth Module Selection

Real-time asset tracking, low power consumption, and reliable communication were primary requirements.

Size Constraints - The available space from the *ZibiPen* autoinjector body was used as an electronic board placement, shown in Figure 5-2. Only a few sections contained sufficient space to house an electronic system. These sections include the safety cap, and the "Gap" space between the outside body and the internal mechanisms, medication cartridge and safety sheath.

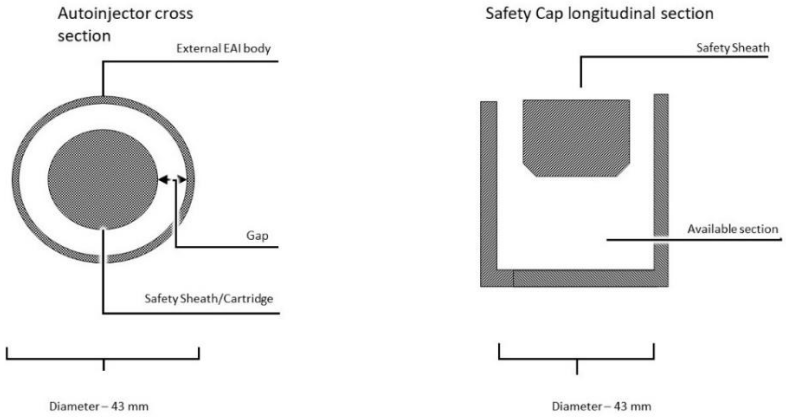

Figure 5-2: A cross-sectional and longitudinal model of the ZibiPen EAI.

The gap space required a flexible electronic board design and could interfere with the mechanism of the ZibiPen. The safety cap was designed with a size constraint that the diameter does not exceed 43 mm to avoid altering the ergonomic properties of the *ZibiPen*.

Microcontroller - A microcontroller with a 32-bit processor to provide high processing power and to host a BLE module with additional GPIO pins for the user feedback and trigger sensing unit.

Antenna Placement -An optimised antenna location to improve radio signal resolution and range. The antenna was placed on the end of the safety cap, away from most electrical components, and the needle to ensure a long-range and less interference.

Two modules were explored, the Bluno Beetle BLE board and the Arduino Ble nano 33 sense shown in Figure 5-3 below. The Bluno Beetle dimensions were slightly bigger than the diameter of the ZibiPen which made the first design prototype unfavourable, see Appendix D. A second iteration utilised the Arduino Bluetooth module. This microcontroller board was selected because it met all the requirements for this application and its rapid prototyping ability. The *Arduino NAO BLE sense,* shown in Figure 5-3[right], is a small, low-power Bluetooth module with a long-range and high data rate. It also has a an integrated 32-bit microcontroller, which provides high processing power.

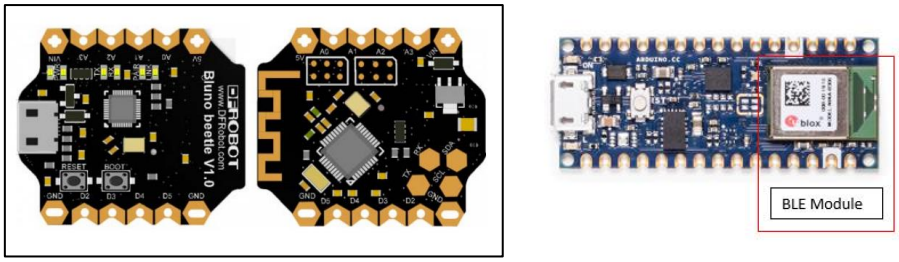

Figure 5-3: BLE modules: Bluno Beetle[left]. Arduino nano BLE sense 33[right]

Table 5-2: Arduino nano BLE sense microcontroller specifications.

Feature	Specification
Model	NINA-B306 Module using nRF52840 architecture
Bluetooth type	Bluetooth 5.0 BLE
Bluetooth class	Class 2
Dimensions	43.16mm x 15.24mm x 4mm
Weight	Five grams
Microcontroller type	Arm Cortex M4F 64MHz
Antenna location	Edge location
GPIO Pins	15 pins
Vendor	Communica South Africa
Cost	R 467.00

5.3.2 Power Input

The power requirement for the Arduino development board was between 6V to 12V. An additional step-down Zener voltage regulator was designed in addition to the microcontroller internal switching regulator. The battery capacity was calculated using the 915 mA the Arduino nano BLE consumes at maximum power consumption when connected in series with 10k resistor and trigger switch. Therefore, the battery capacity was calculated based on full load conditions operating for at least a full 24-hour day.

Equation 1

$$I_{max} = \frac{V}{R} = \frac{12 - 3{,}3}{10000} = 0.87mA$$

$$P = VI = 12 * 0.87mA = 1.05mW$$

Equation 2

$$Capacity = I * BL = 0.87 * 24 = 2.09mAh$$

Two 3.3V high density batteries were required with chemistry like Lithium Polymer or Lithium-ion. However, due to size constraint, batteries with this chemistry take up all the available space. After iterations of the designs considering size constraints and the ergonomics, an A23 12V Alkaline battery was selected, shown below in Figure 5-4.

Figure 5-4: Duracell Alkaline A23 12V battery

The A23 battery contains an alkaline chemistry with an energy density of $55mAh$. The battery life was drastically reduced. The choice, however, was made for proof of concept and better fitment within the smart cap.

5.3.3 Power Management

A power management technique was developed programmatically to reduce battery consumption. An idle mode and tracking mode were designed and developed. In idle mode, the tracker is programmed to indefinitely go to sleep unless an event was detected. This was done using interrupts and sleep functions on the BLE module. Tracking mode is when a user continuously looks for the device using the distance algorithm or using the auditory and/or visual indicators. This is the most power demanding task and it was assumed to only last for a few minutes.

5.3.4 Schematic of the tracker

Figure 5-5 shows the electrical schematic and the electronic board that was developed.

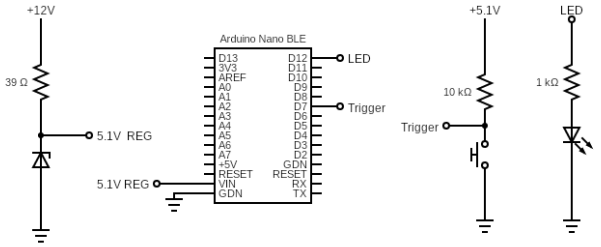

Figure 5-5: Simplified schematic for the circuit board.

5.3.5 Distance Approximation

Both the tracker and the mobile application are responsible for processing the distance algorithm. The mobile phone provides a user interface, whereas the tracker performs the computations. The algorithm was developed using C++. ArduinoBLE version 1.3.4 library was utilized to provide Bluetooth functions, including connection management and accessing connection strength between connected devices.

It is known that all radio devices produce radio signals that propagate in space with the strength of the signal being the function of distance. Radio signal strength decreases logarithmically with an increase in distance. The Received Signal Strength Indication (RSSI) measures the strength of the Bluetooth signal as received by another radio frequency device.

The RSSI was used to approximate the distance between the Bluetooth device and the mobile phone. Many different and advanced algorithms can be used to convert the RSSI to distance. In this application, two methods were used: the Free Space Path Loss (FSPL) equation, and the second method was based on a combined moving average and mode algorithm obtained from an experimental approach to get a line of best fit from measuring the RSSI at known distances.

Free Space Path Loss (FSPL)

The equation incorporates propagation losses and the power transmitted by the Bluetooth source over a clear line of sight. The assumptions are based on ideal conditions that there are no other radio signals close by, and that there is no changing media between the transmitter and the receiver other than air. A simplified equation for approximating distance according to Liu et al. (2020) is shown in Equation 4.

Equation 3

$$FSPL = P(x)_t - P(x)_r$$

Equation 4

$$distance(x) = 10^{(P(x)_r - RSSI(x))/10N}$$

Where N represents an environmental factor that ranges between 2 to 3 depending on whether the signal propagates through air, or a solid medium respectively. An average value of 2.5 was used to approximate distance, as no validated number is available for all conditions. Received power $P(x)_r$ needs to be kept constant, however, this parameter cannot be controlled on the Arduino nano BLE high0 level programming. The $P(x)_t$ increases when there is a weaker RSSI signal detected.

This method showed significant tracking errors. A calibration-based method to minimize error distance conversion can be used. One of the methods is using a Kalman filter calibration approach which works best when other parameters like gyroscope and accelerometer from the mobile phone.

are additionally used as input parameters. Given the low-cost nature of the sensors of the mobile phones, an accurate distance conversion may be rarely achieved (Liu et al., 2020). This research, however, explored alternative methods to enable the application to detect distances of more than ten meters.

Experimental Approach

Using a steel tape measure, marks were made at one-meter intervals marked from 0 to 15 meters as shown in Figure 5-6. The room only had a Wi-Fi router (radio operating at same frequency as Bluetooth), located at least fifteen meters from the BLE module. The airplane mode on the laptop which was used to power the BLE module via a USB port was activated to ensure no WIFI or Bluetooth interference were introduced in the space.

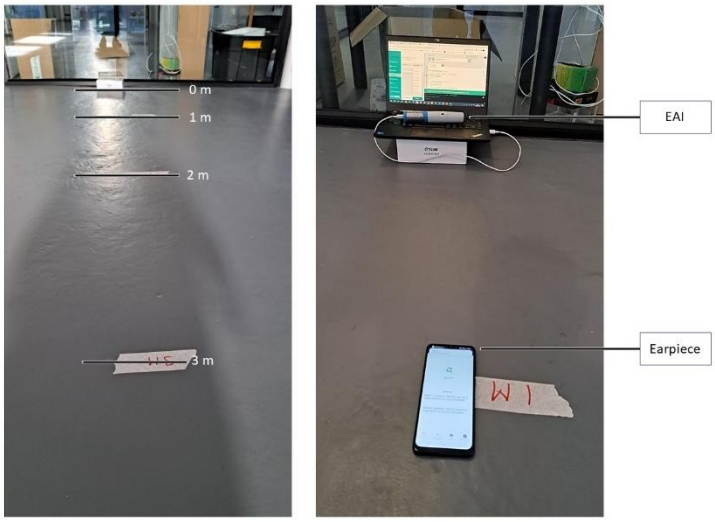

Figure 5-6: Experimental set-up showing the distance markups.

The tracker was placed at zero distance the whole time during the experiment. Moving in a straight line of sight, RSSI values from the mobile application were recorded on the marked distances. These values were reordered and are shown on the curve below.

The mean and mode values of RSSI using two hundred samples at each one-meter interval were plotted and shown in Figure 5-7. The phone's orientation in relation to the tracker was maintained constant throughout the experiment, as shown in Figure 5-6. The earpiece speaker of the phone was facing the tracker, and the screen was facing the upward direction. The orientation was kept the same way when collecting other distance points. This constraint was essential for integrity and

repeatability of the experiment as Bluetooth antenna gains are susceptible to spatial orientation. Changing orientation after every measure may result in inconsistent data, and possible inaccurate distance approximation.

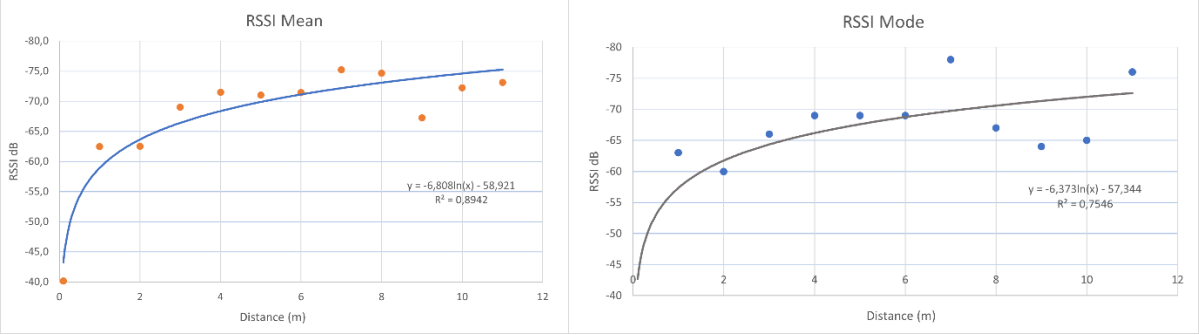

Figure 5-7: Best line of fit equations using mean (left) and mode (right), RSSI(PdB).

Mean based equation:

The equation of best fit,

Equation 5

$$RSSI = -6{,}808\ln(d) - 58{,}92$$

was recorded, with the correlation coefficient $R^2 = 0.894$. Solving for distance $distance, d$, an equation to approximate distance was calculated:

Equation 6

$$distance_{mean} = e^{\frac{RSSI+58{,}92}{-6{,}808}}$$

Mode based equation:

Equation 7

$$distance_{mode} = e^{\frac{RSSI+57{,}344}{-6{,}373}}$$

With the correlation coefficient $R^2 = 0{,}7546$.

Based on the two equations, the distance vs signal power prediction is as shown in Table 5-3.

