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Protocol for a controlled before-after quasi-experimental study to evaluate the effectiveness of a multi-component intervention to reduce gaps in hypertension care and control in low-income communes of Medellin, Colombia

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Abstract

Introduction

Research on public health interventions to improve hypertension care and control in low- and middle-income countries remains scarce. This study aims to evaluate the effectiveness of a multi-component intervention to reduce the gaps in hypertension care and control at a population level in low-income communes of Medellin, Colombia, and assess the process and fidelity of the intervention's implementation.

Methods and analysis

A multi-component intervention was designed based on international guidelines, a cross-sectional population survey results, and consultation with the community and institutional stakeholders. Three main components integrate activities related to (I) Health services redesign, (II) Clinical staff training and (III) Patient and community engagement. The effectiveness of the intervention will be evaluated in a controlled before-after quasi-experimental study, with two deprived communes of the city selected as intervention and control arms. We will conduct a baseline and an endline survey two years after the start of the intervention. The main outcomes assessed will be the gaps in hypertension diagnosis, treatment, follow-up and control. Effectiveness will be evaluated with difference in difference measures. Generalized estimation equations models will be fitted considering the clustered nature of data and adjusting for potential confounding variables. The implementation process will be studied with mixed methods. Implementation fidelity will be documented to assess to which degree the intervention components were implemented as intended.

Ethics and dissemination

The study protocol has been approved by the Medical Ethics Committee at the Antwerp University Hospital (UZA), reference number 18/40/424, and the Institutional Review Board of the Antwerp Institute of Tropical Medicine, number 1294/19. We will share and discuss the study results with the community, institutional stakeholders and national health policymakers. We will publish them in national and international peer-reviewed scientific journals.

Trial registration number

This study was already registered at ClinicalTrials.gov. The NCT number is pending.

Strengths and limitations of this study

- We respond to exhortations to rigorously evaluate multi-component interventions to improve hypertension care and control in low- and middle-income countries.
- The planned intervention is based on formative research and inspired by guidelines from international hypertension care initiatives and has been adapted to the local environment with the participation of all relevant stakeholders.
- We employ a controlled before-after quasi-experimental study design.
- We will rely on quantitative outcomes and qualitative process assessments, combining effectiveness and implementation fidelity indicators, to better inform subsequent adaptation and scaling up.
- The intervention will be implemented in a low-income area of an industrialized city in a middle-income country, and results may not be generalizable to upper-class urban zones or underserved rural settings.

Introduction

Non-communicable diseases accounted for 73.5% of global deaths in 2017 [1]. Their incidence is disproportionately increasing in developing countries [2], and they constitute the first cause of mortality and disability in the Americas region, generating at least 5.5 million deaths each year [3]. Notwithstanding, most Latin American and Caribbean health systems provide inadequate chronic diseases management [4]. Globally, only about one in ten people with chronic conditions are successfully treated [5]. Moreover, most out-of-pocket health payments and catastrophic expenditures are related to these conditions [6, 7].

Uncontrolled hypertension is the main modifiable risk factor for cardiovascular diseases (CVDs) and is associated with more than 10 million deaths worldwide each year [8]. Almost 75% of people suffering from hypertension live in developing countries, where disease awareness is low and health care access is limited [9, 10]. High disease prevalence and poor hypertension control are pivotal factors in the rising epidemic of CVDs in low- and middle-income countries (LMICs) [11], mainly striking the working-age population and further hampering economic growth and social development [10]. Among the 1.6 million people who die from CVDs every year in Latin America and the Caribbean, half a million are below 70 years old [12]. Nevertheless, limited research in this field has been conducted in LMICs [13].

A multi-country cross-sectional study conducted between 2003 and 2009, including 14 LMICs [14], found a prevalence of hypertension of 27.7% in adults with only 46.5% and 32.5% of hypertension awareness and control, respectively, among the affected. A 2019 review focusing on LMICs [15] pooled individual-level hypertension data on people aged 15 years and older from 44 countries and found 17.5% hypertension prevalence. Of the hypertensive individuals, 39.2% were aware of their condition, 29.9% received pharmacological treatment, and barely 10% attained controlled blood pressure (BP). These reports provide information on hypertension control internationally and on variations among populations. To date, most studies assessing patient and health care provider barriers to hypertension care have been conducted at the health facility level and in high-income countries [13]. Research at the population level to document in-depth and tackle the main gaps and barriers hampering equitable and effective hypertension care and control in LMICs is needed.

The Chronic Care Model [16] and its expanded version [5] aim to guide interventions for improving chronic disease management. It is the basis of the Standardized Hypertension Treatment and Prevention (SHTP) Project [17], developed by the Pan American Health Organization and the Centres for Disease Control and Prevention, which identified six key elements to strengthen health systems at

the primary care level and to improve hypertension control, using evidence-based components: guideline-based standardized treatment protocols; effective drug procurement mechanisms using a core set of medications; registries for cohort monitoring and evaluation; patient empowerment; team-based care system and community engagement [17]. This approach was reinforced by the World Health Organization (WHO) Global Hearts Initiative, especially through the Technical Package for Cardiovascular Disease Management in Primary Health Care [18]. Operational research to assess the impact of this and other similar strategies is urgently advocated.

The objective of the present study is to evaluate the effectiveness of a multi-component intervention to reduce the gaps in hypertension care and control in low-income communes of Medellin, Colombia. In addition, we aim to assess the process and fidelity of the intervention's implementation.

Rationale

In 2016, we carried out a cross-sectional survey in a low-income commune of Medellin [19] to estimate the prevalence of hypertension in the adult population and the magnitude and determinants of the main gaps in hypertension care and control. The definitions of those gaps are shown in Table 1. In summary, we found a hypertension prevalence of 43.5%, 28.2% aware and 15.3% unaware hypertensive individuals. Moreover, 14.4% presented a follow-up gap among the aware, 93.4% were prescribed antihypertensive drugs, but 38.9% were not compliant, and 39.0% were uncontrolled. The survey results, the -hypothesized- possible determinants of the identified gaps (Table 2), and potential solutions were discussed with communities and institutional stakeholders in a series of workshops. Based on the workshops' conclusions, in consultation with the main stakeholders and inspired by the SHTP Project and the WHO Global Hearts Initiative [17, 18], we designed a multi-component intervention to improve hypertension care and control in Medellin.

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

Gap	Numerator	Denominator
Diagnosis gap	Number of Unaware Hypertensive individuals[1]	Number of Unaware Hypertensive individuals plus Number of Aware Hypertensive individuals[2]
Follow-up gap	Number of Aware Hypertensive individuals who did not attend a follow-up consultation during the last year	Number of Aware Hypertensive individuals

Pharmacological treatment gap	Number of Aware Hypertensive individuals who received a prescription but either: -do not take the drugs -or are non-adherent	Number of Aware Hypertensive individuals who received a prescription for antihypertensive medication
Control gap	Number of Aware Hypertensive individuals who did not manifest controlled hypertension[3]	Number of Aware Hypertensive individuals

1 Unaware Hypertensive individual: participant not reporting a previous diagnosis of hypertension but presenting an average BP measurement higher than 140/90 mmHg in the survey

2 Aware Hypertensive individual: participant reporting a previous diagnosis of hypertension

3 Controlled hypertension: see text for precise definition

Table 2. Potential determinants at health provider, population and health system level of the main gaps in hypertension care and control. Santa Cruz Commune. Medellin, Colombia, 2016.

