

The cost and cost-effectiveness of a text-messaging based intervention to support management of hypertension in South Africa.

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Declaration

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Dedication

I dedicate this thesis to my family and friends.

Abstract

This project assessed the cost and cost-effectiveness of hypertension management in South Africa within the context of a text messaging-based intervention (StAR* study) conducted in an urban public-sector clinic in Cape Town. The StAR* study is a community randomized trial that investigated the effect of adherence support via short messaging service (SMS) on treatment adherence and patient outcomes for the management of hypertension at Vanguard CHC in Cape Town (Bobrow et al. 2016). Patients received behavioral text messages as reminders for them to collect and take their medication on time. The StAR* study, consisted of three arms that ran in parallel: participants in the control arm received unrelated messages; patients in the information-only arm received one-way information messages twice a week; and patients in the interactive arm received interactive SMS-texts at the same frequency as those in the information only arm (Bobrow et al. 2016). Patients in the interactive arm could respond to the messages and trigger a response from the healthcare provider. The text messaging based intervention was shown to improve hypertension outcomes over a 12-month period in hypertension patients by improving adherence and retention in care. The study showed, in the one-way intervention arm an improvement in adherence (measured by medication refill rates) and a small reduction in systolic blood pressure (2.2mm Hg reduction over 12months) (Bobrow et al. 2016).

In this study, we assessed the cost and cost effectiveness of the StAR* intervention under routine care management at Vanguard CHC. We also assessed the cost of hypertension management from the health system perspective and the cost of accessing hypertension care from the patient perspective. A combination of the ingredients approach and step-down costing was used to cost hypertension care from a health system perspective while a questionnaire was administered to 250 patients to estimate patient costs. The primary outcomes were the average cost of hypertension care and the incremental cost of the text message-based adherence intervention (StAR* intervention), compared to usual care, per millimetre of mercury (mmHg) reduction in systolic blood pressure.

Results of the study show that the average health system cost for hypertension management is R262 per visit and the patient cost of accessing hypertension care is R172 per visit. The text messaging based intervention was found to have low implementation costs in this pilot phase. The monthly incremental cost of the text messaging based intervention cost

was R4 per person. The incremental cost-effectiveness ratio of the intervention was R22 per mm Hg reduction.

This study provides the first contemporary assessment of hypertension management costs and the cost-effectiveness of mobile-based hypertension adherence support in South Africa. Future work will seek to estimate the long-term cost-effectiveness of this intervention and the cost of scaling it to the provincial and national levels.

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List of abbreviations

DMC	Direct Medial Costs
DNMC	Direct Non-Medical Costs
EE	Economic Evaluation
CEA	Cost Effectiveness Analysis
CMA	Cost Minimisation Analysis
CUA	Cost Utility Analysis
CBA	Cost Benefit Analysis
HCA	Human Capital Approach
WTP	Willingness to Pay
MHealth	Mobile Health
Vanguard CHC	Vanguard Community Health Centre

Part A: Protocol

1 Background

Hypertension is the most common reason why South Africans visit health-care facilities (Eksteen, 2015; Mash et al., 2012). Many people are not aware that they have hypertension and this has led to the condition being regarded as a silent killer (Cappuccio & Capewell, 2015). The overall hypertension prevalence rate in South Africa rose from 23.9% in 2001 to 40% in 2010 among adults aged over 25 years (Day et al., 2014; Steyn et al., 1999). On its own, hypertension is the most common risk factor for cardiovascular diseases (CVDs) in South Africa (Eksteen, 2015; Day et al., 2014). Hypertension and its sequelae (i.e. CVDs) are associated with high costs for the health sector as well as loss of human capital owing to morbidity and premature mortality. The management of hypertension is expensive, and large investments are required to maintain the recommended blood-pressure level among affected individuals (Alcocer & Cueto, 2008).

The effectiveness of hypertension management depends on patients taking their medication consistently, which usually requires taking tablets once to three times daily for the rest of their lives. Studies show that improving medication adherence increases the effectiveness of treatment and leads to better patient outcomes (Hamine et al., 2015; Kiselev et al., 2012). Improving adherence may also save costs by averting the development of CVDs in patients with hypertension. To monitor adherence and improve patient outcomes, mobile and wireless technologies (commonly abbreviated as mHealth) such as mobile phones are increasingly being used. Most studies to date examining the effectiveness of mHealth for a wide range of conditions have been carried out in high-income countries and have shown the positive effect on adherence of sending short message service (SMS) texts to patients as a reminder for them to take their medication on time (Anglada-Martinez et al., 2015).

1.1 Problem Statement

There is currently no research on the cost and cost-effectiveness of mHealth interventions for the management of hypertension in South Africa. This research is needed on the one hand to assess the feasibility and affordability of implementing these interventions, and on the other hand to compare mHealth interventions with alternative uses of resources through cost-effectiveness studies. An example of a local study on mHealth interventions is the SMS-Text Adherence Support study (StAR* study), which this cost-effectiveness analysis forms part of. The StAR* study is described below.

1.2 The SMS-Text Adherence Support study (StAR* study)

In Cape Town, a community randomised trial (an SMS-text adherence support study), was conducted recently at Vanguard Community Health Centre (Vanguard CHC) in Bonteheuwel, South Africa, investigating the effects of adherence support via SMS texts on treatment adherence and patient outcomes in the management of hypertension (Bobrow et al., 2016; Leon et al., 2015; Bobrow et al., 2014). The StAR* study, conducted between June 2012 and August 2014, consisted of three arms that ran parallel to each other: patients in the control group received non-intervention messages; patients in the information-only arm received one-way information messages twice a week; patients in the interactive arm received interactive SMS texts at the same frequency as those in the information-only arm (Bobrow et al., 2016; Leon et al., 2015; Bobrow et al., 2014). Patients in the interactive arm could respond to the messages and trigger a response from healthcare professionals. The study showed an improvement in adherence in terms of medicine collection and a small reduction in patients' systolic blood pressure (Bobrow et al., 2016).

1.3 Study Rationale

The aim of this research is to assess the cost of different approaches to hypertension management within the context of the StAR* study. Only a few studies have examined the cost and cost-effectiveness of mHealth interventions (Larsen-Cooper et al., 2015; de la Torre-Díez et al., 2015; Rodrigues et al., 2014; Zurovac et al., 2012; Parker et al., 2007), with no studies conducted to date on hypertension in South Africa. The information on cost and cost-effectiveness can be used to assess the feasibility, affordability and implications of

implementing mHealth in hypertension management in a cost-effectiveness analysis. Using the StAR* trial, this study will therefore estimate retrospectively the cost and cost-effectiveness of the mobile intervention in hypertension management from a societal perspective.

2 Mini Literature Review

2.1 Economic burden of Hypertension

Most studies on the cost of hypertension have been conducted in middle- and high-income countries, with very few studies done in low-income countries. Appendix A shows a summary of some of the cost studies on hypertension care conducted to date. Based on the findings of these studies, hypertension management is costly, making it both a health and an economic burden. The cost of hypertension care varied from country to country, with the United States of America (USA) having the highest cost of care while Nigeria had the lowest cost of care. In the USA, annual direct expenditure of hypertension is as high as US\$54.0 billion (Balu & Thomas, 2006). High-income countries have the highest unit cost of care, followed firstly by middle-income countries, and lastly by low-income countries. Looking at Appendix A, the cost of care is highest in Canada, the USA and China. Nigeria, being the low-income country among them, has the lowest unit cost of care at US\$9.6 per month (Ilesanmi, Ige & Adebisi, 2013).

Regardless of the unit cost of care, the economic impact of hypertension care is huge in all countries. The high cost of care for hypertension subjected many patients residing in the south-western part of China to catastrophic payments. 8.9% of the population experienced catastrophic payments and 4.1% of those households became impoverished after paying the hypertension costs (Le et al., 2012). In Nigeria, hypertension costs led to a 52.8% incidence of catastrophic payments among the study population (Ilesanmi, Ige & Adebisi, 2013). A catastrophic payment occurs when a household uses more than 10% of its total household income on healthcare (in this case, hypertension costs). Impoverishment refers to the percentage of the population that drops below the poverty line after paying healthcare costs (Mills et al., 2012). In 2010, the annual costs of hypertension care in Brazil were so high that

the annual costs represented 0.08% of the country's Gross Domestic Product (GDP) (Dib, Riera & Ferraz, 2010). Considering that the total healthcare expenditure as a percentage of GDP for Brazil was 7.6%, hypertension posed a very huge economic burden, as it accounted for merely 1.1% of that 7.6% in that year.

Looking at the drivers of hypertension costs, the major drivers in most cases are anti-hypertensive drugs (Nguyen et al., 2014; Le et al., 2012; Al-Efan, 2009), except when the study includes hospital care costs (Nguyen et al., 2014). In some instances, antihypertensive drugs were attributable to up to 80% of the total cost of hypertension care (Maetzel et al., 2004). Also, as the number of antihypertensive drugs per patient increases, so does the cost of care (Al-Efan, 2009). Different regions use different first-line antihypertensive drugs for hypertension management. In most studies, diuretics are the first-line treatment (Ganiyu & Suleiman, 2014; Costa, Juvenal Soares Dias da et al., 2002), while in other countries, like Bulgaria and Serbia, the first-line drugs were angiotensin-converting-enzyme inhibitors (ACE inhibitors), followed by treatment with calcium-channel blockers (Ivanova et al., 2009). With different first-line drugs, the cost of hypertension care would differ, since the costs of the individual drugs would be different. Diuretics and the use of no more than 2 antihypertensive drugs per person were found to be cost-effective (Ganiyu & Suleiman, 2014; Costa, Juvenal Soares Dias da et al., 2002). In addition, the presence of co-morbidities and the severity of hypertension affect the cost of hypertension care. Co-morbidities have a significant influence on the total cost of hypertension management (Maetzel et al., 2004). The cost of care for patients with advanced hypertension or for those with comorbid diseases is higher than for those with primary hypertension alone (Ilesanmi, Ige & Adebisi, 2013). A study by Nguyen et al. (2014) indicated that the total cost of hypertension care on its own in Vietnam was lower than the total cost of hypertension care among individuals with both hypertension and hyperlipidaemia.

2.2 Models of Care: mHealth

To improve adherence in hypertension and its outcomes, new models of care are being implemented. Among other strategies, such as nurse- and pharmacist-led interventions, mHealth technologies have recently been introduced for the management of hypertension. mHealth is defined as the use of mobile phones to facilitate communication in the health sector (Adibi, 2015). MHealth has been used in managing chronic diseases like asthma,

obesity, hypertension and diabetes (Nundy et al., 2012). MHealth is increasingly being used in the healthcare sector, owing to the rapid advancements in mobile technologies and the availability of mobile phones within the population (Leon, Schneider & Daviaud, 2012). With mHealth, practitioners can communicate with patients on a larger scale instantaneously (Carter, Bosworth & Green, 2012), and socioeconomic barriers that often reduce access to care are reduced (Leon, Schneider & Daviaud, 2012). For example, in South Africa, the majority of the population, from the poor to the rich, owns a mobile phone (Leon, Schneider & Daviaud, 2012), meaning that the majority of the population can be reached using mobile phones, irrespective of social status.

Randomised control trials have shown the benefits of the use of mHealth in diabetic patients with hypertension, in terms of controlling blood sugar and blood pressure (Fischer et al., 2012; Earle et al., 2010; Logan et al., 2007). Better blood-pressure control was also seen in patients making use of mHealth to monitor their hypertension (Logan et al., 2007). When people can see the changes in their blood-pressure readings over time, they are more likely to adhere to their medication in the future in order to achieve better outcomes (Logan et al., 2007). mHealth, unlike other models of care for hypertension, provides a platform for engaging with patients throughout the treatment process, while offering real-time responses (Logan et al., 2007). It also allows for active patient engagement between providers and patients, which encourages self-management, increases health awareness and makes patients more accountable for their actions (Fischer et al., 2012). Simple and less complicated mHealth interventions such as the use of SMS texts were found to be more favourable among individuals (Logan, 2013).

However, very few studies have been conducted on the cost and cost-effectiveness of mHealth in low- and middle-income countries, none of which were on hypertension or its associated NCDs (Larsen-Cooper et al., 2015; de la Torre-Díez et al., 2015; Rodrigues et al., 2014; Zurovac et al., 2012; Parker et al., 2007). There is a gap in the research when it comes to the cost and cost-effectiveness of mHealth interventions in the management of hypertension. In South Africa, there are no studies to date that have assessed the cost of hypertension management. This study aims to assess the cost and cost-effectiveness of a mobile-based intervention in hypertension management. Based on a few studies that assessed the costs of using mHealth interventions in other diseases, the cost of setting up mHealth interventions and their system-development contributes a larger proportion of the total cost than do their running costs (Zurovac et al., 2012). Also, because the StAR* study mobile

intervention included some donated resources (i.e. free development of the SMS database), knowing the economic cost of intervention is of great importance. Other studies have shown that mHealth may present high costs in small-scale settings, yet when used on a larger scale may be inexpensive (Zurovac et al., 2012). In the next section, we look at the different methods that were used to conduct economic evaluations in mHealth.

2.3 Methodological overview

To measure the effectiveness of new technologies such as mHealth, four types of economic evaluations are commonly used. These include cost-effectiveness analysis (CEA), cost-utility analysis (CUA), cost-benefit analysis (CBA) and cost minimisation (CMA) (Drummond et al. 2005). An economic evaluation is a systematic method used to compare two or more interventions in terms of their costs and consequences (Drummond et al. 2005, Acharya et al. 2011). A cost-benefit analysis is used when the outcome(s) of interest is measured in monetary terms such that the costs and outcomes are in the same units. In a cost-benefit analysis, outcomes are converted into monetary terms using the Human Capital Approach (HCA) or the willingness-to-pay approach. The HCA measures the opportunity cost of an individual based on his or her income, while the willingness-to-pay approach simply assesses the maximum amount that individuals are willing to pay for a certain intervention. The preferred intervention when using the HCA method is the one in which the intervention's benefits outweigh its costs.

A cost-effectiveness analysis is used when the outcome(s) of interest is measured in its natural units, i.e., cost per blood-pressure reduction (in mmHg) (Drummond et al., 2005). Incremental cost-effectiveness ratios (ICERs) are used to determine the preferred intervention, rather than the intervention with the lower ICER. A cost-utility analysis captures both the quantity and quality of outcomes. The quality of life is measured as either a quality-adjusted life year gained (QALY) or a disability-adjusted life year gained (DALY). The latter refers to the number of years lost because of illness, while the former refers to the quality of life years gained because of an intervention or program. In a cost minimisation, the interventions being compared both have the same effect in terms of outcomes, while their costs differ. The intervention with the lowest cost is used.

A cost analysis refers to the quantification and valuation of all the resources used in an intervention. CUA, CBA, CEA and CMA are considered full economic evaluations (Drummond). This study makes use of a cost analysis, which is considered a partial economic evaluation. However, because the other part of the study involves the comparison of the cost-analysis results with the outcomes of the StAR* study in their natural units, the study is referred to as a cost-effectiveness analysis. A full economic evaluation involves the comparison of both the inputs and the consequences of each intervention, whereas a cost analysis is the first part of an economic evaluation (Acharya et al., 2011). Unlike other economic evaluation methods, cost analysis does not involve the outcomes; hence, it is referred to as a partial economic analysis. Even though cost analysis is not considered a full economic-evaluation method, it is still considered an economic evaluation (Acharya et al., 2011).

2.4 Costing and costing perspectives

Assessing the cost of care in a disease-specific cost study is dependent on the costing methodology used, the type of study conducted and the perspective that is taken in the study. Appendix A shows a summary of the costing studies as well as their perspectives. Many of the studies were cross-sectional studies – cross-sectional in the sense that data analysis for a certain population or subgroup was done at a specific point in time. Different perspectives (patient, provider and societal) were taken to analyse the cost of care. The provider perspective is used by researchers when they are interested in the costs borne by the provider (Nguyen et al., 2014). Provider costs include both the direct and indirect costs of providing a service. The provider costs include drug costs, consultation fees, laboratory tests, health workers' salaries and so on (Drummond et al., 2005), and are usually captured through the assessments of patient files and cases (Nguyen et al., 2014; Ivanova et al., 2009). Some studies took the patient perspective, concentrating on the costs borne by the patients themselves (Ilesanmi, Ige & Adebisi, 2013; Maetzel et al., 2004). The common costs assessed included travel costs, consultation fees, admission fees, indirect costs and laboratory costs.

Though some studies use the same perspective (i.e. provider perspective), the choice of the costs considered differed across the studies. Some studies focused on all direct medical-

care costs, meaning that they considered both the direct medical-care costs and the direct non-medical-care costs associated with the disease (Le et al., 2012). An example of a direct medical-care cost is drug cost, while examples of indirect medical-care costs include administration and transport costs. Other studies focused only on the direct costs of drugs that were utilised by different patients (Ganiyu & Suleiman, 2014; Ivanova et al., 2009). This difference alone results in differences in the cost of care, even within the same region.

The type of costs considered in the studies is also a major factor contributing to the differences in costs of care. Some studies make use of financial costs (Ilesanmi, Ige & Adebisi, 2013), while other studies make use of economic costs. Financial costs refer to the actual costs of care paid for the actual use of certain resources (or accounting costs). Economic costs refer to the opportunity costs of each resource utilised: for instance, when conducting a costing study using economic costs, donated goods will have not a value of zero but rather their actual resource value had they not been donated (Drummond et al., 2005). Economic costs capture a more accurate value of the resources than financial costs (Creese & Parker, 1994). Inconsistencies in the inclusion of and estimation methods for indirect costs of care were also seen among the different papers. Indirect costs refer to the best forgone use of time and are measured as the loss of income to the individual or to the household (Drummond et al., 2005; Creese & Parker, 1994). From a provider perspective, these can be the average resource use per visit, while, from a patient perspective, they could refer to the opportunity cost of being at the facility (i.e. lost income or lost time). If costing studies use different methodologies, the costs of care measured will differ and, most importantly, the results will not be comparable.

Some costing studies are incomparable for many reasons. Based on the articles listed in Appendix A, the methodologies are not consistent. Some researchers make use of secondary data sets to draw up their costing data (Balu & Thomas, 2006), while others make use of study tools like questionnaires (Le et al., 2012; Al-Efan, 2009). Even the perspective taken differs with each study, with some deciding to use the patient perspective, some using the provider perspective and others using the societal perspective. Because there is no gold standard when it comes to doing a costing study, the costs measured will always differ and comparisons between studies will be difficult. The societal perspective is the most comprehensive way of doing a disease-specific study as it captures all the costs involved (Drummond et al., 2005). Looking at Appendix A, costing studies are also presented in different currencies and periods. The results are presented as a monthly cost, an annual cost

or, sometimes, as an incremental cost. This makes comparing the results among countries difficult, especially if the results are presented in different currencies. Regardless of all these issues, all costing studies on hypertension cost show that the cost of care is high.

Despite the high cost of care and various methodologies for costing, hypertension on its own is generally undermanaged, with a small percentage of the patients achieving the required blood pressures. For example, in a study by Ilesanmi et al., (2013), only 33.6% of the study population achieved the desired blood pressure, owing to non-persistence and non-adherence to medication. In South Africa, more than 50% of people who are on antihypertensive medication have uncontrolled hypertension (Carter, Bosworth & Green, 2012). Uncontrolled hypertension is defined by a blood-pressure measurement that is above 140/90 mmHg (Steyn et al., 2001). Many people with hypertension in South Africa have uncontrolled hypertension (Steyn et al., 1999).

3 Objectives

The overall objective of the study is to estimate the cost and cost-effectiveness of using a mobile-phone SMS system to improve adherence and health outcomes in hypertensive patients attending Vanguard Community Health Centre.

3.1 Specific Objectives

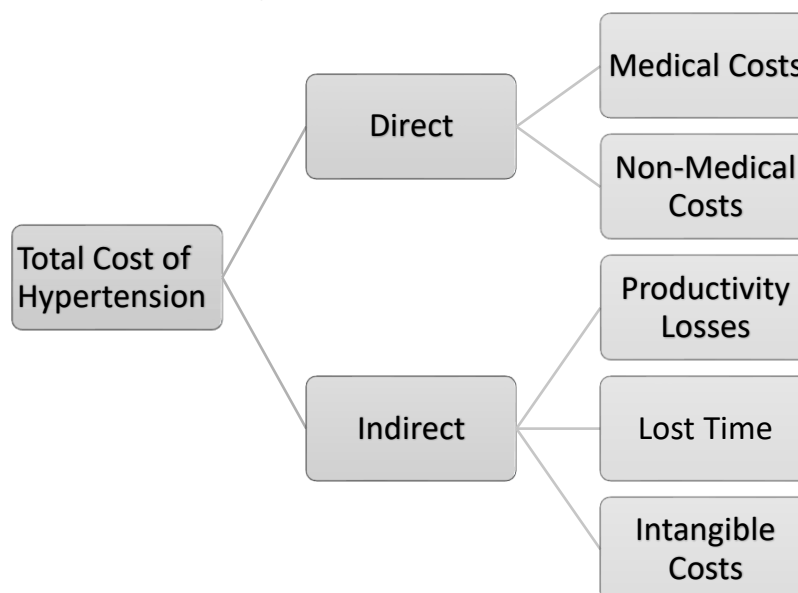
The specific objectives are to:

- estimate the cost of providing hypertension care from both the health service and the patient perspective (societal perspective).
- estimate the economic cost of the SMS-text intervention used in the StAR* trial under routine care.
- establish the cost effectiveness of the SMS-text intervention compared to that of the no-intervention status quo.

4 Conceptual Framework

In this study we will identify and measure all costs related to hypertension, i.e., (1) what does it cost to provide hypertension care (both in current practice and in SMS-text intervention), and (2) what is the cost and the economic burden to the patient of accessing and receiving hypertension care (in current practice)? Costs consist of both direct and indirect costs. Intangible costs such as the cost of suffering and pain will not be considered in this study owing to their complexity and the difficulty of measurement. Direct costs consist of direct medical costs (DMC) and direct non-medical costs (DNMC), of which both can be incurred by patients and providers. An example of a direct medical cost is drug cost; an example of a direct non-medical cost is transport cost. Indirect costs refer to the productivity loss incurred by individuals and households while seeking care (Weinstein et al., 1996). Loss in productivity because of absenteeism and loss of leisure time are examples of indirect costs. We will estimate both financial and economic costs. Financial costs refer to actual monetary expenditure on goods and services, while economic costs refer to the opportunity cost of the resources used (Creese & Parker, 1994). Using economic costs allows us to capture the value of donated resources as well as that of voluntary labour (Creese & Parker, 1994). Figure 1 shows the framework of the cost categories.

