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CORE RESEARCH REPORT:

Research proposal

COST ANALYSIS AND COMPARISON OF TWO GLOBAL CARDIOVASCULAR RISK SCORES IN HYPERTENSIVE PATIENTS AT MAFIKENG PROVINCIAL HOSPITAL

A PRELIMINARY EXPLORATORY STUDY

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Research protocol submitted to seek ethical clearance from the Human Research Ethics Committee of the Faculty of Health Science, University of the Witwatersrand, in **partial fulfilment of the requirements for the degree of Master of Family Medicine**

Johannesburg 2016

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I, Doctor J.P. Mbuilu, hereby declare the following:

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Signed at Mafikeng on 17/01/2015

Dr Mbuilu JP

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LIST OF ABBREVIATIONS

BP:	Blood pressure
CVD:	Cardiovascular disease
CVR:	Cardiovascular risk
CVRE:	Cardiovascular risk estimate
CVRF:	Cardiovascular risk factors
ECG:	Electrocardiography
EHS-ESC:	European Hypertension Society and European Society of Cardiology
GRA:	Global risk assessment
GRS:	Global risk score
HT:	Hypertension/Arterial hypertension
IHD:	Ischaemic heart disease
LB-GRA	Laboratory-based global risk assessment
NCD:	Non-communicable diseases
NLB-GRA	Non-laboratory-based global risk assessment
OPD:	Outpatient Department
SAHS:	Southern African Hypertension Society
WHO:	World Health Organization

INTRODUCTION

1. BACKGROUND AND LITERATURE REVIEW

1.1. Background

Deaths from non-communicable diseases (NCDs) accounted for two out of every three deaths in 2010.[1] Cardiovascular disease (CVD) has been the leading cause of death from 1990 to 2013.[2] By 2020, CVD will have become the leading cause of death and disability in the world, and the current geographic distribution of the burden caused by CVD is not expected to change.[3] However, 80% of the burden of CVD is borne by low and middle-income countries where resources are scarce.[4] Cardiovascular disease is secondary to atherosclerosis that evolved over the years, and is the consequence of a complex interaction between many risk factors. Among major risk factors such as obesity, lipid disorders and tobacco use, hypertension (HT) is the leading condition responsible for deaths due to CVD worldwide.[4] An efficient control of HT and other risk factors is one of the key answers to the CVD pandemic. This response starts with the identification of patients at high risk of developing cardiovascular events like stroke and ischaemic heart disease (IHD), since they represent those who benefit the most from pharmacologic interventions. This discriminative approach of selecting patients on the basis of their potential cardiovascular risk (CVR) is cost-effective and relevant for primary care in low and middle-income countries.[5,6] There are various scoring systems to achieve this cost-effectiveness, but it would be imperative to detect which of these systems are cost-efficient; therefore the need to carry out this study.

1.2. Hypertension, cardiovascular risk factors and cardiovascular diseases

A diagnosis of HT is made when the average of two or more diastolic BP measurements on at least two subsequent visits is ≥90 mm Hg, or when the average of multiple systolic BP readings on two or more subsequent visits is consistently ≥140 mm Hg.[7] Hypertension is prevalent worldwide and studies are predicting a rise in NCDs in general, and HT in particular.[4,8] An increased incidence and prevalence of HT and cardiovascular risk factors (CVRFs) should also be expected in South Africa.[9] Many factors can explain this anticipated trend, including epidemiological transition. Over the next three decades, various reports are predicting a rise in CVDs including HT.[10] In a recent multicentre screening campaign including 47,443 adults in six middle-income countries, HT prevalence was found to vary between 23% and 83%; with up to 87% undiagnosed or untreated hypertensive patients at one site.[11] An early population-based survey conducted in 1998 aiming to determine the prevalence of HT in South Africa found a 21% HT prevalence using the cut-off-point of 140/90 mmHg.[12] A more recent survey result has shown a slight increase in prevalence from 25% in 2003 to 30% in 2013.[13] There is a similar increasing trend in the prevalence of NCDs such as diabetes and HT in Sub-Saharan Africa.[14]

Arterial hypertension (HT) remains a major public health concern. Hypertension is asymptomatic for a long time before and after it has been diagnosed, giving patients a false sense of well-being. During that period end-organ damage takes place, leading to complications many years later. Uncontrolled HT leads to cardiovascular complications or events such as stroke, coronary artery disease and renal failure. All such complications or atherosclerotic CVDs are having a direct impact on productivity and quality of life. Many strategies to control HT have been studied and have shown efficacy.[15.16] Challenges to reach an acceptable control of blood pressure (BP) vary according to local specificity. In high-income countries, challenges lie in individual aspects. In low and middle-income countries, organisational and health systems encounter problems such as unavailability of tools involved in HT care like a calibrated BP machine, an efficient patient record system, the supply of medication and the level of care worker awareness of guidelines. This last aspect is illustrated by a study conducted in Cape Town, South Africa, where primary health care (PHC) practitioners' knowledge of HT and their understanding of the South African national guidelines on HT have been found to be poor.[17]

The high prevalence of HT in PHC in South Africa has been demonstrated by many recent studies. In a large multicentre prospective cross-sectional survey conducted on South African PHC including 24,561 consultations, HT with cardiovascular symptoms appeared to be the leading reason for encounters, comprising 9,5% of reasons to consult a public primary care practice.[18] Adejayan found similar results in an equivalent prospective cross sectional study conducted in the North West Province including 5,000 reasons for encounters and diagnoses recorded in primary care.[19] The leading single cause of these encounters was related to HT, accounting for 16% of all diagnoses. Further results from the same survey have shown that the three leading diagnoses were HT (12.0%), upper respiratory tract infection (5.3%) and HIV/AIDS (3.9%).[18]