Combined Algorithm:

This method is based on questioning the integrity of each distance estimator. Both the moving average and the mode of a particular sample must agree within $\pm 1\ m$, otherwise the distance is recalculated. A high-level flow diagram of this algorithm is shown in the Figure 5-8.

Table 5-3: Distance vs signal strength.

Distance (m)	Mean RSSI (dB)	Mode RSSI (dB)
1	-59	-57
2	-64	-62
3	-66	-64
4	-68	-66
5	-70	-68
6	-71	-69
7	-72	-70
8	-73	-71
9	-74	-71
10	-75	-72

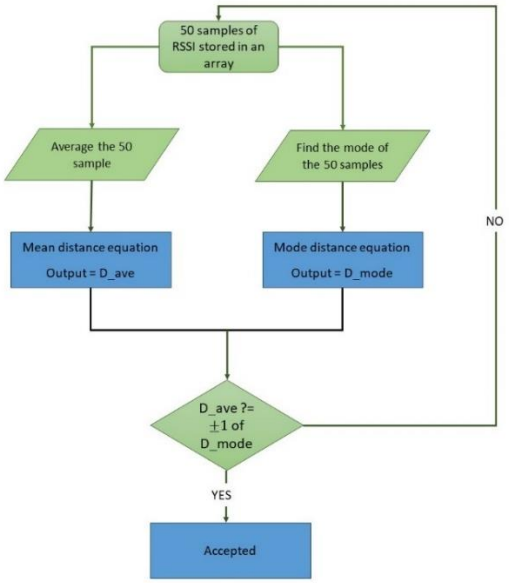

Figure 5-8: Combined tracking algorithm to detect ten meters.

5.4 Tracking User Interface (Mobile Application)

The tracking system was divided into the following two layers. No data layer was implemented for this feature:

- **Presentation layer:**
  - Distance estimator user interface
  - Control buttons

- **Business layer:**
    - Tracking Events
    - Notification Manager
    - Location Manager

The Bluetooth component of the mobile application had to satisfy the following functional requirements.

- The user receives alerts when the distance is more than 10 meters.
- The user must be made aware when the Bluetooth connection between the phone and the smart tracker is disconnected.

- **Non-functional requirements:**
    - An automatic reconnection must initiate when the user is near the tracker.
    - A user must be able to know the distance between the tracker and the phone.
    - Local notifications must always appear at the top of the patient's notification centre. The notifications should be easily readable and accessible by the patient.
    - **Distinguishability**: The tone or the vibration should be different from the daily use phone's setting.
    - Provide useful context regarding whereabouts of the EAI.

The tracking interface was designed to send notification alerts when the distance is more than 10 meters or when there is no longer established connection. Geographical location was sampled to be viewed with the notification bar. The algorithm to perform this task is shown in Figure 5-9.

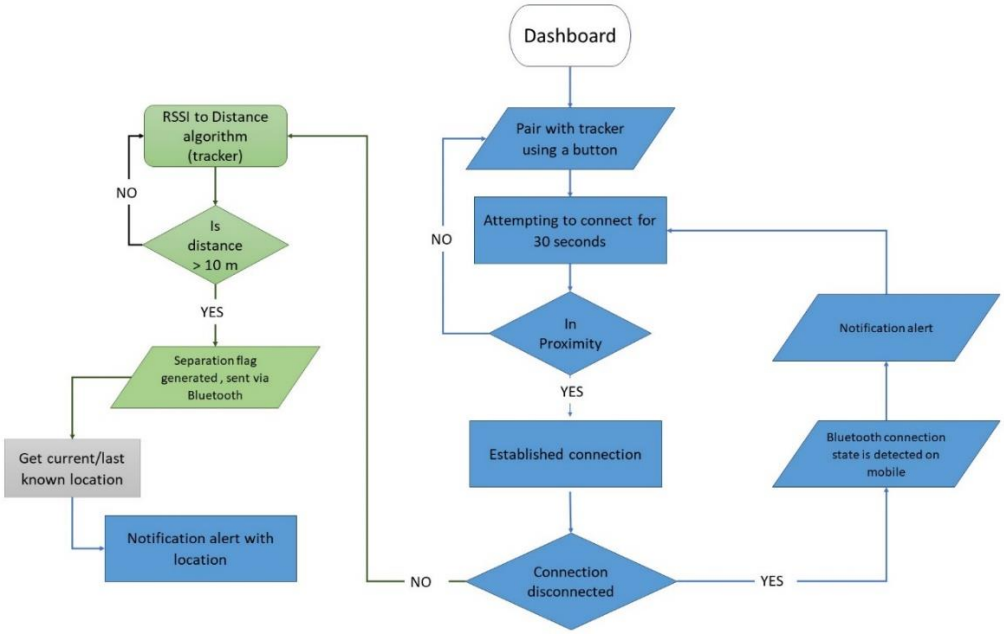

Figure 5-9: Notification reminder flowchart.

5.5 Emergency Sensing Unit

This unit is responsible for the trigger detection of the EAI activation. For power optimisation and reduction of electrostatic effects on the needle, passive components were utilised where possible.

The sensing component was designed using a mechanical tactile push button as shown in Figure 5-10 below. The button pushes against the *ZibiPen* safety sheath to produce a logic high output to the microcontroller.

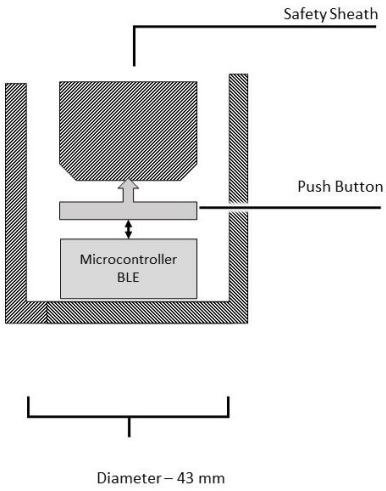

Figure 5-10: A cross-sectional view of the EAI sheath, the trigger button within the safety cap.

Essential consideration was the force required to trigger the safety sheath. According to the *ZibiPen* manufacturers, the minimum force to trigger the EAI is 15 Nm (Impulse Biomedical, 2023). The selection of the button was based on the following two criteria to ensure the button does not trigger the EAI when the cap closed:

- The total length of the button when in pushed position must not exceed 10mm.
- The force required to push the button must be less than 3 Nm (safety factor of 5).

A variety of electronic buttons were explored and compared. Figure 5-11 below shows the tactile button that was selected with its specifications. The button operating force was bench tested using a scale and a minimum of 1,5 N force was required to activate the button. Appendix G.

Figure 5-11: The tactile button used for cap removal detection.

Feature	Specification (datasheet)
Operating force	0,98 Nm
Height	7 mm

A precise positioning slit was designed to hold the button in a fixed position, shown in Figure 5-12 below. The slit holds the button in pressed mode when the safety cap is closed and releases when it open.

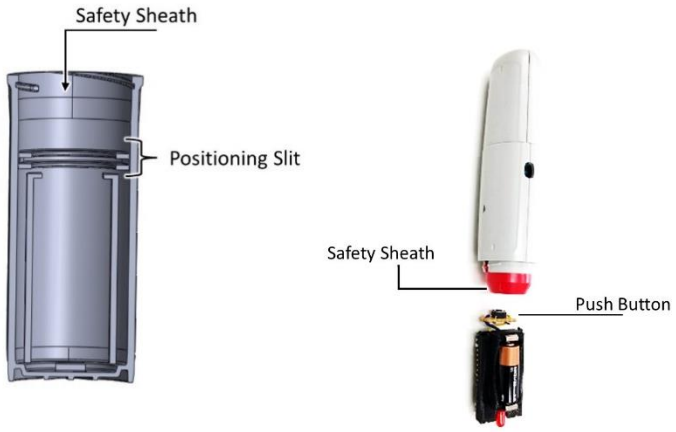

Figure 5-12: Slit design for fixed positioning of the tactile button.

5.5.1 Emergency User Interface

On the three-layered architecture, the emergency alert system was designed utilising the Representational State Transfer (REST) within the business layer. REST is an architectural style that guides the design of web APIs (Purushothaman, 2013). It follows a client-server model where applications (clients) interact with resources (data or functionalities) on servers using a standardised set of rules leveraging HTTP for communication. This focus on HTTP simplifies implementation and fosters interoperability across different platforms and devices on the Internet.

- **Presentation layer:**
  - **Emergency Event Log –** Shows a list of previously detected emergency events.
  - **Contact manager-** Manages the list of emergency contacts on the application.
- **Business Layer:**
  - **SMS API –** Sending an emergency SMS.
  - **Audio player -** Playing an emergency tone when trigger is detected.
  - **Phone Call API –** Automatically makes a call to the emergency list prepopulated by a user.
  - **RESTful API –** Processing patient data during the triggered event.

- **Location Service -** Providing location of the patient.

- **Data layer:**
  - Patient Medical history
  - Past trigger events

The emergency alert system detects the use of an EAI, and initiates communication with emergency contacts by utilizing the algorithm shown in Figure 5-13.

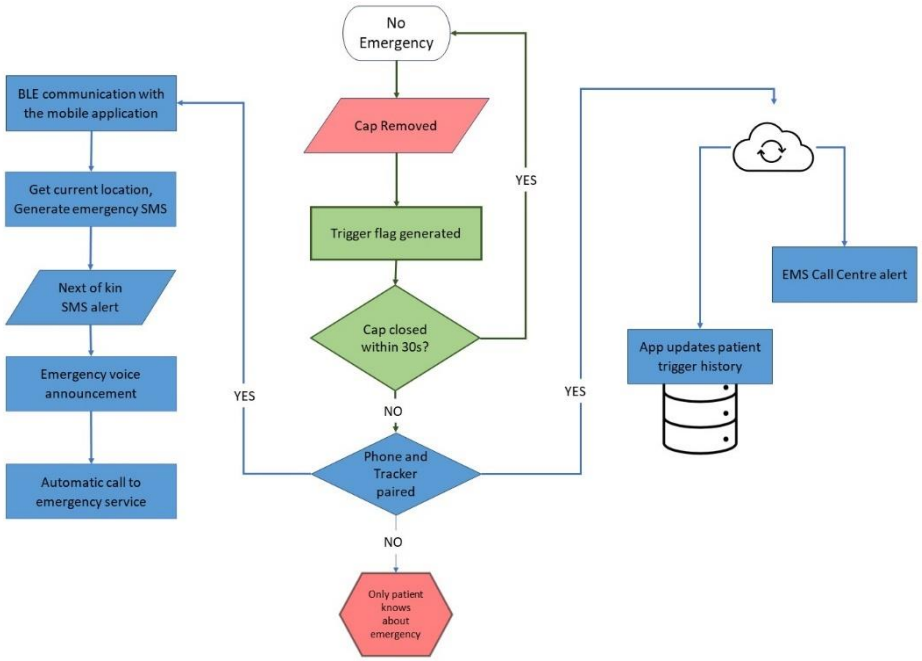

Figure 5-13: Algorithm diagram for cap removal detection.

LED Circuitry Design

The LED system is complementary with both the distance algorithm and the auditory system. LED was specifically designed for dark area location. A toggle button on the mobile application was designed to control the LED on and off modes. The LED is powered by a 3V pin, controlled programmatically using an LED control function that was developed. A red LED was chosen because of its stand-out color when lit in a light and dark room.

5.5.2 Enclosure Design

A battery and circuit board compartment were designed to neaten up the tracker. Flat springs were used for battery terminals to hold the battery in place. The electronic board was mounted at the back of the battery compartment. A clip mechanism to hold the board onto the cap interfaces with

the rectangular compartment was designed. The rectangular compartment also ensures no lateral, and axial movement of the electronic components. The CAD assembly of the tracker with ZibiPen is shown in Figure 5-14.