Figure 1: Framework of the Cost categories



Source: Adapted from Graden, S., (2003)

5 Methods

5.1 Study design

A retrospective cost analysis of hypertension care from the provider perspective will be conducted and will be complemented by a costing study from the patient perspective. Different methods will be used to cost hypertension care for each perspective (see Table 1). The ingredients approach (sometimes referred to as “bottom-up costing”) and step-down costing will be used to cost hypertension care from a provider perspective, as was done in other studies (Settumba et al., 2015; Hansen et al., 2000). A patient-exit survey, which involves the administration of a questionnaire to patients, will be conducted to estimate the cost of hypertension from the patient perspective. Both financial and economic costs will be estimated, since the SMS mobile-intervention programme within the trial was provided largely free of charge. All costs will be estimated in 2016 South African Rand (ZAR). The study sample for the patient perspective will mimic the characteristics of the StAR* trial population sample in terms of demographics. Finally, cost estimates from the cost analysis will be combined with the outcome results from the StAR* trial to establish the cost-effectiveness of the StAR* mobile-phone intervention.

5.2 Study setting

The study population includes hypertension patients at the Vanguard Community Health Centre (CHC), situated in Bonteheuwel, Cape Town, Western Cape. Vanguard CHC serves the people of Langa and Bonteheuwel by providing a range of health services. The clinic serves approximately 28,000 patients a month, while the clinic for chronic diseases serves on average 500 patients a week (Bobrow et al., 2014).

5.3 Sample size

The sample size is based on that of the StAR* trial population 1372. Using a margin of error of 5%, a confidence interval of 90% and a response distribution of 50%, the sample size (n) is calculated as follows:

$$\text{Sample size } (n) = \frac{Z^2 \times p \times (1 - p)}{d^2} \quad \text{Eq. 6.1}$$

Where: Z = Z value (e.g. 1.645 for 90% confidence level)

p = probability of non-response

d = margin of error

The sample size is equal to 227. Assuming a 10% non-response rate, the final sample will consist of 250 individuals.

5.4 Sampling

Given that the StAR* study is complete, we will assume that by using the same inclusion criteria and population, we will interview the same people that would otherwise have been involved in the StAR* trial. On the day of the interviewer's visit to Vanguard CHC, all hypertensive patients presenting to the health facility will be interviewed. If many patients are presenting, systematic sampling with an equal probability method will be applied using the appointment schedule. We will approach the healthcare staff at the beginning of the day on randomly selected days and ask for a list of the patients to be seen that day for hypertension (if available). We will approach the patients after their healthcare visit and invite them to complete the questionnaire. For those that collect their medication on separate sites using "adherence clubs", we will participate in some of the clubs' meetings and invite the patients there to complete the questionnaire. Individuals that are in a hurry and do not wish to complete the questionnaire will be asked if the interview can be conducted over the phone at their convenience. Interviews will be stopped once we reach our target sample-size of 250 patients. Careful consideration will be taken to match the demographics of the StAR* study by doing preliminary analysis of our data.

Patients will be interviewed who (1) meet the inclusion criteria and (2) provide written consent to participate in the study.

Inclusion criteria:

- Patients older than 21 years (as per the StAR* study);
- Patients providing written consent to participate in the study;
- Patients who have hypertension (identified using the ICD-10 code I10);
- Patients on antihypertensive medication or those about to start taking them;
- Patients with a blood-pressure measurement of <220/120 mmHg at enrolment;
- Patients that reside in Langa or Bonteheuwel.

Exclusion criteria:

- Patients who do not have hypertension;
- Patients who do not provide written consent;
- Patients who are pregnant, with a blood pressure of >175/105 mmHg and symptoms of hypertensive emergency (i.e., headache, chest pain, seizure, oedema, etcetera).

5.5 Assessment of costs from the perspective of the health provider.

We will estimate the total cost of hypertension for each intervention (current practice and SMS-based intervention) and the unit cost per outpatient visit to the CHC. Provider costs will include costs from the CHC. The total cost of hypertension from the provider perspective will be estimated using a combination of the ingredients approach and step-down costing. The ingredients approach will be used to estimate the direct medical costs of hypertension care at the CHC, while the step-down approach will be used to estimate the cost per outpatient visit. The latter approach includes only the non-medical recurrent and capital costs.

Ingredients Approach: To estimate the direct medical costs of care we will use the ingredients approach, whereby resource usage (the quantity of inputs used to provide the intervention) is multiplied by the resources' respective prices. Direct medical-care costs such as drugs, laboratory tests, diagnostic tests and consultation fees will be calculated using this method. We will work with local clinicians to develop a list of ingredients that represent a typical encounter for hypertension care. These ingredients will be checked against the medical records of participants in the StAR* trial.

Step-down Costing: This method will be employed to capture the non-medical costs used to deliver hypertension care. Like in other studies, step-down costing will be used to allocate the

costs of running the CHC to the final cost centres where direct provision of hypertension care is provided (Free et al., 2013; Drummond et al., 2005; Creese & Parker, 1994). Step-down costing will be performed, as described by Conteh and Walker (2004). The various departments at Vanguard CHC will be divided into final, intermediate and overhead cost centres (Hansen et al., 2000). Final cost centres refer to those centres that provide medical services directly to patients – in this study, the outpatient department. Intermediate departments provide support services to the final cost centres, such as diagnostic services or drugs, which are supported through the laboratory and pharmacy units, respectively. Overhead cost centres are the departments/units that provide general support services that are necessary to run the CHC (Afriandi et al., 2010; Weinstein et al., 1996; Creese & Parker, 1994) such as administration, cleaning, and maintenance. The costs of the support and overhead departments will be allocated to the final cost centre (outpatient department) in a stepwise fashion. The overhead departments are placed first in the step-down procedure, since they provide services to the whole CHC. Intermediate centres are placed second, since they do not provide services to the overhead centres. Final cost centres are placed last.

Once the cost centres have been identified, we will first assign recurrent and capital costs to the various cost centres directly, based on their actual resource usage (Hansen et al., 2000). For example, the salary cost of a nurse will be allocated to the outpatient department based on the proportion of time he/she spends in the outpatient department, the salary cost of administrative staff will be allocated to the administration cost centre, and so on. Once all recurrent and capital costs have been allocated to the various costs centres, the next step involves the allocation of overhead costs to the intermediate and final cost centres. In the third and final step, the costs of running the intermediate cost centres will be allocated to the final cost centre. Once all the costs have been allocated to the final cost centres, the total cost of the outpatient department will be divided by the total number of outpatient visits to get the unit cost per outpatient visit. The total cost of hypertension care per patient will then be obtained by adding the unit cost per outpatient visit to the average medical cost per person (obtained using the ingredients approach).

Recurrent costs are resources that have a useful lifespan of less than one year, while capital costs are resources with a useful lifespan of more than one year (Creese & Parker, 1994). Capital costs will be valued according to their replacement costs. To allow for depreciation and the opportunity cost of purchase, capital items will be annualised using a discount factor of 3% (Drummond et al., 2005). Discount rates of 0%, 5% and 10% will be used in the

sensitivity analysis. The estimated lifespan used for buildings, furniture and vehicles will be 30 years, 10 years and 5 years, respectively (Drummond et al., 2005; Creese & Parker, 1994).

Data collection: For the ingredients approach, data on direct medical costs and service utilisation will be obtained from medical records. We will review approximately 200 medical records and collect information on demographic characteristics, patient visits, attendance, blood-pressure tests and medication. In addition to the information collected from medical records, direct non-participatory observation will be done to understand the current patient-management process for hypertension (length of the patient-provider contact, types of services provided, etc.). Observations will be conducted for 30 patients. Structured interviews will be conducted with the CHC staff involved in the StAR* trial to collect information on the different activities related to hypertension care as well as on the length of time spent on these activities. Once the care pathway is established, we will list the ingredients and check them against the StAR* participants' medical records. Adjustments will be made to reflect how utilisation differs (in terms of ingredients consumption) between the intervention and usual-care participants.

The information for the step-down costing will be obtained from the most recent financial records (for recurrent expenditures). If personnel costs are not found in the financial records, a list of the staff who work in the departments of interest will be compiled and their salaries will be allocated according to their salary grades. An inventory list will be made (if one is not available) to capture capital items such as building, furniture and vehicles.

5.6 Assessment of costs from the perspective of the patient

Information on direct (medical and non-medical) and indirect costs of hypertension from the patient perspective will be collected using a patient-exit survey. The survey will collect the following information:

- Demographic variables (age, gender, race, education, marital status, etc.);
- Health-seeking behaviour (frequency of clinic visits per month);
- Information on care received (type of care received, duration, type of drugs, dosages, medication instructions, etc.);
- Direct medical and non-medical costs (transport costs, food, administration costs, drug costs, consultation costs, under-the-table costs);

- Socioeconomic status, indirect costs and impact of disease (education, income, coping strategies).

Direct costs consist of out-of-pocket expenditure on medical inputs (consultation, drugs and laboratory tests) and non-medical inputs such as food costs and costs for transportation to and from the health facility. Indirect costs refer to productivity losses incurred by the patient and by informal caregivers and will be estimated using the human-capital method, which consists of valuing the loss of income to patients and caregivers. Income will be measured by asking questions about monthly wages and income from various other sources (e.g. grants). The survey will be pre-tested through a pilot study prior to data collection.

Pilot study: A pilot study will be conducted at Vanguard CHC two weeks prior to the study. The pilot study will be done at the same centre with individuals who meet the inclusion criteria for the actual study, the reason for this being that we want to test whether the study tool measures the required information or not. Ten people will be used in the pilot study. Upon completion of the pilot study, we will also ask the participants whether the questions were simple and easy to answer. Possible responses and challenges to using the tool will be obtained after the pilot study and amendments will be made accordingly, to make the study tool maximally clearer to the study population.

An overview of the costing methods and data-collection tools is provided in Table 1.

Table 1: Summary of costing and data-collection methods

	Perspective			
	Provider		Patient	
Methods	Ingredients approach	Step-down costing	-	Human capital approach
Costs Included	Medical costs (e.g., drugs)	Capital and recurrent costs	Direct costs (e.g., drugs, diagnostic tests, transport and food)	Indirect costs (Productivity loss)
Data Sources	Medical records and direct observation	Facility records	Patient survey	Patient survey
Intermediary Outcome	Median medical cost per patient (a)	Median cost per outpatient visit (b).	Median out-of-pocket expenditure (c)	Median loss of income to the patient and household (d).
Final Outcome	(a)+(b) = Median cost of hypertension-care per outpatient visit		(b) + (d) = Median cost incurred by households per hypertension-care outpatient visit	
	Median cost per hypertension care outpatient visit			

Source: Adapted from Meheus et al. (2013)

5.7 Cost-effectiveness of SMS-based interventions

The study’s objective will be met by analyzing the collected data. Two outcomes will be used in the cost-effectiveness analysis: 1) the odds of adherence, and 2) the average reduction in blood pressure. Data on the patient outcomes will be obtained from the StAR*-trial investigators. The difference in costs and outcomes in the intervention versus in current practice will be presented as an incremental cost-effectiveness ratio (ICER).

$$ICER = \frac{Costs\ of\ StAR^* - Costs\ in\ status\ quo}{Outcome\ in\ StAR^* - Outcome\ in\ status\ quo} \quad q. 6.2$$

Adherence and blood-pressure reduction are the main outcomes of interest in the study. The units of analysis will thus be “cost per adherent patient” and “cost per mmHg blood-pressure reduction”, respectively.

5.8 Sensitivity Analysis

When doing economic evaluations, a lot of assumptions that may influence the results are made. To ensure that the results are comparable across different studies, a sensitivity analysis will be conducted. Using sensitivity analysis will allow us to assess the uncertainty of our

findings while allowing for generalizability to other research settings (Walker & Fox-Rushby, 2001). We will conduct a one-way sensitivity analysis. The effect of changes in parameters (consultation times, SMS costs, discount rate, utilization between interventions, etc.) will be assessed one parameter at a time.

5.9 Data Analysis

Data will be double-entered using Epidata® software. Upon completion, both files will be compared to ensure consistency. Should mistakes and discrepancies be found, the investigator will correct them after reviewing the original forms. Data will be analyzed with STATA (version 13, Texas: StataCorp) and Microsoft Excel. Continuous variables will be analyzed using means/medians and standard deviations/interquartile range, while categorical variables will be analyzed using proportions. The cost of care will be compared across the mobile intervention and the normal standard of care. Differences in the cost of care between different models of care in hypertension at the CHC will be compared (i.e. adherence clubs versus those who are not part of such clubs).

6 Ethical Issues

The ethical and legal issues within this study are limited. The analysis of cost and cost-effectiveness is based on data derived mostly from the StAR* project, which already has ethics approval from the University of Cape Town Human Research Ethics Committee (UCT-HREC) (reference [418/2011]). A copy of that project's ethics approval is attached to this document. In order to carry out this phase, ethics approval will be sought from the UCT-HREC.

6.1.1 Risks and benefits

The study entails minimal risk to the patients and health staff. The provider surveys do not bring any risk. The patient-exit survey may cause some minor psychological discomfort to the respondent. The survey also questions the respondent on sensitive issues related to their income and the income of his or her household. To minimize the discomfort, the respondent will be interviewed in a separate room or some other location away from bystanders. There are no direct benefits to the participants of the study as we will not provide any treatment (nor, however, will any treatment be withheld). No financial or other benefits will be

provided to participants. The study will provide information on the costs of hypertension from a societal perspective. The indirect benefit of the study is that the Department of Health and policymakers will learn about the costs of hypertension and the costs of the mobile-based intervention; in the long run, such information may be used to decide how best to manage hypertension.

6.1.2 Informed Consent

Participation in the study is voluntary and participants (patients and health staff) will be asked for written informed consent, which will offer the possibility to withdraw from the study at any moment without negative consequences for the interviewee. The informed consent will be written in English, IsiXhosa and Afrikaans. The information sheet and consent form will have information on the purpose, procedures, risks and benefits of conducting the study of cost and cost-effectiveness (see Appendices B and C). Trained interviewers will administer the informed consent to the participants as well as explain everything related to the study and the consent forms. Respondents that decline to provide consent will be excluded from the study.

6.1.3 Privacy and confidentiality

We will anonymize the data and protect the confidentiality of participants, by taking the following measures:

- Interviewers will sign the consent form to ensure the confidentiality of all collected data and will receive training on how to maintain patient confidentiality;
- Real names and other personal identifiers will not be used in the study;
- We will not record the names of participants on the patient survey forms. The survey forms will be linked to the participants' consent forms using the survey-form numbers;
- The participant's consent forms will be stored in a locked filing cabinet. Electronic data will be password-protected and accessible only to members of the research team;
- No results when presented can be directly linked to the survey respondents.

7 Budget

An estimate of the budget is summarized in Table 2

Table 2: Budget outline

Item	Description	Quantity	Unit Cost	Total (ZAR)
Travel (average distance 19 km per day)	Travel to and from the facility (average distance 19 km at R3/km) Total km= 1040 km	1040	3	3120
Stationery	Pens, pencils, highlighters, etc.			200
Printing	Informed consent (1 page * 0.3)	260	0,3	78
	Information leaflet (2 pages * 0.3)	260	0,6	156
	Patient questionnaire (15 pages * 0.3)	260	4,5	1170
	Provider questionnaire (2 pages * 0.3)	10	0,6	6
	Observation tool (1 page * 0.3)	30	0,3	9
Translation (to Afrikaans and isiXhosa)	Patient questionnaire (15 pages) * 2	30	350	10500
	Informed consent (1 page) * 2	2	350	700
	Information leaflet (2 pages) * 2	4	350	1400
Fieldworker(s)	All costs including travel and food			20000
Total amount				37339

The travel distance was based on the number of kilometers between the University of Cape Town (UCT) medical campus and Vanguard Community Health Centre (calculated, using Google Maps, as 9.5 km one-way) multiplied by the number of days of the research. The unit price of printing is based on the UCT 2016 printing rates (R0.3 per page). The patient questionnaire, the information sheet and consent form will be translated into isiXhosa and Afrikaans based on a per-page rate (R350 per page). In the Western Cape, isiXhosa and Afrikaans are the dominant languages spoken. Professional translation will be required for both languages.

7.1 Timeline

The timeline of the study is provided in Table 3.

Table 3: Gantt chart

YEAR	2015	2016			2017			
MONTH	Sep-Dec	Jan-Feb	Mar-Jun	Jul-Dec	Jan-Mar	Apr	May	Jun
Proposal Development	■	■						
Submission for Ethics Approval			■					
Data Collection				■				
Data Analysis				■	■			
Report write up					■	■		
Submission of Report						■	■	
Dissemination							■	■

7.2 Dissemination of Findings

The study will be submitted in fulfilment of the Master's in Public Health programme at the University of Cape Town. Research findings will be disseminated through (1) one scientific publication in a national or international peer-reviewed journal, (2) a policy brief, (3) a summary report for Vanguard Community Health Centre and the Western Cape Provincial Department of Health, and (4) a presentation at a national or international conference. The study is a collaboration between the University of Cape Town, the University of Oxford, the Medical Research Council, the University of Washington and the Chronic Disease Initiative for Africa.

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Part B: Literature Review

9 Introduction

Text messaging based interventions are increasingly being used in chronic disease management such as hypertension to improve patients' medication adherence and compliance (Beratarrechea et al. 2014). Medication adherence and compliance has been linked to an improvement in patient outcomes by increasing the chances of achieving the desired outcomes (i.e. desired blood pressure level). When patients with hypertension are compliant and adhere to their medication, less complications are observed (Klein 1988). In the long run, this may reduce the level of health service utilization and costs by avoiding more complicated treatment plans related to uncontrolled hypertension and other Non-Communicable Diseases (NCDs) that are on the rise worldwide.

I shall review the literature on innovative techniques for hypertension management, focusing primarily on mobile health interventions (mHealth). This literature review is organised as follows. In Section 10, I will describe the epidemiology and present data on the burden of hypertension globally and in Africa. In Section 11, I present a brief methodological overview of economic evaluation. I will describe what the different types of economic evaluation techniques are, and focus in more detail on the identification and measurement of costs. In Section 12, I will present cost-effectiveness studies for mHealth interventions and the findings of the review for cost-of-illness studies of hypertension. The last section concludes

10 Epidemiology of hypertension

10.1 What is Hypertension

Blood pressure refers to the force that is exerted onto blood vessels by the blood as it moves through them after being pumped by the heart (Saladin, Miller 1998). Normal blood pressure in adults is 120/80 mm Hg (Cappuccio, Capewell 2015). The first number is the systolic blood pressure and the second number is the diastolic blood pressure. As blood pressure increases, it becomes harder for the heart to pump and this increases the risk of damaging the blood vessels and the heart (Saladin, Miller 1998). Hypertension (or raised blood pressure) is defined as having a blood pressure that is equal to or greater than 140/80 mm Hg (Program, National High Blood Pressure Education 2000). Individuals with a blood pressure measurement between 120/80 mmHg and 140/90 mmHg are pre-hypertensive (Peer 2013, Chobanian et al. 2003). To diagnose hypertension, three physical blood pressure measurements are taken in a clinical setting; should the readings be more than 140/90 mm Hg on two or more occasions, then the individual is hypertensive (Chobanian et al. 2003).

Hypertension is asymptomatic in most individuals, making its detection a challenge (Cohen 2009a). It is often referred to as the “silent killer” as many people are not aware that they have the condition (Eksteen 2015). As a result, hypertension is under diagnosed and undertreated globally (Steyn et al. 2001). Several factors contribute to the emergence of hypertension in the population. The causes and risk factors of hypertension can be broadly divided into social determinants and behavioural risk factors. An ageing population and rapid urbanisation are examples of social determinants. As people get older, blood vessels thicken and get narrower, increasing the risk of hypertension. On the other hand, rapid urbanisation is characterised with the rapid change in diets and lifestyle which puts people at risk of developing conditions such as hypertension (Hofman, Lee 2013). Because of lifestyle changes, hypertension prevalence rates in men and women have increased significantly by almost 100% and 50% respectively in South Africa between 1998 and 2008 (Mungal-Singh 2012). Examples of behavioural risk factors include: lack of exercise, stress, being obese, high salt intake and excessive alcohol intake. Incidence of hypertension can be reduced by reducing these behavioural factors such as eating less salt (less than 5g per day), exercising, reducing alcohol intake and better managing stress (Hypertension guideline working group et al. 2014).

10.2 Effects of Uncontrolled hypertension

Controlled hypertension is defined as having a blood pressure that is less than 140/90 mm Hg while uncontrolled hypertension is having a blood pressure above 140/90 mmHg while on treatment (Hypertension guideline working group et al. 2014). Hypertension damages the walls of the blood vessels which may lead to conditions such as cardiac failure, stroke, congestive heart failure, kidney failure and heart diseases (Cappuccio, Capewell 2015). On its own, hypertension is the leading cause of cardiovascular diseases (CVDs). From as low as 115/75 mmHg, the risk of CVDs doubles with every 20/10 mm Hg increase in systolic and diastolic blood pressure (Chobanian et al. 2003). In South Africa, it is estimated that 4 in every 10 adults aged over 25 years have hypertension and less than 50% of them know that they have the condition (The South African Hypertension Society 2015) and more than 50% of people who are on antihypertensive medication have uncontrolled hypertension (Carter, Bosworth & Green, 2012). More and more people suffer and die prematurely due to strokes, renal diseases, heart attacks and organ damages which are a result of untreated hypertension (Steyn et al. 2001). According to the WHO, hypertension on its own was responsible for 12.8% of all deaths in 2012 (World Health Organisation 2015). Maintaining hypertension levels to below 140/90 in individuals may reduce the incidence of the strokes, myocardial infarctions and kidney problems among other conditions.