1.3. Cardiovascular risk assessment

The World Health Organization (WHO), the International Hypertension Society (IHS) as well as many other guidelines recommend the use of the absolute or global CVR approach rather than the individual risk approach when treating HT.[20,21,22,23] The absolute CVR approach is cheaper and more cost-effective, and saves more lives as compared to the individual risk treatment approach.[24] The global CVR approach is interchangeably referred to as the global risk assessment (GRA).[25] The GRA aims to determine the **global risk score** (**GRS**) by adding, in a mathematical cardiovascular predictive equation, values of CVRF present in an individual.[26] From this cardiovascular grading, a specific treatment modality will be initiated. The cardiovascular grading may be expressed either in cardiovascular level clustering such as low, moderate or high added CVR (South African guideline)

or in percentage (Framingham equation). [20,21] The treatment of individual risk factors was used in the past as opposed to the GRA, but the former is no longer supported as it has been demonstrated to be non-cost-effective and clinically irrelevant.[27] With the single risk factor approach, some individuals presenting with isolated risk factors would be treated with unnecessary medication while others with many risk factors would receive only treatment for the recognised risk factors. There is currently a universal agreement to use the GRA, and this is reflected in different national guidelines.[21, 28]

The most popular equation used in CVR assessment is derived from the Framingham cohort study, which was established in East Boston in the United States of America in 1948. To date, 5,209 adults between 30 and 62 years of age have been recruited, predominantly of white origin.[29] The Framingham risk score derived from this study included non-laboratory-based risk factors such as smoking status as well as laboratory-based risk factors such as the LDL-cholesterol level. One of the advantages of a cardiovascular risk estimate (CVRE) is that it helps in predicting the likelihood of cardiovascular events such as stroke and IHD. A CVR equation such as this assists the clinician in deciding on the level and modality of preventive measures to be prescribed for an individual patient. For example, with the GRS recommended by the European Hypertension Society and the European Society of Cardiology (EHS-ESC), a patient assessed as having low added CVR will start a treatment consisting of lifestyle modification and BP monitoring for three to six months, whereas one who has high added CVR will be immediately started on medication in addition to lifestyle modification.[30] In a given population, the prevalence of certain risk factors combined with environmental and genetic factors will dictate the occurrence of specific cardiovascular events. For example, in India and among Caucasians, IHD is more prevalent than stroke, while in the black population stroke is more predominant as compared to IHD.[31] These geographic repartitions of cardiovascular events imply that the original population must only use a specific CVRE or at least have a validation study prior to its use.

1.4. Laboratory and non-laboratory-based cardiovascular assessments

Many CVR scores with specific advantages and limitations have been developed. The frequently quoted Framingham Risk Score derived from the study carrying the same name is frequently cited in medical literature. The Framingham study is the largest cohort study in the field of cardiovascular estimation with a long follow-up period.[29] This study included various racial and ethnic groups with a dominance of Caucasian participants, and is regarded as a reference in CVRE.[32] Unfortunately the score cannot be used universally because of risk factor prevalence variability and the influence of genetic and ethnic factors on the global CVR level. In Europe, many other scores have been developed, among them the NHAES score, the Q-RISK2-2011 and the Reynold score.[33] They are

validated specifically for European populations. In Sub-Saharan Africa, the estimation of CVR is performed based on research developed elsewhere. The WHO recommends the use of the modified Framingham equation adapted for each region of the world.[5,34] In South Africa, the guidelines developed by the South African Hypertension Society (SAHS) recommend the use of the risk stratification based on the EHS-ESC guidelines.[21] In South Africa, the GRS is calculated using the chart from the SAHS guideline. This is known as the South African Hypertension Society Global Risk Score (**SAHS/GRS**) chart. Using the SAHS/GRS, the patient is classified in one of the two CVR clusters: either low/moderate added risk or high/very high added risk. The first group of patients assessed as having low or moderate CVR will undergo three to six months of lifestyle modification without drug treatment. They will be monitored regularly during this period and will at the end of each cycle be reclassified in one of the two clusters of CVR grading, and be treated accordingly. The second group labelled as high and very high added CVR leave the health care facility with a plan for lifestyle modification and at least one anti-hypertensive drug. The SAHS/GRS is a laboratory-based score.

Some laboratory-based CVRFs used to determine the GRS have included in their equation variables like the LDL-Cholesterol level, which is less accessible in resource-limited settings.[23] Therefore the WHO and the IHS advocate for the non-laboratory-based global risk assessment (NLB-GRA) to be used in low-income countries.[5] The **"WHO-Scores"** ignore the cholesterol level and are developed for each WHO world region.[34] The "Gaziano" and the "Non-Laboratory Framingham" (NLB-Framingham) GRS substitute cholesterol for BMI. [20,35] This makes those scores simple, accessible and clinically available in resource-constrained settings. Many studies have demonstrated the performance of those scores around the world.[26,35] Because of variability in the prevalence of CVRFs, it is recommended that a validation study be conducted locally on a given population before adopting any GRS algorithm developed elsewhere.[32]

1.5. Cost and other implications related to global cardiovascular risk assessment

Establishing CVR on a patient includes a combination of clinical data and laboratory studies such as cholesterol level. A GRS without cholesterol is cost-saving. Patients screened as high risk can then be treated efficiently with a combination of modalities including determining and treating HT and an elevated cholesterol level. Patients stratified as low risk will benefit from lifestyle modification and regular follow-up.

2. RATIONALE AND JUSTIFICATION

South Africa carries a high burden of CVD with HT as the most prevalent risk factor.[12] The efficient and evidence-based approach to the treatment of HT lies in determining the global CVR of the individual. This helps us to set up an efficient and cost-effective treatment. Many GRS systems have been developed, each specific to a given population and its CVR profile.[22] The current national guideline developed by the SAHS recommends the use of a laboratory-based cardiovascular risk score derived from the EHS-ESC: the **SAHS/GRS.**[21] On the other hand, the WHO recommends the use of a non-laboratory-based GRS (**WHO/GRS**) calculated from the chart specific for the Southern African region: the WHO/IHS Chart AFR E.[5, 34]

The current SAHS/GRS used in South Africa implies determination of global CVR after obtaining clinical data from patients, as well as investigations including the cholesterol level and determination of left ventricular hypertrophy by electrocardiography (ECG). On the other hand, the WHO/GRS determines the global CVR after obtaining only clinical data.