Gap	Level		
	Health Provider	**Population**	**Health System**
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 delayed healthcare-seeking	Passive and fragmented health services Limited opening hours of services for hypertension screening
Quality of care (treatment and follow-up gaps)	No pharmacological advice/consultation Limited communication skills of health staff and the poor doctor-patient relationship Interrupted delivery of essential antihypertensive drugs	Low awareness of the importance of non-pharmacological treatment Low educational level hampers communication and treatment compliance	Scarcity of essential antihypertensive drugs Administrative barriers imposed on patients and health providers

Methods and analysis

Overview of study design

The effectiveness of a multi-component intervention in reducing gaps in hypertension care and control will be evaluated in a controlled before-after quasi-experimental study. A graphical summary of the underlying theory of action is depicted in Figure 1. Besides outcomes, the process and implementation fidelity will be studied to assess to which degree the intervention components were implemented as intended. The study will use mixed methods, comprising a baseline and an endline population survey, medical records and health care registers analysis, self-registration forms of intervention activities, non-participant observations, and interviews with key informants such as health care staff, managers, and patients and their caregivers. The intervention will start in the first quarter of 2022 and be evaluated after 24 months.

We checked the completeness and accuracy of our research protocol using the SQUIRE (Standards for QUality Improvement Reporting Excellence) reporting guidelines (online supplementary file 1).

Patient and public involvement

From the onset of the planning phase of the intervention onwards, the main community and institutional stakeholders -the local patient's association, the community representatives to the city council, managers and clinical staff of the city's public health provider (Metrosalud) and public health practitioners from the University of Antioquia- were invited in for a series of workshops to discuss the results of the previous formative research. Hence, they actively proposed pathways to improve hypertension care and control within the community and at the health facility level. We will continuously involve all local stakeholders in monitoring, analysing and learning from the forthcoming intervention.

Study setting and population

Colombia is a middle-income country with a 2019 per-capita gross domestic product of US$6,429 (current US$) [20]. The mortality from CVDs in 2017 was 150.3 per 100.000 population, and 30.5% of all deaths and 16.7% of Years of Life Lost can be attributed to CVDs [21]. The Colombian health system has two different health insurance schemes run by health insurance companies. People able to contribute and their beneficiaries are compulsorily affiliated to the contributory scheme, which covers the formally employed workers, pensioners and part of the self-employed. The State finances the subsidized scheme, which covers people that cannot afford contributions.

Medellin is the second-largest industrialized city in Colombia. It has 16 Communes, and its total 2016 population was around 2.5 million [22]. The intervention will be implemented in Commune 2, located in the northeast of Medellin. Commune 6, located northwest of Medellin, was selected as the control area to deliver routine care. Both communes are among the most deprived areas of the city [23] and share similar characteristics: urban setting, low-income population, typical functioning of the national health system, and commitment of Metrosalud -the city's public health care provider- to develop improvement programmes based on research results.

Intervention

A multi-component intervention to improve hypertension care and control will integrate activities related to 1. Health services redesign, 2. Clinical staff training and 3. Patient and community engagement. Each intervention component will be standardized, and its related activities described in detail in a field manual. The intervention will be implemented by health services staff with technical assistance from the investigators. The three components of the intervention are detailed below:

1. **Health services redesign**
   - 1.1. **"Healthy Hearts" service**: A nursing station will be established, in charge of providing BP measurement, cardiovascular risk assessment and preventive counselling in extended opening hours. It will secure hypertensive patients' effective follow-up, especially for the presumptive hypertensive individuals and those newly diagnosed. It will facilitate serial automated self-measured BP testing to confirm diagnosis within the health facility premises to exclude white coat hypertension. It also will administer periodical anonymous exit questionnaires to patients that attended hypertension-related consultations to assess the quality of care. Results will be communicated to the cardiovascular risk team for analysis.
   - 1.2. **Hypertension screening**: i) The health care flow for patients with a high BP measurement will be standardized employing a written procedure. ii) All adults attending health services who did not have their BP measured by a health care provider in the previous year will be referred to the Healthy Hearts service for screening. iii) Doctors and nurses encountering presumptive hypertensive individuals will refer them to the Healthy Hearts service to confirm the diagnosis.
   - 1.3. **Clinical management**:
     - 1.3.1. **Creation of the cardiovascular risk team**: A group of doctors supervising clinical hypertension management and coordinating action plans for improvement. It conducts

audits, periodically selecting a representative sample of clinical records of hypertensive patients and uses a structured questionnaire to evaluate the fulfilment of the requirements of a complete cardiovascular risk assessment interview and physical examination, doctors' adherence to guidelines and the quality of the provided care. It also will supervise the Healthy Hearts service. This operational body will hold weekly meetings and provide regular feedback and support to health professionals involved in hypertension care.

1.3.2. **Guideline-based standardized diagnostic and treatment protocols**: A simplified diagnostic and treatment algorithm based on the national clinical guidelines and in line with the Global Hearts Initiative will be agreed upon with the general direction of Metrosalud, the direction of the health area and the clinical staff. It will identify a core set of primary and secondary options for each of the major classes of antihypertensive medications.

1.3.3. **Availability of antihypertensive medications**: It will be assured through procurement mechanisms agreed with the central drug store of Metrosalud. To timely inform on possible alternative prescriptions, the availability of antihypertensive medications will be communicated to clinicians at the beginning of each week and *ad hoc* in case of stock-out.

2. Clinical staff training

2.1. **Training on good clinical management of hypertension**: It will be focused on correct BP measurement, use of evidence-based guidelines, cardiovascular risk assessment, a standardized diagnostic and treatment algorithm, correct prescription of pharmacological and non-pharmacological treatment, patient counselling, and prevention of clinical inertia.

2.2. **Training on communication skills and patients' needs assessment:** This training will be designed under the "patient-centred medicine" framework [24], aiming to equip all health workers involved in hypertension care with tools for understanding patients' feelings and experience of illness and improving their capacity to address social, psychological, and behavioural dimensions of hypertension care.

3. Patient and community engagement

3.1. **Patients' empowerment**: "Expert hypertensive patients", under the supervision of a social worker, will provide support and transmit their know-how to other patients in need,

particularly those newly diagnosed or non-adherent to treatment or presenting uncontrolled hypertension.

3.2. **Community engagement**: a Community Hypertension Outreach Group will be set up, composed of existing voluntary community health workers, who will be trained and certified. This group will conduct BP measurements in selected public areas of the commune, referring those with positive screening to the nearest health facility for diagnosis confirmation. It will also provide health information with an emphasis on healthy lifestyles. Additionally, existing local communication channels such as the community radio and the local newspaper will be engaged.

Effectiveness assessment

The primary outcome will be the control gap in the total hypertensive population (aware and unaware hypertensive individuals), whereas the secondary outcomes will be the diagnostic, treatment, follow-up and control gap as defined in Table 1.

Inclusion and exclusion criteria for the baseline and endline surveys

Eligible persons will be all 35 years or older permanent inhabitants of the selected communes, willing and able to provide written informed consent. Potential participants with a mental disability or unable to answer the questionnaire will be excluded.

Sample size and sampling procedures for the surveys

Expecting at baseline 60% non-control in the 35 years or older hypertensive population and at endline 10% difference in difference (baseline minus endline) between the intervention and control arms, a sample of 385 hypertensive individuals per arm is required for 80% power and a 95% confidence level. Given a 45% prevalence of hypertension in individuals aged 35 years or older, screening 856 individuals will allow finding the needed number of hypertensive individuals. We will increase the number to be screened to 1190 individuals, assuming 10% non-response and, based on previous observations, a design effect of 1.25 for our sampling scheme.

A cluster sample will be drawn from a sampling frame made up of the addresses of all premises provided by the municipality and using maps of Medellin detailing house blocks. Given an average of 1.5 individuals ≥35 years old per household, 795 households will be sampled per study arm by selecting 53 clusters of 15 households from the different neighbourhoods of the Communes, with an allocation of the number of clusters proportional to neighbourhood size. A group of trained

interviewers will make up to two repeat door-to-door visits to every selected household to include in the surveys all identified eligible household members aged 35 years or older.