10.3 Global distribution of Hypertension

NCDs are a group of diseases that are not transmissible amongst individuals. The four main types of NCDs are chronic respiratory diseases, cancers, cardiovascular diseases and diabetes (World Health Organisation 2015). For the past few years, NCDs have been on the rise globally. In 2012, 38 million of the reported 56 million deaths worldwide were because of NCDs (World Health Organisation 2015). Of all forms of NCDs, cardiovascular diseases are the main cause of death (World Health Organisation 2015). In 2012 alone, CVDs were responsible for 17.5 million deaths worldwide with stroke and ischemic heart diseases causing 6.7 million and 7.4 million deaths respectively (World Health Organisation 2015). The distribution of NCD related deaths and prevalence is disproportionate across different regions. High income countries have the highest prevalence rates while low income countries have the lowest prevalence yet more deaths occur in low income countries. Recognising the rise of NCDs as a public problem, the WHO drafted an action plan to tackle the NCDs. One of the targets stipulated in the action plan involves achieving a 25% reduction in the

prevalence of hypertension by 2025. Managing hypertension is among the best buys recommended by the WHO to prevent CVDs and other conditions that may occur because of untreated hypertension (Bloom et al. 2011).

Untreated hypertension may lead to conditions such as strokes, heart attacks and kidney diseases which often results in premature deaths (Steyn et al., 2001). On its own hypertension complications account for 9.4 million deaths globally (WHO 2017). With a high prevalence rate for hypertension, the incidence of related NCDs increases. The prevalence rate of hypertension has risen by approximately 67% between 1999 and 2010 (The South African Hypertension Society 2015). High income countries have the highest prevalence in hypertension cases compared to middle and low-income countries (WHO 2017). According to the WHO, hypertension prevalence is highest in Africa (46%) compare to other regions (World Health Organization 2014). The high prevalence of hypertension in Africa is likely due the high population density compared to high income countries and weak health systems resulting into more undiagnosed and untreated hypertension (Chobanian et al. 2003). Globally hypertension is under diagnosed and undertreated (Steyn et al., 2001).

10.4 The importance of Hypertension and NCDs in South Africa

An estimated 6.3 million people in South Africa suffer from hypertension (The Heart and Stroke Foundation, 2015). On its own, hypertension is the most common condition in South Africa (Steyn, Fourie & Temple 2006, Mash et al. 2012). Its prevalence rate rises with age; thus, hypertension is more common in the elderly population (Shisana et al. 2013). South Africa has a large proportion of the elderly, which makes it more prone to many hypertension cases (Eksteen 2015). According to South African National Health and Nutrition Examination Survey, the reported hypertension prevalence amongst South Africans over 15 years of age was 10.2% in 2013 (Shisana et al. 2013). The overall hypertension prevalence among 25 year olds in South Africa rose from 23.9% in 2001 to 40% in 2010 (Steyn et al. 1999, Day et al. 2014). Results from a study on Global Ageing and Adult Health (SAGE) indicate that South Africa has the highest hypertension prevalence among adults aged 50 years and over (77.9%) (Lloyd-Sherlock et al. 2014).

Hypertension alone is the most common risk factor for cardiovascular diseases (CVDs) in South Africa (Eksteen 2015, Cappuccio, Capewell 2015, Day et al. 2014). Thus,

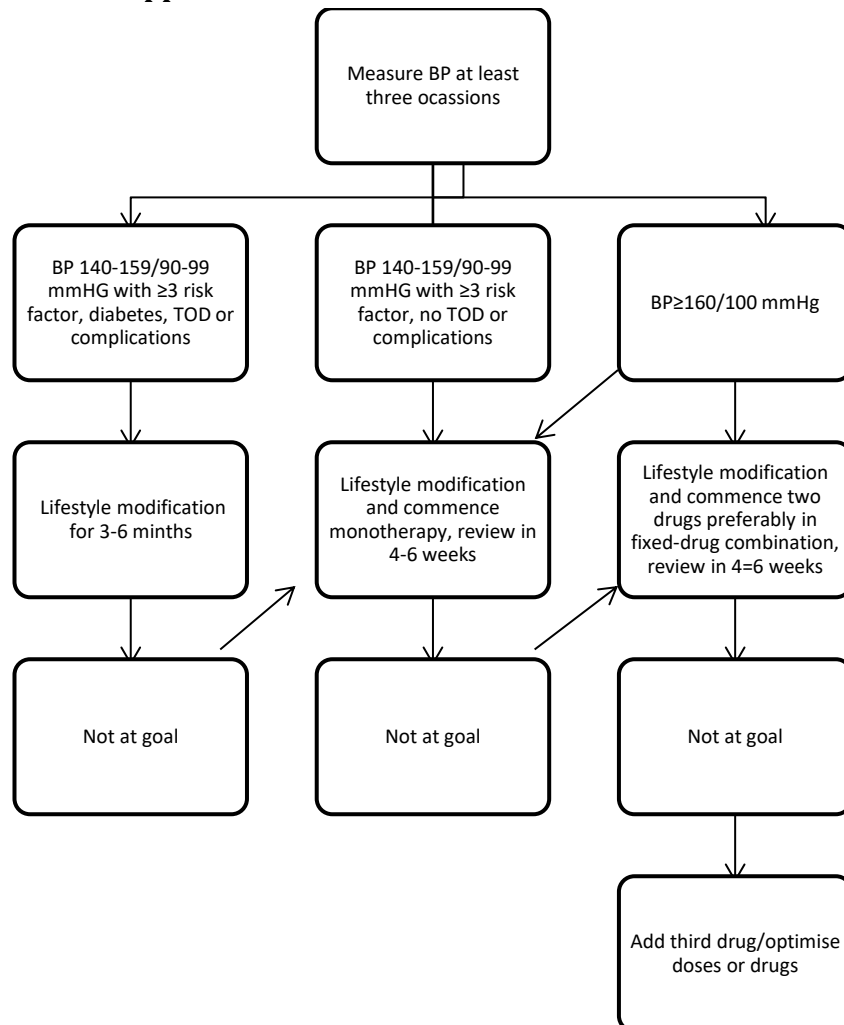
the main reason for managing hypertension is to reduce the risk of cardiovascular events and other associated NCDs (Cohen 2009b). Being a major risk factor for CVDs and other NCDs, the rise in hypertension prevalence has also led to a rise in NCDs in the South Africa. In 2013, strokes and hypertensive diseases were ranked third and fourth respectively on the causes of death list in South Africa (Mail & Guardian, 2013). In South Africa, there are about 130 heart attacks and 240 strokes reported each day of which 50% of strokes, heart diseases and heart failures are a result of hypertension (The South African Hypertension Society 2015).

As a chronic disease, hypertension requires pharmacological and non-pharmacological treatment for a lifetime (Pessanha et al. 2013). Patients have to be persistent and compliant with their medication over a long period of time for better outcomes (Graden, 2003). Even with an effective supply of anti-hypertensive drugs, there still exists a gap between the desired BP control and the actual achievement (Peer 2013). Moreover, hypertension and its sequelae (CVD) are associated with high costs to the health sector as well as loss of human capital due to morbidity and premature mortality. These costs can lead overtime to substantial reductions in the macro-economic output (GDP) (Abegunde et al. 2007). Hypertension requires a large investment to maintain the recommended blood pressure level among affected individuals (Alcocer, Cueto 2008). In the next sections, we look at how hypertension is managed in South Africa.

10.5 Management of Hypertension in South Africa

10.5.1 Hypertension Management Approach

Figure 1: Overview of approach to treatment



Source: (Hypertension guideline working group et al. 2014)

Figure 1 shows the overall approach to hypertension treatment in South Africa (Hypertension guideline working group et al. 2014). Before a person is diagnosed with hypertension, three separate blood pressure readings are taken on separate occasions. If at least two of the readings are above the threshold (140 mmHg) then the person is diagnosed with hypertension. Lifestyle modification strategies such as exercising, consuming less salt and reducing alcohol intake are recommended at the first step of hypertension management in newly diagnosed patients (table 1). Newly diagnosed patients are informed of the lifestyle

modification strategies that they should follow to control their blood pressure. If their blood pressure is too high, then the physician will decide whether to add monotherapy (one drug) or use more than one antihypertensive drug to complement the lifestyle modification strategy. The drugs of choice in the management of hypertension in South Africa include, Thiazide diuretics, Beta-blockers, ACE-inhibitors, Diuretics and Potassium sparing diuretics. A more detailed step by step guideline of hypertension management is provided in a separate document (Hypertension guideline working group et al. 2014).

Table 1: Recommended Dietary modifications

Modification	Recommendation	Approx. ↓ SBP (mmHG)
Weight reduction	BMI 18.5-24.9 kg/m ²	5-20 per 10 kg
Dash diet	↓saturated fat and total fat, ↑fruit and vegetables	8-14
Dietary Na*	<100 mmol or 6 g NaCl/day	2-8
Physical activity	Brisk walking for 30minutes per day most days	4-9
Moderation of alcohol	No more than two drinks per day	2-4
Tobacco	Complete cessation	-

Source: (Hypertension guideline working group et al. 2014)

Several tests are conducted for the diagnosis and management of hypertension. The recommended tests that are run for each patient from time to time based on their risk profile include: urine tests, blood tests, creatinine tests, cholesterol tests and fasting glucose tests. The following tests are done during each clinic visit; measurement of waist circumference, blood pressure measurement, urine tests and assessment of the Body Mass Index (BMI). Tests that are done at least once a year based on how the patient is doing or reacting to the treatment include: blood tests, creatinine tests and uric acid tests. Table 2 shows the summary of all the routine tests conducted on hypertension patients.

Table 2: Summary of hypertension routine Investigations

Test	Comment
Height, weight, BMI	Ideal BMI <25kg/m ² , overweight 25-30 kg/ m ² , obese>30kg/ m ² .
Waist circumference	Men<102 cm; women<88cm. South Asians and Chinese: men<90 cm and women <80 cm.
Electrolytes	Low potassium may indicate primary aldosteronism, or effects of diuretics.
ECG	S in V1 plus R in V5 or V6 >35mm or R in a VL>11 mm or Cornell product (R in aVL+ S in V3 +6 in females) * QRS duration >2440 (mm/ms).
Electrocardiogram (if indicated and facilities available)	LVH: men> 115 g/ m ² and women > 95 g/ m ² .
Fasting glucose	Consider HBA, or GTT if impaired fasting glucose (6.1-7.1 mmol/l).
Cholesterol	If cholesterol> 5.1 mmol/l-fasting lipogram.
Creatinine	Calculate eGFR.
Uric acid	High uric acid is relative contraindication to diuretics.
Dipstick	If abnormal, urine microscopy and protein stimulation.

Source: (Hypertension guideline working group et al. 2014)

10.5.2 Hypertension Care in South Africa

Hypertension care is provided free of charge at primary health care facilities in South Africa and is most commonly managed on an outpatient basis, whereby patients visit the primary health care facilities every month for medical check-ups as well as medication pick-ups. Diagnosis of the condition is made by the doctor while nurses conduct blood pressure tests and other required tests each time the patient visits the clinic as well as counselling the patients. Pharmacists dispense the medication to the patients with hypertension. If the primary health care facility visited is a clinic which does not have a pharmacist, a nurse may dispense the prepacked anti-hypertensive medication to the patients.

Based on the status of the patient's hypertension (controlled or uncontrolled), treatment pathways at public health care facilities may differ. In general, patients with hypertension are

scheduled to visit the primary health care facility at least 12 times a year regardless of the status of their hypertension. Uncontrolled hypertension patients visit the facility more than controlled patients for check-ups and titration of medication doses until their blood pressure is well managed and controlled. The main difference in the number of scheduled visits between the two groups of patients is that controlled hypertension patients make 10 pharmacy visits and 2 follow-up visits to the public health facility while uncontrolled hypertension patients make follow-up visits only which may be more than 12 in a year. Pharmacy visits are less resource intensive as patients only visit the pharmacy to collect their medication, while follow-up visits are more resource-intensive because multiple health professionals (nurse, doctor, and pharmacist) are involved.

10.6 Novel approaches to improve adherence in Hypertension

Hypertension treatment is lifelong and requires patients to take one or more tablets once or twice a day. The effectiveness of a treatment program for managing hypertension therefore depends on the patient taking their medication. Studies show that improving medication adherence produces better disease outcomes (Kiselev et al. 2012, Hamine et al. 2015). Non-adherence on the other hand leads to complications and wastage of resources (Alcocer, Cueto 2008). Considering that the treatment of hypertension is lifelong, non-adherence further increases its prevalence and costs of managing hypertension also increase. Interventions such as nurse or pharmacist led interventions and others including mobile health (mHealth) interventions have been developed to better manage hypertension. This study focuses on the application of mHealth to improve hypertension management. The next section focuses on mHealth and its application in hypertension.

10.6.1 Mobile Health (MHealth)

MHealth makes use of mobile phones to facilitate communication between health providers and patients within the health sector (Adibi 2015). In the healthcare sector, the use of mobile phones is increasing due to the rapid advancements in mobile technologies and the

availability of mobile phones within the population (Leon, Schneider & Daviaud 2012). In South Africa, most of the population (rich and poor) owns a mobile phone and can therefore be reached, irrespective of their social status (Leon, Schneider & Daviaud 2012). MHealth makes it possible for practitioners to communicate with patients on a larger scale instantaneously (Carter, Bosworth & Green 2012), plus it reduces barriers that often reduce access to care such as distance to the facility (Leon, Schneider & Daviaud 2012).

Mobile phones have previously been used in the management of chronic diseases such as asthma, obesity, hypertension and diabetes (Nundy et al. 2012). The use of mHealth in hypertension and other chronic diseases has been found to be effective in (1) improving hypertension outcomes (2) improving adherence and (3) improving self-care and management (Hamine et al. 2015). Several studies have looked at the potential benefits of using mobile-based applications to support people with hypertension. A study by Kiselev et al. (2012) compared the use of a mobile technology in patients with arterial hypertension with those under the traditional care. 77% of the people in the mobile base management achieved the desired blood pressure control. The result was reported to be 5 times higher than those that were in the traditional care (Kiselev et al. 2012).

MHealth was also shown to improve blood pressure control if it is used in blood pressure monitoring (Logan et al. 2007). This is because when patients can see the changes in their blood-pressure readings over time, they are more likely to adhere to their medication to achieve better blood pressure control. Randomised control trials also show an improvement in controlling blood sugar and blood pressure when mHealth is used (Fischer et al. 2012, Earle et al. 2010, Logan et al. 2007). MHealth, unlike other models of care for hypertension, provides a platform for engaging with patients throughout the treatment process, while offering real-time responses and it also allows for active patient engagement between providers and patients, which encourages self-management while increasing health awareness and patient accountability (Fischer et al. 2012). Furthermore, simple and less complicated mHealth interventions such as the use of SMS texts were found to be more favourable among individuals (Logan 2013).

Despite the increasing use of mHealth in health care, there is a lack of economic evaluation studies on them particularly those that focus on costing the interventions. In South Africa, there is a lack of studies that have assessed the cost of hypertension. To cost hypertension and an mHealth intervention that was conducted in South Africa, this literature

review explores the literature that is available on the economic evaluations of mHealth and cost of illness studies on hypertension to inform our study.

11 Introduction to Economic Evaluation and Costing

11.1 Economic evaluation

11.1.1 The role of economic evaluation

An economic evaluation is a systematic method that is used to compare two or more interventions in terms of their costs and outcomes (Acharya et. al., 2011). Economic evaluations improve decisions on the allocation of resources by making comparisons between mutually exclusive and/or complementary interventions (which may include a "do-nothing" scenario) to ensure the best use of scarce resources (McGuire 2001). In health care, we try to make use of the scarce resources efficiently and equitably. Due to the scarcity of resources, trade-offs must be made when allocating resources. With the help of economic evaluations, we can justify our decisions in opting for some interventions over others.

11.1.2 Types of economic evaluation

Drummond et al. (2005) provides a useful classification of the different types of economic evaluations (table 3). Economic evaluations can be classified depending on whether (1) both costs and outcomes are measured, and (2) if there is a comparison between one or more alternatives. Studies whereby only costs or only outcomes are assessed are considered partial economic evaluations. Efficacy of effectiveness studies measure only outcomes (Oparil et al. 2007), while a cost analysis examines only the costs of a program or intervention. The latter provides us valuable information on the costs of the program and is an input for full economic evaluations (see section 11.5 for a more detailed discussion). Evaluations whereby both costs and outcomes are assessed, and a comparison is made between different alternatives are considered full economic evaluations. There are four types of full economic evaluations: Cost Minimisation Analysis, Cost Effectiveness Analysis, Cost Utility Analysis and Cost Benefit Analysis (Drummond et al. 2005, Johannesson 1996).

Table 3: Measurement of costs and consequences in the different types of EE

Type of study	Measurement/ valuation of costs	Measurement/ valuation of consequences
Cost analysis	Monetary units	None
Cost-effectiveness analysis	Monetary units	Natural units (e.g. life-years gained, points of blood pressure reduction)
Cost-utility analysis	Monetary units	Quality adjusted life years (QALYs), disability adjusted life years (DALYs), healthy year equivalents (HYE)
Cost-benefit analysis	Monetary units	Monetary units (e.g. euro, US dollar, Swiss franc)

Source: Adapted from Drummond et al. (2005)

A cost minimisation analysis (CMA) is used when two interventions have the same effectiveness or outcome and the only difference between the two are the costs. The preferred intervention in such a case is the one with the lowest cost (Briggs, O'Brien 2001). This technique is not frequently used primarily because in a CMA one assumes that the effectiveness of different interventions is the same which is rarely the case. In a cost-effectiveness analysis (CEA), the outcome(s) of interest are measured in their natural units and the costs in monetary units (Drummond et al. 2005). The outcomes are a quantifiable unit which can either be behavioural (i.e. adherence to medication intake) or a health outcome (i.e. blood-pressure reduction in mmHg) (Robinson 1993). The results of a CEA are most often presented as a ratio measuring the difference between the costs and effectiveness of the strategies being considered. The ratio is called the incremental cost effectiveness ratio (ICER) and is calculated as follows:

$$ICER = \frac{Costs\ of\ StAR * - Costs\ in\ status\ quo}{Outcome\ in\ StAR * - Outcome\ in\ status\ quo} \quad Eq. 6-2$$

To calculate the cost effectiveness ratio, there must be one dimensional outcome measure which is specific to the disease of interest (i.e. blood pressure reduction measured in mm Hg) that can be used to establish the net costs per unit increase or decrease in the outcome (Robinson 1993). For conditions, such as hypertension, using outcome measures such as mmHg may not reflect the actual benefit of the program since these are considered an intermediary outcome as they do not necessarily give a true reflection on the effect on mortality. A cost utility analysis (CUA) on the other hand is able to capture and reflect the full impact of an intervention by considering both the quantity and the quality of life (Coons, Kaplan 1996). Conditions such as hypertension may lead to strokes and myocardial infarctions (among other things) which often lead to disabilities and a change to quality of

life. It is sometimes important to use a technique which can measure utility by considering both the quantity and quality of life when possible because some interventions may prolong life and significantly improve the quality of life of individuals at the same time. Considering only the quantity of life (life year saved) would undervalue the lifelong condition and this is where the CUA may come in.

The two main outcome measures used in CUA are the “quality adjusted life years” (QALY) and the “disability adjusted life years” (DALY). A QALY considers both the quantity and the quality of life. QALYs are used by health economists to correct an individual’s life expectancy based on their quality of life (Sassi 2006). When used within the context of an economic evaluation, QALYs measure the improvement in the quality adjusted life years resulting from the introduction of an intervention as opposed to no intervention (Sassi 2006). A value of 1 QALY corresponds to a year in perfect health while a value of 0 corresponds to death (Preedy, Watson 2010). An intervention that extends life, but has an impact on its quality will have a QALY between 0 and 1 (i.e. a year is less than perfect health) (Drummond et al. 2005). The quality of life valuation is often referred to as “health utilities” and there are several methods to measure the individual's preferences for different health states (i.e. the utilities). These include; the rating and visual analogue scale, the standard gamble method, and lastly the “time and person” trade off method (Bleichrodt, Johannesson 1997, Torrance 1987). DALYs on the other hand represent the loss of functioning caused by illness (Sassi 2006) and are calculated as the sum of present value of future years of life lost due to premature mortality (YLL) and the present value of future lifetime years lost due to disability (YLD) (Rushby, Hanson 2001). One DALY corresponds to one year of healthy life lost and 0 represents perfect health.

$$DALY = \text{Years of life lost (YLL)} + \text{Years lost due to disability (YLD)} \quad \text{Eq. 11-1}$$

Finally, a cost-benefit analysis (CBA) is a type of economic evaluation which is used when the outcome(s) of interest is measured in monetary terms such that the costs and outcomes are presented in the same units (Goodman, Ahn 1999). In a cost-benefit analysis, outcomes are converted into monetary terms using the Human Capital Approach (HCA), and the willingness-to-pay approach (Drummond et al. 2005). The HCA measures the opportunity cost (or productivity loss) of an individual based on income (value of life = present value of lifetime earnings), while the willingness-to-pay approach simply assesses the maximum

amount that individuals are willing to pay to reduce the probability of dying (Wonderling 2011). CBAs are commonly presented as a benefit-cost ratio (CBR) expressed as:

$$BCR = \frac{\textit{Benefit of strategy 2} - \textit{Benefit of strategy 1}}{\textit{Cost of strategy 2} - \textit{Cost of strategy 1}} \quad \text{Eq. 11-2}$$

The preferred intervention when using the CBA intervention is the one in which the intervention's benefits outweigh its costs (Goodman, Ahn 1999). This makes it easier to compare interventions from different sectors, as it would have not been possible to do so unless a CBA is conducted where the outcomes are converted into monetary units. However, when comparing health interventions, CBA is not often used because of the difficulty of converting health outcomes into monetary terms.

11.2 Perspective

Interventions have different costs and outcomes that affect societies differently. Based on who is consuming the resources, costs and outcomes of a health care intervention can be looked at from different perspectives. The three common perspectives that are used in economic evaluations are: provider perspective, patient perspective and societal perspective (Drummond et al. 2005). The provider perspective only considers costs of an intervention that are borne by the provider such as drug costs and overhead costs; costs incurred by patients are not considered (Creese, Parker 1994). For example, a study by Nguyen et al. examined the cost of hypertension from the health care provider perspective in a hospital in Vietnam (Nguyen et al. 2014). This study included the costs to the hospital of inpatient care (the cost per bed-day,) drug and laboratory costs and overhead costs.

