A Multi-component Intervention to Reduce Gaps in Hypertension Care and Control in Medellin, Colombia

STUDY PROTOCOL AND STATISTICAL ANALYSIS PLAN
dated: 29-Apr-2019

| **Institutional Review Board** | | | Dr. Tullia Battaglioli / Dr. E. Londoño Agudelo
Department of Public Health |

| IRB/AB/AC/101 | OUR REF.
1294/19 | ATTACHMENT(S) | ANTWERP
9/05/2019 |

Concerns: A multi-component intervention to reduce gaps in hypertension care and control in Medellin, Colombia; version 2.0, dated 29/04/2019

Dear Colleague,

I am pleased to inform you that after review by the Chair, the above mentioned protocol has been approved.

We wish to remind you of the following important aspects:

- It is the researchers' responsibility to secure ethics approval in the study country(ies) as required by local regulations, before any study-related activities are started.

- The IRB (+ EC UZA when applicable) should receive a yearly update report to the IRB at the latest one year after the approval date, and an end-of-study report.

- In case you have any questions about data protection or the GDPR, please contact ITMs Data Protection Officer via informatieveiligheid@itg.be.

- Research studies prospectively involving human participants should be registered in one of the WHO-accepted primary registers (e.g. www.clinicaltrials.gov).

Kind regards,

Dr. Raffaella Ravinetto

Chairperson Institutional Review Board

RESEARCH STUDY PROTOCOL

A multi-component intervention to reduce gaps in hypertension care and

control in Medellin, Colombia

Version 2.0, Dated 29 APRIL 2019

Sponsor/Coordinator:	Institute of Tropical Medicine Nationalestraat 155 B-2000 Antwerpen - Belgium
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INSTITUTE OF TROPICAL MEDICINE ANTWERP

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Partnering institutions:	- Facultad Nacional de Salud Pública - Universidad de Antioquia, Medellín-Colombia: Prof. Rubén Darío Gómez, Prof. Paula Díaz, Gesis Viviana Pérez. - E.S.E. Metrosalud, Medellín-Colombia: Dr. Francisco López, Dr. Hernán Aguilar, Dr. José Manuel Vásquez, Dra. Norma Palacio. - Instituto Pedro Kouri (IPK), La Habana-Cuba. Dennis Pérez. - Gent University, Gent-Belgium: Prof. Patrick Van der Stuyft.

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Statement of Compliance & Confidentiality

The information contained in this study protocol is privileged and confidential. As such, it may not be disclosed unless specific permission is given in writing by the ITM or when such disclosure is required by federal or other laws or regulations. These restrictions on disclosure will apply equally to all future information supplied which is privileged or confidential.

Once the final protocol has been issued and signed by the Investigator(s) and the authorized signatories, it cannot be informally altered. Protocol amendments have the same legal status and must pass through the mandatory steps of review and approval before being implemented.

By signing this document, the Investigator commits to carry out the study in compliance with the protocol, the applicable ethical guidelines like the Declaration of Helsinki, the ESF/ALLEA Code of Conduct for Research Integrity, and consistent with international scientific standards as well as all applicable regulatory requirements. The Investigator will also make every reasonable effort to complete the study within the timelines designated.

PRINCIPAL INVESTIGATOR:

Title, Name: Esteban Londoño. MD. MPH. PhD Student   Date: 05/02/2019

Signed:

ITM COORDINATING INVESTIGATOR:

Title, Name: Tullia Battaglioli. MD. MSc. PhD.   Date: 05/02/2019

Signed:

Synopsis

Uncontrolled hypertension is a key factor in the rising epidemic of cardiovascular diseases (CVD), especially in low and middle income countries (LMIC). Nevertheless, research on the main gaps in hypertension care and control and studies evaluating health services interventions to improve hypertension care in LMIC remain scarce. The US Centers for Disease control and Prevention and the Pan American Health Organization recently developed the Standardized Hypertension Treatment and Prevention (SHTP) Project, which was followed by the World Health Organization's initiative "Hearts in the Americas". Both projects provide a practical approach to improve CVD prevention and management using hypertension as the entry point.

In Colombia, 30% of all deaths and 16% of Years of Life Lost can be attributed to CVD. A cross-sectional survey carried out in 2016 in a low-income community in Medellin, aimed to estimate the prevalence of hypertension among the population aged 35 years or older and the magnitude and the determinants of the main gaps in hypertension care and control (utilization of health services, diagnosis, treatment, follow-up) showed a prevalence of hypertension of 43.4%. Among all hypertensive individuals, 36.7% were unaware of their diagnosis. Among the aware hypertensives, 41% had uncontrolled hypertension; 55% of unaware hypertensives had accessed health care in the previous year but health services had failed to diagnose them.

Based on the technical recommendations contained in the SHTP Project, the Technical Package of the "Hearts in the Americas" initiative, on the results of the above-mentioned cross-sectional survey and in consultation with the local partners (Metrosalud and the University of Antioquia) and community leaders, a multi-component intervention for the improvement of hypertension care and control was designed. The components of the intervention integrate activities related to: A) Health services organization, B) Training of clinical staff and C) Patients and community engagement.

The effectiveness of the intervention in reducing the gaps in hypertension care and control will be evaluated in a quasi-experimental, controlled before-after trial, with an intervention arm (a commune of Medellin) where the intervention is deployed and a control arm (another commune of Medellin, with similar socio-economic characteristics) where routine care is implemented. As baseline, the results of the population-based cross-sectional study "Gaps in hypertension care and control in Medellin, Colombia: cross-sectional survey in two Communes", Version 2.0, dated 26-AUG-2018, approved by the UZA Ethics committee on 15/10/2018, will be used. Two years after the start of the intervention, a repeat survey using the same methodology as in the baseline will be carried out in the two communes. The main outcomes (gaps in hypertension care and control) will be assessed with difference in difference measures (endline-baseline changes in the intervention minus endline-baseline changes in the control commune).

The study aims at contributing to the improvement of hypertension care and control in Colombia and may inspire and inform with scientific evidence other initiatives for better chronic care in LMIC, especially in Latin America.

1. INTRODUCTION

1.1 Background

Non-communicable diseases (NCD) are estimated to account for 63% of global mortality nowadays and it is predicted that they will account for around 70% of global deaths by 2030(1). NCD are especially worrying for developing countries, where their incidence is increasing disproportionately. Four out of five deaths caused by chronic conditions occur in low and middle-income countries (LMIC)(2). NCD are also the first cause of mortality and disability in Latin America and the Caribbean (LAC)(3). Notwithstanding, the majority of health systems provide inadequate chronic diseases management, with health services mainly designed for acute curative care. Chronic care, especially in developing countries, is often reduced to the belated management of acute exacerbations of chronic illnesses in specialized settings and at high costs. Consequently, only about one in ten people with chronic conditions are treated successfully(3) and most out-of-pocket health payments and catastrophic expenditure are related to these conditions(4).

Uncontrolled hypertension is the main modifiable risk factor for cardiovascular diseases (CVD) and the related cause of more than 10 million deaths each year(2). Approximately 65% of deaths due to stroke and 50% of deaths due to ischemic heart disease are attributable to uncontrolled hypertension. Furthermore, almost three quarters of people suffering from hypertension (650 million people) live in developing countries, where disease awareness is very low and access to health care is very limited(2;5). Hence, the risk of dying from hypertension at all ages is more than double in LMIC compared to high income countries (HIC)(6).