Data collection

Participants will be interviewed on socio-demographic characteristics, health-seeking behaviour, cardiovascular risk factors and previous hypertension diagnosis employing a structured questionnaire. In addition, participants aware of being hypertensive will be questioned on their follow-up, antihypertensive pharmacological and non-pharmacological treatment, and treatment compliance. BP will be measured using a digital manometer, following international recommendations for standardized BP measurement in population surveys [25, 26].

Operational definitions for the surveys

Hypertensive individual: self-report of previously diagnosed hypertension or without a previous diagnosis but presenting an average repeat BP measurement equal to or higher than 140/90 mm Hg. [14, 27].

Controlled hypertensive individual: self-report of previously diagnosed hypertension and an average repeat BP measurement less than 140/90 mm Hg for patients between 35 and 59 years old or diabetic patients, and below 150/90 mm Hg for patients aged 60 years or older [28].

Data analysis

The difference in difference measures [29, 30] will be calculated (endline-baseline changes in the intervention minus endline-baseline changes in the control commune) for the primary and secondary outcomes. Where relevant, we will stratify on affiliation to subsidized or contributory insurance schemes. Generalized estimation equations models will be fitted, considering the clustered nature of data and adjusting for potential confounding variables. Unadjusted and adjusted odds ratios and their 95% confidence interval will be calculated. The Statistical Package for Social Sciences V.24 (SPSS Inc., Chicago, IL, USA) will be used for data analysis.

Assessment of the implementation process and fidelity

The indicators to be used for measuring results at the health service level are shown in Table 3. They were elaborated considering the performance indicators proposed by the SHTP project, the Global Hearts initiative and other proposals to improve prevention and control of cardiovascular diseases globally [17, 18, 31, 32]. The indicators we constructed for monitoring implementation are listed in

Table 4. The needed data will be collected in the intervention and control areas, at baseline, during implementation, and at the endline. Electronic clinical and billing records of Metrosalud, registers of the "Healthy Hearts" service, exit interviews, and clinical audits will be the data sources.

Table 3. Performance indicators at the health facility level.

Indicator	Operational Definition
Number of hypertensive patients enrolled in the Cardiovascular Risk Program (CVRP)	Number of hypertensive patients enrolled in the CVRP
Prevalence of diagnosed hypertension in the catchment area	Number of hypertensive patients enrolled in the CVRP/Total catchment population.
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
New hypertensive patients enrolled in the CVRP	Total number of new hypertensive patients enrolled in the CVRP per month
Cardiovascular risk assessment	Hypertensive patients with a recorded cardiovascular assessment in the last year/ Number of hypertensive patients enrolled in the CVRP
Prevalence of 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
Prevalence of controlled hypertension	Hypertensive patients with documented systolic BP <140 mm Hg and diastolic BP <90 mm Hg in at the most recent BP measurement during the last year/ Number of hypertensive patients enrolled in the CVRP
Prevalence of controlled hypertension 6 months after enrolment in the CVRP	Hypertensive patients who started treatment 6 months before and have systolic BP <140 mm Hg and diastolic BP <90 mm Hg at follow-up visit / Number of hypertensive patients enrolled in the CVRP who started treatment 6 months.
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

Indicator	Operational Definition
	year/ Number of hypertensive patients enrolled in the CVRP ≥ 6 months before the start of the reporting period
Uncontrolled hypertension	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
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
Six-monthly control of blood pressure among people started on pharmacological treatment for hypertension	Number of patients started on pharmacological treatment for hypertension during the 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)/ Number of patients started on pharmacological treatment of hypertension during the quarter that ended 6 months before

Table 4. Quantitative indicators for monitoring implementation.

Indicators related to BP screening and hypertension diagnosis.	
Indicator	**Operational definition**
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
Effective referral to the Healthy Hearts service and BP screening	Number of people without BP measurement in the last year and referred for BP measurement that reach and receive BP screening at the Healthy Hearts service/ Total number of people without BP measurement in the last year referred for BP measurement to the Healthy Hearts service
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
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 (>=3) BP measurements/ Total number of individuals with high BP detected by BP screening at the Healthy Hearts service.
Result of serial BP measurement	Number of patients with average systolic BP ≥140 mm Hg or diastolic BP ≥90 mm Hg at serial (>=3) BP measurement/ Number of individuals receiving serial BP measurements
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
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
Indicators related to the hypertension management program.	
Indicator	**Operational definition**
Realisation of BP measurements by medical and nursing staff	Number of interviewed individuals referring they had BP measurement/ Total number of exit-interviews
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
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
Use of recommended antihypertensive drugs	Number of patients who received prescription of antihypertensive drugs included in the standardized algorithm/ Sample of hypertensive patients receiving pharmacological treatment
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

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
Indicators related to the training of health care staff.	
Indicator	**Operational Definition**
Trained health care professionals	Number of trained professionals
Effectiveness of training in improving clinical knowledge	Average post-test score minus average pre-test score
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
Indicators related to (stock management and availability of the essential antihypertensive medication.	
Indicator	**Operational Definition**
Number of weeks without availability of essential antihypertensive drugs	Number of weeks without availability of one or more essential antihypertensive drugs
Indicators related to patients and community engagement.	
Indicator	**Operational Definition**
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
Prevalence of high BP among population screened by the Community Hypertension Outreach Group (CHOG)	Number of people with high BP readings during the screening
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

For assessing implementation fidelity [33, 34], we will use self-registration forms for specific intervention activities, alongside non-participant observations and semi-structured key informant interviews. Self-registration forms will be collected monthly to determine whether actual implementation is done as intended and select a heterogeneous sample of activities to be observed purposively and actors to be interviewed. Observations will provide real-time implementation information, while interviews will clarify observed practices and reasons for non-adherence.

Additionally, overall experience with the intervention will be explored through in-depth interviews with stakeholders and patients. Data saturation will be considered to ascertain the frequency of observations and the number of interviews. A local social scientist will analyze data with NVivo 10 (QSR International Pty LTD, Melbourne, Australia, 2010). A senior sociologist not involved in data collection will review the consistency of coding.

We will determine whether intervention components were implemented as planned, or they were modified, deleted or added [35] and assess adherence to the content and dose (i.e., frequency, duration, and coverage) of components and the influence of moderating factors such as comprehensiveness of intervention description, facilitation strategies, quality of delivery, recruitment, participant responsiveness, and context. Factors influencing implementation will be classified using these pre-established categories, and aspects not matching this coding will be categorized as intervention-specific moderating factors [36]. Finally, reasons for adapting intervention components will be identified through an inductive thematic analysis of key informants' interview responses.

Eventually, we will contrast outcome data with implementation data and triangulate quantitative and qualitative results obtained from different information sources to validate and complement our findings.

Data Management

Databases will be electronically encrypted and, when relating to individuals, a single study code will be assigned to each participant. The log of participant names and their assigned codes will be stored in a separate database with restricted access. For the surveys, questionnaires will be filled in employing tablets, and the information will be consolidated using an electronic platform. We will develop checks for data entry with built-in filters and logical constraints to assess the completeness and accuracy of our data. Recorded qualitative information will be transcribed *verbatim* by a local social scientist. Transcripts will be anonymized. Study-related material will be securely stored. Paper documents and tapes will be locked, and electronic databases and backup copies will be password protected. Data will be retained following local legislation.