The patient perspective focuses on the costs that are borne solely by the patients and their households (Weinstein et al. 1996). These costs include direct medical costs (i.e. drug costs), direct non-medical costs (i.e. transport costs) and indirect costs (i.e. productivity losses). A cost of illness study carried out in Malawi, investigated the economic burden of chronic non-communicable disease using the patient perspective (Wang et al. 2016). Costs measured in this study included; direct and indirect costs. Direct costs on their own contributed 72% of the total cost.

The societal perspective is the most comprehensive perspective which considers the health benefits and profitability of interventions to the society (Jönsson 2009). When dealing with chronic conditions such as hypertension that have no cure, the societal perspective is

preferable as it delineates all the positive and negative effects of an intervention together with its costs and how they affect the society. Since both the provider and the patient are subjected to a lifetime of hypertension related costs, it is only logical to consider all costs involved regardless of who bears them. In South Africa, the costs related to hypertension from the provider perspective in the government sector where primary health care services are provided free of charge include; drug costs, consultation costs, laboratory tests and overhead costs. Costs borne by the patient while accessing hypertension services include direct non-medical (i.e. transport costs) and indirect costs (i.e. productivity losses).

11.3 Assessment of costs

A cost analysis refers to the quantification and valuation of all the resources that are used in an intervention (Drummond et al., 2005). It is also the first part of an economic evaluation which is used to assess the cost of care in most disease-specific costing studies (Weinstein et al. 1996). Unlike other economic evaluation methods, a cost analysis does not involve the outcomes; hence, it is referred to as a partial economic analysis (Drummond et al. 2005). The cost analysis element forms an integral part of economic evaluations as it delineates the true costs of an intervention or program (Creese & Parker 1994).

Before interventions or programs are considered, their costs need to be measured and quantified. One may find that an intervention may be very effective in terms of producing the best outcome yet on the other hand it is not affordable. Knowing the costs of an intervention allows us to compare interventions and be able to decide which one amongst the many will benefit everyone within a reasonable budget (cost effective). Cost estimates are also important in determining the feasibility of conducting the intervention or its scale up. Without a cost estimate, it is almost impossible to upscale or even implement a similar intervention elsewhere. We will discuss the various elements of a cost analysis and the issues around cost analysis below.

11.3.1 Financial versus economic costs

Costs are made of 2 components: amount of resources used (q) and the unit cost or prices (p) (Hutton, Baltussen 2005). Financial costs refer to the actual monetary value of the inputs consumed to produce a good or provision of a service (Walker, Kumaranayake 2002). Economic costs represent the value of the next best alternative foregone (opportunity cost) as a result of the use of resources (Drummond et al. 2005). An example of an economic

cost is voluntary labour. This is because voluntary labour in an intervention may have a monetary value of 0 (financial cost) yet the volunteers who opted to provide the service could have been doing something else (i.e. farming) in the community that could have benefited the society (opportunity cost). Economic costs thus include all resources that were used in an intervention even if they were provided for free (i.e. donated goods).

11.3.2 Direct, Indirect and Intangible Costs

The three types of costs that are considered when doing a cost analysis are: direct, indirect and intangible costs (see table 4). Direct medical costs are the health care resources that are used to deliver the health intervention and can be incurred by either the patients or the provider of the health service (see section 2.2 on the perspective of the analysis) (Weinstein et al. 1996). From a patient perspective, direct costs refer to out of pocket payments made by patients while seeking care (Meheus et al. 2006, World Health Organization 2009). Direct costs can be classified as either medical (DMC) or non-medical (DNMC) related costs (Tarricone 2006). Direct medical costs include for instance medicines, laboratory tests, health care personnel, supplies and overheads. Direct non-medical costs consist of non-medical goods and services such as transport cost and food costs.

Who bears direct costs may vary based on who is providing the service. In countries where primary health care services are provided free of charge at public hospitals (i.e. South Africa), direct costs borne by the patients are different from those who do not have free access. An example of a direct medical cost is “drug cost” which are borne by the patient if services are not provided for free, yet when the service is for free then it’s a direct cost from the providers point of view.

Indirect costs refer to the productivity losses incurred by patients or households because of not being able to work due to an illness or loss in economic productivity due to death (Weinstein et al., 1996) and in accounting, indirect costs refer to overhead costs that are shared amongst departments (Tarricone 2006). In this section when we say indirect costs we are referring to productivity losses. Indirect costs may also include the reduced ability to enjoy leisure due to morbidity or unrelated future health care cost. Income losses due to the inability to work or enjoy leisure time due to morbidity are considered a productivity losses (Liljas 1998).

Different methods are used to estimate the productivity losses and these include: the human capital approach and the friction cost method. The most commonly used method in economic evaluations to estimate productivity losses is the HCA (Liljas 1998). Using the human capital approach, indirect costs are estimated by calculating the reduction in future income as a result of mortality or morbidity (i.e. loss of income) (Weisbrod 1961). For example, to estimate productivity losses using HCA, the number of hours lost are multiplied by the hourly wage rate. The Friction cost approach considers the number of hours lost before an absent employee is replaced (Koopmanschap et al. 1995). The period where the employee is unavailable/absent before someone else takes over is called the friction period. HCA takes the patients perspective by considering the number of hours that the patient is not able to work as lost income while the friction cost method only considers the number of hours lost before another employee takes over their role or a replacement is made for those duties van den Hout 2010, Koopmanschap et al. 1995).

The final category of costs are the intangible costs. These represent the cost of e.g. pain and suffering; however, they are usually not taken in to account because of the difficulty of valuing these and will not be discussed here (Creese, Parker 1994, Weinstein et al. 1996).

Table 4: Examples of direct and indirect costs

	Perspective		
	Patient	Provider	Societal
Hypertension related cost			
Direct medical costs ¹		Consultation fees Drug costs Lab tests Admission fees	Consultation fees Drug costs Lab tests Admission fees
Direct non-medical costs	Food costs (bought at the facility) Travel costs		Food costs (bought at the facility) Travel costs
Indirect Costs	Income loss Loss of leisure time		Income loss Loss of leisure time

¹We considered direct costs within the context of South Africa where patients do not have direct medical costs at public health care facilities.

11.3.3 Capital Costs versus Recurrent Costs

Costs can also be classified as either recurrent or capital costs based on their working life and value (Drummond et al. 2005). Resources that are purchased once over a long period of time

(i.e. more than a year) and have a value of more than \$100 are referred to as capital costs. Examples of capital costs include buildings, vehicles, initial service training, furniture and equipment. Resources that are regularly purchased and have a working life of less than a year are referred to as recurrent costs (Creese, Parker 1994). Examples of recurrent costs include; salaries, rates, drugs and electricity. Equipment that has a lifespan of over a year but with a value of less than \$100 are also considered recurrent costs. Equipment valued less than \$100 but with a lifespan of over a year is also considered recurrent (Wonderling 2011).

11.4 Discounting

Discounting is used by researchers to adjust future outcomes and costs to the present time (Walker & Kumaranayake 2002). By applying discounting, you calculate the present value of all future outcomes and costs. Costs have different values when looked at from different time periods. People place different values to resources based on the time that they will receive the benefit (Drummond et al. 2005). Drummond et al explains that this time preference often biases people perceptions on the interventions to prioritise. Because costs and outcomes occur at different time periods, people tend to focus more on the treatment programs as compared to prevention programs. Individuals would rather have the benefits now and pay in the future. To account for this time preference, discounting is used to adjust future costs and future outcomes. A discount rate of between 3 to 5% is normally used by most researchers (Meheus et al. 2013, Hansen et al. 2000, Settumba et al. 2015). Where there is no specific discount rate imposed for discounting, any discount rate can be used as long as a sensitivity analysis is done at different rates for comparability with other studies. Discounting future and present costs using interest rates to represent the opportunity costs of using the money now as compared to the future use is relatively accepted. However discounting outcomes on the other hand is controversial as it might not be the case that people value health less in the future than they do in the present.

11.5 Approaches to Costing

A cost analysis comprises of three stages that include identification, quantification and valuation (Creese, Parker 1994). Identification is the first stage of a cost analysis whereby all the resources that were consumed while providing a service or intervention are comprehensively identified and listed. The identification process is guided by the perspective of the study which determines the frame of costs (and outcomes) to include (Raftery 2000).

Depending on the purpose and reason for the cost analysis, only costs that are of interest are considered. For example, if an intervention is intended to better patients' lives, the patient would want to know how the introduction of such an intervention affects them and in such a case taking a patient perspective is important.

Quantification refers to the process of determining how much was used for each resource change in terms of quantity. This process of quantification is based on the differences in resource usage between interventions. For example, if a trial using mobile phones was conducted to reduce blood pressure over a twelve-month period, the difference in resource usage between the trial and the usual care is used to quantify the resources used in the trial for that period.

Valuation refers to the process of assigning a unit cost to each resource that was consumed during the provision of an intervention or service as well as determining the total costs for each category of resources that were utilised. Total cost is determined by multiplying the unit costs of an intervention by the total number of the resources used which in turn yield outcomes such as cost per mmHg reduction in blood pressure. Unit costs of resources are not always readily available and sometimes even the costs that are available may not reflect the true cost to the society (Weinstein et al. 1996). To value resources, researchers make use of either gross costing or micro costing.

Gross costing refers to the process where researchers allocate a total budget that is readily available to a group of services that are being provided such as outpatient visits (top down approach) (Raftery 2000). Gross costing is a more aggregate technique. Based on the data of resource use available, the unit cost of an event is calculated by obtaining an average cost based on usage. For example, if gross costing is used to calculate the cost per hypertension visit at a facility, the total resource cost by hypertension patients for that period will simply be divided by the total number of hypertension visits. It is often used when costing program of interventions where very large resources are used. Step down approach is a gross costing technique which involves the allocation of expenditure to departments of interest in a step wise fashion. Micro-costing on the other hand is a more detailed approach which involves the collection of detailed measurements of resources used by an intervention or program to provide services Micro costing is time consuming because it is a very detailed method. Researchers must list down every item that was used before assigning them a cost (bottom-up costing or ingredients approach). The unavailability of data in low and middle-

income countries makes micro costing difficult or often not feasible, and researchers therefore use less precise methods or combinations of methods such as top-down and bottom-up costing.

A combination of the ingredients approach and the top down approach is increasingly being used to cost an intervention (Hansen et al. 2000, Meheus et al. 2013, Settumba et al. 2015). In this approach, the hotel cost which is the cost related to the average resource use is separated from the direct medical care costs (Drummond et al. 2005). The top down method is used to estimate the hotel cost and the ingredients approach is used to estimate the medical costs. This approach offers the most appropriate valuation as the general average cost related to the indirect cost is combined with the medical direct cost that is directly attributable to the condition or medical intervention.

12 Empirical Review

12.1 Cost and cost-effectiveness studies in mHealth

As the use mobile technology within the health sector increases, it is important that all aspects related to the mHealth interventions are looked at. To date, they are a lot of efficacy and acceptability studies conducted with very limited economic evaluation studies on mHealth that address both the cost and the outcome side of those interventions. The scarcity of resources in the health sector makes it particularly important that only interventions that are both cost effective and efficient are implemented. In this section, we will review economic evaluations studies that have been conducted in mHealth interventions. A summary synthesis of the mHealth economic evaluation studies that were used for this part of the literature review is provided in table 5

12.1.1 Economic Evaluation of mHealth

Several methods are used to conduct economic evaluations in mHealth studies across different diseases and countries. Regardless of the type of economic evaluation that is conducted, a cost analysis forms the first part of the economic evaluation. In a cost analysis, the costs of all resources consumed by the intervention to produce an outcome are estimated. Costing an mHealth intervention is dependent on several factors which include the perspective, type of costs and most of all, the entity interested in the costs. A combination of methods is often used to fully analyse the cost of mHealth interventions as one method of analysis may not be sufficient to capture all the elements of resources sufficiently. Below we look at economic evaluation studies that were conducted in mHealth.

Chang et al (2013) conducted a cost analysis to estimate the cost of resources that were used to provide a peer health worker supported intervention and a mobile health supported intervention to improve AIDS care in Uganda using a retrospective analytic technique. The ingredients approach and step-down costing methodology was used even though not explicitly specified in the article. The ingredients approach was used to estimate the intervention costs through the aggregation of all the inputs (the ingredients) utilised in the program before assigning a unit cost to each item in-order to get the total costs of the intervention. From the total cost, the average unit cost was determined based on the number

of people served or the number of service output provided (Creese & Parker 1994). The study focussed on recurrent costs and not on capital costs such as buildings and furniture. The seven steps suggested by Conteh et al (2004) were followed while doing the cost analysis and the mHealth intervention was found to produce an additional yearly cost of \$2.35 per patient. The seven steps include (1) defining the final product (2) defining the cost departments (3) identifying the full costs of each input (4) assigning inputs to cost centres (5) allocating all costs to the final cost departments (6) computing the total and unit costs for each department and (7) reporting the results (Conteh & Walker 2004).

A study by Larsen-Cooper et al (2015) in Malawi, assessed the cost per user and cost per contact per user of an mHealth intervention in maternal, new-born and child health. They made use of a base cost model to estimate the unit costs of the intervention. Recurrent costs and capital costs were considered in their analysis and costs that they felt were not necessary should the program be scaled up were left out (i.e. costs that were associated with the pilot studies such as international travel and staff time). This is in alignment with other studies that also leave out costs of resources related to the pilot studies when conducting a cost analysis (Chang et al. 2013). The rationale being that these are one-time costs (sunk costs) that are related to the development and perfection of the intervention (developmental costs) which would however not be incurred again should the intervention be implemented elsewhere.

Rodrigues et al (2014) conducted a study in India to assess how much it would cost the Indian National AIDS Control Programme to implement a mobile intervention to support adherence to antiretroviral therapy in Karnataka State. One-time costs and recurrent costs were considered to cost the intervention. The authors used the concept of avoidable costs where costs that are only incurred once but not incurred again if the intervention is implemented are left out (i.e. developmental costs) (Rodrigues et al. 2014). A sequential costing methodology where resources are identified in their natural units, quantified, assigned a unit cost which subsequently gets used to determine the total cost was used. The cost was determined at national programme level as well as at ART-centre level. The intervention was found to cost between USD1.27-USD1.77 per patient per year depending on the type of reminder, number of ART patients and the total number of functioning ART centres. The cost of the mHealth intervention was found to be of low cost and it improved patient adherence plus it could be implemented at low cost in the country (Rodrigues et al. 2014).

Zurovac et al (2012) conducted a cost and cost effectiveness analysis of using an mHealth intervention to improve adherence to malaria guidelines in Kenya. The programme was aimed at the health workers to ensure that they follow the Malaria guidelines by sending them text messages on their mobile phones regularly. The cost analysis was conducted to assess the cost of the mHealth interventions across three different scenarios; under the trial conditions, if implemented by the ministry of health and lastly if the intervention was expanded to a national scale in Kenya. The costs per additional child correctly managed were highest under study conditions (0.5USD), 0.36 USD under the ministry of health and lowest (0.03) if implemented nationally. The difference in cost per additional child varied since the resources considered for the cost analysis in the different scenarios differed.

The reduction in the unit cost per intervention as the program gets up-scaled is normal. Considering the learning curve effect, it is often the case that to produce the same amount of output, the amount of resources that are required decrease with time and especially when the program is conducted on a larger scale the average long run average costs decrease substantially because of improved technical efficiency (Mogyorosy & Smith 2005). Zurovac et al (2012) did not consider the capital costs such as buildings where the service is being provided but rather focused on the developmental costs and other intervention specific costs related to the programmes implementation and running. Their results show that the major cost contributor of the programme differs depending on the purpose of the programme. Developmental costs were the largest under the study trial conditions when compared to the other scenarios.

Depending on the reason of the cost analysis, developmental costs of an intervention may be important if for example the reason of the analysis was to find out how much the intervention costs to develop (Drummond et al. 2005, Mogyorosy, Smith 2005). Apart from developmental costs, the other cost categories considered in mHealth economic evaluations are; the human resources and management costs, developmental costs, operational and maintenance costs of the intervention, training costs and governance costs (Agarwal et al. 2016). Human resources and management refers to the frontline workers that are responsible for making sure that the interventions run as they are involved in the day to day activities of the intervention. Operational and maintenance cost refer to resources that are used by the intervention daily such as text messaging costs, airtime costs, internet costs and the cost of electricity among other things. Training costs refer to the initial preparation of material that is used to teach the frontline workers how the intervention will be run. Training may be a once

of thing but depending on the type of intervention, it may also be ongoing. Lastly governance costs as described by Agarwal et al (2016) refer to the costs associated with the decision-making process by policy makers and the government regarding the intervention.

Not all cost categories are considered by researchers while doing their analysis. Some researchers include developmental costs in their analysis (Zurovac et al. 2012) yet some researchers consider them onetime costs that would otherwise not be experienced should the intervention be implemented elsewhere and thus leave them out (Chang et al. 2013). Equipment cost and operational costs such as airtime usage and cost of text messages are the most readily available information that is analysed by almost all the researchers doing a cost analysis in mHealth (Chang et al. 2013, Larsen-Cooper et al. 2015, Mogyorosy, Smith 2005, Rodrigues et al. 2014). Training costs are considered in some studies and in other studies they are left out. The issue is that there is no set standard of doing a cost analysis which defines how they are to be done or which metrics to use so that the results of the different studies are comparable. The costing strategy and methodology used in a way also dictates which cost categories to use and which ones to leave out. Micro costing methodology was used to cost most mHealth interventions in most cost effectiveness analysis of mHealth studies. The costing strategy used by Larsen-Cooper et al. (2015) included making a list of the essential programme resources and their quantities before assigning the cost of each item and getting the total amount for the programme; the ingredients approach. The ingredients approach was used in almost all the mHealth cost effectiveness studies analysed (Chang et al. 2013, Larsen-Cooper et al. 2015, Mogyorosy, Smith 2005, Rodrigues et al. 2014). Despite using similar costing techniques, the perspective of the study also determines which cost categories to include in the analysis. The next section looks at how the different perspectives were used the mHealth economic evaluation studies.

12.1.2 Cost Perspectives

The cost perspectives considered while doing a cost analysis are the provider perspective, the patient perspective and the societal perspective (see section 11.2). The provider perspective, sometimes referred to as the health system perspective or implementer perspective was the most commonly used perspective in mHealth economic evaluation studies. Zurovac et al (2012) used the provider perspective to consider the costs of the intervention at different implementation levels which were; study level, under ministry of health as the same sites and at national level. Using the provider perspective helps the program researchers and policy

makers know the costs of conducting the program at trial level as well as at national level. The disadvantage of using this perspective only is that it does not consider costs borne by the people at the receiving end of the intervention. Thus, the intervention may be cost effective from one perspective (provider perspective) whereas from another perspective (patient perspective) it might not be the case. For each intervention, costs are not solely borne by the providers only but also the costs are borne by the recipients of the mHealth intervention. The entities providing the intervention may only consider costs that only concern them and not worry about the other costs that may affect the other parties. Since economic evaluations are based on welfare economics, the societal perspective is the ideal perspective as it would consider the welfare of every party involved (Mogyorosy, Smith 2005). The societal perspective provides a more comprehensive view of the mHealth provision and implementation as it would encapsulate all the costs involved, regardless of who is funding the program. In the next section, we look at the type of costs that were used in the studies. Often the perspective and type of costs used in a cost analysis are based on the reason of the analysis and the entity interested in the results of the analysis.

12.1.3 Type of costs and cost categories

All the studies made use of financial costs to determine the cost of the mobile health intervention (Chang et al. 2013, Larsen-Cooper et al. 2015, Mogyorosy, Smith 2005, Rodrigues et al. 2014). As mentioned in section 11.3.1, financial costs analyse the actual monetary cost of the resources that have a monetary payment. If the aim of a cost analysis is to determine the cost of the program to the study managers and facilitators, financial costs are important to them as they show the actual amount of money that was used to pay for the intervention. However, when costing an intervention that has a possibility of being implemented elsewhere, economic costs should also be considered. In mHealth interventions, economic costs would be beneficial as they can capture the opportunity costs of resources that were used in the intervention. Considering only the financial costs while costing may leave out important costs that may be useful in determining the amount of resources required for an intervention as well as properly assessing the efficacy and effectiveness of such an intervention. It would be advantageous when doing a cost study to report both the financial and economic costs of an intervention as done in other cost analysis for other diseases and interventions (Conteh et al. 2004).

Costs items that are often considered while costing an intervention are those that are most likely to be essential when replicating the same intervention elsewhere. This was seen in all the cost studies in mHealth as sunk costs were not considered. Cost items were categorised either according to activities or function in the studies. It was common practice to first categorise the activities that were exclusive to the intervention and from then, an ingredients approach was usually taken to cost the intervention. The four activities that were common across the mHealth interventions costing studies were; development, pilot testing, implementation and sustenance. Based on the activity, it was easier to identify the resources that were used and then later assigning a cost based on the quantity used. Development is the process of the actual development of the intervention. The mHealth development stage involves the creation of databases, acquisition of equipment and mobilization of the human resources. Pilot testing involves the actual testing of the intervention on a certain number of individuals prior to the study being conducted. Implementation involves the actual implementation of the programme, either at facility level, study level or even at national level. Lastly, sustenance involves the actual process of making sure that the programme runs efficiently over a certain period.

12.1.4 Lessons from the Articles

A couple of lessons were obtained from the review of the articles. First the results have shown that mHealth interventions that use text messaging based platforms are generally associated with low incremental costs when compared to the standard care of most diseases. The low costs of the text messaging based interventions are a result of the low short messaging service (SMS) costs. Depending on the type of mHealth intervention being implemented, start-up costs and developmental costs may form the bulk of the costs. Second, unit costs of mHealth interventions that made use of text messages may be further reduced when interventions are implemented on a larger scale (economies of scale) with improved efficiency. Third, cost analysis results are very context specific. We found out that there are a lot factors that determine the costs. For example, the cost of mobile phones is different across different regions, the costs of sending a text message changes from time to time. Fourth, the importance of a sensitivity analysis in mHealth EEs. Costs are sensitive to many factors and it is important to vary those factors. In one study, it was found that the costs of sending a text message had changed from the period the mHealth intervention trial was conducted to when the EE was conducted (Chang et al. 2013). Because of technological advancements, there is

always be a newer mobile phone or system that will affect the price of the previous model. Fifth, the use of a standard currency facilitates study comparability. Most of the studies used the US\$ to standardise costs. The average exchange rate per year is used for the conversion. However, costs are very responsive to the trading rates. In countries with political instability among other issues, the rate can change overnight and drastically affect the cost per unit. Lastly, the importance of using a checklist to improve transparency and rigour. Using the WHO outcome measures, mHealth interventions in hypertension should ensure efficiency, effectiveness accessibility, acceptability, safety and equity across the whole population before they can be considered for up scaling (Peiris et al. 2014).