CVD are significantly related to premature mortality and disability, hampering economic growth and social development. Current epidemiological data point to CVD striking the working middle-age population in LMIC(7). An estimated 1.6 million people die from CVD every year in LAC (38% of all deaths), half a million of them before 70 years of age(8). High disease prevalence and poor hypertension control are pivotal factors in the rising epidemic of CVD in LMIC(5). Nevertheless, very limited descriptive research in this field has been conducted in LMIC(9). A more in depth assessment of the actual hypertension care and control coverage in LMIC is necessary. Such health coverage evaluation, as stated by Tanahashi(10), requires an assessment at population level.

The recent Prospective Urban Rural Epidemiology (PURE) study in 3 HIC and 14 LMIC(11), found an average age-standardized prevalence of hypertension of 27.7% in adults aged 35 to 70 years. Only 46.5% of participants were aware of their condition; among those aware, 87.5% were receiving

pharmacological treatment but only a minority of treated patients (32.5%) were controlled. The PURE study provided relevant information regarding international rates of hypertension awareness, treatment and control. However, it did not explore the health coverage gaps throughout the hypertension continuum of care nor their determinants. The hypertension continuum of care is a dynamic and interrelated process, from detection to control, that includes access to health services, diagnosis, treatment and follow-up. We define gaps in hypertension care and control as the differences between the actual state of the main components of the continuum of care in a given context and time, compared to the optimal state of each of these components, according to the available evidence and/or the international standards.

There are studies trying to identify patient and health care provider barriers to hypertension care(9), most of them carried-out in HIC and gathering information at health facility level, without including any population assessment. As a result, there is scarce evidence on the main determinants of the gaps in hypertension care and control, especially regarding access to health services and hypertension diagnosis in LMIC.

The Chronic Care Model(12) and its expanded version(3) are the main international references to guide interventions for improving chronic disease management. Nevertheless, studies evaluating health services interventions to improve hypertension care in LMIC are still much more scanty than purely descriptive research. Notwithstanding, in order to provide a practical approach to improve CVD prevention and management using hypertension as the entry point, the US Centers for Disease control and Prevention and the Pan American Health Organization developed the Standardized Hypertension Treatment and Prevention (SHTP) Project(2). The SHTP Project identified six key elements of standardized hypertension management to be addressed to strengthen health systems at primary care level and to improve hypertension control, using evidence-based interventions(2): guideline-based standardized treatment protocols; medications; registries for cohort monitoring and evaluation; patient empowerment; team-based care system; community engagement. This approach was reinforced by the World Health Organization global initiative "Global Hearts" through the Technical Package for Cardiovascular Disease Management in Primary Health Care(13).

In summary, research to document the main gaps and barriers hampering hypertension care and control at population level in LMIC is needed. Furthermore, operational research aimed to improve hypertension care and control and to reduce CVD morbidity and mortality is urgently required throughout the Latin America region.

1.2 Rationale

In Colombia, the death rate from CVD in 2014 was 146.9 per 100.000 population. In this country, 30% of all deaths and 16.3% of Years of Life Lost can be attributed to CVD (14). The Colombian health system is divided in two different regimes, according to individuals' payment capacity. People able to contribute to the social security system and their beneficiaries are affiliated to the Contributory Regime, which is compulsory for formal employees and pensioners. The Subsidized Regime is financed by the State and covers the poor un-employed or informal-employed population. In Colombia, in the context of a market-oriented health system, cost-containment mechanisms imposed by health insurance companies often hamper timely access to health care, especially for those chronically ill, generating harmful consequences to people's lives (15).

In 2016 we carried out a cross-sectional survey in a low-income urban community in Medellin, aimed to estimate the prevalence of hypertension among the population aged 35 years or older and the magnitude and the determinants of the main gaps in hypertension care and control (Table 1).

Table 1. Main Gaps in hypertension care and control – definitions.

Gap	Numerator	Denominator	Remarks
Diagnosis	Number of unaware hypertensive individuals	The total surveyed population	Also calculated for hypertensives (nr. unaware /total hypertensives)
Pharmacological treatment	Number of aware hypertensive individuals who received prescription of antihypertensive medications but do not take any antihypertensive drug	Aware hypertensive individuals who received prescription of antihypertensive medications	
Follow-up	Number of aware hypertensive individuals who did not receive a follow-up consultation in the last year	Number of aware hypertensive individuals	

Control	Number of aware hypertensives with uncontrolled hypertension + Number of unaware hypertensives	The total hypertensive population (aware + unaware)	Also calculated in subgroup aware hypertensives

The study showed a prevalence of hypertension of 43.4%. Among the total hypertensive individuals, 36.7% were unaware of their diagnosis. Of the aware hypertensives, 93% had been prescribed pharmacological treatment, but 7% of those who had been prescribed treatment were not taking any medication and only 65% of those taking treatment referred treatment compliance. Moreover, 15% of the aware hypertensives did not have any follow-up consultation during the previous year. Among the aware hypertensives, 41% had uncontrolled hypertension. Nineteen percent of aware hypertensives and 45% of unaware hypertensives did not have contact with formal health services in the last year, mainly because they did not feel the need. On the other hand, 55% of unaware hypertensives accessed to health care in the previous year but health services failed to diagnose them.

Studies specifically aimed at reducing the gaps and barriers to hypertension care and control at population level in the country are needed.

The results of the baseline study, the possible determinants of the identified gaps and potential solutions were discussed in a workshop held in Medellin-city, with the participation of ITM staff, the University of Antioquia and Metrosalud. A summary of the identified potential determinants of the main gaps, mainly related to disease detection and quality of care, is presented in Table 2.

Table 2. Potential determinants at health provider, population and health system level of the main health coverage gaps for hypertension care and control in the Santa Cruz Commune

Hypertension Coverage Gap / Source of barriers	Health Provision	Population	Health Services
Diagnosis Gap	- No measurement of blood pressure during health care contacts - High blood pressure is detected but confirmation of diagnosis fails due to lack of continuity of care	- Low risk perception of hypertension - Mild or no symptoms determine health seeking	- Passive and fragmented health services - Limited opening hours of services for hypertension detection
Quality of care (treatment and follow-up)	- No pharmacological advise/consultation - Limited communication skills of health staff and poor doctor-patient relationship - Interrupted delivery of essential anti-hypertensive drugs	- Low awareness of the importance of non-pharmacological measures - Low educational level	- Scarcity of essential anti-hypertensive drugs - Administrative barriers imposed to patients and health providers

Based on the technical recommendations contained in the SHTP Project and the "Hearts in the Americas" initiative, on the results of the baseline study and in consultation with the local partners (Metrosalud - the main public health care provider of Medellin city - and the University of Antioquia) and community leaders, we designed, during repeated workshops, a multi-component intervention for the improvement of hypertension care and control in individuals aged 35 years or older in Medellin.