To my knowledge, there is no study comparing the SAHS/GRS Chart and the WHO/GRS in the rural South African region of Mafikeng. Such a study will provide grounds for the use of NLB-GRA in rural primary care in South Africa where it is needed most. Availability of NLB-GRA in South African PHC will assist primary care workers to accurately assess the global CVR, and this will **benefit their patients** from the first visit. Comparing the current SAHS/GRS with the proposed WHO/GRS for Southern Africa in a rural setting will answer many questions such as the level of performance of the WHO/GRS score in classifying rural hypertensive patients on the correct level of CVR. The anticipated cost-saving linked to the non-inclusion of laboratory studies such as cholesterol level testing is imperative in the light of the ongoing dwindling of financial resources in the province and the country at large. This will also decrease the risk of patient loss to follow-up, the loss of specimens to/from the lab, the need for patients to wait for laboratory results (cholesterol levels) as well as the financial burden on patients having to come back for blood results before being risk-categorised. Costs will nose-dive, making quality service delivery less cumbersome for health care workers and patients alike. The WHO/GRS is based on clinical variables, making it easy to use in primary care. Because of time and resource limitations, the present study will be limited to a specific number of patients.

3. RESEARCH QUESTION, AIM AND OBJECTIVES

Research question: In a convenient sample, are the Global Risk Scores (GRSs) using the Southern African Hypertension Society chart (**SAHS/GRS**)[21] and the WHO/IHS Chart AFR E[34] (**WHO/GRS**) **equivalent and cost-effective**?

Aim:

To compare the cardiovascular risk scores calculated from the SAHS/GRS and the WHO/GRS on hypertensive patients attending Mafikeng Provincial (MPH) and to determine the difference in financial cost between the two scores.

Objectives:

1. To describe the socio-demographic profile of participants
2. To determine the proportion of cardiovascular risk factors among participants
3. To grade hypertensive patients using the SAHS/GRS
4. To grade hypertensive patients using the WHO/GRS
5. To evaluate the correlation between the pairs of calculated risk scores in every participant
6. To compare the financial costs of the SAHS/GRS and the WHO/GRS

METHODS

4. STUDY DESIGN

This will be a cross-sectional prospective **preliminary study.**

5. STUDY SETTING

Mafikeng Provincial Hospital (MPH) serves as a level 1 referral hospital for Mafikeng Sub-district health facilities (community health centres, primary health clinics and general practices) and as a level 2 hospital for different district hospitals in Ngaka Modiri Molema district. Mafikeng Provincial Hospital is situated in Mafikeng, the capital of North West Province. The largest part of Mafikeng Sub-district is rural. Mafikeng Provincial Hospital has 409 beds, combining level 1 and 2 services.

The Family Medicine Department together with the Gateway Clinic constitutes the level one component of Mafikeng Provincial Hospital. The Family Medicine Department consists of 4 units: the accident and emergency unit, the general outpatient department, the wellness clinic and the short stay ward. Hypertensive patients from different primary care facilities within Mafikeng Sub-district are referred to Mafikeng Provincial Hospital via the General Outpatient Department where a family physician, a registrar and an intern review them initially. The most frequent reason for referral is uncontrolled HT. The General OPD collaborates with specialised “clinics” or OPDs from different level 2 departments like the “HT clinic” in the Medical Outpatient Department where complex clinical situations and patients who need long-term specialised follow-up are seen. Currently 800 hypertensive patients are registered in the Medical OPD and an average of 1,200 hypertensive patients are seen annually in the General OPD.

6. STUDY POPULATION AND SAMPLING

All hypertensive patients referred from primary care facilities in Mafikeng Sub-district and who are initially seen in the Family Medicine General OPD represent the study population. The recruitment of patients will take place in this department. This study will determine the feasibility of a cardiovascular estimate using the two different scoring systems described above and will include a cost comparison. This preliminary study will serve as a reference for a complete investigation including an adequate sample. This study focuses on hypertensive patients from primary care facilities in Mafikeng Sub-district.

The average number of new and follow-up hypertensive patients registered during 2014 was 1,200. This number was included in the Raosoft sample size calculator using a confidence level of 95%, a variability degree of 50% and a margin error of 5%.[36] The calculator generated a minimum number of 292 patients as a representative sample to be studied. However, to allow parametric statistical

analysis, this pilot study will only include 120 patients: 60 males and 60 females. Consecutive patients consulting the outpatient department at Mafikeng Provincial Hospital who accept to participate in the study will be enrolled until the sample size is reached. Each patient participating in this study will serve as is own control: From each patient data serving to determine cardiovascular risk using both equations will be collected.

7. INCLUSION AND EXCLUSION CRITERIA

All hypertensive patients of 18 years and older referred from Mafikeng Sub-district primary care facilities between March 1st and June 30th 2016 presenting in the outpatient department will be included in this study, depending on their informed consent. Patients who need emergency treatment, those unable to stand or to comply with the anthropometric measurement standards described below, and patients referred from other hospitals will be excluded. Patients with a history of cardiovascular events such as stroke and IHD will also be excluded.