With a lot of studies on mHealth in chronic diseases allegedly being of low standards and a few of high quality, it is hard to say whether the use of mHealth in hypertension is beneficial (Peiris et al. 2014). This is because previously there was no standard of reporting the evidence of the mHealth studies. Recently a team at the WHO published a 14-item checklist which they called mobile health evidence reporting and assessment (mERA) checklist that should be followed when reporting mHealth studies to ensure transparent and rigorous evidence (Agarwal et al. 2016). Item number 9 on the mERA checklist speaks to the inclusion of the cost of the mHealth intervention while reporting the findings. Without the costs of an intervention, it is almost impossible to determine the benefit of the intervention. In the next section, we look at cost of illness studies on hypertension.

Table 5: Summary of economic evaluation on MHealth studies

Author / Country/	Objectives & Perspective	Issue of focus	Strategies used to measure the costs and cost effectiveness of mHealth.	Findings	Limitations and recommendations for future research.
(Rodrigues et al. 2014a) -India	-to assess the costs of implementing a mobile phone reminder to support adherence in ART therapy -Provider Perspective	- cost of mHealth	-used the concept of avoidable costs (did not consider sunk costs in the analysis) -measured onetime costs (equipment), and recurrent costs (mHealth service maintenance, overheads, equipment maintenance, staff operators)	- It would cost between USD (1.27 - 1.77) per patient per year depending on the type of intervention -the total cost of mHealth intervention in India is low -the low cost of telephone services and the use of free software's in LMICs may result in a lower cost of the intervention. -Potential to improve adherence and reduce the number of people to use second line treatment. -Over a 5-year period, the intervention was estimated	-the use of mobile phones may leave out the poor, illiterate and uneducated as they might not have phones -potential for disclosure of private information if intercepted by others i.e. HIV status -costs of the intervention are sensitive to currency exchange rates. -costs may differ depending on the provider. -Text messages and call rates change over time. -Costs very sensible to the context (i.e. Number and

				to account for 0.36% of the total national budget.	type of staff, setting, intervention)
(Chang et al. 2013) -Uganda	- to perform a cost analysis of the Peer Health Workers and mHealth SMS Interventions used by the PHWs -Service Provider perspective	-cost of mHealth & PHW	-used a retrospective cost analytical technique -Ingredients Approach was used -Unit costs determined by the actual amount used (financial costs) -used a threshold analysis to assess potential intervention cost savings. -Cost categories considered for mHealth-startup, training, and maintenance costs.	-PHW cost per patient \$8.74 and \$2.35 for mHealth -PHW and mHealth intervention averts more than 1.5 future second line switches in ART and thus cost saving -The threshold analysis used a means to contextualize the results -costs found to be affordable	-limitations-possibility of task shifting between the interventions which may prevent the accurate measurement of the individual intervention costs -further research in implementing these types of interventions in complex economic models -the costs of mobile phones, airtime varied a big deal (significant change from when the trial was conducted and when the cost analysis was conducted) -Sensitivity analysis-

					calculated total costs with and without staff costs MHealth-airtime costs, charging phones,
(Zurovac et al. 2012) -Kenya	-evaluate costs and cost effectiveness of a mobile phone text message reminder program to improve adherence to Malaria guidelines under three implementation scenarios (study conditions, ministry of health and if implemented nationally) -Program implementer perspective	-costs of mHealth	-Used Financial costs. -used financial records - Cost categories considered include Intervention development, Development of distribution system, cost of collecting HWs mobile numbers and Implementation cost.	-45% of the costs under study conditions were used to develop and pretest the text messages while the cost of developing the text messages accounted for 12% of the costs. - Costs per additional child managed under study conditions was \$0.50, under Ministry of Health \$0.36 and 0.03 if implemented nationally. -SMS intervention found to be effective and inexpensive -the SMS sent to health	-future research to optimize delivery, find out the reasonable SMS frequency and duration of the intervention. - The opportunity cost of sending SMS in the facility - Development of a text messaging intervention addressing integrated management of the most common outpatient diseases. -Sensitivity analysis- complex Malaria management and different diagnostic tests posed the

				<p>workers to optimize adherence to treatment guidelines.</p> <p>-cost of the intervention per additionally managed child under study conditions were higher but low when included in routine practice.</p> <p>-Intervention cost on national scale represent 1% of the allocated money for malaria treatment.</p> <p>-intervention can be seen as a complement and not a replacement.</p>	<p>total costs to be higher for each scenario.</p> <p>-cost per additional child correctly managed dependent on the effect size</p>
<p>(Larsen-Cooper et al. 2015b)</p> <p>-Malawi</p>	<p>-to determine cost per user and cost per contact with users of an mHealth intervention in maternal health</p>	<p>-costs of mHealth</p>	<p>-used a base cost model</p> <p>-selected capital and recurrent costs were used.</p> <p>-Cost data from financial</p>	<p>-intervention cost \$29.33 per user and \$4.33 per successful contact.</p> <p>-Sensitivity analysis showed a possible 48%</p>	<p>Sensitivity analysis- varied the utilization of the various intervention in the study hence the total costs vary across alternate</p>

	<p>-Programmatic Perspective</p>		<p>records, service level agreements and the program budget</p> <ul style="list-style-type: none"> -financial costs used -costs categorized as capital (3% annuatization) and recurrent -Recurrent included administrative, management and oversight, monitoring, techno related fees, travel and transport costs. -only capital costs needed to replicate the service used. 	<p>improved if the service were to operate at full capacity.</p> <ul style="list-style-type: none"> - domestic management and oversight 285 of the total intervention costs, administration fees 7 % tips and reminders also 7% and capital costs only 4%. Labor costs contributed 52.5% of the total costs of the intervention. 	<p>implementation scenarios.</p> <ul style="list-style-type: none"> -Costs dependent on utilization thus hotline costs varied in certain periods. -total programmatic costs could not be disaggregated to service type, multiple outcomes not accounted for in other individuals, exclusion of volunteer time. -Future research-monetize benefits and use BCA for easy comparison, - consider costs and cost savings from patient perspective.
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12.2 Cost of Illness Studies on Hypertension

12.2.1 Summary of results

Most studies on the cost of hypertension have been conducted in middle- and high-income countries, with very few studies done in low-income countries as summarized in Table 6. Evidence reported in these studies shows that hypertension management is costly, making it both a health and an economic burden. The cost of hypertension care varied from country to country, with the United States of America (USA) having the highest cost of care while Nigeria had the lowest cost of care. In the USA, annual direct expenditure of hypertension was as high as US\$54.0 billion (Balu & Thomas, 2006). High-income countries have the highest unit cost of care, followed firstly by middle-income countries, and lastly by low-income countries.

Regardless of the unit cost of care, the economic impact of hypertension care is huge in all countries. The high cost of care for hypertension subjected many patients residing in the south-western part of China to catastrophic payments. 8.9% of the population experienced catastrophic payments and 4.1% of those households became impoverished after paying the hypertension costs (Le et al., 2012). In Nigeria, hypertension costs led to a 52.8% incidence of catastrophic payments among the study population (Ilesanmi, Ige & Adebisi, 2013). A catastrophic payment occurs when a household uses more than 10% of its total household income on healthcare (in this case, hypertension costs) (O'Donnell et al. 2008). Impoverishment refers to the percentage of the population that drops below the poverty line after paying healthcare costs (Mills et al., 2012). In 2010, the annual costs of hypertension care in Brazil were so high that the annual costs represented 0.08% of the country's Gross Domestic Product (GDP) (Dib, Riera & Ferraz, 2010). Considering that the total healthcare expenditure as a percentage of GDP for Brazil was 7.6%, hypertension posed a very huge economic burden, as it accounted for merely 1.1% of that 7.6% in that year.

Looking at the drivers of hypertension costs, the major drivers in most cases are anti-hypertensive drugs (Nguyen et al., 2014; Le et al., 2012; Al-Efan, 2009), except when the study includes hospital care costs (Nguyen et al., 2014). In some instances, antihypertensive drugs were attributable to up to 80% of the total cost of hypertension care (Maetzel et al., 2004). Also, as the number of antihypertensive drugs per patient increases, so does the cost of care (Al-Efan, 2009). Different regions use different first-line antihypertensive drugs for

hypertension management. In most studies, diuretics were the first-line treatment (Ganiyu & Suleiman, 2014; Costa, Juvenal Soares Dias da et al., 2002), while in other countries, like Bulgaria and Serbia, the first-line drugs were angiotensin-converting-enzyme inhibitors (ACE inhibitors), followed by treatment with calcium-channel blockers (Ivanova et al., 2009). Diuretics and the use of no more than 2 antihypertensive drugs per person were found to be cost-effective (Ganiyu & Suleiman, 2014; Costa, Juvenal Soares Dias da et al., 2002). In addition, the presence of co-morbidities and the severity of hypertension affects the cost of hypertension care. Co-morbidities have a significant influence on the total cost of hypertension management (Maetzel et al., 2004). The cost of care for patients with advanced hypertension or for those with comorbid diseases is higher than for those with primary hypertension alone (Ilesanmi, Ige & Adebisi, 2013). A study by Nguyen et al. (2014) indicated that the total cost of hypertension care on its own in Vietnam was lower than the total cost of hypertension care among individuals with both hypertension and hyperlipidaemia.

12.2.2 Findings and Lessons from the Studies: cost of illness studies

Assessing the cost of care in a disease-specific cost study is dependent on the costing methodology used, the type of study conducted and the perspective that is taken in the study. Most costing studies shown in Table 6 were cross-sectional studies. Cross-sectional in the sense that data collection and analysis for a certain population or subgroup was done at a specific point in time. Different perspectives (patient, provider and societal) were taken to analyse the cost of care. The provider perspective is used by researchers when they are interested in the costs borne by the provider (Nguyen et al., 2014). Provider costs include both the direct and indirect costs of providing a service. The provider costs include drug costs, consultation fees, laboratory tests, health workers' salaries and so on (Drummond et al., 2005), and are usually captured through the assessments of patient files and cases (Nguyen et al., 2014; Ivanova et al., 2009). Some studies took the patient perspective, concentrating on the costs borne by the patients themselves (Ilesanmi, Ige & Adebisi, 2013; Maetzel et al., 2004). The common costs assessed included travel costs, consultation fees, admission fees, indirect costs and laboratory costs.

Some studies focused on all direct medical-care costs, meaning that they considered both the direct medical-care costs and the direct non-medical-care costs associated with the disease (Le et al., 2012). An example of a direct medical-care cost is drug cost, while

examples of direct non-medical-care costs include administration and transport costs. Other studies focused only on the direct costs of drugs that were utilised by different patients (Ganiyu & Suleiman, 2014; Ivanova et al., 2009). This difference alone results in differences in the cost of care, even within the same region.

Inconsistencies in the inclusion of and estimation methods for indirect costs of care were also seen among the different papers. Indirect costs refer to the best forgone use of time and are measured as the loss of income to the individual or to the household (Drummond et al., 2005; Creese & Parker, 1994). From a provider perspective, these can be the average resource use per visit, while, from a patient perspective, they could refer to the opportunity cost of being at the facility (i.e. lost income or lost time). If costing studies use different methodologies, the costs of care measured will differ and, most importantly, the results will not be comparable.

Some costing studies are incomparable for many reasons. These reasons include inconsistent methodology. Some researchers make use of secondary data sets to draw up their costing data (Balu & Thomas, 2006), while others make use of study tools like questionnaires (Le et al., 2012; Al-Efan, 2009). Even the perspective taken differs with each study, with some deciding to use the patient perspective, some using the provider perspective and others using the societal perspective. Since there are currently no set rules of conducting a cost analysis, the costs measured will always differ and comparisons between studies will be difficult. The societal perspective is the most comprehensive way of doing a disease-specific study as it captures all the costs involved (Drummond et al., 2005). Looking at table 6, costing studies are also presented in different currencies and periods. The results are presented as a monthly cost, an annual cost or, sometimes, as an incremental cost. This makes comparing the results among countries difficult, especially if the results are presented in different currencies. Regardless of all these issues, all costing studies on hypertension cost show that the cost of care is high.

Despite the high cost of care and various methodologies for costing, hypertension on its own is generally undermanaged, with a small percentage of the patients achieving the required blood pressures. For example, in a study by Ilesanmi et al., (2013), only 33.6% of the study population achieved the desired blood pressure, owing to non-persistence and non-adherence to medication. In South Africa, more than 50% of people who are on antihypertensive medication have uncontrolled hypertension (Carter, Bosworth & Green,

2012). Most people with hypertension in South Africa have uncontrolled hypertension (Steyn et al., 1999). As an initiative to control and manage hypertension in South Africa, several models of care have been implemented in the republic. Addressing medication adherence being one of the major areas being target. One such model of care is the use of text messaging based interventions and other mHealth programs.

12.3 Conclusion

In this literature review we looked at economic evaluation studies in mHealth and the cost of illness studies in hypertension. MHealth interventions in most cases were found to be cost saving in the long run when upscaled despite having a high initiation cost. With the rapid advancements in mobile technology, the cost of using such interventions will decrease with time. For example, the price of text messages in the last ten years has gone down in South Africa. Text messages (operational cost) being one of the major cost drivers of mHealth costs, any reduction in the price is welcome. Partnerships with other sectors (i.e. NGOs and private sector) and the government to provide efficient mHealth interventions may further reduce their average costs as they are shared among the different sectors, after all the interventions have the potential to benefit everyone.

Looking at the cost of illness studies in hypertension, drug costs were found to be the major cost driver followed by consultation costs. However, in countries where primary health care services are provided for free, patients are faced with direct nonmedical costs and indirect costs such as transportation costs and lost income. In some instances, the patient costs had the potential to become catastrophic and possibly impoverish households. Considering that hypertension is a chronic disease with no cure, patients costs are always going to be there and it is thus important to know how much they are and how they affect households.

The literature shows to date that there has been no cost study done to assess the cost of hypertension care in South Africa. There is currently no research on the cost and cost-effectiveness of mHealth interventions for the management of hypertension in South Africa. This research is needed on the one hand to assess the feasibility and affordability of implementing these interventions, and on the other hand to compare mHealth interventions with alternative uses of resources through cost-effectiveness studies.

Table 6: Summary of Hypertension Costing Articles

Study Author(s)	Country	Study Type and Data extraction tools	Costs Measured	Perspective	Hypertension costs
(Ganiyu, Suleiman 2014)	Nigeria	Cross sectional study <ul style="list-style-type: none"> • Case Notes 	<ul style="list-style-type: none"> • Direct (drug costs) 		Average monthly cost per: <ul style="list-style-type: none"> • Diuretics= NGN858.6 (\$5.51) • Blockers a= NGN1101.1 (\$7.07) • Fixed dose combinations = NGN10 425. (\$66.93).
(Maetzel et al. 2004)	Canada	<ul style="list-style-type: none"> • Questionnaire • Telephone Surveys 	<ul style="list-style-type: none"> • Direct • Indirect 	<ul style="list-style-type: none"> • Patient 	Annual cost US\$3900
(Le et al. 2012)	China	Prevalence based cross-sectional survey <ul style="list-style-type: none"> • Questionnaire 	<ul style="list-style-type: none"> • Direct • Indirect • Intangible 	<ul style="list-style-type: none"> • Societal perspective 	Mean unit cost of illness \$9393.3
(Costa, Juvenal Soares Dias da et al. 2002)	Brazil	Cross-sectional study <ul style="list-style-type: none"> • Interviews • Questionnaire 	<ul style="list-style-type: none"> • Direct • Indirect 	<ul style="list-style-type: none"> • Patient 	Monthly mean costs of care (R\$ 89.90)
(Balu, Thomas 2006)	United States of America	Survey <ul style="list-style-type: none"> • Secondary data 	<ul style="list-style-type: none"> • Direct 		Total incremental annual direct Expenditure= \$US 54.0 billion Mean incremental annual direct

Study Author(s)	Country	Study Type and Data extraction tools	Costs Measured	Perspective	Hypertension costs
					expenditures per individual = \$US 1,131.
(Nguyen et al. 2014)	Vietnam	Retrospective survey <ul style="list-style-type: none"> Financial records 	<ul style="list-style-type: none"> Direct 	<ul style="list-style-type: none"> Provider 	Median total direct costs per patient = US\$65
(Dib, Riera & Ferraz 2010)	Brazil		<ul style="list-style-type: none"> Direct 		Estimated direct annual cost in: Public health system= US\$ 398.9 million Private health system =US\$ 272.7
(Ilesanmi, Ige & Adebisi 2013)	Nigeria	Cross-sectional survey <ul style="list-style-type: none"> Chat Review 	<ul style="list-style-type: none"> Direct (drug costs) Indirect 	<ul style="list-style-type: none"> Patient 	Mean cost of treatment \$9.6 Median monthly drug cost \$6
(Al-Efan 2009)	Malaysia	Prevalence-based and incidence-based cross-sectional study. <ul style="list-style-type: none"> Case record form Questionnaire 	<ul style="list-style-type: none"> Direct Indirect 	Patient	The total costs for pre-hypertensive, stage 1 and stage 2 <ul style="list-style-type: none"> Direct costs: RM1612.38, RM1741.85 and RM2718.21 Indirect: RM8078.70, RM6654.52 and

Study Author(s)	Country	Study Type and Data extraction tools	Costs Measured	Perspective	Hypertension costs
					RM7511.41
(Ivanova et al. 2009)	Bulgaria and Serbia.		<ul style="list-style-type: none"> • Direct (drug costs) 	Provider	<p>Monthly cost of hypertension</p> <ul style="list-style-type: none"> • Serbia = 12.56 Euro • Bulgaria= 8.23 Euro <p>Monthly cost for complicated hypertension</p> <ul style="list-style-type: none"> • Serbia 13.39 Euro • Bulgaria 8.23 Euro

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Part C: Journal manuscript

Proposed Journal: BMC Public Health¹

¹ Figures and tables have been imbedded in the text to improve readability. Appendix I shows the instructions for the author. For this thesis, the student is the sole author.

**The cost and cost-effectiveness of a text-messaging
based intervention to support management of
hypertension in Cape Town, South Africa.**

Abstract

Background: The consequences of uncontrolled hypertension are increasingly becoming an economic burden both to the public and the government. Non-adherence to medication is one of the factors contributing to poor blood pressure control. Several strategies have been studied to improve adherence to blood pressure lowering treatments, including mobile-phone based health interventions such as sending text-messages targeting support and behaviour change. The objective of this study was to examine the cost and cost-effectiveness of a text-messaging based intervention to support management of hypertension within the context of a text-messaging based intervention (the SMS-text Adherence support trial, StAR*-BP) conducted in an urban public-sector clinic in Cape Town.

Methods: A combination of the bottom-up approach and step-down costing was used to estimate the cost of treatment a health system perspective. One-way univariate sensitivity analysis was conducted to deal with uncertainty. All costs were estimated in 2016 South African Rand and discounted at 5%. The cost data and the StAR*-BP interventions main outcome; blood pressure reduction (expressed in mm HG) were combined to estimate the cost-effectiveness of the intervention. A total of 250 patient interviews were undertaken to estimate the cost from the patient perspective.

Results: The primary outcomes were the average cost of blood pressure lowering care and the incremental cost of the text-message based adherence intervention, compared to usual care, per millimetre of mercury (mmHg) reduction in systolic blood pressure. The average health system cost for hypertension care was R262 per visit and patient cost was R172 per visit. The incremental cost of the text-messaging based intervention cost was R4 per month. The incremental cost-effectiveness ratio of the intervention was R22 per mmHg reduction over the twelve-month period.

Conclusions:

This is the first study to estimate of the societal cost of hypertension management in an urban South African environment and it demonstrates that a text messaging based intervention to improve hypertension treatment adherence in South Africa can provide good value for money at an incremental cost of R49 per patient per year and an incremental cost effectiveness of R22 per mmHg reduction in systolic blood pressure. Our findings support ongoing efforts by the Department of Health to study and invest in mHealth solutions that can improve patient

adherence and quality of care. Given the importance of hypertension as a risk factor for premature death and disability among South African adults, there is urgent need for research on mHealth for cardiovascular disease prevention and care.

Keywords: Hypertension; blood pressure lowering; cost analysis; adherence; cost-effectiveness analysis; mobile health

Background

Between 2001 and 2010, the hypertension prevalence rate among South African adults aged 25 years and older rose from 24% to 40% (1,2). This is a concern since, raised blood pressure/hypertension is the most important modifiable biological risk factor for cardiovascular diseases (CVD) (1,3). Uncontrolled high blood pressure and its sequelae (i.e. CVDs such as stroke, heart failure, and ischaemic heart disease) lead to high levels of resource use in the health sector as well as loss of human capital due to morbidity and premature mortality. Over time, uncontrolled high blood pressure could lead to reduced worker productivity, which in turn reduces economic output which may lead to substantial reductions in the macro-economic output (GDP) of a country (4).

Management of high blood pressure, which is a common condition, consumes a large proportion of outpatient care budgets. Because the condition does not usually have symptoms and adherence to medical treatment is poor, large investments are required to maintain the recommended blood pressure level among affected individuals (5). Non-adherence to anti-hypertensive medication on its own is a huge problem as it can lead to 'difficult-to control hypertension' which substantially increases the risk of developing serious life-threatening conditions such as CVDs, strokes and heart attacks (6,7). The effectiveness of blood pressure treatment on reducing CVD risk depends on the patients taking their medication consistently, usually once to three times daily from the time of diagnosis throughout the rest of their lives. Studies have shown that improving medication adherence increases the effectiveness of treatment and leads to better patient outcomes(8,9). Improving adherence may also be cost saving by averting the development of CVD. Efforts to monitor medication adherence have been made through the use of pill counts, blister packs, text messages and electronic monitors (7,10). However, there is no gold standard to monitor or measure non-adherence and it is almost impossible to detect intentional non-adherence among patients as none of the previously tested methods can show if the medication was taken (10).

This study focuses on the use of text messages to improve patient adherence to hypertension medication. Mobile and wireless technologies (commonly abbreviated as mHealth) such as mobile phones are increasingly being used to monitor adherence and improve patient outcomes. To date, most studies examining the effectiveness of mHealth have been carried out in high-income countries for a wide range of conditions. These studies have generally

shown a positive effect, especially when short text-message services (SMS) are used to remind patients to take their medication (11).