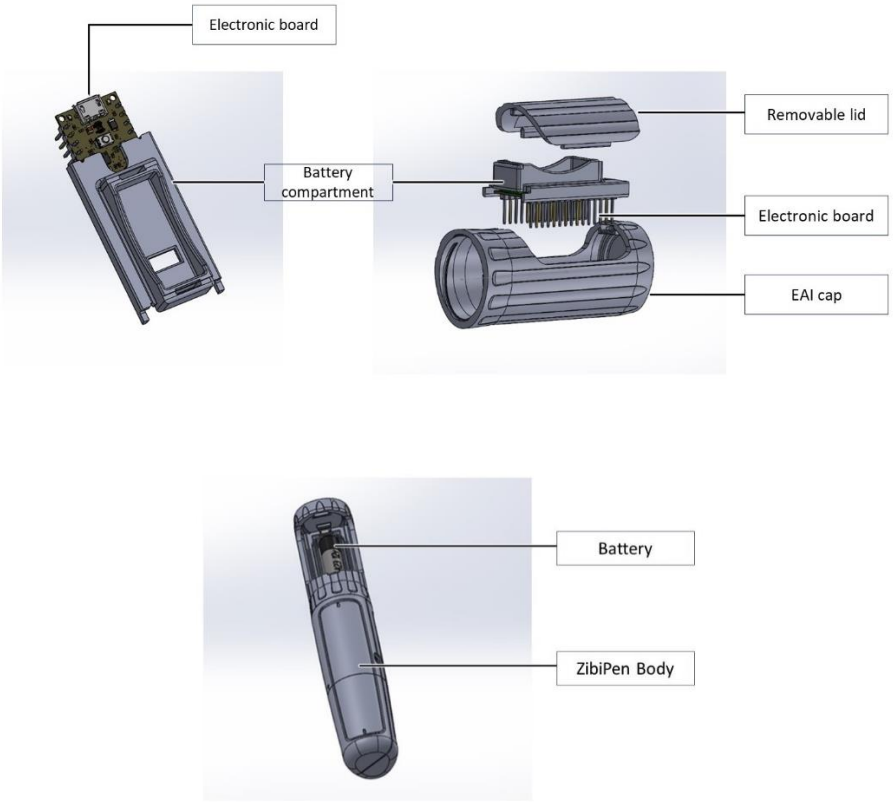

Figure 5-14: Smart tracker subcomponents and enclosure. CAD assembly

The final image of the Integrated ZibiPen with the battery powered smart cap is shown in Figure 5-15. The image shows the whole EAI device with and without the battery lid.

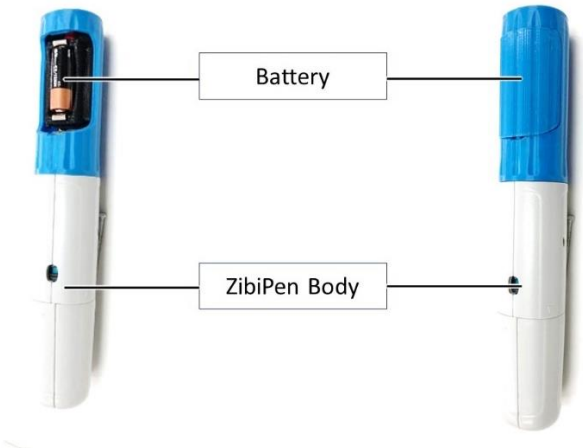

Figure 5-15: Image of assembled battery powered tracker with ZibiPen EAI.

5.6 Storage Integration

Google Firestore database was utilized. RESTful API was used to communicate with the server. Data of interest stored includes Event Records, high risk areas and are shown on the relational database schema in Figure 5-16. Relational databases organise data into tables, which are made up of columns and rows. Each column represents an attribute that describes the data in the table, and each row represents a distinct record. Furthermore, keys are used to construct associations between tables, facilitating data linking and integrity (Elmasri & Navathe, 2016). Relational databases are useful in this application to link each trigger event to its EAUID.

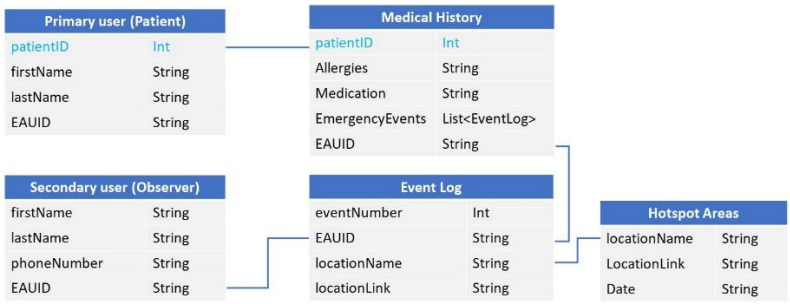

Figure 5-16: Firebase relational database design.

The patient data stored in the database includes medical history, which is used when EMS attend the patient. Event records are associated with the patient's smart autoinjector and stored in the event log, which contains data for all past events across users registered on the application.

5.7 How It Works

5.7.1 System Features

The mobile application dashboard in Figure 5-17 shows the system's features with the UI layout design. This section will outline the operation of the overall system.

Figure 5-17: Smart tracker features.

Table 5-4: Guardian application main features.

Feature	*Description*
A	**User Management -** Forms part of the access control to the application
B	**Bluetooth Manager** – Handles the Bluetooth connection between the tracker and the app. It is essential for real time tracking and detecting emergency triggers.
C	**Emergency Events** – Provides a list of all recorded emergency events showing the date, and location of the event.
D	**Contact Manager –** Manages the emergency contacts that receive an SMS/ phone call when a trigger is detected.
E	**Learning** – Makes use of external medical journals, and websites to provide education on better anaphylaxis management plan.

5.8 User Profile Management: A

The mobile application was designed to consist of two user profiles: the patient and the observer as shown in Figure 5-18. The patient's profile is the admin of the application and has complete control over all features available, including adding observers. The user could be the patient or their guardian and approves access to observer users. The two-profile design was chosen to ensure access control due diligence.

An observer is a user that receives cloud notifications during an emergency and has limited privileges on the mobile application, unlike the patient. This secondary user can only view the activities on the mobile application and cannot change the primary user's settings.

Access Control

First time users are required to register. The registration process requirements are the ownership of a smart EAI cap and its associated unique ID. When a patient submits their name and medical history using the smart EAI code, their data is stored on the server. The backend server was developed using a combination of Google Firebase and UCT 5G testbed as a redundant database. Google Firebase was used for authentication, storage, cloud messaging and notification.

Registration Process

On the login page, the user indicates whether they are a patient or an observer, and then a log-in page corresponding to their profile is rendered. First-time users are required to register via a Google

account or create a new profile by providing their name, email address and phone number. The information is stored in a database(server) and locally on the user's device. For users registering as patients, no authentication method is required.

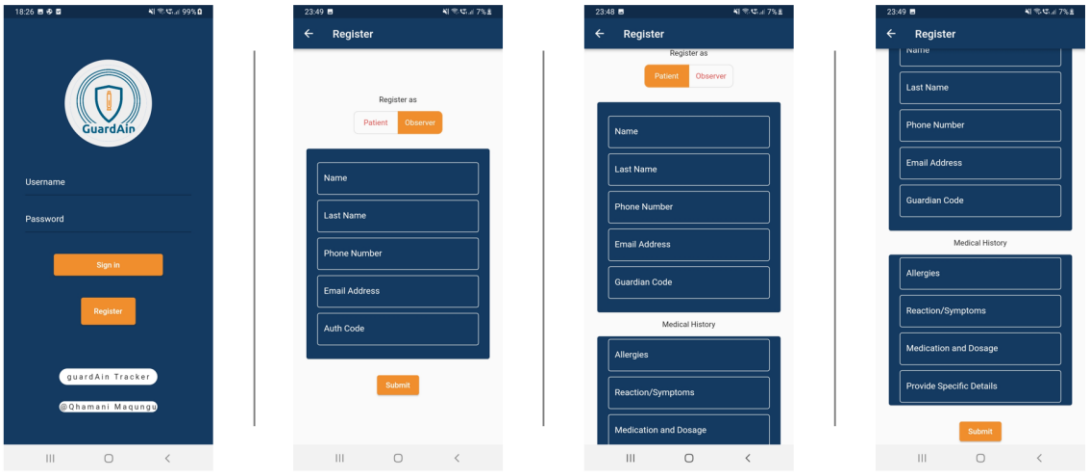

Figure 5-18: Register and Login screens.

EAI unique identifier (EAUID), which is the same as the BLE module UID, is used to link observers to the correct patient. The EAIUI is generated on the smart tracking module and shared with when the user connects with the mobile application. The patient and observer are required to enter the EAI unique ID for the system to know which account the patient is linked with. This method also ensures the unnecessary creation of user profiles for users that do not hold an anaphylaxis EAI prescription.

Login Process

A form was designed to facilitate a login process for a registered user. A username and the EAI are required for signing in. Credentials are locally stored on a mobile phone on an encrypted file that a user cannot directly access for offline authentication, SHA256 hashing algorithm.

5.9 Bluetooth Manager: B

A Bluetooth button is located at the landing screen, the dashboard as shown in Figure 5-19. When the button is long pressed, it connects or disconnects depending on the current state of the connection between the phone and the smart tracker. During registering, the EAIUI is extracted and used, together with the smart tracker name, to automatically connect to the EAI when it is in proximity. To facilitate for the better usability and experience, a loading screen was developed to inform the user about the process occurring in the background. The loading icon ensures that the connection process does not get disturbed when it is performing the verification. The verification confirms the EUID, and the smart tracker name corresponds to the authorised user. When the mobile application successfully connects to the smart tracker, the Bluetooth icon dynamically turns

green. Figure 5-20 shown the user interface representation. The user can be able to track via notifications and detect emergencies using SMS.

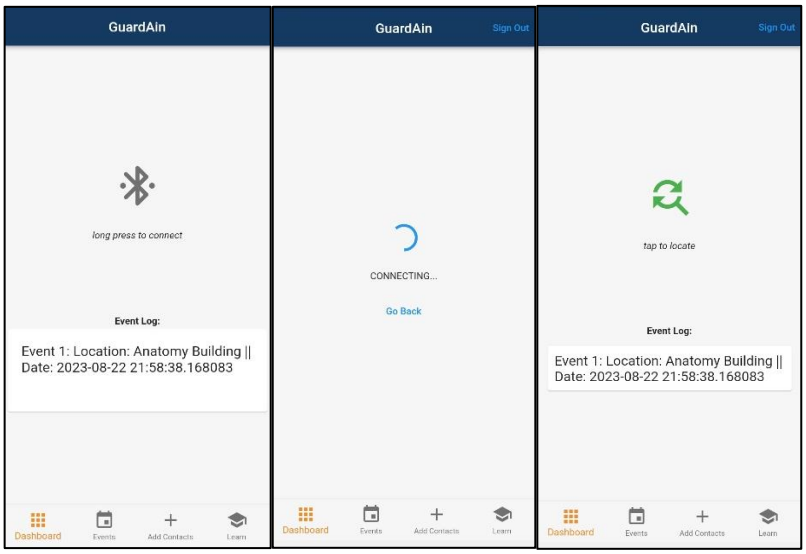

Figure 5-19: Dashboard when GuardAin has disconnected and connected.

5.9.1 Notification-base Tracking

Local notifications are used to remind patients when there is a significant distance between them and their autoinjector. Monitoring of the approximated distance, the Bluetooth connection state, and high-priority notification reminders are shown to the user.

Local notifications are shown to the user when the algorithm predicts a distance of more than 10 meters. Meanwhile, the Bluetooth connection state monitors trigger notifications when the state changes to disconnected. Whichever comes first, the user is alerted. The notifications are of high priority. The high priority nature ensures a highly disruptive behaviour to the user to quickly notice the notification. The notifications have no time limit for appearance unless the user intentionally closes them. A different notification is displayed when the application detects one of the devices has switched off. Figure 5-20 shows screenshots of the notification alerts when a separation has been detected(top) and when the EIA battery died (bottom).

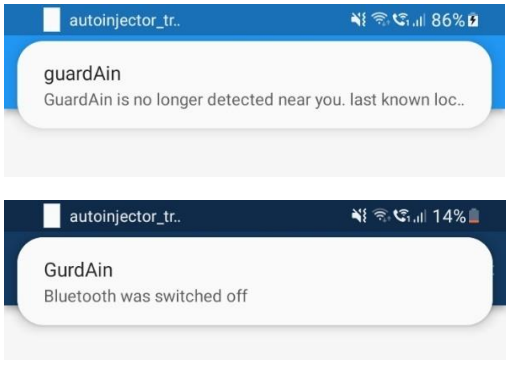

Figure 5-20: Notification alert when distance is more than ten meters [top] and when the Bluetooth is off [bottom].

5.9.2 Bluetooth-Distance Tracking

When the user intends to locate the smart tracker using the distance algorithm, they tap the green icon to enter the distance tracking mode. A circular indicator was colour-coded to give an indication of proximity to the smart module is shown in Figure 5-21. A full green circular bar represents a distance less than one meter between the two devices, and a full red represents a distance more than or at 10 meters.

The colour bar updates in real time as the user moves around. The distance shown in the centre of the circle is the radial/polar distance from the tracker.

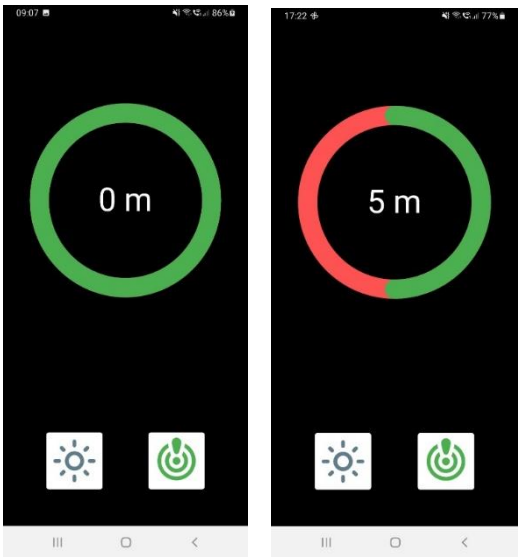

Figure 5-21: Distance estimator screen. The user is within five meters (left) and above five meters (right).