8. DATA COLLECTION

8.1. Data collection tool

The WHO stepwise approach to non-communicable disease risk factor surveillance (STEPS) will be used for data collection. The WHO STEPS Instrument will serve as a support for data collection. A data collection sheet with identifiers is attached in appendix 4. This is a standardised and validated data collection instrument developed by the WHO intending to generate local data comparable with other sites worldwide, and it is recommended for collection of CVRFs.[37]

8.2. Process of data collection

All hypertensive patients will be approached individually while in the pre-vitals room. A research team member will give an extensive verbal explanation of this study. Patients willing to participate in the study will undergo an informed consent process following the points detailed in the consent form (see Appendix 1). At the end of this dialogue all hypertensive patients, irrespective of whether they agree to participate in this study, will receive an explanation of how to collect a urine sample. A urine sample bottle will be given to each one and they will be invited to collect urine and return it to the vital signs room. Patients who agree to participate in the study will be invited to sign the consent form in the presence of a nurse who is not a member of the study team and who will act as a witness. Patients not willing to participate will be given normal care according to hospital standards and current national guidelines. After signing the informed consent form, a special sub-file will be included in the hospital record. This sub-file will contain the WHO STEPS Instrument designed to assist in data collection.[37] A discriminating colour-coded “orange dot” will be glued to the front of the file cover

to avoid replication of recruitment. The patient will be invited into the vital signs room where a nurse trained for this study will record his/her weight, height, BP, heart rate and urine dipstick results. The patient will then be invited into the interview room, where a nurse trained to use the WHO STEPS approach Instrument will administer a questionnaire in English or Setswana. After the interview, the patient will undergo a clinical consultation including a repeat of the BP measurement and a physical examination. The patient will enter the investigation room where a blood sample will be drawn and an ECG will be recorded. The sub-file will be withdrawn from the patient file and kept for data capturing. Before being discharged, the patient will receive a brief feedback on the entire consultation and will be invited for a subsequent visit where definitive management will be offered according to the findings and the national guidelines. To conduct this process, a team of four members will be needed: three nurses and one doctor. Nurse one will be in the pre-vital room to invite hypertensive patients, nurse two in the vital room, the researcher in the consulting room and nurse three in the investigation room.

8.3. variables to be collected

At the end of this study, I will need to establish the cardiovascular risk stratification of each participant using both the SAHS/GRS and the WHO/GRS. The calculated risk will be compared mutually for concordance. This simply means that each participant will be the patient and his own control. The only factor changing will be the test used to determine the cardiovascular risk level.

9. DATA ANALYSIS

Data recorded during the clinical interaction with the patient will include the variables listed in the Appendix 4. In total, 11 variables will be recorded. The data will be recorded onto an Excel spreadsheet and then transferred to SPSS 17.0 for summary and analysis. Categorical variables will be summarised by their frequency and percentage; continuous variables will be summarised by their mean +/- standard deviation (SD). Clusters of CVR categories will be compared using a Chi-square test to assess similarity. Tables and charts will be used to describe and present different data summaries.

9.1. Establishing global cardiovascular risk using the SAHS/GRS

Using Table 4 (Appendix 6), the number of risk factors will be plotted in the first column of the table and the level of the mean BP in the first row. Among the risk factors, the left ventricular hypertrophy will be determined using information from the ECG to populate the cornel score as detailed in the guideline.[21] The intersection corresponds to the level of CVR.

The SAHS/GRS discriminates four groups of CVR namely low, moderate, high and very high added CVR groups. According to this guideline, the first group identified as having low added CVR will be

followed up for six to twelve months of lifestyle modification. The second group identified as having moderate added CVR will be prescribed a lifestyle modification and followed up for three to six months. The third group identified as having high added CVR will immediately be started on one antihypertensive drug in addition to advice/health education on lifestyle modification. The fourth group classified as having very high CVR will also be commenced on one antihypertensive drug in combination with lifestyle modifications.

From a therapeutic perspective, all four CVR groups can be divided into two groups. The first group will start treatment with one lifestyle modification and the patients in this group will be reviewed during 3, 6 and 12-month follow-up, with treatment changes depending on the level of risk. The second group will be combining one antihypertensive drug with lifestyle modification from the beginning. For this study, the first group of patients managed with lifestyle modification only will be included in the first category and the second group will include those managed with at least one antihypertensive drug.

9.2. Establishing global cardiovascular risk using the WHO/GRS

Using Table 3 (Appendix 5), every patient's clinical data will be plotted to determine the percentage of CVR. Patients scoring less than 30% will be classified as Category 1. Those scoring equal to or more than 30% will be included in Category 2, since they will be managed with at least one antihypertensive drug from the beginning.

9.3. Comparison of the two scores: WHO/GRS vs. SAHS/GRS

All patients will be classified into one of the two categories of CVR: low and low to moderate or with a CVR less than 30% (Category 1), or high to very high or with a CVR equal to or more than 30% (Category 2). Using the current SAHS/GRS as reference score ("gold standard"), the sensitivity and specificity of the WHO/GRS to correctly classify patients into one of the two CVR clusters will be established. This result will be presented in a 2X2 table. Multivariate statistical manipulation will be done to improve the performance of the WHO/GRS by including different clinical variables in a multivariate model. Multiplying the number of patients correctly classified as low to moderate risk with the cost of cholesterol testing, the total cost saving will be established. The ratio of high-risk patients falsely classified as low risk will be determined and the number needed to harm (NNH) will be established. The statistical test plan is presented in Table 1 below.

Table 1. Statistical test plan

Objectives	**Data collection** (Variables and/or data needed)	**Planned statistical analysis**
1. To describe the socio-demographic profile of participants	Categorical variables like race and education	Frequency and percentage
	Continuous variables like age	Range, mean and standard deviation
2. To determine the proportion of CVRFs among participants	Proportion of risk factors such as smoking status, high cholesterol level and left ventricular hypertrophy present in hypertensive patients	Percentage
3. To grade hypertensive patients using the Global Risk Assessment from the South African Hypertension Society Chart (GRA/SAHS Chart)	Risk factors, SAHS-GRA Chart to obtain two clusters of grading (A) low or moderate and (B) high and very high added CVR	Frequency and percentage
4. To grade hypertensive patients using the World Health Organization and International Hypertension Society Chart for the South African region (WHO/HIS Chart AFR E)	Combine risk factors according to WHO/IHS and AFR E charts to obtain two clusters of grading: (C) low or moderate and (D) high and very high added CVR	Frequency and percentage
5. To compare the CVR score of hypertensive patients in MPH calculated from the GRA/SAHS Chart and the WHO/HIS Chart AFR E	Comparison of percentage of patients classified into one of the two clusters or categories of cardiovascular grading from SAHS/GRS and WHO/GRS charts	Sensitivity and specificity