In South Africa, a recent randomized trial (the SMS-text Adherence support trial, StAR-BP) investigated the effect of adherence support via Short Message Service (SMS) on blood pressure and treatment adherence in adults diagnosed with hypertension and managed in an outpatient primary care facility(12). The StAR-BP study, conducted between June 2012 and August 2014, allocated participants to one of three groups (arms) that ran in parallel: usual care group, information only group and interactive group. Participants allocated to the usual care group only received the SMS-texts sent to all trial participants. These messages are sent no more frequently than one SMS text-message every four weeks. The messages are a welcome SMS text-message, a text confirming enrolment, an SMS text-message on a birthday, and other SMS text-messages about participation in the trial.

Participants allocated to the interactive adherence support received the same messages as the information-only group but could also respond to selected messages using free-to-user “Please-Call-Me” requests. These generated an automated series of responses from the text-message delivery system offering trial participants several options including cancelling or changing an appointment, and changing the timing and language of the text-messages. The information-only adherence support group were sent messages to motivate collecting and taking medicines, and to provide education about hypertension and its treatment. Additional reminders were sent when medicines were ready for collection or about scheduled clinic appointments. All trial participants were given a phone number to contact the research team.

The trial showed in the information-only intervention arm, compared to the control arm, an improvement in adherence (measured by medication refill rates) and a small but statistically significant reduction in systolic blood pressure (12). Despite the numerous effectiveness studies on mHealth, to our knowledge, only a few studies have examined the cost and cost-effectiveness of mHealth interventions, and to date no studies have been conducted in the South African context (13-15). The objectives of this study were: (1) to estimate the cost of providing routine hypertension care, (2) to assess the incremental cost of the effective one-way SMS text-message intervention, and (3) to assess the cost-effectiveness of this intervention.

Materials and Methods

Study setting

The study was carried out in 2016 in the context of the StAR-BP trial at Vanguard Community Health Centre (CHC) in Bonteheuwel, Cape Town. Vanguard CHC is a day-clinic serving patients on an outpatient basis only. The clinic serves people of Langa and Bonteheuwel by providing a range of primary health services. In 2015, the clinic served approximately 27,000 patients monthly. A dedicated clinic for chronic diseases (including hypertension and diabetes) serves on average 500 patients weekly.

Hypertension care pathway

Vanguard CHC follows the South African standard treatment guidelines for the management of hypertension (16). Patients who have been diagnosed with high blood pressure are managed within a chronic disease service. The service is staffed by doctors and clinical nurse practitioners. At Vanguard CHC patients with hypertension are seen at a disease specific clinic which runs two days a week (one of these days is a combined high blood pressure and diabetes mellitus clinic.) Patients with appointments for routine high blood pressure care arrive at the facility and proceed by collecting their paper-based medical record from reception, they are then seen by a nurse who measures their vital signs and checks the record for routine screening activities which may be required. Thereafter patients are seen in a disease specific club room either by a clinical nurse practitioner or doctor depending on the appointment type (annual review, medication review) and clinic-measured blood pressure on the day (for example patients with a blood pressure above 160/100 mmHg will be evaluated by a doctor and may be referred to the emergency unit.) As per the country guidelines controlled hypertension is defined as systolic blood pressure measurement equal to or below 140 mmHg, with higher values considered uncontrolled.

Individuals with hypertension may visit the facility as infrequently as four times per year (an annual review and medication collection, medication review and medication collection, and two medication collection only visits (prescriptions are valid for a maximum of six months and the pharmacy will dispense a maximum of three months medication at one time.) Uncontrolled hypertension patients generally visit the facility more than controlled patients for check-ups and titration of medication doses until their blood pressure is controlled. The main difference in the number of scheduled visits between the two groups of patients is that controlled hypertension patients make between two and ten pharmacy medication collection

visits and two clinical follow-up visits to the facility while uncontrolled hypertension patients may require monthly or more frequent clinical follow-up visits (may be more than 12 per annum) and include medication collection. Pharmacy visits are less resource intensive as patients only visit the pharmacy (i.e. bypass reception) to collect their medication (which may already have been pre-packaged and dispensed via a third-party provider), while clinical follow-up visits are more resource-intensive because multiple health professionals (nurse, doctor, and pharmacist) are involved.

Costing Methods

We conducted a retrospective cost analysis for patients with a diagnosis of hypertension treated for raised blood pressure from the health system (provider) perspective using a combination of the bottom-up approach and step-down costing to estimate the monthly outpatient cost per visit. A costing analysis from the patient perspective was conducted using a structured questionnaire to estimate the monthly cost per visit to access hypertension care. All costs from the provider perspective were collected between June 2016 and February 2017. The patient survey was conducted between September 2016 and December 2016. “Both financial and economic costs were estimated. Financial costs represented the actual expenditure on goods and services, while economic costs valued the cost of all inputs, even if these were provided for free (e.g. voluntary labour) or where the price did not reflect its true value such as subsidized goods.” All costs were estimated in 2016 South Africa Rand.

Costs from the provider perspective

The objective of the provider costing was to estimate the monthly cost per outpatient visit for hypertension. Two different estimation approaches were used: direct medical costs of hypertension care, such as the cost of drugs, were estimated using the bottom-up approach, while other resources were estimated using the step-down approach (i.e. capital costs and recurrent costs not directly related to hypertension care).

Bottom-up costing: This method was used to estimate the direct medical costs associated to hypertension management at Vanguard CHC. These costs include; human resources, medical drugs, laboratory tests and other medical services related to hypertension care. To identify and measure these costs we conducted 10 non-participatory observations on patient’s management at the CHC, reviewed 200 medical records and conducted five structured interviews with CHC staff involved in hypertension care. All human resources involved in hypertension management were based on the allocation of time per related activity. The

schedules of visits and other laboratory tests used in the cost estimation were based on the standard treatment guidelines (costed per protocol). Price lists were obtained from the Western Cape Department of Health for medical drugs, and from Vanguard CHC for laboratory investigations. The direct medical cost per patient was calculated by multiplying resource utilisation of inputs obtained from medical records and treatment guidelines by their respective price.

Step-down costing: Other costs that are not directly related to the provision of hypertension care, including capital costs (building, equipment and furniture) and recurrent costs incurred by support departments (e.g. overhead costs linked to administration, cleaning and maintenance) were allocated to hypertension care using step-down costing(17-19). Recurrent costs information was obtained from the latest financial expenditure report (2015/2016) for Vanguard CHC. Capital cost information was obtained from an inventory list of all the furniture and equipment provided at Vanguard CHC. The cost per square meter office space was used to estimate the buildings costs. Straight-line depreciation was used to calculate the financial costs of capital items while annualization was used for the economic costs. Capital items were annualized using a discount factor of 3% to allow for depreciation and the opportunity cost of purchase (17). The estimated lifespan used for buildings, furniture and vehicles was 30 years, 10 years and 5 years, respectively (17,18).

Departments at Vanguard CHC were divided into two categories, overhead department and final service departments (20). Final service departments referred to those departments that provide medical services directly to patients and consisted in this study of the chronic disease service and a category "other departments". The overhead (or support) departments do not provide medical services directly to patients, but are essential for the CHC to run and provide services such as cleaning, administration, maintenance and security (18,21,22). The pharmacy department is often considered an intermediate department (17) but was included with the overhead departments. Overhead departmental costs were allocated to the final service departments in a stepwise fashion. First, we allocated recurrent and capital costs to the various departments directly, based on their actual resource usage (20). For example, the cost of building was allocated directly to the various departments based on the surface area in square meters of these departments.

Subsequently, costs were allocated by the overhead departments to the chronic disease clinic. A set of allocation keys that describe the actual resource usage to allocate the overhead costs

was used. For example, maintenance costs were allocated to the chronic disease unit based on the floor space. A final step in this study included the allocation of costs from the chronic disease service to hypertension management. There was no specific department for managing raised blood pressure and hypertension at Vanguard CHC so we created a virtual hypertension department based on the time schedules at the clinic. Patients with hypertension use all rooms within the chronic disease clinic three days of the week, which is equivalent to 60% of the clinic days in a week. Therefore, we assigned 60% of all costs allocated to the chronic disease clinic using the step-down allocation to the virtual hypertension department.

Once all the costs had been allocated to the virtual hypertension department, the total cost was divided by the total number of hypertension visits to obtain the monthly unit cost per outpatient visit. However, as information on hypertension visits for the year 2015 was not available, the total number of visits at the facility was utilised. This figure was not disaggregated by type of care received. The latest detailed information on hypertension at Vanguard CHC was from 2011, where 6% of total visits were related to hypertension care. We applied this percentage of hypertension visits for 2011 to estimate the total number of hypertension visits for the year 2015.

Costs from the patient perspective

We conducted a patient exit survey to obtain information on direct (medical and non-medical) and indirect costs of hypertension from the patient perspective. Direct costs consisted of out-of-pocket expenditure on medical inputs (consultation, drugs and laboratory tests) and non-medical inputs such as food costs and costs for transportation to and from the health facility. Indirect costs incurred by the patient and informal caregivers were estimated using the human capital method, where we valued the loss of income to patients per hour spent away from an economically productive activity. The questionnaire also collected information on demographics, health-seeking behaviour, medical services received at Vanguard CHC, socio-economic status, and impact of disease (i.e. sex, income, transport costs and food costs). Income was measured by asking questions about monthly wages and income from various other sources (e.g. grants). The questionnaire was piloted on ten participants at Vanguard CHC prior to data collection.

Incremental cost estimation of the StAR-BP Intervention

We estimated the monthly incremental cost of the text-message based intervention under routine Vanguard CHC using the bottom-up approach. The incremental cost per patient was

calculated by multiplying resource utilisation of inputs by their respective price. Incremental costs denoted the difference in total costs between usual care and the intervention. To identify and measure the costs of the text message intervention under routine care conditions, structured interviews were conducted with both Vanguard CHC staff and the StAR-BP intervention staff. Only costs borne by the government if the intervention was run under routine care at Vanguard CHC were considered. Costs included in the analysis were: human resources, furniture and equipment, short messaging service costs, internet costs, and other operational costs related to the text message based intervention in managing hypertension care at Vanguard CHC. The salaries for human resources used in the intervention cost estimation were based on the governments average pay scale, the cost of SMS and internet usage were based on the average 2016 rates for the top three mobile and internet providers in South Africa (Vodacom, MTN and Cell-C).

Cost-effectiveness of StAR-BP Intervention

For the effectiveness information, the results of the StAR-BP trial were used to estimate the incremental cost effectiveness of the text message based intervention (12). The cost data and the StAR-BP interventions main outcome; blood pressure reduction (expressed in mm HG) were combined to estimate the cost-effectiveness of the intervention. The incremental cost effectiveness ratio was estimated by calculating the difference in costs between the usual care and the intervention divided by the difference in outcome (average blood pressure over twelve months) between the usual care and the intervention.

$$ICER = \frac{Costs\ of\ StAR - BP * - Costs\ in\ usual\ care}{Outcome\ in\ StAR - BP * - Outcome\ in\ usual\ care}$$

Data analysis

Data was double entered into Epi-Data software and analyzed using STATA (version 12, Texas: StataCorp) and Microsoft Excel®. Continuous variables were analyzed using means or medians and standard deviations or interquartile range, while categorical variables were analyzed using proportions.

Sensitivity Analysis

To examine how changes in the value of input variables affected the cost outcomes, we carried out a series of one-way deterministic sensitivity analyses. One-way sensitivity analysis was applied to the following variables: the discount rate for costs was varied from

0% to 10%, with the upper range corresponding to the maximum discount rate sometimes used in cost-effectiveness studies for South Africa. The utilisation rate at the facility was varied from 50% to a 100%. The average utilisation rate that is sometimes used in cost effectiveness studies for South Africa is 80%. For all other input variables (number of text messages and average blood pressure reduction, the baseline value was varied by 50 % in each direction.

Ethics Approval

Prior to commencement of the study, written informed consent was obtained from the participants (health workers and the patients). Anonymity was maintained throughout the medical records review process and we did not collect any patient identifying information (i.e. names and identity number). Ethics approval for this study was obtained from the University of Cape Town Human Research Ethics Committee (UCT_HREC: 418/2011) and the Western Cape Department of Health.

Results

Costs from the provider perspective

Current management of hypertension

Table 1 shows a summary of hypertension costs by the three perspectives of the analysis (health system, patient and societal). The total financial cost of hypertension management per patient visit at Vanguard CHC was R262, while the economic cost was similar at R263. This total cost includes the (non-medical) cost per outpatient visit estimated through the step-down costing, and the direct medical cost per visit from the bottom-up costing. The majority of the total cost per visit consisted of direct medical costs on drugs, laboratory investigations and medical staff (R228); the other costs per outpatient visits were R35. Drug costs alone contributed 54% (R140) of the direct medical costs while laboratory tests contributed 2% (R6).

Table 1: Summary of Unit Costs from the different Perspectives

Perspective (Usual care) Type of Costs	Health System		Patient	Societal
	Financial (a)	Economic (b)	- (c)	Economic (e)=(b)+(c)
Unit cost per outpatient visit	34.43	35.06		35.06
Medical cost per outpatient visit	227.69	227.69		227.69
Food Costs at facility			37.20	37.20
Travel costs			11.44	11.44
Productivity loss			122.88	122.88
Total Unit Cost per visit (ZAR)	262.12	262.75	171.52	434.27

Costs from the patient perspective

Demographic and socio-economic background of study participants

Demographic and socioeconomic characteristics of the study respondents are presented in table 2. A total of 246 patient exit interviews were conducted; four patients declined to participate. Of the 246 patients, 139 were diagnosed with hypertension with no comorbidities (HPT) while the other 107 were diagnosed with hypertension together with another comorbidity (HPT+Co). The average age of the respondents was 59 years and most of the respondents were women (74%). About 34% of the respondents reported having either

a full-time or part-time job; the majority (62%) reported social grants as their source of income. Ninety-one percent of respondents reported visiting the facility in the previous month. The medication dispensed to participants lasted for a month for the majority (80%), while the other 20% used the dispensed medication for longer, indicating incomplete adherence.

Table 2: Demographics and Socioeconomic characteristics

	ALL¹ (N=246)	Hypertension ONLY (N=139)	Hypertension & Co-Morbidity (N=107)
Mean Age (Years)	57	54	59
Mean Income (ZAR)			
Working	3902.12 (n=52)	3577.58 (n=33)	4465.79 (n=19)
Not Working ²	1555.47 (n=129)	1524.41 (n=68)	1590.10 (n=61)
Sex			
Male	26.42%	27.34%	25.33%
Female	73.58%	72.66%	74.77%
Race			
Black	42.68%	51.08%	31.78%
White	0.81%	0.72%	0.93%
Coloured	56.10%	47.48%	67.29%
Other	0.41%	0.72%	0.00%
Education			
No formal education	2.47%	3.65%	0.94%
Primary education	22.63%	18.25%	28.30%
Secondary education	70.37%	74.45%	65.09%
Tertiary Education	4.53%	3.65%	5.66%
Income Source			
Working full time job	25.26%	27.93%	21.69 %
Working part time job	8.26%	10.81%	4.82 %
Social Grant	62.37%	56.76%	69.88 %
Gifts	4.12%	4.5%	3.61 %
Mode of Transport			
Bus/taxi	17.55%	17.39%	17.76%
Car	15.55%	9.42%	23.36%
Walking	66.94%	73.19%	58.88%
Missed a dose last month			
Yes	11.38%	6.47%	17.76%
No	88.62%	93.53%	82.24%
Reason for not missing a dose			
Alarm reminders	16.00%	22.73%	6.45%
Family	7.56%	9.09%	5.38%
Feeling Sick	1.78%	2.27%	1.08%
I just knew/remembered	68.00%	60.61%	78.49%
Other	6.67%	5.30%	8.60%
Took alternative treatment ³			
Yes	26.34%	24.82%	28.30%
No	73.66%	75.18%	71.70%

¹ Individuals with hypertension combined with those that have hypertension & a comorbidity

² Refers to those unemployed, retired or disabled

³ Alternative treatment here refers to anything else that the patients took to manage hypertension i.e. vitamins or herbs from the traditional healer.

Direct and Indirect costs

The costs from the patient perspective were analysed separately for patients with HPT and HPT+Co (see tables 3 and 4). A summary of total patients' costs for both groups combined is presented in table 1. The average patient cost of HPT was R172 per month (see table 1). This cost consisted of direct non-medical costs (food and transportation) and indirect costs. None of the patients reported direct medical costs (e.g. drug costs). User fees for primary care were abolished in South Africa in 1994 and 1996. (23). Food costs and travel costs were modest since most of the people walked to the facility (67%) and did not buy any food at the facility (82%). Table 4 provides an overview of direct non-medical costs by type of patient (HPT and HPT+Co). Transport costs (one-way) were slightly higher for HPT patients compared to HPT+Co patients (R37 for HPT and R34 for HPT+Co).

Table 3 : Productivity costs for patients seeking hypertension care at Vanguard CHC in 2016 ZAR

Population Group	N	Travel time (one way) (a)	n	Total Time at facility (b) min	n	Acute Treatment (hours)	Admission in min (c)	Total Time (2 ¹ a)+(b)+(c) (min)	Productivity Loss (a+b+c)* income per min ²
HPT³									
Working	43	16.72	41	187	9	3.89	233.4	453.84	169.13
Not working	96	18.11	84	156	13	6.69	401.4	593.62	94.26
All HPT	139	17.68	125	169	22	5.55	333.0	537.36	122.88
HPT+Co⁴									
Working	22	18.18	14	190	7	4.85	291.0	517.36	240.67
Not working	85	22.52	59	164	14	3.42	205.2	414.24	68.6
All	107	21.63	73	168	21	3.90	234	445.26	105.42

¹ "2" refers to the two-way transport cost (to and from the facility)

² Average salary is calculated per minute assuming an individual works 9600 minutes a month

³ HPT represents patients with hypertension only

⁴ HPT+Co represents patients with hypertension together with one or more conditions such as Diabetes and Asthma

The costs for food bought by patients while at the facility were also similar between the two groups of patients (about R11 for both). The average time spent at the facility was similar between HPT and HPT+Co patients (169mins and 168mins, respectively). The travel time from home to the facility and back was 33 min for HPT and 43 minutes for HPT+Co. In some cases, participants reported having a very high blood pressure reading at the facility and had to stay for a couple of hours while being monitored. Total time spent at the facility was higher for working patients compared to non-working patients. Total time consisted of travel time and time spent at the facility. Indirect costs (i.e. loss of productivity) accounted for 71% of the patient cost. In both groups, participants who were working had a higher average direct non-medical and indirect cost compared to those not working or receiving social grants. The average productivity losses for HPT were higher than those of the HPT+Co patients (R123 and R105 respectively) (see table 4).

Table 4: Monthly Direct costs for people with hypertension (all costs in 2016 ZAR)

Patient Group	HPT (N=139)					HPT+Co (N=107)				
	n	Mean	(SD)	Min	Max	n	Mean	(SD)	Min	Max
Direct non-medical costs										
<i>Food Costs</i>										
Working	5	16.40	14.65	2	40	4	7	3.55	3	10
Not Working	13	9.54	5.94	2	20	13	10.9	8.32	3	30
Total	18	11.44	9.24	2	40	17	10.7	7.64	3	30
<i>Transport Cost</i>										
Working	10	54.50	64.24	5	200	7	45.28	39.84	6	100
Not Working	20	28.55	29.39	5	100	25	29.28	31.27	2	100
Total	30	37.20	44.73	5	200	32	34.37	33.82	2	100
Summary of direct non-medical costs										
Working		70.90					52.28			
Not Working		38.09					40.18			
Total		48.64					45.09			

Costs from the societal perspective

Given the negligible difference between financial and economic costs, we used only economic costs in the estimation of total costs from the societal perspective. The societal costs include all costs, irrespective of who bears the costs and who receives the benefits in this case combining patient and provider costs. We found the monthly cost of hypertension from a societal perspective to be R437. Of the total cost per visit from the

societal perspective, costs from the provider perspective represented 61%, while patient costs represented 39%. The largest cost category was the direct medical costs (53%) followed by indirect costs (28%) and overhead costs were the smallest cost category (8%). Table 1 shows a summary of HPT costs from the different perspectives.

Incremental costs and cost-effectiveness of StAR-BP intervention

Table 5 shows the monthly incremental cost per patient and the ICER for the text message intervention under routine care at Vanguard CHC. It would cost the hypertension service an additional R4 to add low frequency text message adherence support to the current package of care. With a yearly cost of R49, the ICER of the intervention is R22 per mm HG reduction at Vanguard CHC.

Table 5 Incremental costs and ICERs for text message intervention under routine care in 2016 ZAR

Monthly incremental cost per participant (ZAR) ¹	4.06
Yearly incremental cost per participant (ZAR)	48.72
Average mm HG reduction in StAR-BP intervention over 12 months	2.2 ²
Cost per mm Hg reduction (ICER) ³	21.95

¹ZAR= South African Rand

² Bobrow, K., Farmer, A.J., Springer, D., Shanyinde, M., Yu, L.M., Brennan, T., Rayner, B., Namane, M., Steyn, K., Tarassenko, L. & Levitt, N. 2016, "Mobile Phone Text Messages to Support Treatment Adherence in Adults with High Blood Pressure (StAR-BP): A Single-Blind, Randomized Trial", *Circulation*,

³ ICER= Incremental Cost Effectiveness Ratio

One-way Univariate Sensitivity Analysis

Figure 1: One-way univariate sensitivity analyses results.