5.10 Emergency Alert System

- **Contact list:**

Using the contacts screen, a user can add, up to three, a list of emergency contacts that receive an emergency SMS during an alert. The application sends the emergency SMS and initiates a call to an emergency number, typically 112 or user defined. Figure 5-22 below shows emergency contact list screen with only one contact added.

- **Emergency use:**

When the safety cap is removed while the tracker and phone are still Bluetooth-connected, an emergency signal triggers an alert on the user's phone. A 30-second waiting period to confirm if the trigger is genuine was implemented, as shown in Figure 5-[right]. The user can only stop the emergency trigger by closing the smart cap back to the EAI. The application assumes an emergency when the 30-second period has passed without user action.

An emergency message is sent automatically via SMS to emergency contacts without the user's intervention. The message contains the location, date, and time of the patient at the time of the trigger and the Google Maps link associated with it. The date and time were included on the emergency SMS to timestamp the exact moment the SMS was triggered on the patient's mobile phone. The structure of the emergency SMS goes as follows:

"{UserName}'s epinephrine autoinjector has been triggered at this location: {LocationName}. This user can be located using this Google Maps location finder {ClickableLocationLink}."

UserName, LocationName, and *ClickableLocationLink* are all dynamic and change based on the location of that particular user at that moment in time. The SMS is sent sequentially over to all the recipients listed as an emergency contact.

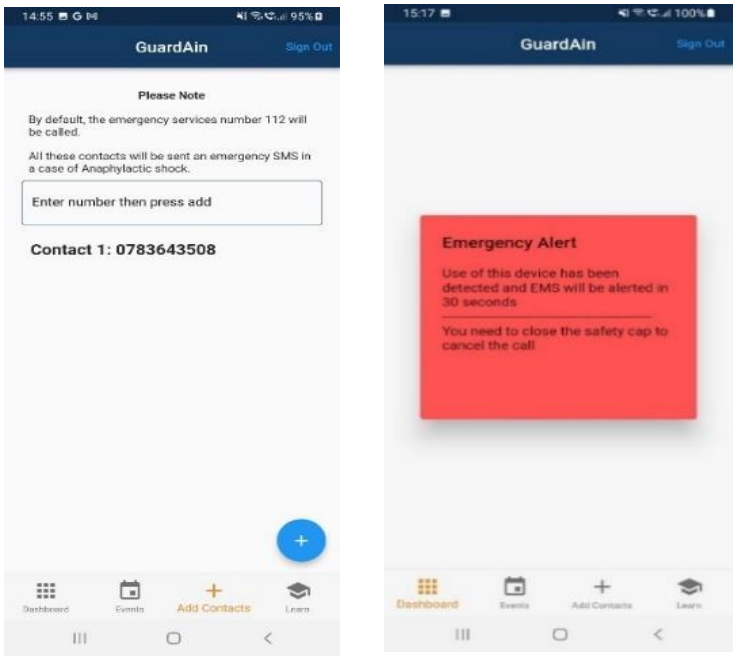

Figure 5-22: Emergency contacts [left] and emergency alert message [right].

Following the emergency SMS, an audio recording was developed using a speech technology that plays when an emergency event is detected. The audio relies on the media volume of the mobile phone. The audio goes as follows:

"Attention! Attention! This user is experiencing a severe allergic reaction. A phone call to an emergency contact will initiate after this recording. Please assist by speaking with the person on the phone"

A phone call is initiated immediately after the recording. The application automatically dials an emergency contact when the SMS has been sent. This is to facilitate a fast reaction from bystanders

by contacting the patient's next of kin without difficulties. Due to the limitations of voice call technology, only one number can be dialled during an emergency.

- **Event Log:**

An emergency event log to store past events was developed, shown in Figure 5-23 below. It is responsible for storing all the emergency triggers that the patient has experienced in the past. Data including the date of the incident, the location and the associated smart module that detected the trigger, are stored on an online server. The location can be used to inform a patient about possible areas that might contain allergy triggers.

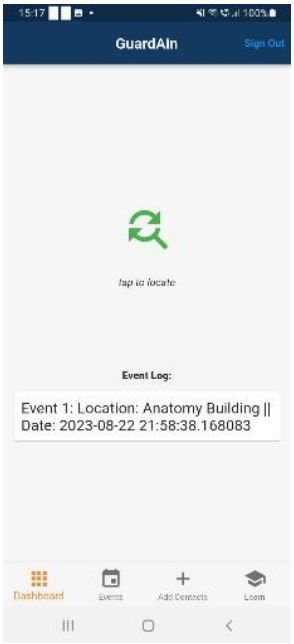

Figure 5-23: Emergency Event Log.

5.11 Learning Resources

The learning resources serve as the training material to equip a user with the necessary steps needed to perform during an emergency. The user can navigate to links regulated outside the mobile application to gain such information. The information includes the following:

- Understanding the SA EMS Triage process
- Anaphylaxis management plan
- Anaphylaxis signs and symptoms

6. Chapter 6: System Evaluation

This chapter evaluates the objectives of this research against the design outcomes of the GuardAin tracker implementation. The evaluation was conducted at Impulse Biomedical's laboratory following Guiliano et al. (2020). Data recording and analysis was conducted in Microsoft Excel. A brief statistical test was conducted using one sample single- and two-sided t-test owing to the nature of the data. The occurrence of the triggers extremely above and below the trigger distance (10 meters in horizontal direction, and 3 in vertical direction) were much more of a risk concern.

A further discussion on the feasibility of the technologies used to provide the solution was assessed.

A reminder of the research objectives below is shown:

- **OBJ1:** Design and develop a mobile-based tracker to alert patients to carry their EAI at all times.
- **OBJ2:** Integrate the tracker with Impulse Biomedical's EAI *ZibiPen* to detect an emergency usage and alert EMS.
- **OBJ3:** Evaluate the smart device guided by medical software and hardware standards and evaluate the feasibility in SA context.

These objectives are validated below:

- **OBJ1:** A system capable of detecting ten meters in a horizontal direction was designed and developed to provide notification alerts to the patient via an Android mobile application.
- **OBJ2:** Developed a sensing unit for ZibiPen, communicating with emergency contacts and EMS via a phone call and SMS.
- **OBJ3:** The system was evaluated for security and risk guided by ISO 14971. Secondly, the device was ranked against existing solutions looking particularly at the feasibility implementation with existing South African emergency digital ecosystem.

A series of tests to validate the system functionality were performed using a 5V, 2200mAh power bank to provide longer battery life for the whole duration of the testing. A general discussion of the technology feasibility in the South African context is also included.

6.1 Notification Alerts

An indoor interwall and a free line-of-sight test were performed. Vertical and horizontal movements were investigated. Distances at which the notification triggered were recorded in Excel.

6.1.1 Horizontal direction:

The device was placed on a stool at a fixed point (zero meters), the same height as the phone as shown in Figure 6-1.

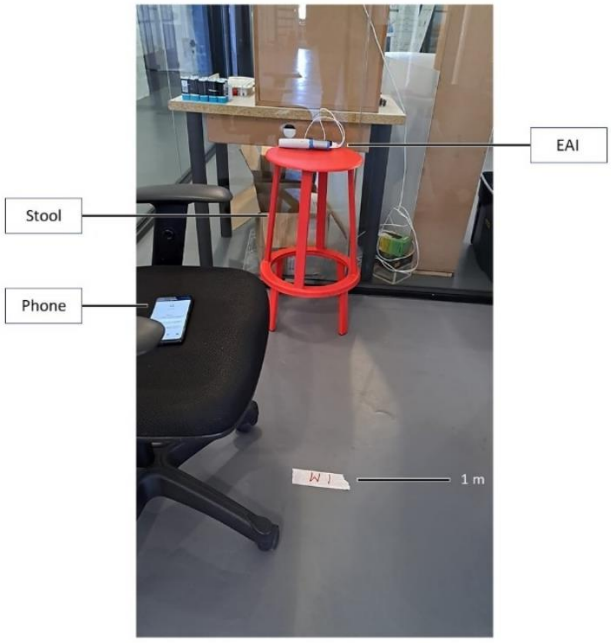

Figure 6-1: Experimental set-up for horizontal direction validation.

A series of cases were performed; Holding a phone in hand (PIH), placed in a room with a wall separation, shown in Table 6-1, and a phone in pocket (PIP), shown in Table 6-2. The conditions for the test were as follow.

- User walks in a natural pace, and gesture.
- User walks in a straight line and stop at 10 meters.
- If the notification does not trigger at 10 meters, the user walks further at natural pace until it sends a notification alert.

Distances of reminder notification were recorded and are tabulated in Table 6-1.

Table 6-1: Notification alert results for in hand test in a horizontal direction.

Trial	**Distance (m)**	
	Phone in hand	Phone in room
1	9	13
2	12	13
3	14	9
4	12	15
5	10	9
6	15	14

7	8	9
8	10	11
9	8	7
10	10	9
Average	10.8	10.7
STDV	2.27	3.45

- Pocket test results for two different participants with different gaits.

Table 6-2: Notification alert results for pocket test in a horizontal direction.

Trial	**Distance (m)**	
	Participant one (PIP1)	Participant two (PIP2)
1	14	10
2	8	11
3	7	14
4	6	13
5	11	11
6	8	13
7	12	9
8	10	13
9	7	8
10	8	9
Average	9.1	11.1
STDV	2.42	1.97

The data was summarised and shown in the statistical charts in Figure 6-2. The distribution charts show the overall distribution of the horizontal direction test.

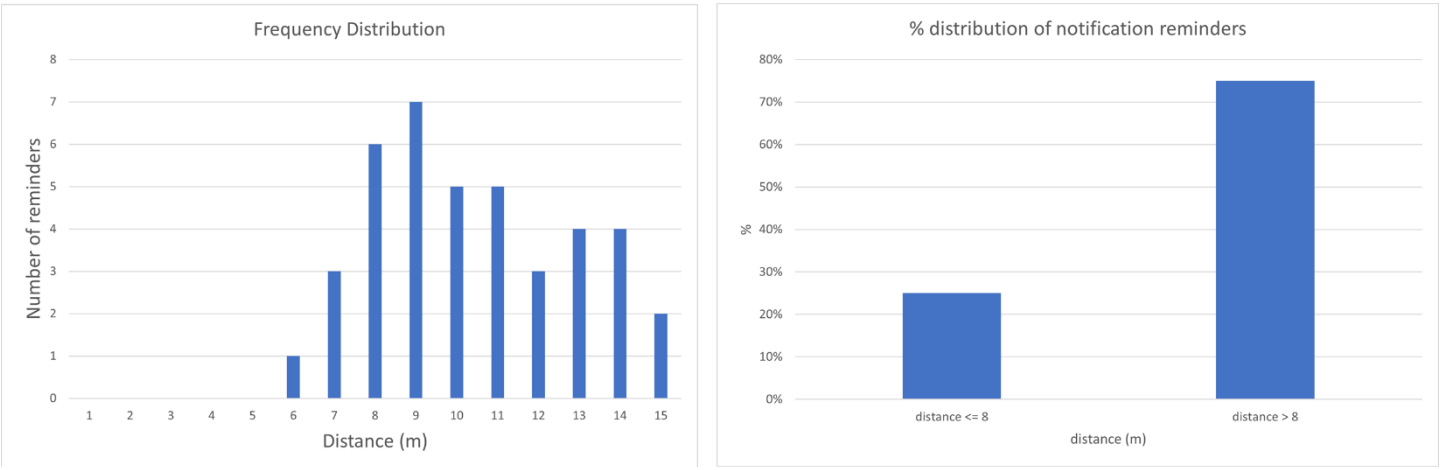

Figure 6-2: Frequency distribution chart for combines cases in a horizontal test.

The results indicate a predominant occurrence of reminder notifications at distances closer to 10 meters. The bar graph illustrates a distribution resembling a normal distribution around the 9–11-meter range for all conditions. Notably, no false triggers were detected within five meters, and only

25% of triggers occurred between 6-8 meters in the 40 test runs. The majority (75%) of reminders were detected above 8 meters, with additional notifications noted between 13-15 meters.

The observed reminder notifications above 12 meters were more prominent in the hand test due to the BLE module attempting to increase $P(x)_t$ power around 10 meters to compensate for detected weaker RSSI. Consequently, more triggers occurred beyond 12 meters.

A comparison of the spread for all four conditions is presented in the box plot below in Figure 6-3, revealing the following key observations:

- **Centre and Spread:**

The median notification reminder for PIH, PIP2, and tracker in a room appears higher than that of PIP1, with medians closer to their means. However, the interquartile range (IQR) for PIP shows greater variability, potentially leading to false 10-meter detections at lower radii.

- **Outliers:**

Notably, there are no significant lower outliers resulting in false, short-distance detections of 10 meters in the collected samples.