6.1. To calculate the cost-saving derived from the WHO/GRS 6.2. To calculate the number needed to harm (NNH)	Number of patients correctly classified using WHO/GRS Ratio of number of wrongly classified as low risk by the WHO/GRS and ratio of patients classified as low risk using the SAHS/GRS	Cholesterol test price multiply by the number of patient correctly classified using WHO/GRS. Inverse of the absolute risk increase (ARI) from the ratio of patients wrongly classified as Category 1 or low risk

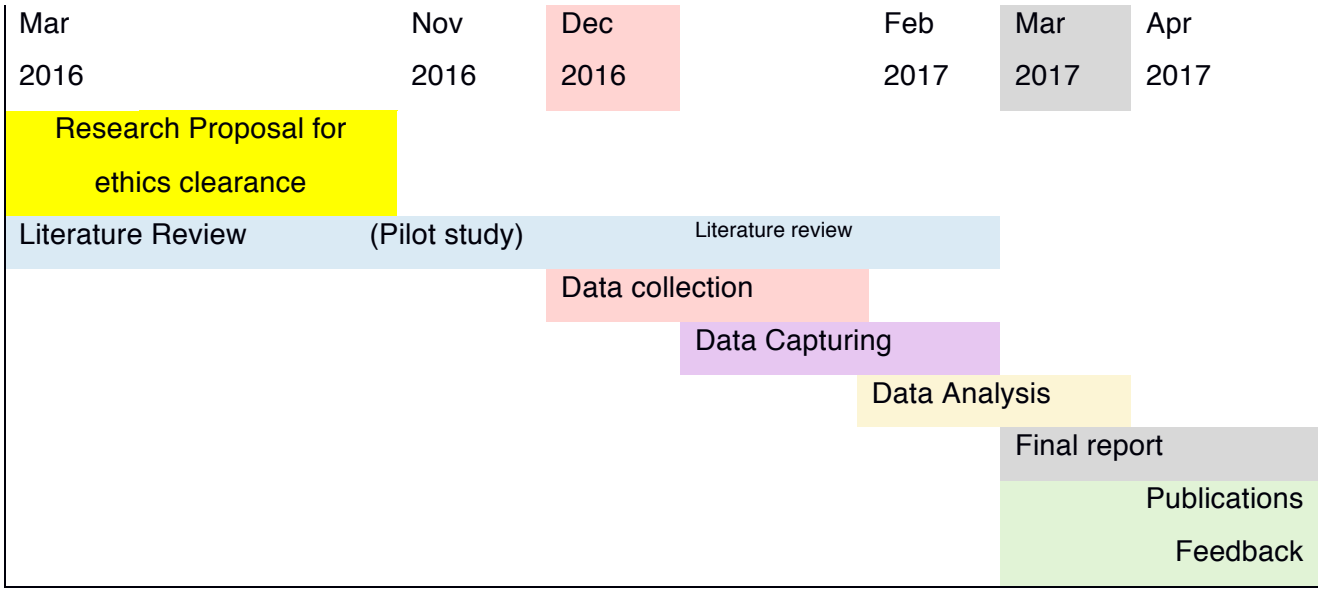
10. TIME FRAME AND FINANCES

Table 2. Financial plan

Item	Quantity	Price	Total price
Printing and stationary	120 x 15 = 900 pages, sub-file covers & miscellaneous	R1/copy R1.50/sub file	R1,980
ECG paper and leads	2 packs of paper and 1 box of 1000 disposable leads	R800	R800*
Cholesterol level test	120 tests	R125	R15,000*
Data collection and capture, team transport and incentives	4 team members	R2,000	R8,000
Proof reading	X2	R1,000	R2,000
Publication fees (CVJA)		R600	R600
Pitfalls			R1,000
Total			R29,380
Without sponsored items			**R13,580**

* Sponsored items

Fig.1. Gantt chart



11. ETHICAL CONSIDERATIONS

11.1. Confidentiality and autonomy to participate in the study

Interviews and physical examinations will be conducted in private rooms ensuring participants' privacy and dignity. Patient information will be kept **confidential** and treated with anonymity, as explained in the following sentence. A codification number will be linked to each patient's information and the file linking the specific code to the corresponding patient will be stored under lock and key at a location with restricted access, only accessible to the researcher. Individual **informed consent** will be sought after a full explanation of the study aim, objectives and methodology. A copy of the signed consent form will be kept in the patient's folder. There will be no discrimination should the patient refuse to be part of the study. Since this study will only benefit indirectly to the patient; they will be made aware of this during the informed consent process.

Ethical clearance will be requested from the WITS Human Research Ethics Committee, as well as authorisation from the hospital management to conduct this study.

11.2. Finances and cost

This study will **not create extra costs for the Department** of Health or the institution where it will be conducted. Patient data, particularly those related to costly investigation (Cholesterol and ECG), will be collected according to the guideline. In fact, according to the national guideline on HT in South Africa, hypertensive patients are required to have an annual ECG and cholesterol testing. When those results are available and not older than twelve months, no new investigation will be required. Those results will be used for the study since they will still be valid according to the national guideline. An ECG and a cholesterol level test will be sought only when they are either not available or older than twelve months. Authorisation to comply with the guideline and to request new investigations when not available has been requested from the hospital management.