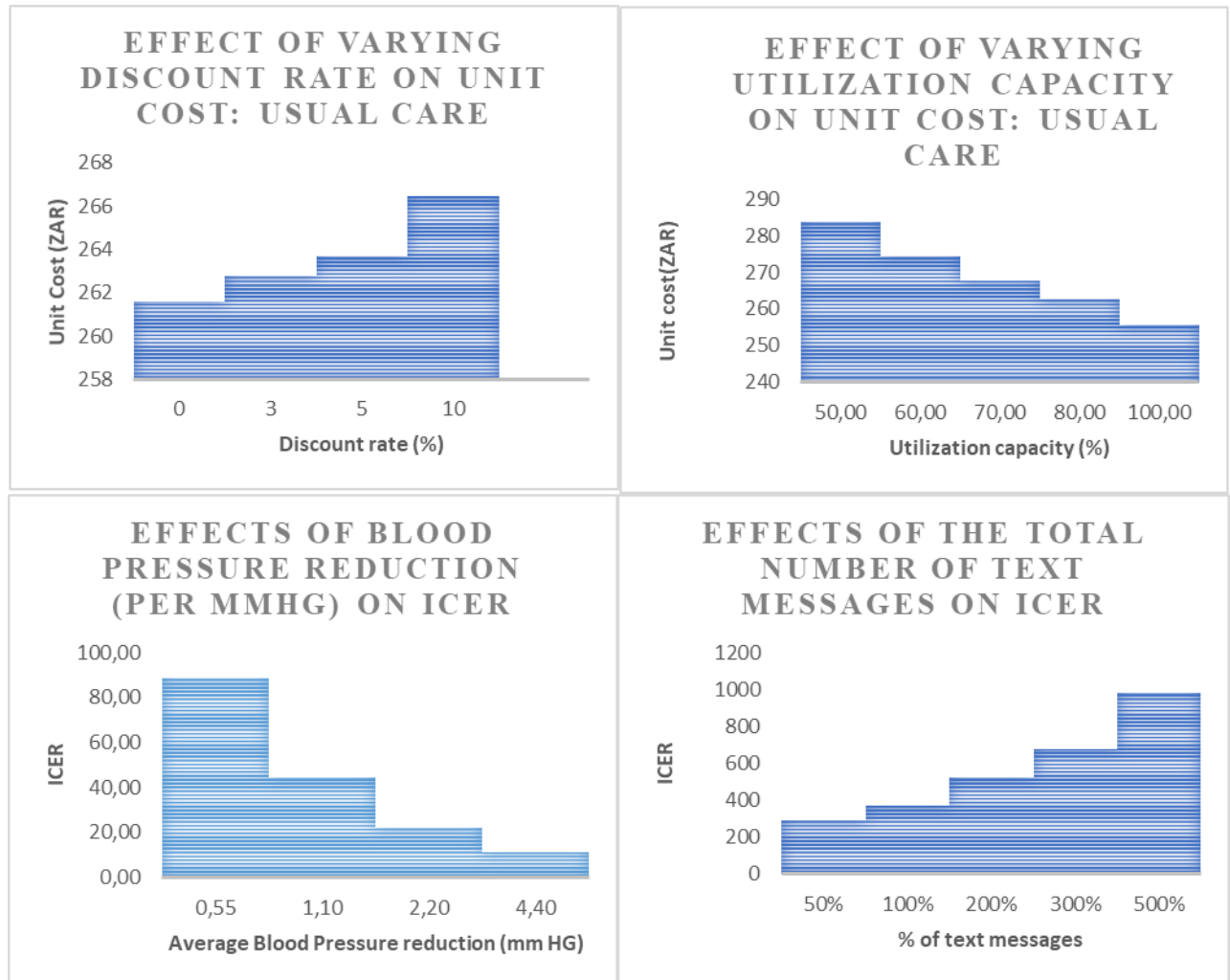


Figure 1 shows the impact of varying the different inputs on the incremental cost as well as to the total unit cost from the provider perspective. The total unit cost in the usual care arm was sensitive to the discount rate and utilization capacity, which was varied between 50% and 100%. As the capacity increased, the total unit cost decreased. The effect of discount rate was directly proportional to the total unit cost. We also varied the number of staff involved in the StAR-BP intervention and the total number of text messages sent to estimate the effect on the incremental costs. The incremental costs were sensitive to both the number of staff and the number of text messages.

Discussion

This is the first study estimating the cost of HPT management in South Africa. Results of the study show that hypertension costs R434 per patient per month in an outpatient primary care setting in South Africa. The average cost per patient of medication alone was R140, which is comparable to other studies that reviewed the average cost of anti-hypertensive drugs (20-22).

Adding the text messaging-based intervention to usual care leads to an incremental cost of R4 per visit. The StAR-BP study saw a 2.2 mmHg reduction in blood pressure over a 12-month period (12). Our cost effectiveness analysis shows that it would cost R22 for every mm Hg reduction in blood pressure. Based on the literature, in people aged over 50, the risk of strokes, CVDs and other hypertension related non-communicable diseases (NCDs) doubles for every 20/10 mmHg increase in blood pressure above 140/90 mmHg (24). Thus, any reduction in blood pressure is important. To put this 2 mm Hg reduction in context, Watkins et al (2016) estimated the cost-effectiveness of a salt reduction policy in South Africa; this policy was anticipated to reduce population systolic blood pressure in South Africa by slightly more than 2 mmHg on average and result in about 5600 fewer deaths and 23,000 fewer cases of CVDs annually, or about 11% of total deaths (25). Furthermore, uncontrolled hypertension may lead to even more severe and debilitating sequelae over time, and thus higher mortality and morbidity rates. One study showed that almost 50% of all coronary heart diseases and strokes are as a result of uncontrolled hypertension (26). A previous study in South Africa estimated that 50% of stroke, 42% of ischaemic heart disease, 72% of hypertensive heart disease, and 22% of other CVD in adults is attributable to high blood pressure” (27). Thus, adequate control of hypertension, including measures to improve medication adherence, should be focused on in public sector primary care.

At the same time, the cost of maintaining an mHealth intervention at scale in South Africa would be significant. Extrapolating the R50 incremental cost per patient per year would imply an annual additional investment by the national Department of Health of approximately R560 million or 0.3% of current public-sector expenditure (28). While this figure appears modest, health expenditure in South Africa has been increasing about 4% per year on average since 1995, though it has flattened out more recently. These trends suggest that mHealth for hypertension will need to provide very good value for money at scale in order to justify any investments on the order of one rand out of every additional ten rand

spent by the public health sector. In order to provide the Department of Health with better information for resource allocation, future work in this area will seek to (a) estimate the long-run cost of operating the mHealth intervention at a national scale and (b) estimate reductions in long-run health outcomes such as averted death and disability from stroke and heart failure

In terms of the transport and food costs of HPT and HPT+Co patients, we observed only a small difference between these two groups of patients. This is because we measured these costs based on each visit and it is not unreasonable that both groups of participants use the same transport systems or buy the same type of food while seeking care at the facility. Considering the number of times that both groups of participants visit the health facility in a year, we would expect the yearly total costs for transport and food to be different. The HPT+Co group utilised the facility more than the HPT group. Ninety-four percent of HPT participants reported visiting the health facility every month compared to 90% among the HPT+Co participants, with the other HPT and HPT+Co patients reporting visiting the facility every 2-3 months. Furthermore, 18% HPT+Co patients reported not taking at least one dose in the previous month compared to 6% in the HPT group.

The study was context specific and based on clinical trial conducted at a single health care setting using intermediary outcomes, as such the study had a number of limitations. The results are not generalizable as we used natural units making it difficult to compare the results across different diseases. Due to the limited availability of detailed utilisation statistics and medical records as well as information by type of hypertensive patient (i.e. controlled versus uncontrolled), our analysis estimated the costs for an "average" hypertension patient combining controlled and uncontrolled. It is therefore likely that the cost has been overestimated for controlled patients and underestimated for uncontrolled patients. Utility data pertaining to electricity and water usage was only available at an aggregate level as it is managed by the district as it was not possible to accurately allocate retrieve utilisation at the facility level these costs were excluded in the cost estimations. However, in our study, the outpatient unit cost accounted for 13% of the total cost for hypertension per month from the health system perspective. To estimate the productivity losses in the patient perspective, we used the human approach for both the working participants and the not-working participants. Average hourly rates were used in both groups, however social grant was used to calculate the hourly rate in the not working group. The study was based on one facility nor did we know the total number of patients in the province making it difficult to assess whether the intervention was affordable in the Western Cape. Our cost estimations for the StAR*-BP

intervention under routine care represent a crude cost estimation that may either be overestimated or underestimated.

The Western Cape Government recognises that the use of mHealth technologies may be beneficial and included mHealth as part of its 2030 vision for wellness plan (29). In some circumstances mHealth can become the “human face” of the medical staff to patients, improving both patient adherence and motivation. A study that made use of a telecommunication technology showed an improvement in adherence, reduced the number of visits at facilities and people were generally happy with the new system (30). A further inquiry to see (1) how the intervention might be modified to different provinces/ethnicities/languages and (2) what investments would be needed to operate at scale and be integrated with other mHealth interventions that would be beneficial to the government.

Conclusion

This study provides two novel contributions to the scientific literature. It is the first estimate of the societal cost of hypertension management in an urban South African environment. Second, it demonstrates that a text messaging based intervention to improve hypertension treatment adherence in South Africa can provide good value for money at an incremental cost R49 per patient per year and an incremental cost effectiveness of R22 per mmHg reduction in systolic blood pressure. Importantly, the next phase of this research will need to incorporate long-term cardiovascular outcomes as well as estimates of economies of scale and scope that may be realised by rollout of this intervention nationally and, potentially, integrating it with other mHealth initiatives. Our findings support ongoing efforts by the Department of Health to study and invest in mHealth solutions that can improve patient adherence and quality of care. Given the importance of hypertension as a risk factor for premature death and disability among South African adults, there is urgent need for research to on mHealth for cardiovascular disease prevention and care.

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Part D: Policy Brief

Hypertension management and mobile technology (mHealth) in South Africa

June 2017

POLICY BRIEF



**HEALTH
ECONOMICS
UNIT**

This policy brief was prepared by Danleen Hongoro as part of a dissertation for a Master of Public Health degree at the School of Public Health & Family Medicine of the University of Cape Town. The author received support from the National Research Foundation (NRF). Opinions expressed and conclusions arrived at, are those of the author and are not to be attributed to the NRF.

INTRODUCTION

Hypertension complications account for 9.4 million deaths globally (Lim *et al.* 2013). A study comparing 6 countries using data collected between 2007 and 2010 showed that the prevalence of hypertension amongst adults aged 50 years and more was highest in South Africa at 78% (Lloyd-Sherlock *et al.* 2014). With hypertension causing 50% of strokes, heart diseases and heart failure), the disease is an important public health problem in the country (The South African Hypertension Society 2015).

Nearly 50% of all hypertension patients either partially adhere to their medication or not at all, this reduces the success rate of controlling hypertension. Novel approaches to better manage hypertension and improve patient adherence such as mobile health (mHealth) are becoming increasingly popular. A recent community randomized trial (the StAR* trial) which investigated the effect of adherence support via SMS on treatment adherence and patient outcomes for the management of hypertension showed an improvement in

Key Points

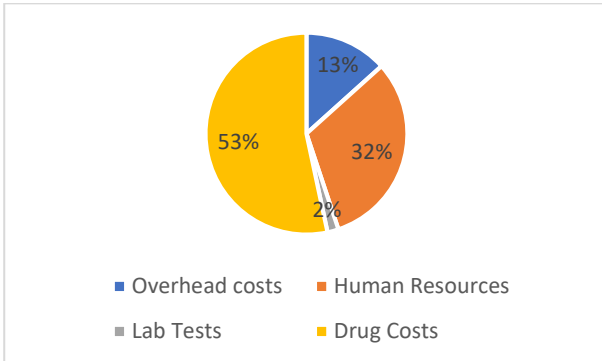
1. Hypertension has a high economic burden to the patient (28% out of pocket non-medical costs) and is linked to more costly conditions.
2. Drug costs are the major cost driver for hypertension costs from the provider perspective.
3. MHealth shows a potentially low cost of implementation.

adherence (measured by medication refill rates) and a small reduction in systolic blood pressure (Bobrow *et al.* 2016).

This policy brief reports on the findings from a costing and cost-effectiveness study that was conducted at Vanguard Community Health Centre (Bonteheuwel, Cape Town). The study estimated the cost of providing routine hypertension care and hypertension care in the context of the StAR* trial from the government and patient's perspective as well as the cost-effectiveness of the StAR* trial intervention.

The cost and cost effectiveness of hypertension management in the Western Cape.

Figure 1: Monthly percentage distribution of Hypertension Costs per person: Provider perspective



*Human resources here refer to staff directly in contact with hypertension patients and were not included in the overhead costs calculation.

The costing study at Vanguard CHC was carried out between August 2016 and January 2017. The annual cost per patient to the government of providing hypertension care attending Vanguard Community Health Centre was R3144, or R262 per month. The cost elements considered include: overhead costs (i.e. building costs, maintenance costs and operational costs) and the medical costs (i.e. drug costs). The major cost driver being the drug costs, contributing 53% (R140) of the total cost as shown in Figure 1.

Despite hypertension care being provided for free at public health facilities, patients still bear costs of accessing the health facilities. To estimate the patient costs, we interviewed 250 patients at the facility. The annual cost of seeking hypertension care per person at Vanguard Community Health Centre was R2064, or R172 per month. Patients did not

experience direct medical costs such as drug costs since the government of South Africa provides hypertension care free of charge at the facility. Patients only experienced direct non-medical costs (i.e. transport costs and food costs) and indirect costs (i.e. productivity losses) as shown in Figure 2. The direct non-medical out of pocket accounted for 29% of the total patient cost. The waiting time at the facility resulted in the high productivity losses. Hypertension patients spend on average 168 minutes waiting for a service at the facility.

From the social perspective, the total annual cost of hypertension was R5208 or R434 per month. Figure 3 shows the percentage distribution of hypertension costs from a societal perspective. Drug costs contributed 32% of the total costs and travel costs were the least contributor at 3%. Thirty eight percent of the societal cost was borne by the patient alone.

Figure 2: Monthly Hypertension Costs per patient: Patient perspective

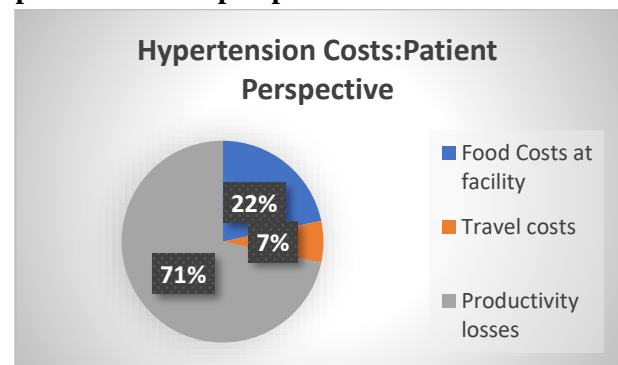
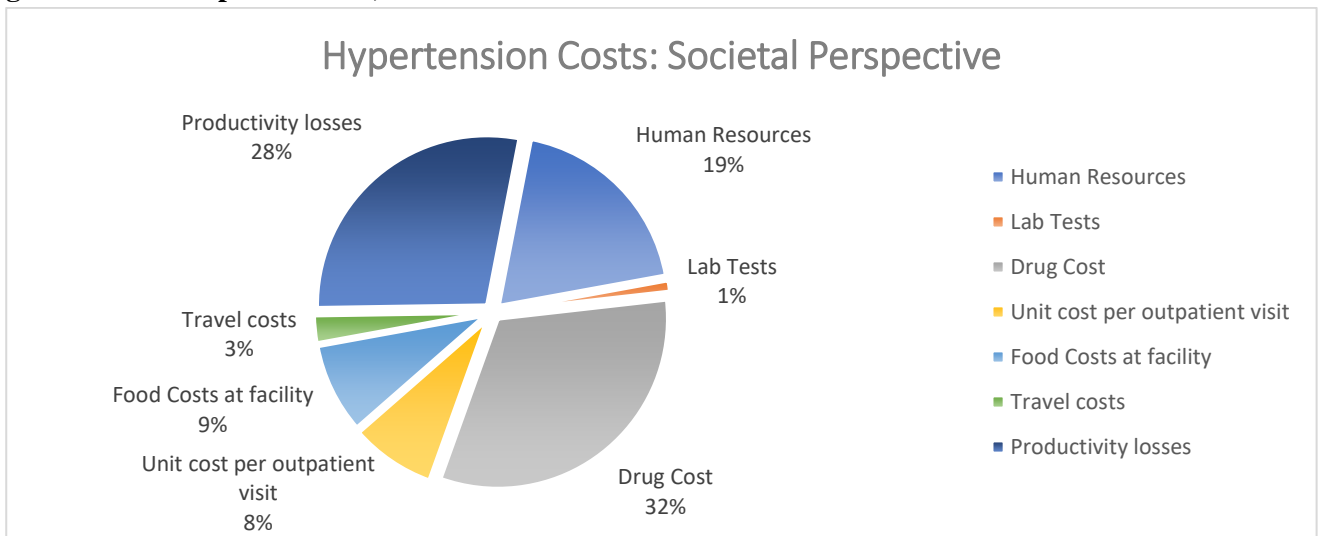


Figure 3: Monthly cost of hypertension per patient from the societal perspective (including government and patient costs)

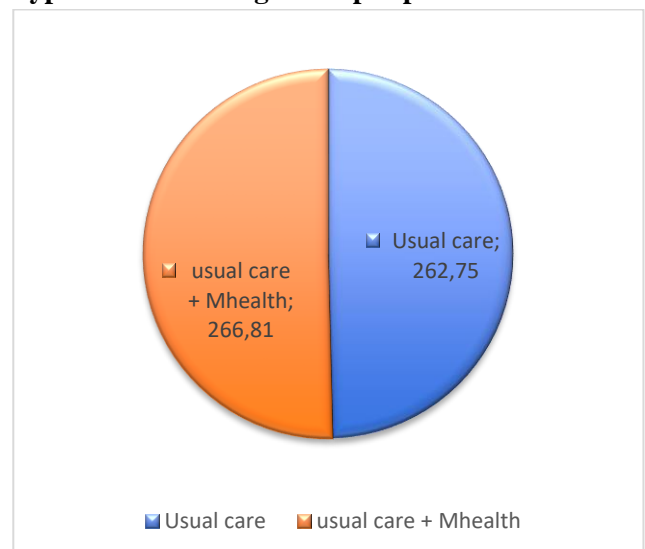


Mobile Health in Hypertension Management.

The monthly total cost of mHealth with usual health is R266.81 compared to R262.75 without the intervention as indicated in figure 4. The difference in cost between the two is marginal 1.4%(R4). Based on the effectiveness data from the StAR* trial (Bobrow et al. 2016), the text messaging based intervention showed an incremental cost effectiveness ratio (ICER) of R24 per mm Hg. This implies that for each unit reduction in blood pressure, it would cost the government R24 per patient if this messaging system is introduced under routine hypertension care. With hypertension, the risk of developing more debilitating and costly conditions such as strokes and cardiac infarctions increases with an increase in blood pressure so any small reduction in blood

pressure is important (Yusuf et al. 2004). For example, Watkins *et al.* (2016) estimated that a reduction of systolic blood pressure in the population of about 2 mmHg would result in 5600 fewer deaths and 23,000 fewer cases of CVDs annually.

Figure 4: The monthly cost of using mHealth in hypertension management per patient.



Policy recommendations

To improve the effectiveness of hypertension management, the following policy interventions ought to be considered:

- Since the Economic Burden of hypertension is a major issue in the country:
 - The government needs to develop policies to support patients that experience direct non-medical costs such as food costs and transport costs while seeking hypertension care.
 - The government to target waiting time of patients in the public health facilities in-order to reduce productivity losses.
- The government provides hypertension drugs for free, yet they are the major cost driver:
 - It may be worthwhile to implement strategies that target the risk factors of hypertension to reduce its incidence. This will in future reduce the need for hypertension medications which will reduce economic burden on the health system.
- Given the marginal difference in the cost of introducing mHealth (compared to the usual care) and effectiveness of the mobile intervention shown, it would be of great value to conduct larger demonstration projects using mHealth at population level to improve adherence as well as management.

Conclusion

Hypertension management is not cheap, both to the patient and the provider (the government). Non-compliance to medication by hypertensive patients potentially drives these costs even higher since uncontrolled hypertension is linked to even more costly conditions (i.e. strokes). The use of an

mHealth intervention to improve hypertension outcomes was found to be of low cost. A further inquiry to see (1) how the intervention might be modified to different provinces/ethnicities/languages and (2) what investments would be needed to operate at scale.

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Part E: Appendices

Appendix A: Summary of Hypertension Costing Articles

Study Author(s)	Country	Study Type and Data extraction tools	Costs Measured	Perspective	Hypertension costs
(Ganiyu, Suleiman 2014)	Nigeria	Cross sectional study • Case Notes	• Direct (drug costs)		Average monthly cost per: • Diuretics= NGN858.6 (\$5.51) • Blockers a= NGN1101.1 (\$7.07) • Fixed dose combinations = NGN10 425. (\$66.93).
(Maetzel et al. 2004)	Canada	• Questionnaire • Telephone Surveys	• Direct • Indirect	• Patient	Annual cost US\$3900
(Le et al. 2012)	China	Prevalence based cross-sectional survey • Questionnaire	• Direct • Indirect • Intangible	• Societal perspective	Mean unit cost of illness \$9393.3
(Costa, Juvenal Soares Dias da et al. 2002)	Brazil	Cross-sectional study • Interviews • Questionnaire	• Direct • Indirect	• Patient	Monthly mean costs of care (R\$ 89.90)
(Balu, Thomas 2006)	United States of America	Survey • Secondary data	• Direct		Total incremental annual direct Expenditure= \$US 54.0 billion Mean incremental annual direct expenditures per individual = \$US 1,131.
(Nguyen et al. 2014)	Vietnam	Retrospective survey • Financial records	• Direct	• Provider	Median total direct costs per patient = US\$65
(Dib, Riera &	Brazil		• Direct		Estimated direct annual cost in:

Study Author(s)	Country	Study Type and Data extraction tools	Costs Measured	Perspective	Hypertension costs
Ferraz 2010)					Public health system= US\$ 398.9 million Private health system =US\$ 272.7
(Ilesanmi, Ige & Adebisi 2013)	Nigeria	Cross-sectional survey • Chat Review	• Direct (drug costs) • Indirect	• Patient	Mean cost of treatment \$9.6 Median monthly drug cost \$6
(Al-Efan 2009)	Malaysia	Prevalence-based and incidence-based cross-sectional study. • Case record form • Questionnaire	• Direct • Indirect	Patient	The total costs for pre-hypertensive, stage 1 and stage 2 • Direct costs: RM1612.38, RM1741.85 and RM2718.21 • Indirect: RM8078.70, RM6654.52 and RM7511.41
(Ivanova et al. 2009)	Bulgaria and Serbia.		• Direct (drug costs)	Provider	Monthly cost of hypertension • Serbia = 12.56 Euro • Bulgaria= 8.23 Euro Monthly cost for complicated hypertension • Serbia 13.39 Euro • Bulgaria 8.23 Euro

Appendix B: Consent form

Survey number			
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Patient Exit Survey

Title of Research Project: The cost and cost-effectiveness of a text-messaging based intervention to support people with hypertension

Before we start with the interview, we want to make sure you understand the following information about the study:

- Your participation in this study is voluntary.
- There will be no reimbursement for participation to the study
- You may stop the interview at any time, or you can refuse to answer individual questions. However, we hope that you will participate fully in this survey since the information you provide us is important.
- The survey will take approximately 30minutes to complete.
- The survey may bring some minor psychological discomfort to the respondent. The survey questions the respondent on sensitive issues related to their income and the income of the household i.e. Questions asking how much you earn, how much you use to get to the facility and whether you borrowed money (or sold some personal assets) to cover hypertension costs)
- The information you provide will be kept strictly confidential. The consent form will be detached and kept separately from the questionnaire.
- The data will be used for research purposes; your responses in the survey will not be linked to your identity in anyway. The completed survey and the consent form will be kept in a locked cabinet and only the research team will have access to the locked filing cabinet; electronic data will be password protected and only accessible to the members of the research team.
- Do you have any questions regarding this study? Answer any questions.
- Do you agree to participate in this study?