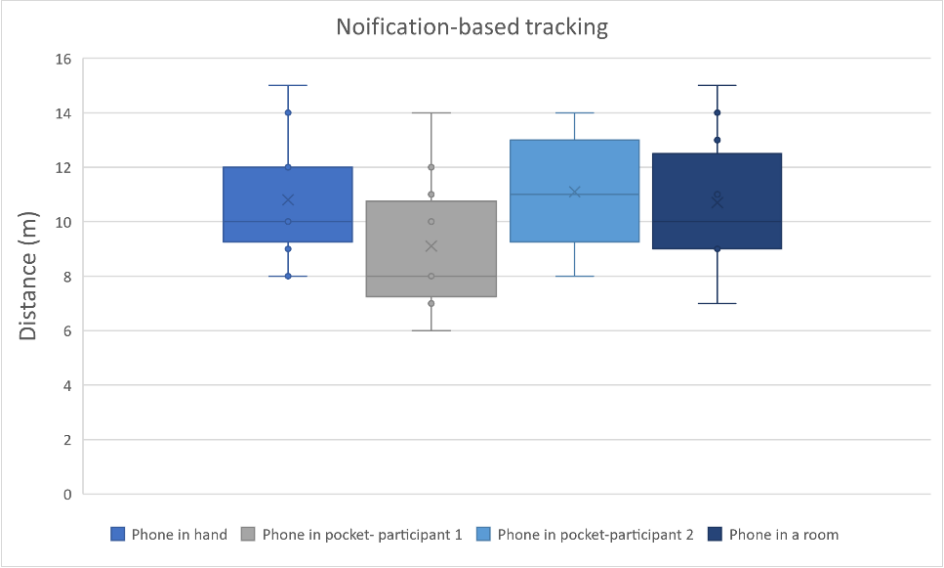

Figure 6-3: Box-whisker plot showing the variance between each case.

Given the small sample size of the data, a one-sample t-test analysis was conducted to see the repeatability of the observed data with a hypothesis of accurate tracking at 10 meters at 90% confidence level [9m – 11m].

The findings were tabulated as shown in Table 6-3.

Table 6-3: One-sample t test results for horizontal direction test.

t-Test: One-sample	
	Distance
Mean	10,775
Variance	5,255769231
Observations	40
Hypothesized Mean	10
df	39
t Stat	2,138028815
P(T<=t) one-tail	0,019418541
t Critical one-tail	1,684875122
P(T<=t) two-tail	0,038837082
t Critical two-tail	2,02269092

The results ($p<0.04$) of the two-tail test show a great variance of the sample mean (10.8 m) from the hypothesized mean (10 m) at 10% significance level. The sample size does not provide enough evidence to support notification alerts repeatability at 10 meters. However, the underlying distribution shows consistent alerts around 8-12 meters, and therefore reducing early triggers (less than 8 metres) that could cause notification fatigue, and late triggers (more than 12 meters) that could put patient at risk of forgetting the EAI.

6.1.2 Vertical Distance

This test focused on measuring the distance at which notification trigger when a user climbed up a staircase in an indoor setting as shown in Figure 6-4. The test was conducted at Impulse Biomedical offices making use of the office staircase, and outside staircase. Similarly, a PIH and PIP test were conducted, and results were recorded.

Figure 6-4: Vertical distance indoor (office) set-up.

The test was repeated ten times under two conditions. During the entire test, the EAI was placed at the bottom and the user climbed up the stairs until a notification reminder was triggered. The height of the staircase was measured to be 3 meters above the ground, and the reminder notification triggered at the top of the staircase with both the PIH and PIP cases. All the observed notification reminders for this test were 3 meters.

It was suspected the material (steel) of the indoor staircase could have had an effect of the signal causing interference. The test was repeated with concrete staircase as shown in Figure 6-5. Each floor is made up of three sections that were approximated to vertical 3 meters based on the step height and width.

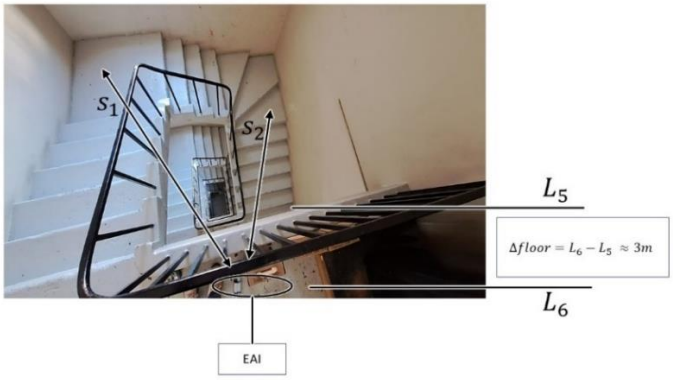

Figure 6-5: Experimental set-up for vertical distance using outside staircase.

Unlike the previous vertical direction test, the starting position was floor 6, and the user climbed down the stair until the notification was triggered. After a several trials, the results were recorded as shown in Table 6-4.

Table 6-4: Notification alert results for in hand test in a vertical direction.

Trial	***Phone in hand***		***Phone in pocket***	
	Distance (m)	$\Delta floor$	Distance (m)	$\Delta floor$
1	5.1	1	4.5	1
2	6.1	2	1.6	1
3	1.5	0	3.1	0
4	6.1	2	1	0
5	2	0	4.5	0
6	3.1	1	1	0
7	5.1	1	2.1	0
8	9.2	3	2.1	0
9	5.1	1	10.4	4
10	2	0	10.9	4
Average	**4.5**	**1.1**	**4.1**	**1**
STDV	**2.2**	**0.9**	**3.4**	**1.5**

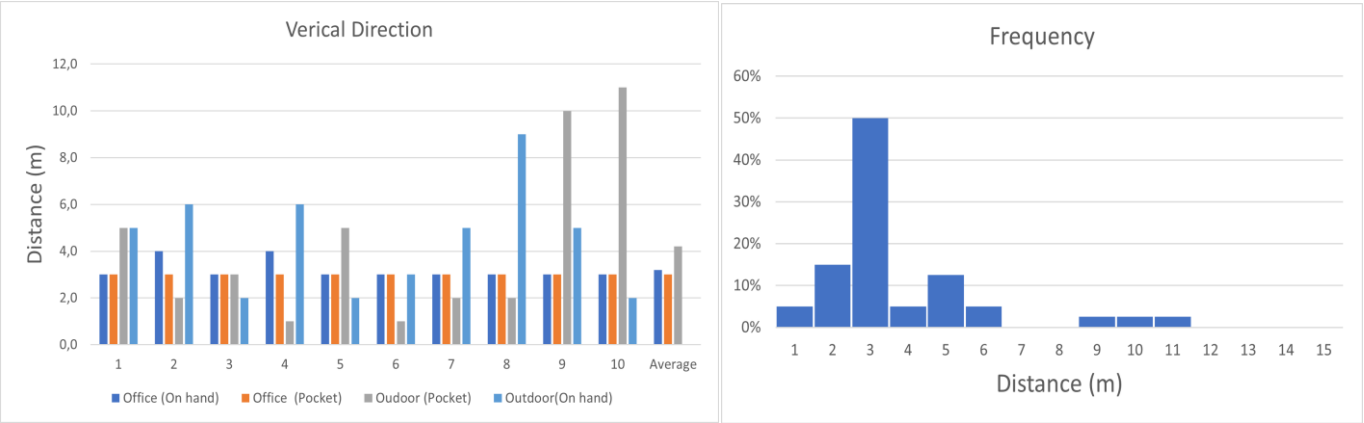

Figure 6-6:Frequency distribution for overall vertical distance tracking.

The results for the vertical direction consistently indicated alert triggers with each floor change. The trigger distance was significantly lower than ten meters. The trials were plotted on a frequency graph and depicted a normal distribution centred around 3-4 meters. Two outliers at 9 and 10 meters were concluded using the upper bound formula = Q3 + 1.5*IQR = 7.4 when considering all 40 vertical tests.

88% of reminders were activated when the user moved a floor up or down in a building. Only 12% of reminders were triggered at more than two floors away from the EAI. A spread analysis, shown in Figure 6-7, focusing on the outdoor staircase revealed the following observations:

- **Centre and Spread:**

Minimal dispersity was observed in the indoor vertical test for when the PIH condition. It can be seen from Figure 6-7 that the mean and median are almost aligned at 4.5 meters. However, for PIP there is a great dispersity.

- **Outliers:**

In both cases, PIH and PIP, outliers were observed that skewed the data.

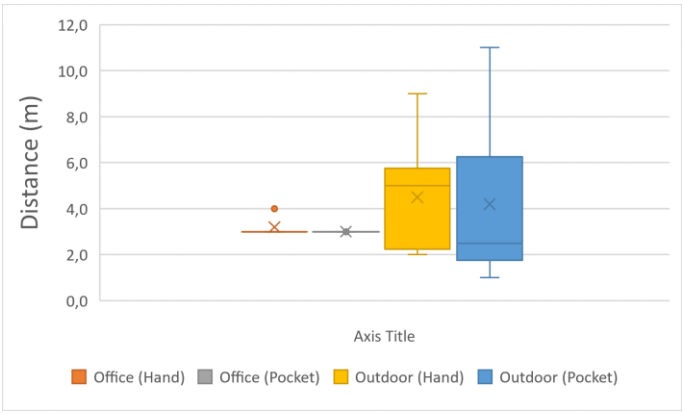

Figure 6-7:Box-whisker plot showing the variance between each case (vertical distance).

The test conducted outside the office showed significantly different behaviour from that of the indoor tracking. Table 6-5 summarises the analysis of the vertical distance triggers. A mean distance of 3,7 meters (p<0,04) was observed.

Table 6-5: One-way t test results for vertical direction test.

t-Test: One-sample	
	Distance
Mean	3,725
Variance	4,666025641
Observations	40
Hypothesized mean	3
df	39
t Stat	2,122728455
P(T<=t) one-tail	0,020089447
t Critical one-tail	1,684875122
P(T<=t) two-tail	0,040178893
t Critical two-tail	2,02269092

There are few factors contributing to this observation including signal loss over thick floors, and the BLE antenna design limitations. When the BLE antenna design was investigated further, it was discovered that the radiation pattern for the NINA-B306 Module Bluetooth® Low Energy 5.0 Module is not symmetrical in all directions. Horizontal direction gains were more dominant than the vertical direction. Likewise with the phone BLE antennas, signal strength was more dominant in one direction than the other.

A spherical analysis of the NINA-B306 adopted from a datasheet is shown in Figure 6-8.

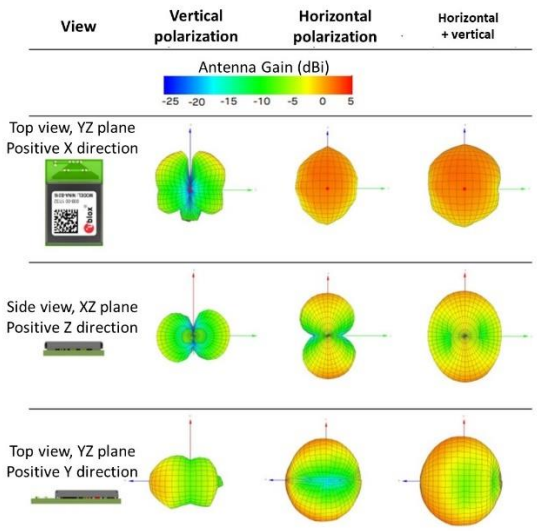

Figure 6-8: NINA-B306 spherical analysis for antenna gain (u-blox, 2023).

The red areas show a signal gain of 5 dB, the maximum, and the blue regions show the weakest gain of -25 dB. The orientation of the EAI w.r.t the phone when it was either below or above it could have been in a direction of slow signal gain, and therefore triggering at an average of 3.5 meters.

6.1.3 Notification priority

This test aimed to observe if the priority nature of the notification can be overridden by user setting that can potentially block the reminder notifications.

The mobile application was set into “Do not disturb” mode and the user were allowed to walk over the 10-meter radius in both horizontal and vertical direction. The results showed that notifications of “high importance” and “high priority” override the “do not disturb” feature. The user was able to receive the notifications as shown in Figure 6-9.

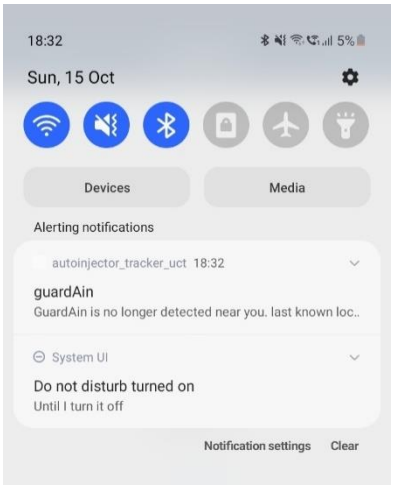

Figure 6-9: Notification bar at "do-not-disturb" mode.

The ringer profile however was not overridden by the priority nature of the notifications. It was observed that the mobile application only follows the global setting of the ringer profile. This could cause potential risk for users that do not check their devices regularly and have the silent mode activated.