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APPENDICES

APPENDIX 1A. Informed consent (Version 2)

Consent Form

STUDY TITLE: COST ANALYSIS AND COMPARISON OF TWO GLOBAL CARDIOVASCULAR RISK SCORES IN HYPERTENSIVE PATIENTS AT MAFIKENG PROVINCIAL HOSPITAL: A PRELIMINARY EXPLORATORY STUDY

Dear Patient,

You are currently consulting the Out Patient department of Mafikeng Provincial Hospital for treatment of problems you are currently experiencing. Mafikeng Provincial Hospital not only renders treatment but is also actively involved in conducting research aimed at improving the quality of care that we deliver.

You are invited to participate in the study with the title is written above. You have been handed an information sheet giving details of the current study. In summary this study aims to compare 2 risk stratifications formula for people with hypertension in our region. The result of this study will benefit future user of health care in our district because stratification will be possible from the first consultation without using invasive and laboratory procedures. You will also benefit from this study by having your cardiovascular risk review and updated. The researcher will give you an individual feedback on your risk. This study includes answering questions, measurements and blood tests. Collection of blood test, 8 ml form the back of the hand or the forearm is linked to a needle prick pain.

All data collected during this study will be handled anonymously. The recording will be made under a code generated as soon as you agree to participate to maintain anonymity. A specific consent is needed to remove decode any data. You are free to decline participation to this study or to withdraw any time during the study. This will not affect your care in any way whatsoever. This study has been approved by the Human Research Ethics Committee (Medical) of the University of the Witwatersrand, certificate number: …….

Should you wish to contact us at any stage regarding consent, contact Dr MBUILU JP at 0837662832.

(Please tic) A. Consent Given B. Consent Not Given

I_____ hereby give consent to participate freely in the above described research:

PATIENT: _____ DATE: _____

APPENDIX 1B. INFORMATION DOCUMENT (v2)

Study title: Cost analysis and comparison of two global cardiovascular risk scores in hypertensive patients at Mafikeng Provincial Hospital: a preliminary exploratory study

Greeting:

Introduction:

I, Dr Mbuilu JP, am doing research/study on Hypertension. In this study I want to learn if the stratification of hypertension risk can be made without using some information from the laboratory as recommended by the current South African guideline. We hope that results from this study will benefit future patient consulting our peripheral health facility for hypertension.

Invitation to participate: I am inviting you to take part in a research study.

What is involved in the study – If you agree to participate in this study, I will ask you few questions about your age, smoking and drinking habit and history related to hypertension on you and your family during a 8 minutes interview, record some measurement on your body (7 minutes) and collect 8 ml of blood (two big spoon) from your forearm or back of your hand. This blood will be tested for the level of cholesterol and renal function. This study need 120 participants to be completed.

Risks: drawing of blood is accompany by a needle prick pain.

Benefits of being in the study include an update of your cardiovascular risk and an adjustment of your treatment accordingly (counselling on diet and exercise and prescription). This is an indirect benefit from this study.

The participant will be given pertinent information on the study while involved in the project and after the results are available.

Participation is voluntary, that refusal to participate will involve no penalty or loss of benefits to which the participant is otherwise entitled, and that the subject may discontinue participation at any time without penalty loss of benefits to which the participant is otherwise entitled.

No extra cost when consenting to this study

Confidentiality: Efforts will be made to keep personal information confidential. Absolute confidentiality cannot be guaranteed. Personal information may be disclosed if required by law.

Organizations that may inspect and/or copy your research records for quality assurance and data analysis include groups such as the Research Ethics Committee and the Medicines Control Council (where appropriate).

If results are published, may lead to individual / cohort identification.

Contact details of researcher – for further information / reporting of study related adverse events: Dr Mbuilu, Tel.: 0837662832

Contact details of HREC administrator and chair – for reporting of complaints / problems: WITS University,Tel: +27 (0)11-717-1252

APPENDIX 2. WHO STEPS Instruments and GPAQ links:

http://www.who.int/chp/steps/GPAQ_EN.pdf

http://www.who.int/chp/steps/STEPS_Instrument_v2.1.pdf

FOR DATA COLLECTION

APPENDIX 3. Authorisation from Mafikeng Provincial Hospital CEO

Dr Jody P. Mbuilu

Third Year Registrar in Family medicine
Student number 444840 - WITS University
Based in Family Medicine department
Mafikeng provincial Hospital
0837662832
jodymbuilu@gmail.com

July 2, 2015

Ms JCE TALJAARD
Acting CEO - Mafikeng Provincial Hospital
Danville - Mafikeng
NW, RSA

Dear Ms Taljaard,

As requested by my curriculum, I must conduct a reasearch during my fourth year of training. In the process of obtaining an ethical approval, I first need to obtain an authorisation from the site where the research will be conducted.

I am planning to research an easy way to characterise hypertension patient in different grading of risk as recommended by the national guideline. My study will compare the current recommendation with a method of grading less expensive, using only clinical informations and excluding laboratory tests. This study will have local and national impact.

The current study title is: "Non-Laboratory Based Cardiovascular Risk Estimate on Hypertensive Patients Attending Mafikeng Provincial Hospital." For more details, please found attached my research proposal that will be submitted once I have your authorisation. I am available for additional informations. This letter is written to request an official authorisation to conduct this research at Mafikeng Provincial Hospital during the first semestre 2016.

Sincerely yours,

Dr JP. Mbuilu

9/7/2015
Approval is granted.
Kind regards
Acting CEO. MPH.

health
Department of
Health
North West Province
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POLICY, PLANNING, RESEARCH, MONITORING AND EVALUATION

Name of researcher : Dr J. Mbuilu
University of the Witwatersrand

Subject : Conditional Approval Letter- Cost Analysis and Comparison of Two Cardiovascular Risk Scores in Hypertensive Patients at Mafikeng Provincial Hospital.

This letter serves to inform the Researcher that Conditional Approval to undertake the above mentioned study has been granted by the North West Department of Health subject to:

1. The Researcher submitting the Ethical Clearance Certificate.

This letter should be signed and a copy returned to the department with required information.