2. STUDY OBJECTIVES

Main objective:

To implement and evaluate the effectiveness of a multi-component intervention with evidence-based activities, to reduce the gaps in hypertension care and control at population level

Secondary objectives:

- To improve the quality of hypertension care provided by the public primary health care services in the Commune 2-Santa Cruz.

- To increase detection of hypertension by blood pressure screening outside the clinical settings and contribute to the public awareness on the importance of healthy behaviour and self-care to prevent cardiovascular diseases.

- To carry out a process evaluation of the intervention and its implementation fidelity in order to assess to which degree the components of the intervention were implemented as intended and how the intervention actually influenced hypertension control outcomes.

3. STUDY DESIGN

A multi-component intervention for the improvement of hypertension care and control in individuals aged 35 years or older will be implemented and evaluated. The components of the intervention integrate activities related to: A) Health services organization, B) Training of clinical staff, and C) Patients and community engagement. The effectiveness of the intervention in reducing the gaps in hypertension care and control will be evaluated in a quasi-experimental, controlled before-after trial, with an intervention arm (a commune of Medellin) where the intervention is deployed, and a control arm (another commune of Medellin, with similar characteristics) where routine care is implemented. As baseline, the results of the population-based cross-sectional study "Gaps in hypertension care and control in Medellin, Colombia: cross-sectional survey in two Communes", Version 2.0, dated 26-AUG-2018 approved by the UZA Ethics committee on 15/10/2018, will be used. Twenty-four months after the start of the intervention, a population-based cross-sectional survey with similar methodology as the baseline survey will be carried out in the intervention and control commune. The main outcomes (magnitude of the gaps in hypertension care and control) will be assessed with difference in difference measures (endline-baseline changes in the intervention minus endline-baseline changes in the control commune). The total duration of the study will be 32 months, of which 24 allocated to the implementation of the intervention. Implementation fidelity will be evaluated in order to assess to which degree the components of the intervention were implemented as intended and how the intervention actually influenced hypertension control outcomes.

The proposed research is part of a concerted effort within the Latin American Network for Multidisciplinary Research on Chronic Diseases, which is co-coordinated by the principal investigator of the study, Dr Esteban Londoño. This is a regional network for multidisciplinary research on the prevention and control of chronic non-communicable diseases in Latin America, comprised of partner institutions and supported by ITM (Unit of General Epidemiology and Disease Control). Parallel studies, following comparable research protocols and applying data collection tools with a common core part, are being conducted in Havana-Cuba and Quito-Ecuador.

The study is part of the PhD research of Dr Esteban Londoño entitled "Addressing gaps in hypertension care and control in Medellin, Colombia: formative research, multi component quasi-experimental intervention".

4. METHODS

4.1 Study Setting, Population and Sampling Strategy

4.1.1 Study setting

Medellin is the capital of the department of Antioquia, in Colombia. It has a population of 2,5 million people and 16 Communes. The intervention will be implemented in the "Santa Cruz" Commune, located in the northeast side of Medellin. It has 11 neighbourhoods, an area of 2.2 Km^2, a total population of 113.024 inhabitants (53% women and 47% men) in 2018. In Santa Cruz, Metrosalud counts with a Hospital Unit and two health centers. In Metrosalud diagnosed hypertensive patients are enrolled in the Cardiovascular Risk Program (CVRP) that foresees periodic consultations for the management of their hypertension, called cardiovascular risk consultations. Different community organizations, represented by community leaders, have been supporting Metrosalud´s work in community- and health-related activities for many years. The Commune 6-"Doce de Octubre" has been selected as control area. It is located in the northwest side of Medellin, has 12 neighbourhoods, an area of 3.8 km2, and a total 2018 population of 193.657 inhabitants (53% women and 47% men). The commune was chosen purposively, especially due to its socio-economic similarities with the Santa Cruz Commune and after discussion with the Director General of Metrosalud, who approved the selection of these two areas.

4.1.2 Study population, Sampling, Sample Size and Power

The study communes are chosen purposively according to the following inclusion criteria: urban setting; low and/or middle-income population; typical functioning of the national health system; commitment of the main actors in health care provision in the area to develop improvement programmes based on research results.

All health structures and their catchment population aged 35 years or older will be involved in the study.

For the endline survey, the same methodology applied for the aforementioned baseline survey will be used. Expecting a baseline hypertension control gap of 45%, a sample of 280 hypertensive individuals 35 years or older is required to estimate a 10% difference in the magnitude of the control gap in the intervention vs the control area at endline, with power 0.75 and alfa 0.10. Given a 40% prevalence of hypertension (see 4.1.4 for definitions) in individuals aged 35 years or older, screening around 700 individuals 35 years or older in each Commune, will allow to find the needed number of hypertensive individuals. This is increased to 1150 individuals, assuming a percentage of non-response of 10% and a design effect of 1.5, given the sampling strategy outlined below. From a sampling frame containing the addresses of all homes of the Communes, provided by the Planning Office of the Municipality, a stratified one-stage cluster sampling will be implemented in order to obtain a representative sample of the population aged 35 years or older living in the selected Communes. Considering that in households there are on average 1.5 individuals 35 years old or older, 765 households will be included in each Commune. In each Commune, clusters of 15 contiguous households will be defined with the help of maps and 51 clusters will be selected by randomly sampling each neighbourhood of the Commune. The number of randomly selected clusters in each neighbourhood will be proportional to the neighbourhood size (weights assigned to each neighbourhood according to its total number of households). The module for complex samples of the Statistical Package for Social Sciences (SPSS) V.24 (SPSS Inc., Chicago, IL, USA) will be used. Door to door visits to every single household of each selected cluster will be made by a group of trained surveyors. All identified eligible consenting individuals aged 35 years or older will be interviewed.

4.1.3 Inclusion and Exclusion Criteria

- In order to be eligible for the endline survey, study participants must meet the following criteria:

» Aged 35 years or older

- » Permanent inhabitant of the selected Commune
- » Willing and able to provide written informed consent.

- In order to be eligible for in-depth interviews and non-participant observation (qualitative component):

» Adult patient aged 35 years or older or health staff of Metrosalud.

» Active participant of any component of the intervention or subject of any intervention activity.

» Willing and able to provide written informed consent.

Potential participants meeting any of the following criteria will not be enrolled in the study:

» Mental disability or unable to answer the questionnaire.

4.1.4 Definitions

Hypertensive individual (operational definition for survey): self-report of previously diagnosed hypertension or without previous diagnosis but presenting an average blood pressure (BP) measurement higher than 140/90 mmHg(11;16).

Presumptive hypertensive individual: no self-report of previously diagnosed hypertension but presenting an average BP measurement higher than 140/90 mmHg.

Controlled hypertensive individual: self-report of previously diagnosed hypertension and an average BP less than 140/90 mm Hg for patients between 35 and 59 years old or diabetics and 150/90 mm Hg for patients aged 60 years or older (17).

4.2 Procedures

A multi-component intervention, detailed below, will be implemented in the intervention area, while standard hypertension care will be provided in the control area.

Each intervention component will be standardized and described in a field manual for the improvement of hypertension management. For each component we will clearly define: subcomponents or activities specifying implementation level and units, responsible, target population, content, methodology and way of delivery, time, duration, key improvement factors, functioning principles and expected results per activity.