Ethics and dissemination

All field staff will be trained in responsible conduct of research. Informed consents will be obtained from survey participants and partakers in the qualitative research components (online supplementary file 2). A convenient place and time for interviews will be assured. Confidentiality will be guaranteed throughout. In particular, exit interviews will be anonymous and will not inquire into the identity of the health personnel the interviewee consulted with. Patients who are hypertensive in the survey and without follow-up or treatment will be referred for care to a provider of their health insurance scheme.

The planned intervention is based on formative research and inspired by guidelines from international hypertension care initiatives and has been adapted to the local environment with the participation of all relevant stakeholders. It does not pose health risks to beneficiaries as it implies implementation in the routine setting of evidence-based best practices. The local patients' association, Metrosalud central authorities, and study site health staff have agreed upon any new procedure related to patient care. All activities are implemented conditional on adjustment when needed and planned to be continued beyond the study period.

The study protocol (online supplementary file 3) has been reviewed and approved by the Medical Ethics Committee at the Antwerp University Hospital (UZA), reference number 18/40/424 dated 15/10/2018, and the Institutional Review Board of the Antwerp Institute of Tropical Medicine, number 1294/19, dated 09/05/2019. Therefore, the study will adhere to the principles stated in the Declaration of Helsinki.

The study findings will be shared and discussed in workshops with the local health authorities, health staff, representatives of Metrosalud and patient organizations to adjust activities where needed, strengthen sustainability and prepare to scale up the intervention. Finally, results will be further disseminated through the media, presented in national and international conferences and published in peer-reviewed scientific journals.

Implications of this research

There is an urgent need, particularly in LMICs, to develop and test public health approaches that tackle the rising burden of the non-communicable diseases epidemic [37]. Doing so within an integrated framework of care will benefit all patients [5]. When developing our proposal, we started from international hypertension initiatives' guidelines [17, 18, 31, 32] and stepped them up considering the local context. We will thus implement and evaluate a comprehensive multi-component strategy

involving stakeholders spanning from community members to health program administrators, who all participated in the protocol's design. We believe that this ensures social relevance and will lead to increased intervention uptake at the health service and the community level.

The quasi-experimental nature of our design will provide solid evidence on the outcome of the intervention, which can form the basis for further economic evaluation. Relevant lessons will also be learned on what functioned, for whom, and why within the complex hypertension continuum of care dynamics in a specific national health system. Findings should not be extrapolated to upper-class urban zones or underserved rural areas. Still, over half of the Colombian population is living in low-income urban environments, to which they may be generalizable.

Finally, our research involves Metrosalud, the most significant public health care provider of Medellin. As such, it should act on primary care for non-communicable diseases in the Colombian health system. Its findings can also inform and inspire other initiatives for better chronic care in LMICs, particularly in Latin America. Furthermore, assessing the implementation fidelity of the intervention and its determinants may provide valuable insights on the scalability of the WHO Global Hearts initiative.

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Contributors: Tullia Battaglioli and Esteban Londoño contributed equally to this paper. Patrick Van der Stuyft, Esteban Londoño and Tullia Battaglioli conceived the study and took the lead in designing the intervention. José Vásquez, Hernán Aguilar, Viviana Pérez, Rubén Gómez and Esteban Londoño coordinated the stakeholder involvement and the workshops in which the intervention content and procedures were defined. Dennis Pérez supported the development of process assessment and implementation fidelity matters. All authors contributed to refining the research protocol and the data collection tools. Esteban Londoño, Tullia Battaglioli and Alonso Soto drafted the manuscript with Patrick Van der Stuyft' involvement. All authors commented on subsequent versions of the paper and read and approved the final manuscript.

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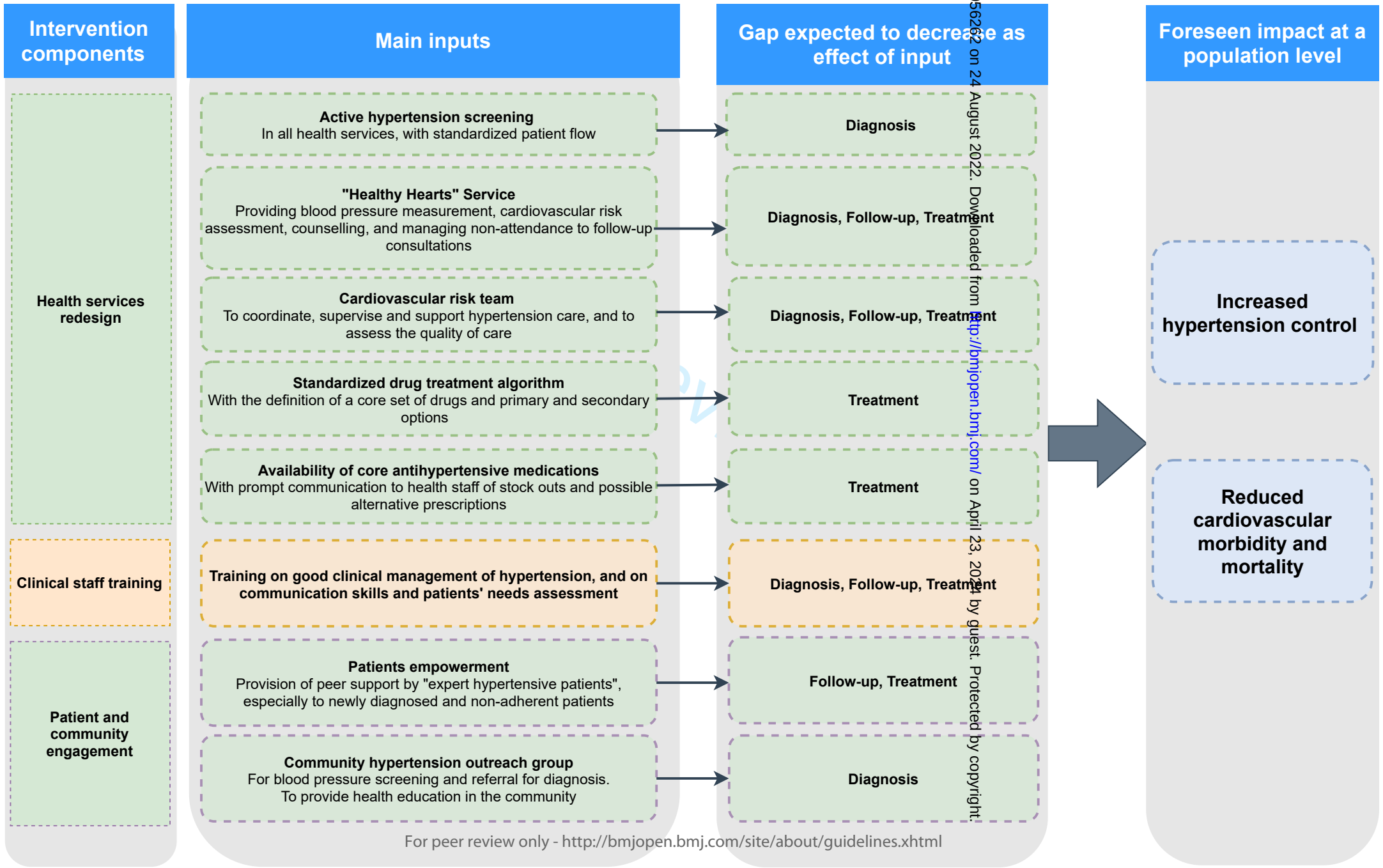
Competing interests: None declared.

Figure legend

Figure 1. Model conceptualizing the theory of action of a multi-component intervention to improve hypertension care and control in low-income Medellin, Colombia.



Reporting checklist for quality improvement in health care.

Based on the SQUIRE guidelines.