Kindest regards

Dr. FRM Reichel
Director: PPRM&E

21/01/2016
Date

Researcher

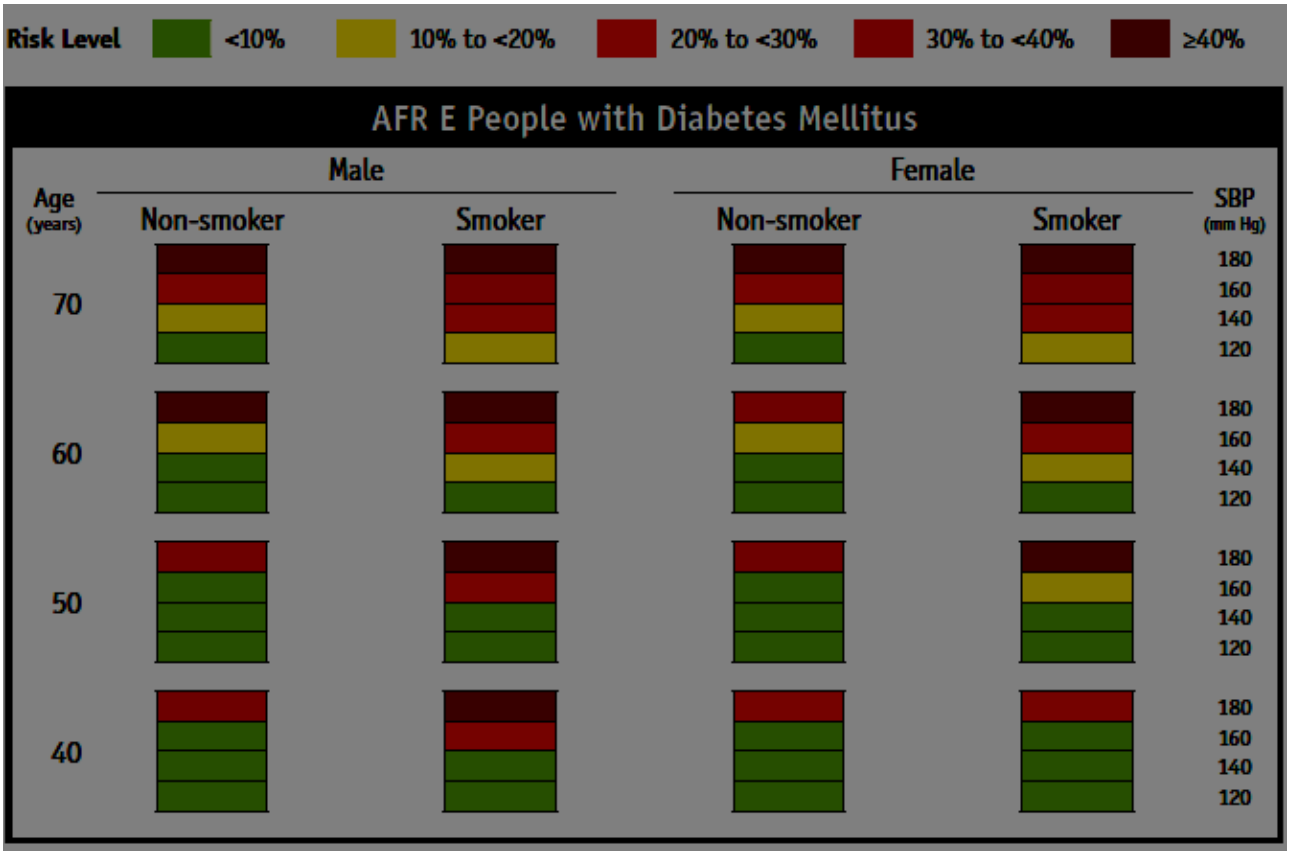
Date

LEPAPHA LA BOITEKANELO
DEPARTMENT OF HEALTH
Kgetsana Poso /Private Bag X2068
Mmabatho, 2735
23 JAN 2016
NORTH WEST PROVINCE
REPUBLIC OF SOUTH AFRICA

APPENDIX 4. List of variables to be collected

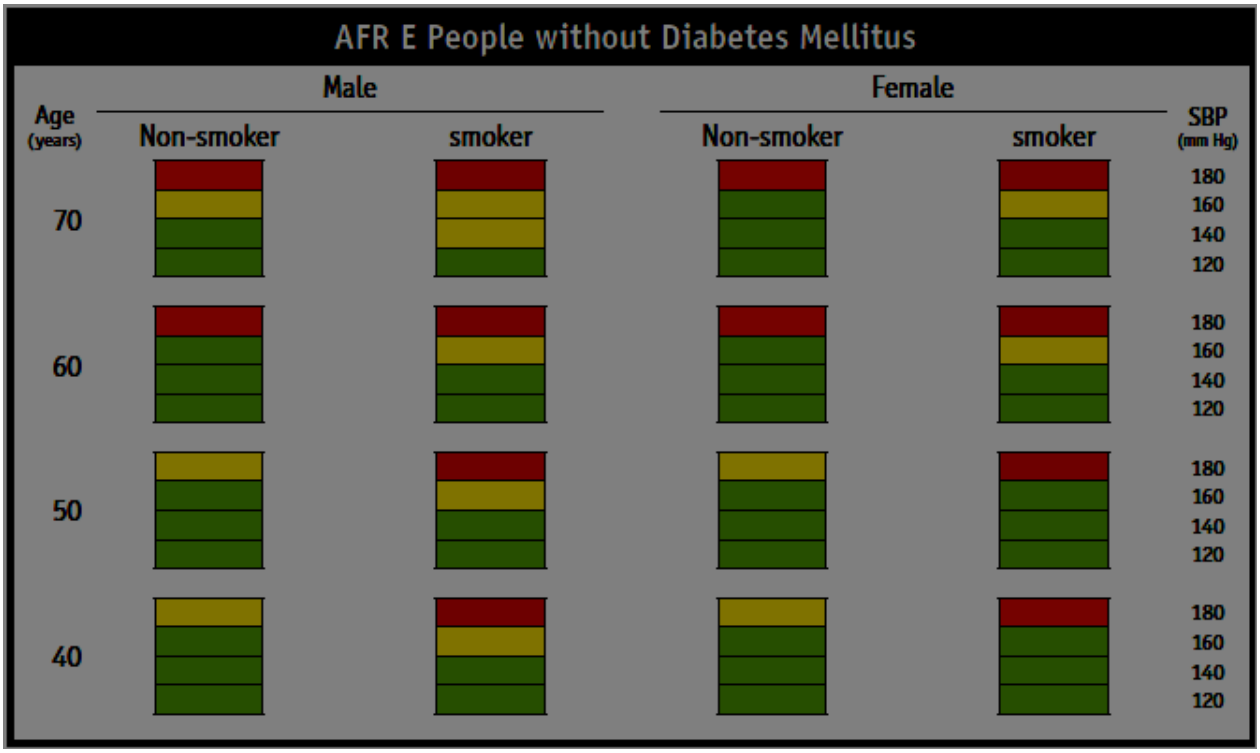
1. Age (years as at the last birthday)
2. Gender (Male or female)
3. Level of systolic and diastolic BP (mmHg)
4. Smoking status
5. Dyslipidaemia defined by:
    - total cholesterol >5.1 mmol/l OR
    - LDL >3.0 mmol/l OR
    - HDL men<1 and women < 1,2 mmol/l
6. Diabetes mellitus
7. Family history of early onset of CVD (men <55 years; women <65 years)
8. Waist circumference (Cm)
9. ECG with standard calibration of 10 mv = 10mm and 25 mm/sec
10. Cornell score: (R in aVL + S in V3 + 6 in female) X QRS duration > 2440 (mm/ms)
11. Microalbuminuria and eGFR (serum creatinine)