A logic model of the intervention will be elaborated to provide a graphical depiction of the inputs, processes, immediate, short-term, and long-term outcomes, and the relationship and sequence between the different intervention components and critical points in the implementation process as a whole. Critical points are stages or activities in the process, susceptible to be measured, in the

absence of which other stages or activities cannot be implemented. The intervention activities will be implemented by Metrosalud staff of the health structures in the Commune with technical assistance from the investigation team.

4.2.1 Intervention

The components of the intervention aim to integrate activities related to: A) Health services organization, B) Training of clinical staff, and C) Patients and community engagement. Taken together, through these components, most elements of the SHTP project and the Technical Package for Cardiovascular Disease Management in Primary Health Care(13) will be covered in a context-adapted intervention.

A. Health services organization

    A.1. Hypertension screening: 1) all adults aged 35 years or older presenting to any health service (including clinical and support services) will be asked if they had their BP measured in the previous year. If not, they will be referred to a specific nursing hypertension service ("Healthy Hearts" service, see A.2 below) for a BP measurement, using a ticket stub for referral. 2) Doctors and nurses encountering presumptive hypertensive patients (individuals not reporting a previous diagnosis of hypertension but presenting BP higher than 140/90), will refer them to the "Healthy Hearts" service for confirmation of the diagnosis with serial BP measurement. 3) The entire health care flow for patients with a high BP measurement within health facilities will be standardized in order to guarantee continuity of care and correct diagnosis.

    A.2. "Healthy Hearts" service: an auxiliary nursing station with extended opening hours and providing services such as BP measurement, global cardiovascular risk assessment and preventive counselling. It oversees serial self-measured BP monitoring within the health facility premises to exclude white coat hypertension, providing devices and patient education on self BP measurement. It will ensure retention and follow-up of all people with a high BP measurement at screening (at service level or in the community - see C.2 below) in order to guarantee that final diagnosis (hypertensive or not) is reached. It will refer to clinicians of the CVRP all newly diagnosed hypertensive patients. Through phone calls and/or SMS to patients and linkage with community agents, it will promote effective referral and manage non-attendance to follow-up CVRP consultations. It will administer periodical anonymous exit-questionnaires (annex 6) to hypertensive patients exiting from CVRP

consultations in order to assess effective BP measurement and the quality of pharmacological and non-pharmacological advice during medical consultations. Results will be transmitted to the cardiovascular risk team (see A.3.1 below).

A.3. <u>Improvement of clinical management of patients with hypertension</u>

A.3.1. <u>Creation of the cardiovascular risk team (CVRT)</u>, which will include the head and one leading medical doctor of the hospital unit, and the coordinating doctors of the two health centres. The CVRT will be responsible of supervising good clinical management of hypertension. It will conduct audits of clinical records, periodically selecting a representative sample of clinical records of hypertensive patients and using a structured questionnaire – see annex 5 - to evaluate if the clinical records fulfil the requirements of a complete cardiovascular risk assessment interview and physical examination, doctors' adherence to the hypertension management guideline and some parameters to assess the quality of the provided health care. The CVRT will also provide regular active feedback and support to health professionals involved in the CVRP. It will also supervise the Healthy Hearts service.

A.3.2. <u>Guideline-based standardized diagnostic and treatment protocols</u>: before the start of the intervention, the diagnostic algorithm will be standardized and a simplified and implementable drug treatment algorithm will be defined, based on the national clinical guidelines and in agreement with the general direction of Metrosalud, the direction of the health area and the clinical staff. A core set of antihypertensive medications will be identified and primary and secondary options will be defined for each of the major pharmacologic classes of antihypertensive drugs (diuretics, angiotensin-converting enzyme inhibitors/angiotensin II receptor blockers, calcium channel blockers and Beta-blockers).

A.4. <u>Availability of antihypertensive medications</u>: the availability of the defined core set of antihypertensive medications will be assured through the central store of Metrosalud. Any (un-)availability of antihypertensive medications will be communicated to clinicians at the beginning of each week and *ad hoc* in case of intervening stock-out, in order to timely inform them on possible alternative prescription.

B. Staff Training

B.1. Training of clinical staff on good clinical management of hypertension focused on correct BP measurement, use of evidence-based guidelines, cardiovascular risk assessment, use of standardized diagnostic and treatment algorithm, correct prescription of non-pharmacological treatment and anti-hypertensive drugs, patient counselling, and how to tackle clinical inertia. The content, duration, responsible staff and target groups for the training component of the intervention is outlined in annex 1.

B.2. Training of all health workers involved in hypertension care (doctor, nurses, pharmacists and other non-medical staff) on communication skills and patients' needs assessment. This training will be designed under the "patient-centered medicine" framework (14), aiming at equipping health providers with tools for understanding patients' unique feelings and experience of illness, and to improve their capacity to detect and address social, psychological and behavioural dimensions of hypertension care and control.

C. Patients and community engagement

C.1. Patient empowerment: sessions where "expert hypertensive patients" will provide support and peer-education to other patients in need, such as those newly diagnosed or non-adherent to treatment or with uncontrolled hypertension, under the supervision of a social worker.

C.2. Community engagement: A Community Hypertension Outreach Group (CHOG) will be set up, composed by three voluntary community health workers who will be trained and certified. The CHOG will be created in partnership with the patients' association, which is a very dynamic organization already present in the Commune and interested in engaging in the project. The CHOG will conduct screening activities with measurements of BP in selected public areas of the commune on a weekly rotation basis, for all adults without BP readings in the previous year and referral of those with a positive screening to the nearest health facility for diagnosis confirmation. The CHOG will provide health education with emphasis on healthy lifestyles (tobacco cessation, physical activity and healthy diet). It will contribute to increase community awareness on the importance of hypertension control and on cardiovascular risk detection and prevention. Existing local communication channels such as the community radio and the local newspaper will also be used.

4.2.2 Data Collection

4.2.2.1 Quantitative Data Collection

4.2.2.1.1 Endline population based survey:

*T*he structured questionnaire "Gaps in hypertension care and control in Medellin, Colombia" (annex 2 to this protocol and Annex 12.1 in protocol "Gaps in hypertension care and control in Medellin, Colombia: cross-sectional survey in two Communes", Version 2.0, dated 26-AUG-2018,) will be used. The survey questionnaire has been standardized within the Latin American Network for Research on Chronic Diseases for being applied in Colombia, Cuba and Ecuador and has also be validated for each country.

Participants will be interviewed on their socio-demographic characteristics, health seeking behaviour, risk factors (e.g. smoking, alcohol abuse, physical inactivity) and previous and current health problems (e.g. diabetes, dyslipidaemia). Those referring previous diagnosis of hypertension will be asked on their treatment, follow-up, anti-hypertensive pharmacological and non-pharmacological treatment and compliance with the treatment.

4.2.2.1.2. Data collection at health services:

Data sources: databases of the Subsidized Regimen and of the non-insured poor population, electronic clinical and billing records of Metrosalud, registers of the "Healthy Hearts" service (Annex 3, 4 and 5), exit-interview forms (Annex 6), audit form (Annex 7, an adapted format for the audit of clinical records in use at Metrosalud), lists of participants and minutes of meetings and training activities, test results during trainings, registers and inventory at the pharmacy service, and report of activities by health professionals.