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Complete this checklist by entering the page numbers from your manuscript where readers will find each of the items listed below.

Your article may not currently address all the items on the checklist. Please modify your text to include the missing information. If you are certain that an item does not apply, please write "n/a" and provide a short explanation.

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		Reporting Item	Page Number
Title			
	#1	Indicate that the manuscript concerns an initiative to improve healthcare (broadly defined to include the quality, safety, effectiveness, patientcenteredness, timeliness, cost, efficiency, and equity of healthcare)	1
Abstract			3
	#02a	Provide adequate information to aid in searching and indexing	
	#02b	Summarize all key information from various sections of the text using the abstract format of the intended publication or a structured summary such as: background, local problem, methods, interventions, results, conclusions	
Introduction			

Problem description	#3	Nature and significance of the local problem	5
Available knowledge	#4	Summary of what is currently known about the problem, including relevant previous studies	5-6
Rationale	#5	Informal or formal frameworks, models, concepts, and / or theories used to explain the problem, any reasons or assumptions that were used to develop the intervention(s), and reasons why the intervention(s) was expected to work	6-7
Specific aims	#6	Purpose of the project and of this report	6
Methods			
Context	#7	Contextual elements considered important at the outset of introducing the intervention(s)	8-9
Intervention(s)	#08a	Description of the intervention(s) in sufficient detail that others could reproduce it	9-11
Intervention(s)	#08b	Specifics of the team involved in the work	9-11
Study of the Intervention(s)	#09a	Approach chosen for assessing the impact of the intervention(s)	
Study of the Intervention(s)	#09b	Approach used to establish whether the observed outcomes were due to the intervention(s)	11-12
Measures	#10a	Measures chosen for studying processes and outcomes of the intervention(s), including rationale for choosing them, their operational definitions, and their validity and reliability	12-17
Measures	#10b	Description of the approach to the ongoing assessment of contextual elements that contributed to the success, failure, efficiency, and cost	12-17
Measures	#10c	Methods employed for assessing completeness and accuracy of data	17
Analysis	#11a	Qualitative and quantitative methods used to draw inferences from the data	12-17
Analysis	#11b	Methods for understanding variation within the data, including the effects of time as a variable	12

Ethical considerations	#12	Ethical aspects of implementing and studying the intervention(s) and how they were addressed, including, but not limited to, formal ethics review and potential conflict(s) of interest	18
Results			
	#13a	Initial steps of the intervention(s) and their evolution over time (e.g., time-line diagram, flow chart, or table), including modifications made to the intervention during the project	n/a (it is a protocol)
	#13b	Details of the process measures and outcome	12-17
	#13c	Contextual elements that interacted with the intervention(s)	n/a (it is a protocol)
	#13d	Observed associations between outcomes, interventions, and relevant contextual elements	n/a (it is a protocol)
	#13e	Unintended consequences such as unexpected benefits, problems, failures, or costs associated with the intervention(s).	n/a (it is a protocol)
	#13f	Details about missing data	n/a (it is a protocol)
Discussion			
Summary	#14a	Key findings, including relevance to the rationale and specific aims	n/a (it is a protocol)
Summary	#14b	Particular strengths of the project	4, 18-19
Interpretation	#15a	Nature of the association between the intervention(s) and the outcomes	n/a (it is a protocol)
Interpretation	#15b	Comparison of results with findings from other publications	n/a (it is a protocol)
Interpretation	#15c	Impact of the project on people and systems	18-19
Interpretation	#15d	Reasons for any differences between observed and anticipated outcomes, including the influence of context	n/a (it is a protocol)
Interpretation	#15e	Costs and strategic trade-offs, including opportunity costs	n/a (it is a protocol)

Limitations	#16a	Limits to the generalizability of the work	4, 19
Limitations	#16b	Factors that might have limited internal validity such as confounding, bias, or imprecision in the design, methods, measurement, or analysis	4, 19
Limitations	#16c	Efforts made to minimize and adjust for limitations	4, 12-17
Conclusion	#17a	Usefulness of the work	18-19
Conclusion	#17b	Sustainability	18-19
Conclusion	#17c	Potential for spread to other contexts	18-19
Conclusion	#17d	Implications for practice and for further study in the field	18-19
Conclusion	#17e	Suggested next steps	n/a (it is a protocol)
Other information			
Funding	#18	Sources of funding that supported this work. Role, if any, of the funding organization in the design, implementation, interpretation, and reporting	24

Annex 10. Informed consent for endline survey

Study title: Gaps in hypertension care and control in Medellin, Colombia: cross-sectional survey in two Communes.

Principal Investigator: Dr. Esteban Londoño Agudelo, MD. MPH. Institution: ITM, Belgium – University of Antioquia, Colombia.

Metrosalud E.S.E. (Medellin, Colombia), the University of Antioquia (Medellin, Colombia) and the Institute of Tropical Medicine (Antwerp, Belgium) are conducting a study on the gaps in the process of care and control of hypertension at population level in Medellin city, Colombia.

This informed consent form has two parts:

Part I: Information sheet (to share information about the study with you)
Part II: Signature of Consent (for signature if you choose to participate)

You will be given a copy of both parts.

Part I: Information sheet

Introduction: We invite you to participate in this research study on how to improve the medical care and treatment for high blood pressure in the city. It is important that you understand the information given in this sheet before you decide to be part of this study. This sheet explains your rights and our responsibilities to you. We are going to give you information on the study and invite you to be part of this research. This sheet is asking for your consent. It may contain words that you do not understand, so please feel free to ask any question regarding this study before you decide to participate. If you have questions later, you can ask them to the study responsible, **Dr. Esteban Londoño** or to any member of the team. You can also go directly to the Direction of the Hospital of Metrosalud in Santa Cruz, asking for Dr. Hernán Aguilar; or to the Direction of the Hospital of Metrosalud in Doce de Octubre, asking for Dr. Valentina Sossa.

Purpose and description of the research:
People with high blood pressure readings (that is, hypertension), who are still not detected or not properly treated by a doctor can suffer from serious health problems. Uncontrolled high blood pressure can lead to serious problems like heart attacks, strokes, heart failures, and renal failures. If a community has a lot of people with uncontrolled high blood pressure, we can expect to find a lot of individuals suffering from serious health problems or prematurely dying. We want to find out how many people have high blood pressure readings among individuals 35 years or older in your Commune and what are the main problems that prevent the health personnel to detect people suffering from high blood pressure and to properly treat them. The results of this study can help to detect the main problems for the people of this Commune to receive timely and good health care for high blood pressure. We will use the results of this research to design strategies to improve the quality of health care for people living with high blood pressure.

Participants selection: People aged 35 years or older who live in the Commune can join this study. Using a computerized program, we have randomly selected a group of homes in each neighborhood, which will take part in this study. Then, in each selected home we will interview all the inhabitants aged 35 years or older.

Voluntary participation: Your decision to join this study is totally voluntary. It is your choice whether to participate or not. On the other hand, if you decide to join, you can choose to answer only the questions that you like. You can also leave the study at any time, even after you have signed this Informed Consent Form.

Procedures: Using a questionnaire, we will ask questions about your health, how often you use health services, what are your health problems and general health. We will especially ask you if you suffer from high blood pressure. In case you do, we will ask you about your treatment and how often you get follow-up consultations. This won't take much time, approximately 60 minutes, a professional survey taker for this study, will carry out the interview. The survey taker will also measure your blood pressure readings three times during the interview.

Risks and discomforts: There is no physical risk. You will only share personal information and if you feel any question too personal or you feel uncomfortable you do not have to answer. The study will not interfere with the health care that you receive.