APPENDIX 5. Table 3. WHO/GRS – 2 Charts for estimation of cardiovascular risk.



Note: - Low and moderate cardiovascular risk or Category 1: equivalent to less than 30%.

- High and very-high cardiovascular risk or Category 2: equivalent to equal or more than 30%



APPENDIX 6. Table 4. SAHS/GRS - Chart

2013 ESH/ESC Guidelines for the management of arterial hypertension

Other risk factors, asymptomatic organ damage or disease	Blood Pressure (mmHg)			
	High normal SBP 130–139 or DBP 85–89	Grade 1 HT SBP 140–159 or DBP 90–99	Grade 2 HT SBP 160–179 or DBP 100–109	Grade 3 HT SBP ≥180 or DBP ≥110
No other RF	• No BP intervention	• Lifestyle changes for several months • Then add BP drugs targeting <140/90	• Lifestyle changes for several weeks • Then add BP drugs targeting <140/90	• Lifestyle changes • Immediate BP drugs targeting <140/90
1–2 RF	• Lifestyle changes • No BP intervention	• Lifestyle changes for several weeks • Then add BP drugs targeting <140/90	• Lifestyle changes for several weeks • Then add BP drugs targeting <140/90	• Lifestyle changes • Immediate BP drugs targeting <140/90
≥3 RF	• Lifestyle changes • No BP intervention	• Lifestyle changes for several weeks • Then add BP drugs targeting <140/90	• Lifestyle changes • BP drugs targeting <140/90	• Lifestyle changes • Immediate BP drugs targeting <140/90
OD, CKD stage 3 or diabetes	• Lifestyle changes • No BP intervention	• Lifestyle changes • BP drugs targeting <140/90	• Lifestyle changes • BP drugs targeting <140/90	• Lifestyle changes • Immediate BP drugs targeting <140/90
Symptomatic CVD, CKD stage ≥4 or diabetes with OD/RFs	• Lifestyle changes • No BP intervention	• Lifestyle changes • BP drugs targeting <140/90	• Lifestyle changes • BP drugs targeting <140/90	• Lifestyle changes • Immediate BP drugs targeting <140/90

BP = blood pressure; CKD = chronic kidney disease; CV = cardiovascular; CVD = cardiovascular disease; DBP = diastolic blood pressure; HT = hypertension; OD = organ damage; RF = risk factor; SBP = systolic blood pressure.

Note

- Low and moderate cardiovascular risk or Category 1: equivalent to less than 30%.

- High and very-high cardiovascular risk or Category 2: equivalent to equal or more than 30%

APPENDIX 7. DATA COLLECTION SHEET AND TABLE FOR CODE AND ANONYM

DATA COLLECTION SHEET:
Cost Analysis of Two Global Cardiovascular Risk Scores in Hypertensive Patients at Mafikeng Provincial Hospital: A Preliminary Exploratory Study

ID CODE:.....

A. DEMOGRAPHIQUE DATA

1. AGE	
2. GENDER	
3. EDUCATION	
4. RACE	

B. RISK FACTORS & CLINICAL DATA

5. SMOKING	
6. ALCOHOL	
7. PERSONAL HISTORY OF CVD	
8. FAMILY HISTORY OF CVD	
9. SYSTOLIC BP	
10. DIASTOLIC BP	
11. WAIST CIRCUMFERENCE	
12. PROTEINURIA	
13. ECG -LVH	
14. T. CHOLESTEROL	
15. LDL CHOLESTEROL	
16. HDL CHOLESTEROL	

Asymptomatic Organ Damage

				Comments
17. LVH	Sokolow:		Cornell:	
18. Ankle-brachial index (ABI)				
19. eGFR				
20. microalbuminuria				
LVH: left ventricular hypertrophy; eGFR: estimated glomerular filtration rate				

Established Organ Damage

	Yes	No		Comments
21. Stroke				
22. CHD				
23. Heart Failure				
24. PVD with symptoms				
CHD: coronary heart disease; PVD: peripheral vascular disease				

ANONYMOUS TABLE FOR CODES

ID CODE	NAME	SURNAME	FILE NUMBER	OTHER