Besides the data explicitly mentioned in the annexes and tables of this protocol, we will collect the data mentioned below.

Data extracted from the databases of the Subsidized Regimen and of the non-insured poor population (data will be extracted either in the intervention and in the control commune):

- the total adult population (by sex, age, place of living and health insurance affiliation)for whom Metrosalud is responsible in the catchment area (target population).

Data extracted from the billing and electronic clinical records of Metrosalud (data will be extracted either in the intervention and in the control commune):

-number of patients enrolled in the CVRP.

-regarding patients enrolled in the CVRP: sex, age, frequency and results of cardiovascular risk assessment, prescribed pharmacological/non-pharmacological treatment, BP figures, major comorbidities and complications.

-number of patients who have missed a hypertension-related appointment

 4.2.3 Qualitative componentThe qualitative component will be carried out by a social scientist with previous experience in the use of qualitative methods, under the supervision of a senior sociologist from the Latin American Network for Multidisciplinary Research on Chronic Diseases with expertise in implementation fidelity.

We will collect data concerning the implementation process and its fidelity, following the modified version of the Conceptual Framework for Implementation Fidelity (18; 19). This framework defines fidelity as a measurement of adherence, with its subcategories: content, frequency, duration, and coverage (dose). It identifies six moderating factors: comprehensiveness of intervention description, strategies to facilitate implementation, quality of delivery, recruitment, participant responsiveness, and context (20). The nature of adaptations that are likely to occur during implementation and their implication for fidelity should be also analysed prospectively for each intervention (21).

Our fidelity assessment will focus on all intervention components. Data collection methods will include non-participant observations, key informant interviews and document analysis. To measure the subcategories of adherence, specific forms will be created for self-registration for each component of the intervention. All actors responsible with the implementation will be trained in self-registration of all the activities. Self-registration forms will be collected monthly.

This information will be used to monitor the process and identify those activities and relevant actors that will be subject of interviews and non-participant observations. The observation will have the purpose to triangulate self-registration information by providing real-time information on whether actual implementation is done according to the plan. Observations will be accompanied by semi-structured interviews to clarify the observed practices, moderating factors, adaptations introduced by the different stakeholders and possible explanations for adaptations. Observation and semi-structured interviews will be systematically applied to a purposive heterogeneous sample of

implementation units and actors. While exploring moderating factors, a specific section will be added to the semi-structured interview guide to explore socio-economic evolutions, health system & service changes and other activities and events that might bear on the outcomes. Similar aspects will be explored also in the control area.

The overall experience of patients with the implementation of the intervention will be explored through in-depth interviews, carried out at different phases of implementation. The estimated sample size for the interviews will be 25 – 30 for each phase. Data saturation will be taken into consideration. The qualitative data collection will fit the overall process evaluation plan.

4.3 Data Analysis

4.3.1 Quantitative Data Analysis

The main outcomes (dependent variables) of the analysis at population level will be the gaps in hypertension care and control (Table 1). Uni, bi- and multivariate analysis will be performed. For the main outcomes, difference in difference measures will be calculated (endline-baseline changes in the intervention minus endline-baseline changes in the control commune). Where relevant, we will stratify on affiliation to Subsidized or Contributory insurance schemes. Logistic regression models adjusting for potential confounding variables will be fitted. Unadjusted and adjusted Odds Ratios (ORs) and their 95%CI will be calculated.

The indicators for monitoring the implementation and measuring the results and effects of the intervention at health service level are listed in the following table (Table 3). They have been elaborated also taking into account the standardized performance indicators proposed by the SHTP and Global Hearts project (2). The indicators will be measured both in the intervention and in the control area, at baseline, at regular intervals during implementation, and at endline.

Table 3. Performance indicators at health facility level.

Indicator	Numerator	Denominator	Data Source	Breakdown	Frequency of collection
1. Number of hypertensive patients enrolled in the Cardiovascular	Number of hypertensive patients enrolled in the CVRP	NA	Billing and electronic clinical records	Cardiovascular risk level (low, medium, high),grade of hypertension (I,	Monthly

Risk Program (CVRP)				II, resistant), sex, age, pharmacological treatment (yes, no), co-morbidities, complications, health care setting	
2. Prevalence of diagnosed hypertension in Metrosalud's catchment area	Number of hypertensive patients enrolled in the CVRP	Total population for whom Metrosalud is responsible in the studied Commune	For the numerator: Billing and electronic clinical records For the denominator: Database of the Subsidized Regime and non-insured assigned population	Cardiovascular risk level (low, medium, high), grade of hypertension (I, II, resistant), sex, age, pharmacological treatment (yes, no), co-morbidities, complications, health care setting	Quarterly
3. Ratio of prevalence of diagnosed hypertension to the expected prevalence of hypertension in Metrosalud's catchment area	Prevalence of diagnosed hypertension in Metrosalud's catchment area	Expected prevalence of hypertension in the population for whom Metrosalud is responsible in the catchment area	For the numerator: Billing and electronic clinical records For the denominator: Survey "Gaps in hypertension care and control in two Communes".	Sex, age, health care setting	Quarterly
4. New hypertensive	Total number of new	NA	Billing and electronic	Cardiovascular risk level (low,	Monthly

patients enrolled in the CVRP	hypertensive patients enrolled in the CVRP during a month		clinical records	medium, high), grade of hypertension (I, II, resistant), sex, age, pharmacological treatment (yes, no), co-morbidities, complications, health care setting	
5. Cardiovascular risk assessment	Hypertensive patients with a recorded cardiovascular assessment in the last 1 year	Number of hypertensive patients enrolled in the CVRP	Billing and electronic clinical records	Cardiovascular risk level (low, medium, high), grade of hypertension (I, II, resistant), sex, age, pharmacological treatment (yes, no), co-morbidities, complications, health care setting	Annual
6. High calculated cardiovascular risk	Hypertensive patients with calculated cardiovascular disease risk ≥20% in 10 years and systolic blood pressure (BP) ≥140/90 mm Hg at last BP measurement during the last year.	Number of hypertensive patients enrolled in the CVRP	Billing and electronic clinical records	Pharmacological treatment (yes, no), sex, age	Biannual
7. Prevalence of controlled	Hypertensive patients with documented	Number of hypertensive patients	Billing and electronic clinical	Pharmacological treatment (yes,	Biannual

hypertension	systolic BP <140 mm Hg and diastolic BP <90 mm Hg in at the most recent BP measurement during the last year.	enrolled in the CVRP	records	no), sex, age	
8. Prevalence of controlled hypertension 6 months after enrolment in the CVRP	Hypertensive patients who started treatment 6 months before the reporting trimester and have systolic BP <140 mm Hg and diastolic BP <90 mm Hg at follow-up visit during the reporting trimester	Number of hypertensive patients enrolled in the CVRP who started treatment 6 months before the reporting trimester	Electronic clinical records	Sex, age, pharmacological treatment (yes, no), non-pharmacological treatment (yes, no)	Quarterly
9. Uncontrolled hypertension in patients with cardiovascular disease, renal disease or diabetes	Hypertensive patients diagnosed ≥ 6 months before the start of the reporting period, and cardiovascular disease, renal disease, or diabetes mellitus, who had systolic BP ≥140 mm Hg or diastolic BP ≥90 mm Hg at the most recent BP measurement during the last	Number of hypertensive patients enrolled in the CVRP ≥ 6 months before the start of the reporting period	Electronic clinical records	Pharmacological treatment (yes, no), sex, age	Quarterly