Benefits: You will not receive direct benefits from this study, neither incentives to participate. With no doubt you will

obtain more information on what high blood pressure is, what are the measures you can take to prevent the disease and also how to get medical control. If during the interview the survey taker finds out that you have high blood pressure or any medical complication, you will be informed and referred to the health center where you are subscribed. Furthermore, the results of this study can help to improve how to provide health care to people with high blood pressure in Medellin and in Colombia.

Confidentiality: The information that you provide us will be kept confidential and will be accessed only by the study investigators. All formats in the study will be recognized by a number code, not by your name. Your name or any data that could identify you will not be revealed by the research team. Your identity will never be revealed in any report or publication resulting from this study.

Sharing the results: The results of this study will be shared with the managers of Metrosalud E.S.E. and of the health insurance companies of the Contributory Regimen; and may be published in national and or international scientific journals.

Right to Refuse or Withdraw from the study: The participation in this study is voluntary and you are not obliged to participate. If you prefer not to participate this won't influence the medical care and treatment that you receive. You can withdraw from the study at any time. You can refuse to answer any question that you feel uncomfortable. Should you have any question on the study, you can ask all questions that you want, either now or at any other time. In this case you can contact the principal investigator of this study, *Dr.* Esteban Londoño Agudelo (see below).

Part II: Signature of the consent.

Part for the participant

I declare that I have been informed about this study and that I have received a copy of the Informed Consent. I have been explained and read the information and I understand the objectives and procedures of the study, and that the collected data will be used only for this investigation. I had the chance to ask questions on the study and clarify doubts.
I freely consent to participate in this study and understand that I have the right to withdraw from the study at any time, without any consequence for me.

In consideration of the above, I sign this document on

Date: day ____ month _____ year _____

Name and surnames of the participant

_____

Signature: _____

Part for the investigator: I duly read the informed consent form to the potential participant, and the person had the opportunity to ask questions. I confirm that the person has given his/her consent voluntarily.

Date: day ____ month _____ year _____

Name and surnames of the Investigator: _____ **Signature**:

_____

Any question on the study can be addressed to the study responsible: **Dr. Esteban Londoño Agudelo, Facultad Nacional de Salud Pública, Universidad de Antioquia. Calle 62 No. 52-59. Phone: +57(4) 2196822, email:** estebanlondonoag@gmail.com

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Part for the participant I declare that I have been informed about this study and that I have received a copy of the Informed Consent. I have been explained and read the information and I understand the objectives and procedures of the study, and that the collected data will be used only for this investigation. I had the chance to ask questions on the study and clarify doubts.

I freely consent to participate in this study and understand that I have the right to withdraw from the study at any time, without any consequence for me.
In consideration of the above, I sign this document on
Date: day ____ month _____ year _____

Name and surnames of the participant

_____

Signature_____

Part for the investigator: I duly read the informed consent form to the potential participant, and the person had the opportunity to ask questions. I confirm that the person has given his/her consent voluntarily

Date: day ____ month _____ year _____ **Signature**:

Name and surnames of the Investigator: _____ _____

Reducing gaps in hypertension care and control in Colombia

Study title: "A multi-component intervention to reduce gaps in hypertension care and control in Medellin, Colombia"
(Qualitative data collection of process evaluation in the intervention commune).

Principal Investigator: Dr. Esteban Londoño Agudelo, MD. MPH.
Institution: ITM, Belgium – University of Antioquia, Colombia.

Metrosalud E.S.E. (Medellin, Colombia), the University of Antioquia (Medellin, Colombia) and the Institute of Tropical Medicine (Antwerp, Belgium) are conducting a study on the gaps in the process of care and control of hypertension at population level in Medellin city, Colombia.

This informed consent form has two parts:

Part I: Information sheet (to share information about the study with you)
Part II: Signature of Consent (for signature if you choose to participate)

You will be given a copy of both parts.

Part I: Information sheet

Introduction: We invite you to participate in this research study on the improvement of hypertension care and control in the Commune. It is important that you understand the information given in this sheet before you decide to be part of this study. This sheet explains your rights and our responsibilities to you. We are going to give you information on the study and invite you to be part of this research. This sheet is asking for your consent. It may contain words that you do not understand, so please feel free to ask any question regarding this study before you decide to participate. If you have questions later, you can ask them to the study responsible, **Dr. Esteban Londoño** or to any member of the team. You can also go directly to the Direction of the Hospital Unit of Metrosalud in Santa Cruz, asking for Dr. Hernán Aguilar.

Purpose and description of the research:

People with hypertension, who are still not detected or not properly treated can suffer from serious health problems. Uncontrolled high blood pressure can lead to serious problems like heart attacks, strokes, heart failures, and renal failures. If a community has a lot of people with uncontrolled high blood pressure, we can expect to find a lot individuals suffering from serious health problems or prematurely dying. We want to contribute to address the main problems that prevent the timely detection and adequate treatment of people with hypertension in the Commune. To achieve this, we have implemented a number of improvement interventions in the Commune's Metrosalud health services and in the community. For this purpose, a few months ago, you were explained about the intervention activities and invited to implement them. You were provided with the skills, guidelines and all the resources required to improve hypertension care and control actions within your health service. As part of the study, we are going to monitor and evaluate the implementation of the activities assigned to you and the rest of the involved health workers. We will use the results of this research to identify the main difficulties and to improve the implementation of the different components of the intervention. The results of this study can contribute to improve the quality of the health care provided to people living with hypertension.

Participants selection: Health providers involved in implementation of the different components of the intervention to improve hypertension care and control in the intervention commune.

Voluntary participation: Your decision to join this study is totally voluntary. It is your choice whether to

participate or not. On the other hand, if you decide to join, you can choose to answer only the questions that you like. You can also leave the study at any time, even after you have signed this Informed Consent Form.

Procedures: If you agree to participate in the research, you could be subject of observation of your activities and semi-structured interviews. Observations will be conducted by research staff ("observers") in a systematic way and at different points in time. The exact moment of the observation will not be communicated not to interfere with your activities and not to influence or bias your performance. The observer will take notes of the activities you conduct as part of the intervention. Based on those notes you could be further interviewed by the research staff. The time and the place of the interview will be arranged with you in advance. The interview could take between 45 minutes and one hour. The interviewer will ask you some questions. If you do not wish to answer any of the questions during the interview, you may say so and the interviewer will move on to the next question. We foresee to tape-record the entire interview unless you do not allow us doing so. Your name will not be identified on the tape. The recorded information will be confidential and the tapes will be destroyed after three months.

Risks and discomforts: The risks related to observation and interview are minimal. There is no physical risk. You will only share personal information and if you feel any question too personal or you feel uncomfortable you do not have to answer. The study will not represent an evaluation or report of your performance.

Benefits: You will not receive direct benefits from this study, neither incentives to participate. The results of this study can help to improve how to provide health care to people with hypertension in Medellin and in Colombia.

Confidentiality: The information that you provide us will be kept confidential and will be accessed only by the study investigators. All formats of the study will be recognized by a number code, not by your name. Your name or any data that could identify you will not be revealed by the research team. Your identity will never be revealed in any report or publication resulting from this study.

Sharing the results: The results of this study will be shared with the managers of Metrosalud E.S.E. and of the health insurance companies of the Contributory Regimen; and may be published in national and or international scientific journals.

Right to Refuse or Withdraw from the study: The participation in this study is voluntary and you are not obliged to participate. If you prefer not to participate this won't have any implication for your job or work-related evaluation. You can withdraw from the study at any time. You can refuse to answer any question that you feel uncomfortable. You can also stop the interview at any time if you decide to do so.

Should you have any question on the study, you can ask all questions that you want, either now or at any other time. In this case you can contact the principal investigator of this study, *Dr.* Esteban Londoño Agudelo (see below).