6.2 Emergency Alert Test

The purpose of this test was to detect an emergency and alert EMS and patient emergency contacts with accurate information about the patient. This section explores the validation tests about the accuracy of the location pin, the time it takes for an SMS to be sent to a list of emergency contacts, under different conditions.

- **Emergency Trigger Alerts:** The areas of interests were school/workplace environment, shopping/restaurant, and mountainous regions as shown in Figure 6-10 with the red pins.

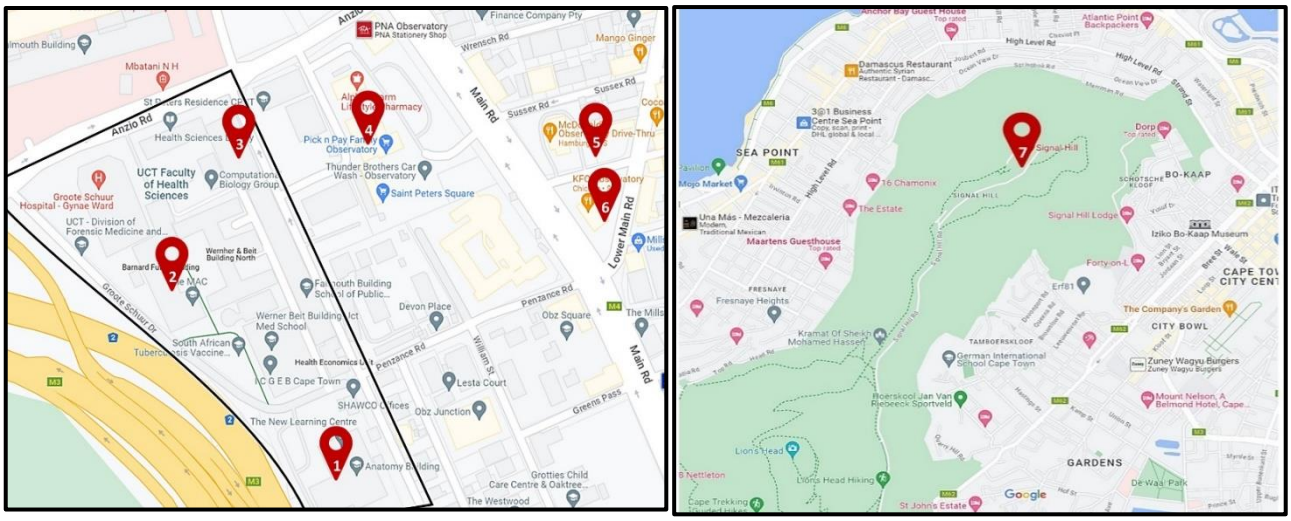

Figure 6-10: Geographical location used for testing the emergency alert system.

Two emergency contacts were added on the mobile application, and only one contact could be contacted at a time. At each location, the device was triggered and left the cap off for more than 30 seconds to trigger the SMS and phone call. The location detected was compared to the actual location using the Google maps application from a Samsung A53 phone. The time from the trigger to the time the message was received by emergency contacts was recorded.

This process was repeated twice at eight different locations. The results are summarised in Table 6-6. It can be observed in the last column that the distance from the Google pin location and the detected location was within a few meters off. The maximum error on the sample data recorded in a well-defined urban region was 49 meters, and the lowest was 7 meters. The average location error was 24 meters. The tracker could point the EMS to the exact location of the patient, given that the patient does not change locations. The tracker was successfully able to detect different buildings within the FHS campus and detect open areas, Signal Hill, region where a few landmarks were available with minimum errors.

- **Eligibility to be an emergency alert device**

According to the emergency alert guideline by US Homeland security, an emergency alert system could either be audible or visual alarms. Audios are mostly used to address to a large group of people, assisted by visual alarms if the noise levels of the population are high. GuardAin contains an audio alarm and a visual alarm.

- An automated audio message stating the patient is experiencing a severe reaction and guiding what a potential bystander should do to assist the person in an emergency.
- The LED flashes when the cap is removed from the EAI at the emergency alert frequency: 0.5 seconds ON and 0.5 seconds OFF.

- **Device Classification**
  - **Primary Purpose:** GuardAin tracks the location of an epinephrine autoinjector using BLE to ensure it is available when needed for emergency treatment of anaphylaxis.
  - **Classification:** The device can be classified as a Class I device under FDA as it designed to assist, and should not be relied to it sorely, to locate the EAI. A reminder system poses non-significant risk to the patient since it is not in direct contact with or controls the mechanism that provide an invasive access with the patient. However, the software application contains patient information that can be used to treat a patient and can be classified separately.

6.2.1 Emergency Phone call

When the automated emergency voice finished playing, and an SMS has been sent to emergency contact, the automatic call API is triggered. A few screenshots showing the phone call received by an emergency contact with the patient location shown in Figure 6-11.

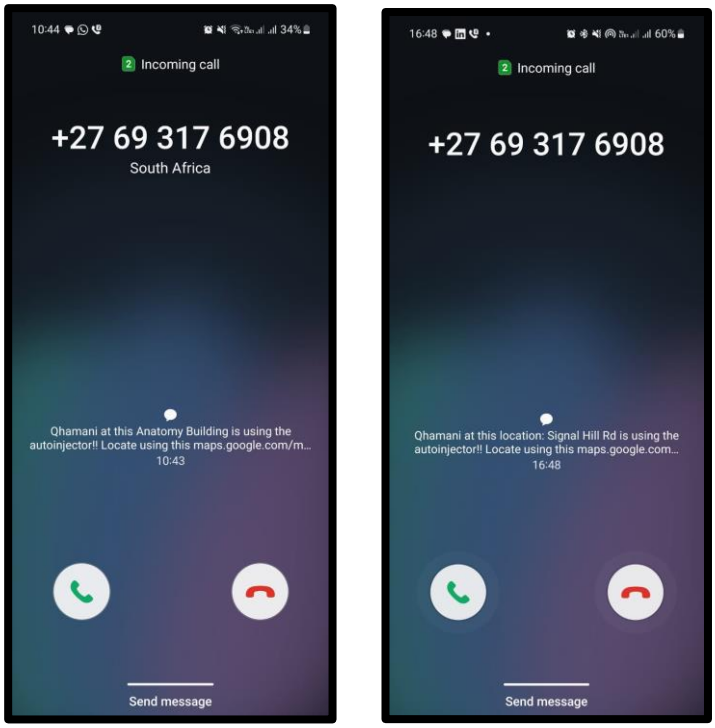

Figure 6-11: An automatic phone call received with an emergency SMS.

Table 6-6: Location tracking result at different location in Cape Town, Western Cape.

Landmark Name	Detected Latitude	Detected Longitude	Detected Location name	Google Maps Location (Lat, Long)	Error (Lat, Long)	Distance (m) error
1. Anatomy Building (FSH)	-33.944466	18.466350	• Anatomy Building (FSH)	(-33.9441307669292, 18.466467110472927)	(0.00037, 0.00020)	20
2. Barnard Fuller Building	-33.942954	18.465066	• Barnard Fuller Building	(-33.94285560154714, 18.46503605670043)	(0.00010, -0.00003)	11
3. Chris Barnard Heart Institute	-33.942459	18.465663	• 7 Anzio Rd	(-33.94202017013074, 18.46567637344814)	(0.00044, 0.00001)	49
4. Pick n Pack Observatory grocery store	-33.942078	18.467045	• 453 Main Rd	(-33.94199976050027, 18.466776437522373)	(0.00008, -0.00027)	13
5. McDonalds Observatory	-33.942143 -33.9424434	18.468139 18.468264	• 477 Main Rd • 491 Main Rd	(-33.94191446099925, 18.468088335668696)	(0.00053, -0.00018)	7.0 42
6. KFC Observatory	-33.942477 -33.944177	18.468327 18.466366	• 6 Norfolk Rd • 2 Norfolk Rd	(-33.94236766061081, 18.468455868212292)	(0.00181, 0.00209)	9.0 12
7. Impulse Biomedical Woodstock	-33.9288287	18.436441	• 160 Sir Lowry Rd	(-33.92813423296626, 18.436481752866417)	(0.00069, 0,00004)	52
8. Signal Hill	-33.917333	18.404617	• Signal Hill Rd	(-33.91698442393443, 18.404614081701954)	(0.00035, 0.00000)	23

6.3 Overall system evaluation

GuardAin's overall system performance was compared to the existing trackers discussed in literature review and is shown in Table 6-7.

Table 6-7: Comparison between GuardAin and other tracking devices.

Device	Availability in SA	EMS connected	EAI integrated	Distance algorithm	Notification alert conditions
GuardAin	It is designed to integrate with SA EIA ZibiPen.	Connect with EMS using automatic phone call and SMS technology.	Integrates with the EAI from the safety cap, providing an option to interchange tracker with new EAI.	Detects 10 meter and 0 meters.	When distance is more than 10 meters. When Bluetooth connection is broken
Epi-Trak	N	N	N	N	Uses GPS to track a change in location name and compares with home location.
Epi-Reminder	N	N	Y	N	Makes use of Bluetooth connection state to track the proximity tag.
Veta Smart Case	N	Y	Y	N	Makes use of the Bluetooth connection state to track the smart case.
AnApphylaxis	N	Sends an alert to emergency contacts using SMS technology.	Y	No distance algorithm.	Only when Bluetooth connection is broken.

The South African EMS uses phone trained operators to triage patients when they dial 112. One way of integrating the EAI with EMS is to ensure the ECC operator is alerted about the incident. GuardAin automatically calls the EMS number when usage of EAI is detected. Additionally, an alert is sent over to the server to alert the subscribed EMS about the patient with anaphylaxis alert. In this way, the patient can also be aware of the necessary crucial step to visit ER for a possible relapse.

6.3.1 Solution feasibility

While the tracker provides good benefits, it has a few challenges.

- **Benefits:**
    - The tracker uses Bluetooth, a widely available technology for many smartphones.

- Reliable short-range communication between EAI and smartphone results in a guaranteed reminder when the user is not detected near the EAI.
- A potential increase in the number of EAI carrying adherence through separation reminders.
- The tracker provides location to EMS; an easy and accurate form of locating patients when they are experiencing anaphylaxis.
- A more accessible learning resources to enforce proper anaphylaxis management strategies.
- It can be integrated with wearable devices like smart watches, which a patient can use to track the EAI.
- The choice of placement of the tracker within the safety cap makes it favourable to be interchanged to a different ZibiPen EAI when it is expired or used.

- **Challenges:**
  - Bluetooth does not provide a highly accurate distance approximation, due to surrounding interference. This could lead to potential notification fatigue for false ten-meter distance detection.
  - Additionally, the assumption of owning a phone poses a challenge to patients who do not own a smartphone like children.
  - Lack of knowledge about anaphylaxis may result from ECC to under triage patients showing symptoms of commonly known allergies and delayed response time.
  - Lack of good EMS system in SA could hinder the full implementation of the solution. This means the server integration would have to meet each private institution's ICT infrastructure differently and not integrate with the public sector.
  - There is no standardised digital portal that links patients to health institutions. Only telephonic communication would be utilised; however, the solution could still be ineffective for public healthcare where EMS still have long response times.

7. Chapter 7: Discussion and Conclusion

This study aimed at addressing the need for a better anaphylaxis management plan by focusing on the two clinical issues. Firstly, a reminder system for patients owning an EAI to alert them when they are not near the life-saving device. Secondly, to facilitate fast response and locating of a patient by EMS and other emergency contacts by sharing patients whereabouts.

7.1 OBJ 1: Design and develop a mobile based tracker to alert patients always to carry their EAI.

The research project focused on designing a smartphone tracker to send notifications to patients, reminding them to always carry their epinephrine autoinjector. GuardAin showed good repeatability for detecting distances 10 meters from the EAI with a p-value < 0.02 in the horizontal direction.

The horizontal direction hand and pocket test produced a mean notification alert distance of 10.6 meters with a standard deviation of 2.2 meters. The vertical direction test produced a much lower notification alert distance of 3.3 meters, equivalent to moving from one floor level to another, with standard deviation of 1.4 meters. These results were accepted as sending notification alert every floor change would be more beneficial to a user compared to two floor changes or more. There was no significant performance variation between a hand and pocket test for both horizontal and vertical tracking evaluated independently.

The notifications were developed to gain user attention by ensuring they do not disappear unless the user switches off the notification. However, this can be overridden by user settings if they chose not to activate silence mode notifications.

Using GuardAin's tracking algorithm, it was shown that notification reminders can be triggered when a user exceeds ten meters in the horizontal distance, and at three meters in the vertical direction and therefore reminding the patient always carry the EAI.

7.2 OBJ 2: Integrate the tracker with Impulse Biomedical's EAI ZibiPen to detect an emergency usage and alert EMS.

The tracker was designed successfully for the ZibiPen, with no alteration of the EAI mechanism and potential risk to the medication and patient. This was achieved by using passive components inserted in the safety cap.