	year				
10. Uncontrolled hypertension 2	Hypertensive patients diagnosed ≥ 6 months before the start of the reporting period who had systolic BP ≥160 mm Hg or diastolic BP ≥100 mm Hg at the most recent BP measurement during the last year	Number of hypertensive patients enrolled in the CVRP ≥ 6 months before the start of the reporting period	Electronic clinical records	Pharmacological treatment (yes, no), sex, age	Quarterly
11. Resistant hypertension	Hypertensive patients diagnosed ≥6 months before the start of the reporting period and who are treated with three or more antihypertensive drugs, who had systolic BP ≥160 mm Hg or diastolic BP ≥100 mm Hg at the most recent BP measurement during the last year	Number of hypertensive patients enrolled in the CVRP ≥ 6 months before the start of the reporting period	Electronic clinical records	Sex, age	Quarterly
12. Six-monthly control of blood pressure among people started on pharmacological treatment for	Number of patients started on pharmacological treatment of hypertension during the	Number of patients started on pharmacologi cal treatment of hypertension	Electronic clinical records	Sex, age	Quarterly

| hypertension | quarter that ended 6 months before, with controlled blood pressure (SBP<140 and DBP<90) at the last clinical visit in the most recent quarter (just before the reporting quarter) | during the quarter that ended 6 months before | | | |

The indicators for measuring the process implementation of different components of the intervention are listed in Table 4.

Table 4. Quantitative indicators for measuring process implementation.

> A. **Indicators related with the performance of the "Healthy Hearts" service in the quality improvement of BP screening and hypertension diagnosis**

Indicator	Numerator	Denominator	Data Source	Breakdown	Frequency of collection
13. Effective availability of the Healthy Hearts service	Number of effective opening hours of the Healthy Hearts service in a week	Number of programmed opening hours of the Healthy Hearts service per week	Register of opening hours of the Healthy Hearts service. Staff shift chart (initial and final)	Days, time	Weekly
14. Effective referral to the Healthy Hearts service and BP screening	Number of people without BP measurement in the last 1 year and referred for BP	Total number of people without BP measurement in the last 1 year referred for BP measurement to the Healthy	Numerator: register of people without BP measurement in the last 1 year who receive BP measurement at	Referring service, age, sex, health insurance scheme, patient or caretaker, result of BP measurement	Monthly

	measurement that reach and receive BP screening at the Healthy Hearts service	Hearts service	the Healthy Hearts service Denominator: ticket stubs for referral to Healthy hearts service	(high BP or not)	
15. Referral for serial BP measurement to the Healthy Hearts service	Number of patients not previously enrolled in the CVRP, with high BP at doctor or nurse consultation, referred for serial BP measurement to the Healthy Hearts service during the reporting month	Total number of patients not previously enrolled to the CVRP with high BP at doctors or nurses consultation during the reporting month	Electronic clinical record (referral to Healthy Hearts services)	Type of consultation, age, sex, chronic patient (yes, no)	Monthly
16. Realization of serial BP measurements at Health hearts service	Number of individuals with high BP detected by BP screening at the Healthy Hearts service who receive serial BP measurements	Total number of individuals with high BP detected by BP screening at the Healthy Hearts service	Electronic clinical records. Register of individuals who receive serial BP measurements at the Healthy Hearts service	Referring service (Healthy Hearts service, clinical services or A Community Hypertension Outreach Group (CHOG)) Age, sex, patient or caretaker, chronic patient (yes, no)	Monthly
17. Result of serial BP measurement	Number of patients with average systolic BP ≥140 mm Hg or diastolic BP ≥90 mm Hg at	Number of individuals receiving serial BP measurements	Register of serial BP measurements at Healthy Hearts service	Referral service (Healthy Hearts service, clinical services or CHOG)	Monthly

				Age, sex, patient or caretaker, chronic patient (yes, no) Cardiovascular risk level.	
18. Indication of serial self-measured BP monitoring	Number of individuals with indication of serial self-measured BP monitoring	Number of individuals with average systolic BP ≥140 mm Hg or diastolic BP ≥90 mm Hg as result of a serial BP measurement	Register of serial self-measured BP monitoring at Healthy Hearts service	Age, sex, patient or caretaker, health insurance scheme	Monthly
19. Realization of serial self-measured BP monitoring	Number of patients with serial self-measured BP monitoring	Number of patients with indication of serial self-measured BP monitoring	Register of serial self-measured BP monitoring at Healthy Hearts services	Age, sex, patient or caretaker, health insurance scheme	Monthly
20. Result of serial self-measured BP monitoring	Number of patients with average systolic BP ≥140 mm Hg or diastolic BP ≥90 mm Hg as result of a serial self-measured BP monitoring	Number of patients with serial self-measured BP monitoring	Register of serial self-measured BP monitoring at Healthy Hearts services	Age, sex, patient or caretaker,	Monthly

B. **Indicators related with the clinical management of the cardiovascular risk program for hypertensive patients**

Indicator	Numerator	Denominator	Data Source	Breakdown	Frequency of collection
21. Realisation of BP measurements by medical and	Number of interviewed individuals referring they	Total number of exit-interviews	Annex 4 (Exit-interview on adherence of clinical staff to	Age, sex, patient or caretaker, chronic patient (yes, no), kind of	Every 2 months

nursing staff	had BP measurement		cardiovascular duties	consultation / service	
22. Missed hypertension-related appointment	Number of patients who missed their last hypertension-related appointment during the reporting week	Patients with scheduled hypertension follow-up visit during the reporting week	Electronic records of Metrosalud	Sex, age, pharmacological treatment (yes, no)	Weekly
23. Management of missed hypertension-related appointment 1	Patients who missed a hypertension-related appointment in the reporting week that were contacted and provided with a new appointment	Patients who missed a hypertension-related appointment in the reporting week	Register of missed hypertension-related appointment in the Healthy Hearts service	Sex, age, pharmacological treatment (yes, no)	Weekly
24. Management of missed hypertension-related appointment 2	Patients who missed a hypertension-related appointment that presented at the new appointment provided by health services	Patients who missed a hypertension-related appointment that were contacted and provided with a new appointment	-Register of missed hypertension-related appointment at CVRP - clinical records	Kind of contact to provide the new appointment (by phone or through community leaders)	Weekly