Annex 11. Informed Consent for semi-structured interviews on health providers. Version 2.0, dated 29-APR-2019

Reducing gaps in hypertension care and control in Colombia

Part II: Signature of the consent.

Part for the participant

I declare that I have been informed about this study and that I have received a copy of the Informed Consent. I have been explained and read the information and I understand the objectives and procedures of the study, and that the collected data will be used only for this investigation. I had the chance to ask questions on the study and clarify doubts.
I freely consent to participate in this study and understand that I have the right to withdraw from the study at any time, without any consequence for me.

I agree that the interview can be recorded: Yes No

In consideration of the above, I sign this document on **Date:** day ____ month _____ year _____

Name and surnames of the participant

_____ **Signature**: _____

Part for the investigator: I duly read the informed consent form to the potential participant, and the person had the opportunity to ask questions. I confirm that the person has given his/her consent voluntarily.

Date: day ____ month _____ year _____ **Signature**:

Name and surnames of the Investigator: _____ _____

Any question on the study can be addressed to the study responsible: **Dr. Esteban Londoño Agudelo, Facultad Nacional de Salud Pública, Universidad de Antioquia. Calle 62 No. 52-59. Phone: +57(4) 2196822, email:** estebanlondonoag@gmail.com

✂---------- ----------

Part for the participant: I declare that I have been informed about this study and that I have received a copy of the Informed Consent. I have been explained and read the information and I understand the objectives and procedures of the study, and that the collected data will be used only for this investigation. I had the chance to ask questions on the study and clarify doubts.

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I agree that the interview can be recorded: Yes No
In consideration of the above, I sign this document on **Date**: day ____ month _____ year _____
Name and surnames of the participant

_____ **Signature**: _____

Part for the investigator: I duly read the informed consent form to the potential participant, and the person had the opportunity to ask questions. I confirm that the person has given his/her consent voluntarily

Date: day ____ month _____ year _____ **Signature**:

Annex 11. Informed Consent for semi-structured interviews on health providers. Version 2.0, dated 29-APR-2019

Reducing gaps in hypertension care and control in Colombia

Name and surnames of the Investigator: _____

_____

Annex 11. Informed Consent for semi-structured interviews on health providers. Version 2.0, dated 29-APR-2019

Reducing gaps in hypertension care and control in Colombia

Study title: "A multi-component intervention to reduce gaps in hypertension care and control in Medellin, Colombia"
(Qualitative data collection of process evaluation in the intervention commune).

Principal Investigator: Dr. Esteban Londoño Agudelo, MD. MPH.
Institution: ITM, Belgium – University of Antioquia, Colombia.

Metrosalud E.S.E. (Medellin, Colombia), the University of Antioquia (Medellin, Colombia) and the Institute of Tropical Medicine (Antwerp, Belgium) are conducting a study on the gaps in the process of care and control of hypertension at population level in Medellin city, Colombia.

This informed consent form has two parts:

Part I: Information sheet (to share information about the study with you)
Part II: Signature of Consent (for signature if you choose to participate)

You will be given a copy of both parts.

Part I: Information sheet

Introduction: We invite you to participate in this research study on the improvement of hypertension care and control in the Commune. It is important that you understand the information given in this sheet before you decide to be part of this study. This sheet explains your rights and our responsibilities to you. We are going to give you information on the study and invite you to be part of this research. This sheet is asking for your consent. It may contain words that you do not understand, so please feel free to ask any question regarding this study before you decide to participate. If you have questions later, you can ask them to the study responsible, **Dr. Esteban Londoño** or to any member of the team. You can also go directly to the Direction of the Hospital Unit of Metrosalud in Santa Cruz, asking for Dr. Hernán Aguilar.

Purpose and description of the research:

People with hypertension, who are still not detected or not properly treated can suffer from serious health problems. Uncontrolled high blood pressure can lead to serious problems like heart attacks, strokes, heart failures, and renal failures. If a community has a lot of people with uncontrolled high blood pressure, we can expect to find a lot individuals suffering from serious health problems or prematurely dying. We want to contribute to address the main problems that prevent the timely detection and adequate treatment of people with hypertension in the Commune. To achieve this, we have implemented a number of improvement interventions in the Commune's Metrosalud health services and in the community. For this purpose, a few months ago, you were explained about the intervention activities and invited to implement them. You were provided with the skills, guidelines and all the resources required to improve hypertension care and control actions within your health service. As part of the study, we are going to monitor and evaluate the implementation of the activities assigned to you and the rest of the involved health workers. We will use the results of this research to identify the main difficulties and to improve the implementation of the different components of the intervention. The results of this study can contribute to improve the quality of the health care provided to people living with hypertension.

Participants selection: Health providers involved in implementation of the different components of the intervention to improve hypertension care and control in the intervention commune.

Voluntary participation: Your decision to join this study is totally voluntary. It is your choice whether to participate or not. On the other hand, if you decide to join, you can choose to answer only the questions that you like. You can also leave the study at any time, even after you have signed this Informed Consent Form.

Procedures: If you agree to participate in the research, you could be subject of observation of your activities and semi-structured interviews. Observations will be conducted by research staff ("observers") in a systematic way and at different points in time. The exact moment of the observation will not be communicated not to interfere with your activities and not to influence or bias your performance. The observer will take notes of the activities you conduct as part of the intervention. Based on those notes you could be further interviewed by the research staff. The time and the place of the interview will be arranged with you in advance. The interview could take between 45 minutes and one hour. The interviewer will ask you some questions. If you do not wish to answer any of the questions during the interview, you may say so and the interviewer will move on to the next question. We foresee to tape-record the entire interview unless you do not allow us doing so. Your name will not be identified on the tape. The recorded information will be confidential and the tapes will be destroyed after three months.

Risks and discomforts: The risks related to observation and interview are minimal. There is no physical risk. You will only share personal information and if you feel any question too personal or you feel uncomfortable you do not have to answer. The study will not represent an evaluation or report of your performance.

Benefits: You will not receive direct benefits from this study, neither incentives to participate. The results of this study can help to improve how to provide health care to people with hypertension in Medellin and in Colombia.

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Sharing the results: The results of this study will be shared with the managers of Metrosalud E.S.E. and of the health insurance companies of the Contributory Regimen; and may be published in national and or international scientific journals.

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Should you have any question on the study, you can ask all questions that you want, either now or at any other time. In this case you can contact the principal investigator of this study, *Dr.* Esteban Londoño Agudelo (see below).

Annex 11. Informed Consent for semi-structured interviews on health providers. Version 2.0, dated 18-APR-2019

Reducing gaps in hypertension care and control in Colombia

Part II: Signature of the consent.

Part for the participant

I declare that I have been informed about this study and that I have received a copy of the Informed Consent. I have been explained and read the information and I understand the objectives and procedures of the study, and that the collected data will be used only for this investigation. I had the chance to ask questions on the study and clarify doubts.
I freely consent to participate in this study and understand that I have the right to withdraw from the study at any time, without any consequence for me.

I agree that the interview can be recorded: Yes No

In consideration of the above, I sign this document on **Date:** day ____ month _____ year _____

Name and surnames of the participant

_____ **Signature**: _____

Part for the investigator: I duly read the informed consent form to the potential participant, and the person had the opportunity to ask questions. I confirm that the person has given his/her consent voluntarily.

Date: day ____ month _____ year _____ **Signature**:

Name and surnames of the Investigator: _____ _____

Any question on the study can be addressed to the study responsible: **Dr. Esteban Londoño Agudelo, Facultad Nacional de Salud Pública, Universidad de Antioquia. Calle 62 No. 52-59. Phone: +57(4) 2196822, email:** estebanlondonoag@gmail.com

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I freely consent to participate in this study and understand that I have the right to withdraw from the study at any time, without any consequence for me.