GuardAin has shown accuracy in detecting geographical locations within a 50-meter radius to the true location. EMS alerts were achieved via automatic phone dials to an emergency number, and

SMS alert notification, containing the patient's location, to a customisable emergency contact list. Hence contributing towards rapidly locating and attending to a patient experiencing anaphylaxis.

7.3 Objective 3: Evaluate the smart device guided by medical software and hardware standards and evaluate the feasibility in SA context.

One of the major concerns when introducing an mHealth application is securing sensitive personal information. Security concerns of this solution may include:

- Access to the platform by unauthorised users.
- Risk of exposing patient health data to third parties other than authorised health professionals.

GuardAin is a restrictive platform that only allows user with EAI unique ID to use the application, and therefore restricting only the access of data to only authorised users. Sensitive information including patient health data is stored on a server that can only be accessed by medical personnel only when a detection of an emergency has been sent over the server. Only the trigger history can only be viewed by patient from the application. Data transmitted via Bluetooth is restricted only to non-personal information such as distance algorithm, and emergency trigger signals. Therefore, no sensitive information is transmitted wirelessly between the EAI to the phone.

By understanding the ICT infrastructure in SA, GuardAin was developed to integrate to existing communication methods using automatic, phone calls and SMSs without the need to create a new EMS system. Additionally, GuardAin was found to be including more clinical benefits when compared with other existing devices and therefore validated the completion of the identified gap in literature.

7.4 Research Gap and Limitation

The gaps and limitations of this research are listed below. Considering these cases would have improved the prototype, but because of time constraints and the project scope, they were not explored fully.

- The end users of the tracker were not surveyed to develop a refined prototype.
- The tracking functionality was only tested on one Android mobile phone that performed well; however, this does not guarantee the same performance on other smartphone architecture, and further investigation is required.

- Although the tracker's purpose is to provide prompt response to the patient by EMS, the system does not account for or control the South African EMS response time when an anaphylactic patient is triaged.
- The tracking of the EAI assumed that the patient will always have their smartphone on hand with them.
- The location tracker was only tested in the Cape Town, urban region, and no rural settings tests were conducted to understand the GPS performance in those regions.
- The performance metric of the reminder system was based on the 80 test trials collected in the daytime on a sunny day.
- The hardware component of the tracker was designed specifically for ZibiPen EAI.

7.5 Possible Future Work

Future-work on the reminder system for EAI from this research includes:

- Design recommendations
  - Use of wearable device to track the EAI without the need for a smartphone to overcome challenges including the need always to have a smartphone.
  - Build a custom board to optimize battery life and use small batteries for a long-term study with subjects.
- Validation recommending
  - Perform usability testing of the device on anaphylaxis patient or EAI user.
  - Perform the tracking validation tests on a bigger scale to get a better long-term behaviour.
  - Test the location tracker in rural areas where geographical landmarks such as restaurants and shopping centres are less prominent compared to urban areas.
  - Investigate the performance of the tracking algorithm for at least ten different, in specifications and advancement, Android phone models.

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Appendices

Appendix A Anaphylaxis Management

A personalized emergency medical management plan for anaphylaxis, adopted from Australian Society of clinical immunology and Allergy.

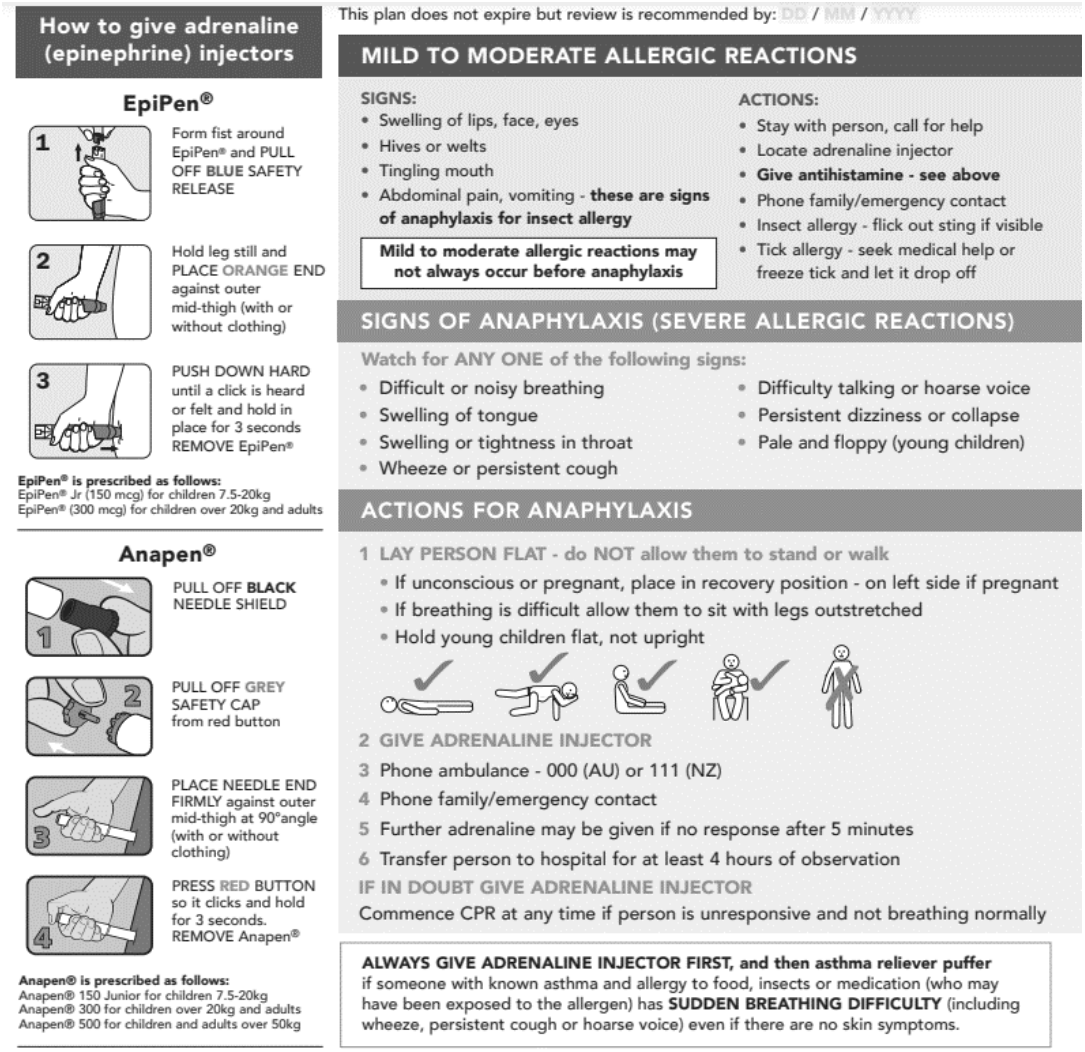
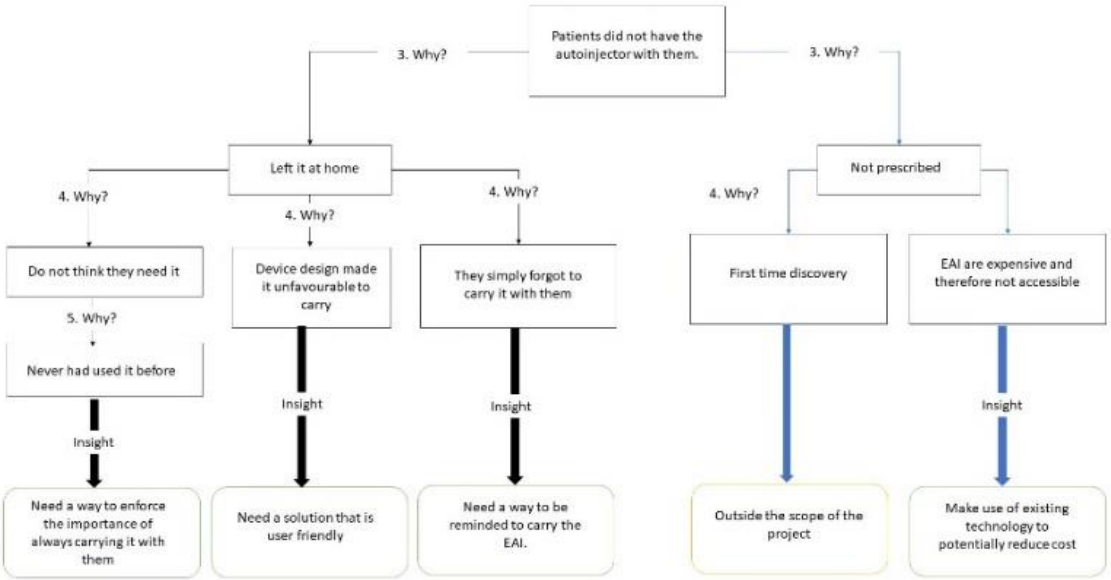


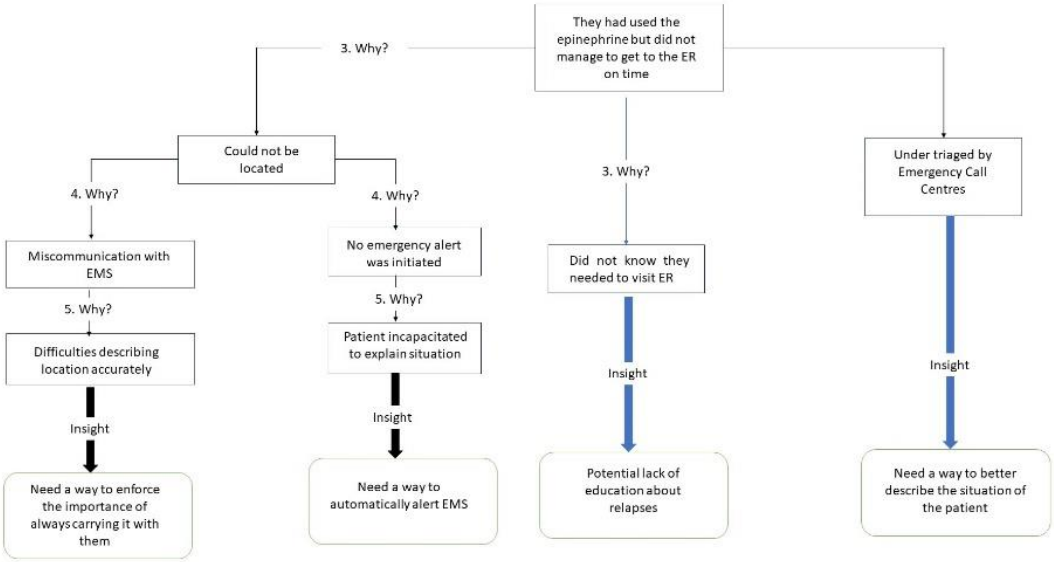
Figure A-1: Generalised anaphylaxis emergency action plan for patients with prescribed EAIs (ASCIA, 2023).

Appendix B The Five Whys Framework

The framework following the five whys to determine the root need. A series of "why" questions answered by literature to understand why EAI carrying adherence is extremely low.

	Five Questions	Response
1	Why is there a high number of anaphylaxis hospitalisation and death incidents?	a) EAI carrying compliance is rated very low.
2	Why is the carrying compliance very low.	a) Patients did not have the autoinjector with them. b) They had used the epinephrine but needed emergency medical backup. c) They were unsure on whether it was okay to use it. d) The epinephrine had expired and did not think it was going to be effective.





Appendix C Project Software and codes

The source codes for the system can be obtained in the following repository.

Mobile application source code

- **Models:** https://github.com/Qhamani/uct_autoinjector_app/tree/master/lib/models
- **Screens:** https://github.com/Qhamani/uct_autoinjector_app/tree/master/lib/screens
- **Services:** https://github.com/Qhamani/uct_autoinjector_app/tree/master/lib/services
- **Widgets:** https://github.com/Qhamani/uct_autoinjector_app/tree/master/lib/widgets

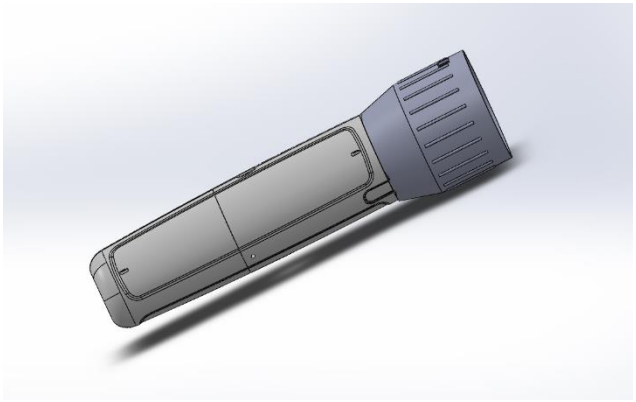
Arduino source code:

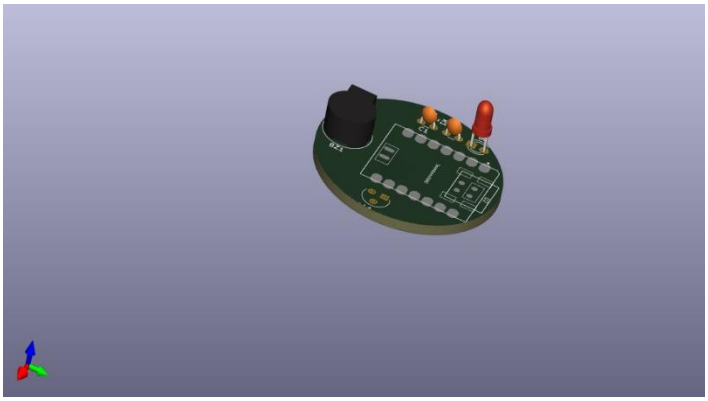
- https://uctcloud-my.sharepoint.com/:f:/r/personal/mqnqha001_myuct_ac_za/Documents/Masters_Biomedical%20Eng/THESIS/tracker_Code?csf=1&web=1&e=M7Ah09

Appendix D Design Iterations

- **Iteration one**

The first CAD iteration made use of the Bluno Beetle module.