25. Effective meetings of CVRT for programme follow-up	Number of meetings realized	Number of programmed meetings	List of participants. Minutes of the meetings.	NA	Quarterly
26. Audits of clinical records of patients enrolled in the CVRP	Number of audits of clinical records realized	Number of programmed audits to clinical records	Audit format: Audit of clinical records of hypertension CVRT audit plan of the	NA	Every 2 months
27. Collective feedback to health professionals of the CVRP	Number of feedback meetings involving health professionals of the CVRP	Number of programmed meetings	List of participants. Minutes of the meetings. CVRT meetings schedule	NA	Every 2 months
28. Correct prescription of pharmacological treatment	Number of patients who received a correct prescription of pharmacological treatment according to clinical condition and defined algorithm	Total number of audited clinical records	Report of audit of clinical records	Age, sex, health facility, cardiovascular risk level	Every 2 months
29. Use of recommended antihypertensive drugs	Number of patients who received prescription of antihypertensive drugs included in the standardized	Sample of hypertensive patients receiving pharmacological treatment	Electronic clinical records	Name of anti-hypertensive, age, sex, health facility, cardiovascular risk level, time of diagnosis	Quarterly

	algorithm				
30. Pharmacological advice by the medical doctor during consultation	Number of interviewed hypertensive patients who referred they received pharmacological advice by the medical doctor	Total number of interviewed patients during the audit	Annex 4 (Exit interview on adherence of clinical staff to cardiovascular duties)	Age, sex, health facility, cardiovascular risk level	Every 2 months
31. Percentage of hypertensive patients who received prescription of non-pharmacological treatment	Number of interviewed who refer they received prescription of non-pharmacological treatment by the doctor	Total number of exit interviews	Annex 4 (Exit-interview on adherence of clinical staff to cardiovascular duties)	Age, sex, health facility, cardiovascular risk level	Every 2 months

C. Indicators related with the clinical training of health care staff for improvement of hypertension care

Indicator	Numerator	Denominator	Data Source	Breakdown	Frequency of collection
32.Realized trainings	Number of realized training sessions for health care staff	Number of programmed training sessions for health care staff	Training plan List of attendance	Type of training	Annual
33. Trained health care professionals	Number of trained professionals	Total number of professionals	Training plan List of attendance	Type of health professional Type of training Health facility	Annual

34.Effectiveness of training in improving clinical knowledge	Average post-test score minus average pre-test score	NA	Pre- and post-test	Type of health professional Training session Health facility	Once
35. Effectiveness of training on acquiring BP measurement skills	Number of trained professional passing post-training practical test	Total number of trained professionals undergoing post-training practical test	Post-training practical test for certification on BP measurement following international standards	Type of health professional Health facility	

D. Indicators related with the management of the pharmacy service to guarantee the availability of the essential anti-hypertensive medication

Indicator	Numerator	Denominator	Data Source	Breakdown	Frequency of collection
36. Notification on availability of core set of anti-hypertensive drugs	Total number of notifications made in a month	Number of weeks in the respective month	Register of notification at the pharmacy service	Type of health facility	Monthly
37. Number of weeks without availability of essential antihypertensive drugs	Number of weeks without availability of one or more essential antihypertensive drugs	NA	Pharmacy inventory	Type of health facility Name of the antihypertensive	

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E. Indicators related with patients and community engagement for improving hypertension care and the prevention of cardiovascular diseases

Indicator	Numerator	Denominator	Data Source	Breakdown	Frequency of collection
38. Attendance to peer support group	Number of hypertensive patients who participate in the meetings of the peer support group	Number of hypertensive patients enrolled in the CVRP eligible for peer support and referred	Attendance list Denominator: Billing and electronic clinical records of Metrosalud	Sex, age, pharmacological treatment (yes, no), hypertension control (yes, no), health facility, cardiovascular risk level	Quarterly
39. Prevalence of high BP among population screened by the Community Hypertension Outreach Group (CHOG)	Number of people with high BP readings during the screening	Number of screened people for hypertension by the CHOG	Report of activities by the social worker of Metrosalud	Kind of environment, place, target population	Monthly
40. Meetings of the CHOG	Number of meetings of the CHOG	NA	Report of activities by the social worker of Metrosalud List of attendance	NA	Quarterly
41. Participation of community leaders in the meetings of the CHOG	Number of community leaders participating in the meetings of the CHOG	Total number of community leaders in the CHOG	Report of activities by the social worker of Metrosalud List of attendance	NA	Quarterly

4.3.2 Qualitative Data Analysis

Based on the logical model and the detailed description of the intervention, one to three process evaluation questions will be elaborated to determine whether each aspect of the intervention was implemented as intended (e.g. was each of the intervention components implemented as planned? Were the intervention components implemented as often and for as long as planned? Was the methodology and way of delivery followed as described?).

Semi-structured interviews with health providers involved in the implementation and project leaders or coordinators, as well as patients, will be conducted by a social scientist (outline of interview guides in annex 8 and 9). To determine if each intervention component was implemented as specified, the content of collected documents, semi-structured interviews, and observation notes from the same level, unit and actor will be analysed independently by three independent researchers (evaluators). The components will be categorized according to the analytical framework mentioned above (content, frequency, duration, and coverage) and also by establishing at which level (individual, team, organizational) adaptations are introduced. The analysis will be conducted systematically for every previously identified critical point.

Three types of adaptations to the original design of the intervention will be identified by the evaluators, following the categorization proposed by Rebchook et al.(22): deletion (when a component is omitted or modified so radically that the programme is no longer implemented as intended), modification (a component is implemented with minor or major modifications while still respecting the original purpose) and third, additional activities or components are added. The algorithm to categorize adaptation will be as follow: if all three evaluators independently agree that a given aspect of the intervention was implemented as specified, it will be classified as "implemented". If all agree that a given component was not implemented, it will be classified as such. If any of the evaluators consider that a component was modified, it will be classified as such. Added components will be also identified. Modified and added aspects will be classified as positive or negative in relation to the expected outcome, taking into consideration the functioning principles. Those adaptions classified as negative will be corrected.

Besides, an inductive thematic analysis of the semi-structured interviews will be conducted to identify, define and organize participant responses regarding reasons for introducing adaptations and general factors either positively or negatively affecting or moderating implementation. Then, transcripts will be reviewed, using a constant comparative technique to expand or merge themes. Finally, findings will interpreted according to the six moderating factors pre-established by the

theoretical framework. Factors not matching the deductive coding scheme will be classified as intervention-specific moderating factors.

In depth interviews with patients will be analysed firstly inductively looking for experiences and views of the intervention across different stages and component of the intervention, as well as region and health centres within the commune. In a second stage, data will be reclassified according to the subcategories of fidelity and the moderating factors of the framework to triangulate with data provided by the implementers and with quantitative results.

The qualitative data analysis will be conducted by the social scientist. To increase internal validity, the senior sociologist not involved in data collection will review the data and consistency of the coding system. Besides, findings from the data analysis and triangulation with quantitative results will be discussed systematically with a wider group of the research team, composed of professionals with diverse backgrounds (epidemiologists, public health practitioners, health care managers, nurses and general practitioners).

To identify when and under which circumstances the intervention was successful we will used qualitative comparative analysis (QCA) by contrasting outcomes data with implementation data collected at different stages and critical points of the intervention along process evaluation. Qualitative analysis will be carried out using the software Nvivo v.10.

5. ETHICAL ISSUES

Confidentiality of the retrieved individual information will be guaranteed. The collected information will be used only for research purposes and at no time the identity of participating individuals will be disclosed.