YES	NO
-----	----

WRITTEN CONSENT: I give my permission to be interviewed

Name of the participant:.....

Signature: Date:

Appendix C: Information Sheet

Project Title: The cost and cost-effectiveness of a text-messaging based intervention to support people with hypertension

Who we are

Hello, my name is, and I am a member of a research team from the Health Economics Unit, School of Public Health and Family Medicine, University of Cape Town.

What we are doing

We are collecting information for a project entitled: **The cost and cost-effectiveness of a text-messaging based intervention to support people with hypertension.** In South Africa, hypertension is the most common reason why people visit health care facilities. It is also a risk factor for other diseases that cause a relatively large number of deaths in the country. To understand hypertension care in South Africa, we want to assess the cost of care for hypertension. This information will be used in other studies that aim to improve hypertension care in the country.

Your Participation

We are contacting you because of your knowledge as a patient with hypertension. We are asking you whether or not you will be willing to participate in the research project that examines the cost of accessing care for hypertension. We would like to ask you some questions about the services you received at this health facility for hypertension care, the costs you incurred while seeking care, your income and any income losses you may have incurred as a result of your condition. Additionally, we would like to review your medical record and retrieve information regarding your hypertension care and other related conditions. Such information includes; when, how and where you got diagnosed, the diagnostic tests done, the laboratory tests, the blood-pressure tests, the drugs that you take, how often you take each drug, the departments that you consult per clinic visit, how often you consult the clinic and demographic characteristics.

Appendix D: Provider Interview Questionnaire

Vanguard Community Health Centre

Section A: Identification

A1	Questionnaire number			
A2	Name of Interviewer			
A3	Date of interview (dd/mm/yyyy)	__ __ / __ __ / __ __ __ __		
A4	Interview start time	__ __ : __ __		
A5	Type of health professional	You need to make a list here: Assistant nurse Professional nurse Facility manager etc.		

Section B: Questions on Hypertension management at the facility.

Diagnosis process

How are patients with hypertension diagnosed at the facility? Are there guidelines on how to diagnose hypertension?

Who diagnoses them? What tools or equipment are used during the process of diagnosis?

From time of arrival at the facility, what processes do patients that have been diagnosed with hypertension follow?

Which departments do they go to?

Management or treatment of hypertension

How are patients with hypertension managed at the facility? Are there treatment guidelines for hypertension? How is it decided what medication or treatment regimen a patient is to be initiated on?

How many days' supply of medication do they get?

How often do the patients visit the facility for reasons linked to their condition (hypertension)?

Services Offered

What services are available for patients with hypertension?

Who provides what services?

Which department do you work in?

What is your role in managing patients with hypertension?

What services do you offer patients with hypertension in your department?

Service Delivery

How long does it take to serve one patient in your department?

From time of arrival, how long does it take for one patient to be seen by a health provider?

How many patients with hypertension are seen per day or hour?

How long does it take to take the blood pressure?

How long does it take to collect medication at the pharmacy?

Questions related to the StAR trial interventions

Activities

What activities were carried out in the StAR* study?

Can you explain how the SMS intervention worked?

Were there any guidelines for using the SMS intervention?

Which departments were involved?

How was it different from the normal standard of care?

Were you involved in the StAR* study?

What was your role in the study?

How many people were involved in each activity?

Who else was involved in the StAR* study?

Times

How long did it take for each activity i.e. sending SMS?

How many times did you send messages to individuals per day?

Did you have a specific day to send the SMS?

How long did you spend per patient with hypertension?

Challenges

Were there any challenges in using the SMS intervention?

How did you overcome them?

Appendix E: Patient Exit Survey

Vanguard Community Health Centre

Introduction to the patient:

My name is _____. I work for the University of Cape Town and we are interested in the costs that people face when they are seeking health care. Hypertension being a chronic disease that is known to be the most common reason why people visit health facilities in South Africa, this questionnaire seeks to collect information on the costs that are incurred by people with hypertension. This information will be used in other studies that aim to improve hypertension care in the country.

A1.1	Patient questionnaire number			
------	------------------------------	--	--	--

A1.2	Name of Interviewer	
A1.3	Date of interview (dd/mm/yyyy)	__ __ / __ __ / __ __ __ __
A1.4	Interview start time	__ __ : __ __

A1.5	Do you want to participate to the survey	1 Yes GO to next section 2 No
A1.6	Reason for not participating	1. Language not good enough 2. Time constraint 3. Not comfortable 4. Unspecified

SECTION A: PATIENT INFORMATION

A2.1	Sex	1 Male 2 Female
A2.2	What is your date of birth?	__ __/__ __/__ __ __ __ (day/month/year)
A2.3	Race	1. Black African 2. White 3. Indian or Asian 4. Coloured 5. Other (specify)_____
A2.4	Marital Status	1 Married 2 Living with partner 3 Single/never married 4 Widow/widower 5 Separated 6 Divorced 88 Other, specify _____
A2.5	Date of First Diagnosis	__ __/__ __/__ __ __ __
A2.6	Date of first treatment	__ __/__ __/__ __ __ __
A2.7	How was the patient diagnosed?	1 Routine screening in clinic 2 Routine screening in community (e.g. mobile unit, health fair) 3 Having symptoms (e.g., headache) 4 Diagnosed while in clinic or hospital for some other problem Other (explain): _____
A2.8	Other Comorbidities	1 Diabetes 2 Epilepsy 3 Asthma 4 Hyperlipidaemia 5 Rheumatoid Arthritis 6 Ulcerative Colitis 7 Hypothyroidism 8 Chronic obstructive pulmonary disorder 9 Schizophrenia 10 Chronic renal disease 11 Glaucoma 12 Coronary artery disease 13 HIV 14 None 88 Other? (specify)

Note down the current medication regime of the patient

	A2.9.1 Name	A1.9.2 Dosage/strength	A1.9.3 Frequency
a			
b			
c			
d			
e			

SECTION B: HEALTH SEEKING BEHAVIOUR

No	Question	Code
B1	Are you visiting this facility for the first time for hypertension?	1. Yes 2. No -> GO TO B3
B2	Where did you seek care previously for hypertension?	1 Hospital 5 Pharmacy 2 Clinic 6 Health Shop 3 Traditional 88 Other (Specify) Healer _____ 4 Faith Healer
B3	Why did you choose this health facility TODAY for your hypertension care?	1 Location close to home 2 Trust in providers/ high quality of care 3 Availability of drugs 4 Availability of female provider 5 Recommendation or referral 6 I was asked to come here 88 Other, specify: _____ 98 Do not know
B4	What type of hypertension care are you receiving TODAY ?	1. Pharmacy visit 2. Physician visit 3. Adherence club 4. All 88 Other _____
B5	How many times did you visit this facility last month because of your hypertension?	_____
B6	Did you ever have to stay long for observation because of Hypertension?	1 Yes 2 No -> GO TO SECTION C
B7	How long did you stay?	_____ hours

SECTION C: TRAVEL COSTS AND WAITING TIME

I will now ask you some questions related to your visit **TODAY**. These questions are related to your mode of travel, how long it took you to come here, and how it affected your usual activities.

No	Question	Code
C1	How did you travel to this health facility today?	1 Public transport 2 Car (private transport) 3 Walking 4 Cycling 88 Other (specify) 98 Don't know
C2	How many minutes did you take to get to this facility TODAY from your house (one-way)?	_____minutes
C3	When you came to the facility TODAY , did anyone accompany you here such as family or a friend?	1 Yes -> GO TO C7 2 No

Question No	C4. What is your relationship with that person?	C5. Did they miss school/work because of this clinic visit?	C6. How much does the person accompanying you earn per day?	C7. How many hours of school did they miss?
Person 1	1 Relative 2 Friend 3 Child 4 Care giver 5 Other (specify)	1 Yes 2 No	1 Nothing 2 R_____	_____hrs
Person 2	1 Relative 2 Friend 3 Child 4 Care giver 5 Other (specify)	1 Yes 2 No	1 Nothing 2 R_____	_____hrs
Person 3	1 Relative 2 Friend 3 Child 4 Care giver 5 Other (specify)	1 Yes 2 No	1 Nothing 2 R_____	_____hrs

C8	At what time did you arrive at this facility TODAY ?	___ __/___ __ Hrs	
C9	How much did you pay to come to this health facility TODAY (one-way)?"	1. Nothing 2. R_____	notes
C10	If you did not have to come to this facility, what would you be doing TODAY ?	1 Working 2 Relaxing at Home 3 Working at Home 4 Looking after Children 5 Other? (specify) _____	
C11	What are you doing after this clinic visit?	1 Going Home Skip to Section D 2 Going to work 88 Other (specify)? _____ 98 Don't Know	
C12	Will you get your normal day's wage for today?	1. Yes 2. No -> GO TO C14	
C13	Will you able to work a full day?	1 Yes -> If YES skip to section D 2 No	
C14	How many hours will you able to work TODAY ?	_____hours	

SECTION D: TREATMENT COSTS

I will now ask you some questions about the costs you incurred. These will include treatment costs, travel costs, food costs and costs to the people accompanying you, if any.

About how much did you spend on each of the following items during **TODAY's** visit (*for all that don't apply mark N/A*)

D1	Administration fees	R_____
D2	Consultation fees	R_____
D3	Laboratory tests	R_____
D4	Medication	R_____
D5	Under the table fees	R_____

SECTION E: FOOD AND GUARDIAN COSTS

N°	Question	Code
E1	When you came did you bring something to eat?	1. Yes 2. No
E2	If No, did you buy anything to eat?	1 Yes 2 No -> GO TO E4
E3	How much did you pay in total for the food?	R_____
E4	Did you get someone to look after your children or the house while you visited the clinic? (i.e. guardian or caregiver)	1. Yes 2. No -> GO TO Section F
E5	How much are you paying them?	R_____

SECTION F: MEDICATION COMPLIANCE AND ADHERENCE

N°	Question	Code
F1	During the past month, did you on any occasion not take your blood pressure medication?	1. Yes -> GO TO F3 2. No
F2	If NO , what made you remember to take your medication on time?	1. Caregiver 2. Reminders (e.g. alarm) 3. Adherence clubs 4. Family 5. Headache 6. Phone app 7. Feeling sick 8. I just knew 88 Other (please specify) 98 Don't know
F3	In the past month, did you at any moment feel the need to stop taking hypertension medication?	1. Yes 2. No -> GO TO F5
F4	Why did you feel like not taking the tablets?	1. I was feeling fine 2. Tired of taking medication. 3. Too much medication 4. Side Effects 5. Consulting with other health care practices (e.g. traditional healers) 88 Other (specify) 98 Don't know
F5	Thinking back last month, did you take anything else other than your normal hypertension tablets to control your hypertension? E.g. vitamins	1. Yes 2. No 98 Don't know
F6	How long will the supply of medicine that you received TODAY last?	1. One Month 2. Two Months 3. Three Months
F7	Have you ever used your phone to search for health information?	1. Yes 2. No

F8	Are there any other costs that you incurred because of TODAY'S visit that I haven't asked?	1. Yes 2. No 98 Don't know
----	---	----------------------------------

Please list the costs and their respective amounts below.

	F9 Cost	F10 Amount (ZAR)
a		
b		
c		

SECTION G: SOCIO-ECONOMIC INFORMATION

G1	What is your employment status?	1. Employed full-time 2. Self-employed (formal sector) 3. Part-time/contract/temporary 4. Casual 5. Self-employed (informal sector) 6. Unemployed 7. Housewife 8. Pensioner 9. Student/learner/child 10. Disabled and unable to work 98. Don't know 88 Other (specify) _____
G2	Is the reason for your unemployment your chronic illness (hypertension)?	1 Yes 2 No
G3	If yes, when was the last time you were working? (month/year)	
G4	Are you receiving any income?	1 Yes 2 No
G5	What is your source of income?	1 Working at a full-time job 2 Working at a part time job 3 Social Grant 4 I receive money from other people
G6	What was your total average monthly income PRIOR to your diagnosis with hypertension?	R_____
G7	What is your income NOW ?	R_____/Day

		R_____ /Week R_____ /Month
G7	Have you ever stopped working/going to school/doing housework due to your hypertension?	1 Yes 2 No -> GO TO G9
G8	If yes, for how long?	1 Less than 1 month 2 One month 3 2-3 months 4 4-5 months 5 More than 6 months
G9	Do you have children?	1 Yes 2 No -> GO TO G11
G10	How many children do you have?	1 One 2 Two 3 Three 4 Four 5 More than five
G11	What is your relation to the household head?	1. Me 2. Husband/wife/partner 3. Son/daughter 4. Adopted son/daughter 5. Stepchild 6. Brother/sister 7. Parent (mother/father) 8. Parent-in-law 9. Grand/great grandchild 10. Son/daughter-in-law 11. Brother/sister-in-law 12. Grandmother/father 13. Other relative Non-related person
G12	What is your highest level of education?	1 No formal education 2 Primary education 3 Secondary education 4 Tertiary education 88 Other (specify) _____
G13	Are you covered by a Medical Aid or Medical Benefit Scheme or any scheme that helps you pay for health-care services or medicines?	1 Yes 2 No

SECTION H: COPING COSTS

I will now ask you some questions about how you cover the cost of your care.

N°	Question	Code
H1	Did you borrow any money when you came for this clinic visit?	1. Yes 2. No -> GO TO H4
H2	How much did you borrow?	R _____
H3	Does the money have interest?	1. Yes 2. No -> GO TO H5
H4	How much interest do you have to pay?	R_____
H5	Did you take up any extra work to cover the costs for TODAY'S visit?	1. Yes 2. No
H6	Was there anything that you sold to cover the costs for TODAY'S clinic visit i.e. jewellery, radio, television or furniture?	1. Yes 2. No -> GO TO H9
H7	How much did you get from the sale?	R_____
H8	For TODAY'S clinic visit, did you withdraw any money from your savings account?	1. Yes 2. No -> GO TO H10
H9	How much did you withdraw?	R_____
H10	Did you have to modify your diet due to Hypertension?	1 Yes 2 No
H11	Is this diet modification costing you any money?	1 Yes 2 No
H12	How much is this diet modification costing you per month?	R_____

Thank You for participating in the survey!

Appendix F: Observation Tool

WAITING TIMES AND CONSULTATION TIMES

Date:	_ / _ / _ _ _ _
Facility:	
Observer's name	
Observation number	

Unit/Section	Time of arrival at the Unit/Section (a)	Time of Leaving the Unit/section (b)	Total Time spent (b-a)
Admission			
Prep Department			
Adherence Club			
Medical Officers (MOs)			
Pharmacy			
Other Section (s)			
(1)			
(2)			

Observer's signature _____

Appendix G: UCT Ethics Approval letter (HREC)



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



Room E52-24 Old Main Building
Groote Schuur Hospital
Observatory 7925
Telephone [021] 406 6338 • Facsimile [021] 406 6411
Email: nosi.tsama@uct.ac.za
Website: www.health.uct.ac.za/fhs/research/humanethics/forms

07 April 2016

14 HREC REF: 157/2016

Dr O Alaba
Health Economics Unit
Public Health & Family
Medicine Falmouth
Building

Dear Dr Alaba

PROJECT TITLE: THE COST AND COST-EFFECTIVENESS OF A TEXT-MESSAGING BASED INTERVENTION TO SUPPORT PEOPLE WITH HYPERTENSION (Masters candidate D Hongoro) sub-study linked to 418/2011.

Thank you for your response letter to the Faculty of Health Sciences Human Research Ethics Committee received on the 07 April 2016.

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

Approval is granted for one year until 30 April 2017.

Please submit a progress form, using the standardised Annual Report Form if the study continues beyond the approval period. Please submit a Standard Closure form if the study is completed within the approval period.

(Forms can be found on our website:

www.health.uct.ac.za/fhs/research/humanethics/forms)

We acknowledge that the student Dan/een Hongoro will be involved in this study.

Please quote the HREC REF in all your correspondence.

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

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

Yours sincerely

15 PROFESSOR M BLOCKMAN
CHAIRPERSON. FHS HUMAN RESEARCH ETHICS COMMITTEE

Federal Wide Assurance Number: FWA00001637.

Institutional Review Board (IRB) number: IRB00001938

16 HREC
157/2016

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

The Human Research Ethics Committee granting this approval is in compliance with the ICH Harmonised Tripartite Guidelines E6: Note for Guidance on Good Clinical Practice (CPMP/ICH/135/95) and FDA Code Federal Regulation Part 50, 56 and 312.REC 157/2016

Appendix H: Western Cape Provincial Approval



STRATEGY & HEALTH SUPPORT

Health.Research@westerncape.gov.za
tel: +27 21 483 6857; fax: +27 21 483 9895
5th Floor, Norton Rose House., 8 Riebeeck Street, Cape Town, 8001
www.capegateway.gov.za

REFERENCE: WC_2016RP54_748
ENQUIRIES: Ms Charlene Roderick

University of Cape Town

Rondebosch

Cape Town

7700

For attention: Mr Danleen Hongoro, Dr Olufunke Alaba

Re: **The cost and cost-effectiveness of a text-messaging-based intervention to support people with hypertension.**

Thank you for submitting your proposal to undertake the above-mentioned study. We are pleased to inform you that the department has granted you approval for your research.

Please contact the following people to assist you with any further enquiries in accessing the following sites:

Vanguard CHC

Luntu Mbanga

021 695 8242

Kindly ensure that the following are adhered to:

1. Arrangements can be made with managers, providing that normal activities at requested facilities are not interrupted.
2. Researchers, in accessing provincial health facilities, are expressing consent to provide the department with an electronic copy of the final feedback (**annexure 9**) within six months of

completion of research. This can be submitted to the provincial Research Co-ordinator (Health.Research@westerncape.gov.za).

3. In the event where the research project goes beyond the *estimated completion date* which was submitted, researchers are expected to complete and submit a progress report (**Annexure 8**) to the provincial Research Co-ordinator (Health.Research@westerncape.gov.za).
4. The reference number above should be quoted in all future correspondence.

Yours sincerely

DR A HAWKRIDGE

DIRECTOR: HEALTH IMPACT ASSESSMENT

DATE:

7/6/2016.

Cc:

K.GRAMMER

DIRECTOR: SOUTHERN WESTERN

Appendix 1: Journal Instructions for the author: BMC Public Health Journal

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2.21

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Overview of manuscript sections for Research articles

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For reporting standards please see the information in the [About](#) section.

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The title page should:

provide the title of the article

list the full names, institutional addresses and email addresses for all authors

indicate the corresponding author

Please note:

the title should include the study design, for example "A versus B in the treatment of C: a randomized controlled trial X is a risk factor for Y: a case control study"

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if a collaboration group should be listed as an author, please list the Group name as an author.

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be searchable through their individual PubMed records, please include this information in the "acknowledgements" section in accordance with the instructions below.

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The Abstract of the manuscript should not exceed 350 words and must be structured into separate sections: Background, the context and purpose of the study; Methods, how the study was performed and statistical tests used; Results, the main findings; Conclusions, brief summary and potential implications. Please minimize the use of abbreviations and do not cite references in the abstract. Trial registration, if your research article reports the results of a controlled health care intervention, please list your trial registry, along with the unique identifying number (e.g. Trial registration: Current Controlled Trials ISRCTN73824458). Please note that there should be no space between the letters and numbers of your trial registration number. We recommend manuscripts that report randomized controlled trials follow the [CONSORT extension for abstracts](#).

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The Background section should be written in a way that is accessible to researchers without specialist knowledge in that area and must clearly state - and, if helpful, illustrate - the background to the research and its aims. Reports of clinical research should, where appropriate, include a summary of a search of the literature to indicate why this study was necessary and what it aimed to contribute to the field. The section should end with a brief statement of what is being reported in the article.

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Results and discussion
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This should state clearly the main conclusions of the research and give a clear explanation of their importance and relevance. Summary illustrations may be included.

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Endnotes

Endnotes should be designated within the text using a superscript lowercase letter and all notes (along with their corresponding letter) should be included in the Endnotes section. Please format this section in a paragraph rather than a list.

References

All references, including URLs, must be numbered consecutively, in square brackets, in the order in which they are cited in the text, followed by any in tables or legends.

Each reference must have an individual reference number. Please avoid excessive referencing. If automatic numbering systems are used, the reference numbers must be finalized and the bibliography must be fully formatted before submission.

Only articles, clinical trial registration records and abstracts that have been published or are in press, or are available through public e-print/preprint servers, may be cited; unpublished abstracts, unpublished data and personal communications should not be included in the reference list, but may be included in the text and referred to as

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Smith JJ. The world of science. *Am J Sci.* 1999;36:234-5.

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Rohrmann S, Overvad K, Bueno-de-Mesquita HB, Jakobsen MU, Egeberg R, Tjønneland A, et al. Meat consumption and mortality - results from the European Prospective Investigation into Cancer and Nutrition. *BMC Medicine.* 2013;11:63.

Article within a journal by DOI

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Name: Danleen James Hongoro

Student Number: HNGDAN003

Course: Master of Public Health (Health Economics)

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