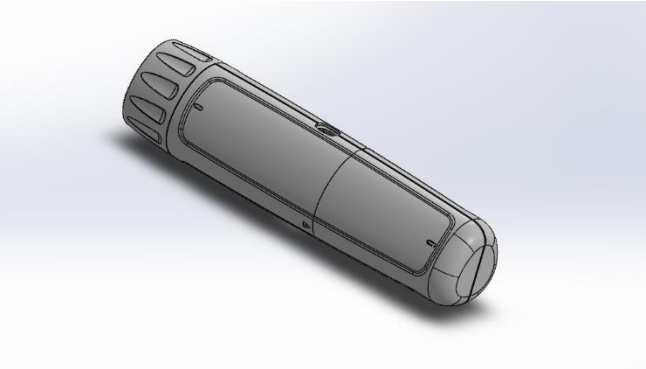


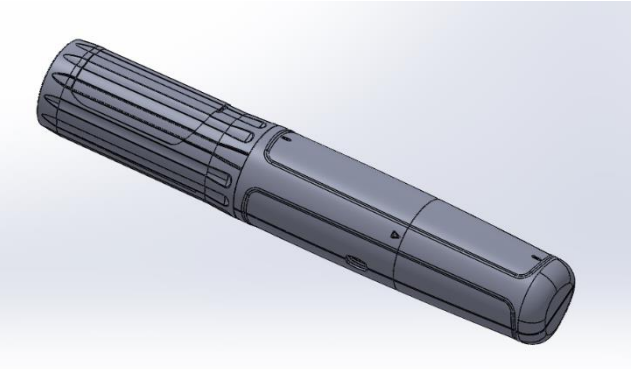


- **Iteration two**

Appendix E ZibiPen CAD

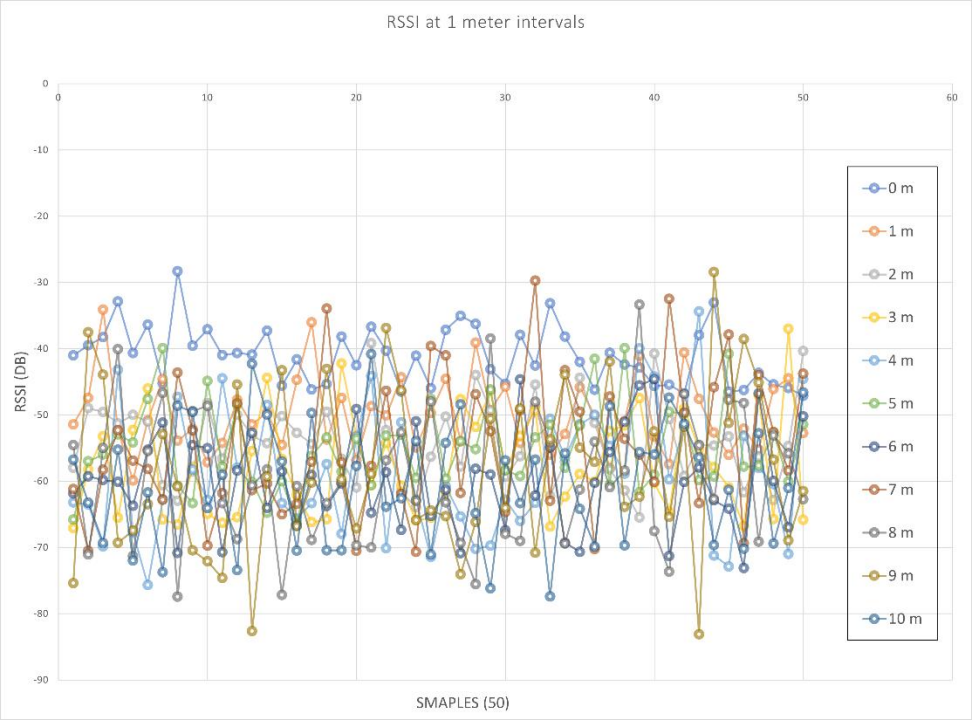
The CAD image of the ZibiPen before incorporating the smart tracker and after smart tracker.





Appendix F Notification Reminder

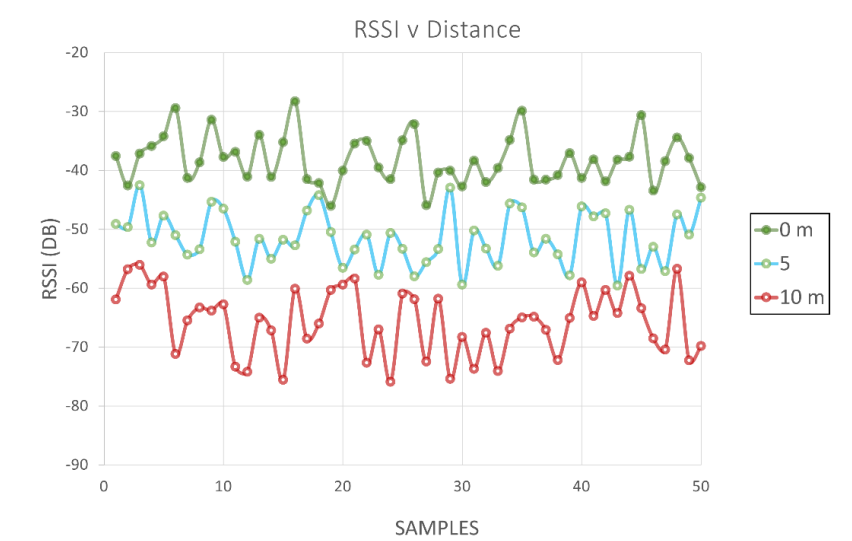
Raw data for signal strengths based on moving average and mode algorithm.



Distance Estimator:

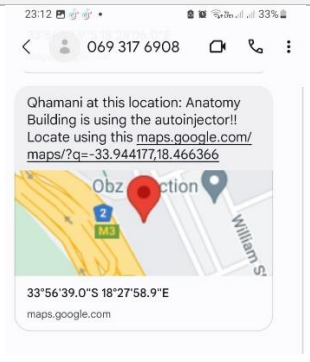
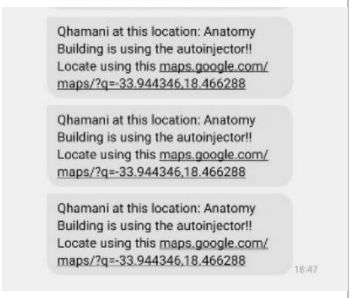
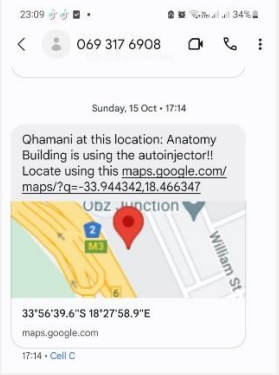
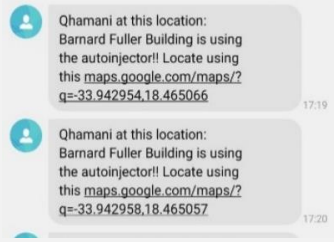
This test involves using the signal strength to locate the EAI. Initially all one-meter distances between 0-10 m were estimated. Because of a huge overlap between the signal strength detected at

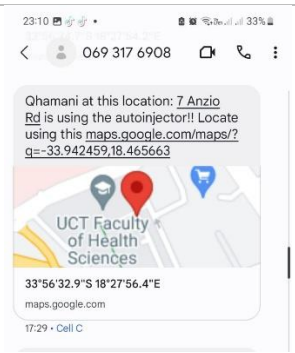
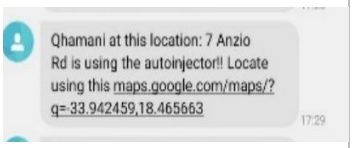
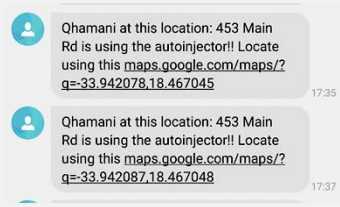
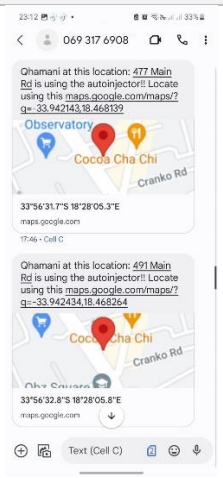
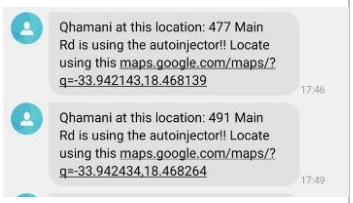
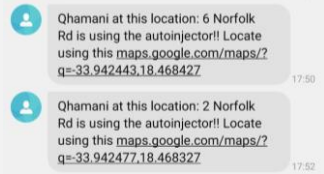
each interval, estimated distances contained huge errors. A more refined approach involved locating the device using sections, tracking only within a five-meter radius and over the five meter-radius.

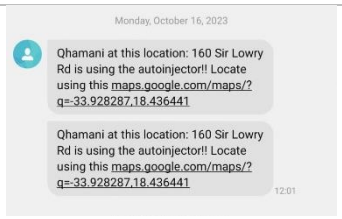
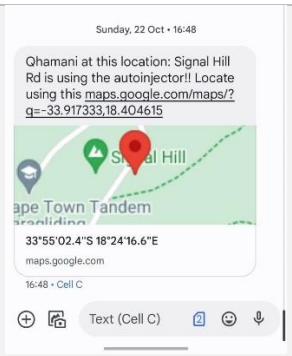
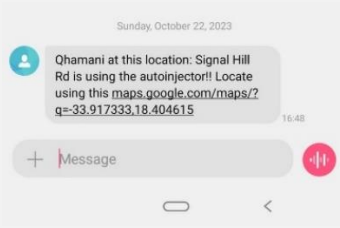


Appendix G Trigger Alert

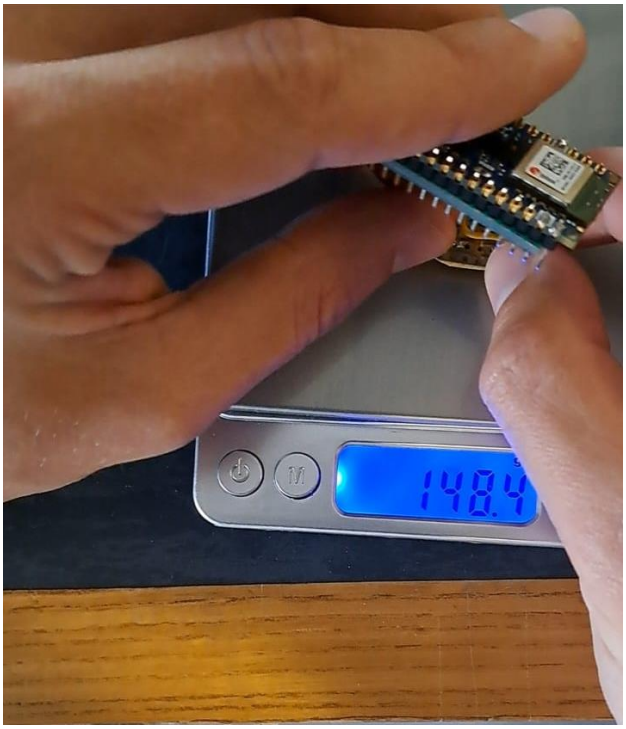
SMS screenshot for emergency alert to two emergency contacts.

Location Name	SMS evidence		Location Picture
	Emergency Contact 1	Emergency Contact 2	
Anatomy Building			
Barnard Fuller Building			

Chris Barnard Heart Institute			
Pick n Pay Observatory			
McDonalds Observatory			
KFC Observatory			

Impulse Biomedical			
Signal Hill			

- **Bench Testing of the tactile button**



The force was calculated as follow:

$$f = weight = mg = 0.148 * 9.81$$

$$f = 1.5\ N$$