During the endline survey, confidentiality at the time of interview will be also guaranteed interviewing participants belonging to the same household one by one and in separate spaces. All surveyors will be trained in identifying patients with severe abnormal conditions. They will identify and refer to the nearest health center, individuals with very high BP figures or reporting health complications or acute symptoms. In Colombia, health care for hypertension is free of charge in both regimes of the health insurance system (Subsidized and Contributory). Patients found to be hypertensive without follow-up or treatment will be referred for care to the provider of the corresponding patients' health insurance scheme.

Exit-interviews to patients will be anonymous and the identity of the consulting medical doctor or nurse won't be recorded. The results will be evaluated by the CVRT who will give collective

constructive feedback to the medical staff; the patient survey results won't be used as an individual evaluation of the medical staff.

The intervention does not pose any risk to beneficiaries and it implies the implementation into the routine setting of evidence based best practices. Any procedure that influences directly patient care has been agreed with the Metrosalud central authorities and site health staff. All activities are implemented under standard practice and, conditional on adjustment when needed, will continue beyond the end of the study period.

Patients eligible for the qualitative component, will be asked by the local health staff if they would be interested in learning more and participate in the study. If they are interested, they will be invited to participate by the PI or the research assistant at the health setting. Health staff will be contacted directly by the research staff. The objectives and procedures will be explained as well as the benefits and risks and written informed consent will be obtained (see below).

The research team will guarantee to allocate the most convenient place and time for interviews. A place as enclosed for privacy and as neutral as possible for participants will be chosen. Participants will be asked if they consent for the discussion to be tape-recorded.

5.1 Ethical (and regulatory) Review

This study protocol will be submitted for formal review and approval to the Institutional Review Board of ITM, the Ethics Committee of University of Antwerp Hospital and the Research Ethics Committee of Metrosalud E.S.E. No participants will be enrolled or participant related activities performed before written approval from these bodies is obtained.

The study will be carried out according to the principles stated in the Declaration of Helsinki, all applicable regulations and according to established national and international scientific standards.

5.2 Obtaining Informed Consents

Informed consent for participation inf the study will be sought for the endline survey (Annex 10) and the qualitative component (Annexes 11 and 12). For the endline survey, during the household visit all eligible individuals will be explained about the study in lay language by the research team and handed over the informed consent form.

Participant information sheets will describe the purpose of the study, the procedures to be followed, the risks and benefits of participation, etc. Study participants will be informed that participation on

the study is completely voluntary and that they can withdraw from the study at any time without any negative consequences. A copy of the informed consent will be handed over to participants. No informed consent will be sought for other intervention components, as all implemented activities are part of routine practice.

5.3 Insurance

The Coordinator of this study, the Antwerp Institute of Tropical Medicine, has obtained an umbrella insurance for low risk research to cover any potential damage or loss to study participants and which is caused directly or indirectly by their participation in the study.

6. MONITORING AND QUALITY CONTROL

All research staff will be trained in responsible conduct of research. For the endline survey, the surveyors will be trained on the study, the study tools and BP measuring. For the intervention at health services, the participant health staff will be trained on the study procedures tools for data collection and self-reporting. They also will be subject of random supervision visits and audits to check the implementation of the planned activities, its accuracy and reliability. The PI will be responsible of the monitoring and quality control of the implementation of study procedures, data collection, entry and analysis. The qualitative component will be carried out by trained research staff.

7. TIMELINE

	Year 1				Year 2				Year 3			
	Q1	Q2	Q3	Q4	Q1	Q2	Q3	Q4	Q1	Q2	Q3	Q4
Preparation of the Intervention	■											
Ethical Approval of intervention protocol	■											
Intervention		■	■	■	■	■	■	■	■	■	■	■
Data collection		■	■	■	■	■	■	■	■			
Endline survey										■		
Data analysis				■	■	■	■	■	■	■	■	■
Dissemination of results						■	■	■	■	■	■	■

█ = intervention activities continue to be implemented by Metrosalud as part of routine practice

8. DATA MANAGEMENT AND ARCHIVING

8.1 Data Management

Data will be collected as described in section 4. Databases will be electronically encrypted, and a single study code will be assigned to each participant and they will be password-protected, with a password known only to the research team. The list of participant names and their assigned study codes will be stored in a separate database with restricted access to the study investigators that did the process of identification. Data will be analysed as described in section 4. The obtained individual information will be known only by the research team, where information access levels will be established, in particular for personal identification data. For the endline survey, questionnaires will be filled in by using tablets, and the information will be consolidated through an electronic platform provided by a professional statistics enterprise. The access to each electronic questionnaire is restricted to specifically authorized surveyor. The software of the electronic platform will allow to record in real-time every applied single questionnaire, obtaining reliable databases. Only aggregate data will be extracted from the billing and electronic clinical records of Metrosalud and from the databases of the subsidized regimen and of the non-insured poor population. Qualitative information will be transcribed *verbatim* by trained personnel. Transcripts and data will be stored in Nvivo v.10 and analysed as described in section 4.3.2. Anonymity of participants will be maintained, a code will be assigned to every participant and transcripts will be anonymous for transcribers. Data protection and confidentiality will be responsibility of the PI and the responsible for qualitative analysis.

8.2 Archiving

The Principal Investigator will ensure a secure and appropriate location for storage of the paper documents and any other study related documentation, as well as for ensuring that only research staff that is competent and delegated to work for the study has got access to the files.

The paper documents will be kept locked and the electronic databases will be protected by a unique password accessible only to investigators and stored with a backup copy in a safe location accessible

only to the research staff. Data will be retained for a period of time in accordance to the local legislation.

9. DISSEMINATION OF RESULTS

The results of the study will be shared with the local health authorities and staff. The study will be published in peer reviewed scientific journals and presented at national and international conferences and workshops. A summary of the results in an adapted language might be communicated to the involved communities and institutions.

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11. LIST OF ABBREVIATIONS

BP	Blood Pressure
CVD	Cardiovascular diseases
NCD	Non-communicable diseases
SHTP	Standardized Hypertension Treatment and Prevention Project
LMIC	Low and Middle Income Countries
LAC	Latin America and Caribbean
HIC	High Income Countries
PURE	Prospective Urban Rural Epidemiology study
CVRP	Cardiovascular Risk Program
CVRT	Cardiovascular Risk Team
CHOG	Community Hypertension Outreach Group
ESE	[Empresa Social del Estado]
IC(F)	Informed Consent (Form)
(I)EC	(Independent) Ethics Committee
IRB	Institutional Review Board
ITM	Institute of Tropical Medicine
PI	Principal Investigator

12. ANNEXES

- Annex 1: Training of clinical staff for improving CVD management
- Annex 2: Endline survey questionnaire
- Annex 3: Outline of Healthy Hearts register
- Annex 4: Register of opening hours of Healthy Hearts service
- Annex 5: Register of missed appointments at CVR program
- Annex 6: Exit interview on adherence of clinical staff to cardiovascular duties

- Annex 7: Format for audit of electronic clinical records of CVRP

- Annex 8: General questions for the evaluation of fidelity

- Annex 9: Topics for in-depth interviews with patients

- Annex 10: Informed Consent for endline population survey

- Annex 11: Informed Consent for semi-structured interviews on health providers

- Annex 12: Informed consent in-depth interviews