I agree that the interview can be recorded: Yes No
In consideration of the above, I sign this document on **Date**: day ____ month _____ year _____
Name and surnames of the participant

_____ **Signature**: _____

Part for the investigator: I duly read the informed consent form to the potential participant, and the person had the opportunity to ask questions. I confirm that the person has given his/her consent voluntarily
Date: day ____ month _____ year _____ **Signature**:

Annex 11. Informed Consent for semi-structured interviews on health providers. Version 2.0, dated 18-APR-2019

Reducing gaps in hypertension care and control in Colombia

Name and surnames of the Investigator: _____

_____

Annex 11. Informed Consent for semi-structured interviews on health providers. Version 2.0, dated 18-APR-2019

Institutional Review Board

Dr. Tullia Battaglioli / Dr. E. Londoño Agudelo
Department of Public Health

IRB/AB/AC/101	OUR REF.	ATTACHMENT(S)	ANTWERP
	1294/19		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

UZA / Wilrijkstraat 10 / 2650 Edegem
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Tel +32 3 821 30 00
www.uza.be / BE0874.619.603

Universiteit Antwerpen

COMITE VOOR MEDISCHE ETHIEK

Dr. T. Battaglioli

Instituut voor Tropische Geneeskunde
Nationalestraat 155
2000 Antwerpen

VOORZITTER
Prof. dr. Patrick Cras

SECRETARIAAT
tel: 03 821 38 97

Gaps in hypertension care and control in Medellin, Colombia: cross-sectional survey in two Communes (ProtocolNr: ITG 1202/17)

Belgisch Registratienummer: B300201837708

datum	ons kenmerk	contact
15/10/2018	18/40/424	Secretariaat Ethisch Comité ethisch.comite@uza.be

DEFINITIEF GUNSTIG ADVIES

Geachte Collega,

Het Ethisch Comité van het Universitair Ziekenhuis Antwerpen en de Universiteit Antwerpen bevestigt dat bovenvermelde studie voldoet aan de criteria gesteld in de wet van 7 mei 2004 en geeft een gunstig advies dd. 15/10/2018 .

De volgende bijlagen werden volgens de ICH-GCP richtlijnen door het Ethisch Comité goedgekeurd:

- Bewijs van "no-fault" verzekering
  Amlin Corporate Insurance, Polisnr 99.002.067
- CV onderzoeker
  Dr. T. Battaglioli, Dr. E. Londono Agudelo
- Informatie- en toestemmingsformulier
  ENG IC for questionnaire Annex 12.2 Version 2.0 dd 26/08/2018
- Protocol
  ITG 1202/17 version 2.0 dd 26/08/2018
- Diverse dd. 28/08/2018
  Approval letter from ITM's Institutional Board
- Vragenlijst(en)
  Questionnaire Annex 12.1 Version 1.0 dd 22/11/2017

De volgende opmerkingen werden nog gemaakt:
Het ICF is in het Engels: is het niet beter om deze in het Spaans op te stellen voor Colombia?

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Universiteit Antwerpen

Vervolg blz. 2 van het adviesformulier betreffende project EC UZA 18/40/424

datum	ons kenmerk	contact
15/10/2018	18/40/424	Secretariaat Ethisch Comité ethisch.comite@uza.be

Deze goedkeuring is geldig tot een jaar na bovenvermelde datum. Wij verzoeken u ons te melden wanneer de eerste deelnemer werd geïncludeerd, wanneer en waarom de studie (vroegtijdig) werd stopgezet of nooit werd opgestart.
Indien de studie nog loopt na een jaar verwachten we een follow-up rapport waarin eventuele voorvallen worden gemeld.
Tot slot wijzen we er op dat, voor in het UZA lopende studies, de ernstige ongewenste voorvallen dienen gerapporteerd via het incidentenmeldingssysteem

Met vriendelijke groeten,

Prof. Dr. G. Ieven

Ondervoorzitter Ethisch Comité

Cc: FAGG - Research & Development Department, Victor Hortaplein 40, bus 40 - 1060 Brussel
Prof. dr. M. Boelaert, Instituut voor Tropische Geneeskunde - Volksgezondheid, Nationalestraat 155 - 2000 Antwerpen

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Universiteit Antwerpen

Vervolg blz. 3 van het adviesformulier betreffende project EC UZA 18/40/424

datum	ons kenmerk	contact
15/10/2018	18/40/424	Secretariaat Ethisch Comité ethisch.comite@uza.be

Samenstelling Ethisch Comité sinds 15/10/2018.
Deze studie werd besproken op vergadering van 15/10/2018.

	Functie	M/V	Aanwezig
Voorzitter			
CRAS Patrick	Voorzitter/Neuroloog	M	-
Ondervoorzitter			
IEVEN Greet	Ondervoorzitter/Klinisch Bioloog	V	+
Leden EC UZA			
BLAUMEISER Bettina	Medisch geneticus	V	+
DE BAETSELIER Elyne	Verpleegkundige	V	+
HENS Kristien	Ethicus	V	-
MICHIELS Barbara	Huisarts	V	+
MICHIELSEN Peter	Gastro-enteroloog	M	-
PAELINCK Bernard	Cardiochirurg	M	+
SPECENIER Pol	Oncoloog	M	+
VAN DE WIELE Miranda	Patiëntenbegeleiding	V	-
VAN DEN EEDE Filip	Psychiater	M	+
VAN DYCK Pieter	Radioloog	M	+
VANSWEEVELT Thierry	Jurist	M	+
VERLOOY Joris	Pediater	M	+
Toegevoegde leden UA			
DE MEESTER Ingrid	Farmacoloog / Onderzoeker UA	V	-
GRANAAS Kristina	Medewerkster Dep. Onderzoek	V	+
Uitgenodigde Experten			
AERTSEN Veerle	Patiëntenvertegenwoordiger	V	-
DOCKX Celine	Jurist	V	+
IDES Kris	Kinesitherapeut	M	-
LUYTEN Leon	Arts in het beheer van gezondheidsgegevens	M	+
MICHIELSENS Inge	Jurist	V	+
MOONS Pieter	Coördinator bio- en weefselbank	M	+
VAN BORTEL Paulus	Filosoof	M	-

The Ethics Committee states that no individual member of the Ethics Committee who may have an affiliation with the study or sponsor, has voted in
the deliberations for this trial.
The Ethics Committee states that it is organised and operates according to the ICH/GCP guidelines, the applicable laws and regulations, and
their own written operating procedures.

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
Principal Investigator:	Esteban Londoño. MD. MPH. ITM PhD Student

Title:	A multi-component intervention to reduce gaps in hypertension care and control in Medellin, Colombia
Version:	Version 2.0 dated 29 APRIL 2019
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.

Funder:	Institute of Tropical Medicine, Antwerp-Belgium, with partial support from Metrosalud E.S.E., Medellin-Colombia.
Sponsor:	Institute of Tropical Medicine, Antwerp, Belgium
ITM Coordinating Investigator:	Tullia Battaglioli, Bruno Marchal.
Department:	Public Health
Address:	Institute of Tropical Medicine, Nationalestraat 155, 2000 Antwerp, Belgium
Telephone:	+32 3 247 07 81
Fax:	+32 3 247 62 58
Email:	tbattaglioli@itg.be

Contents

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. Improvement of clinical management of patients with hypertension

A.3.1. Creation of the cardiovascular risk team (CVRT), 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. Guideline-based standardized diagnostic and treatment protocols: 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. Availability of antihypertensive medications: 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:

The 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 pharmacological 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

	serial BP measurement			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	

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.

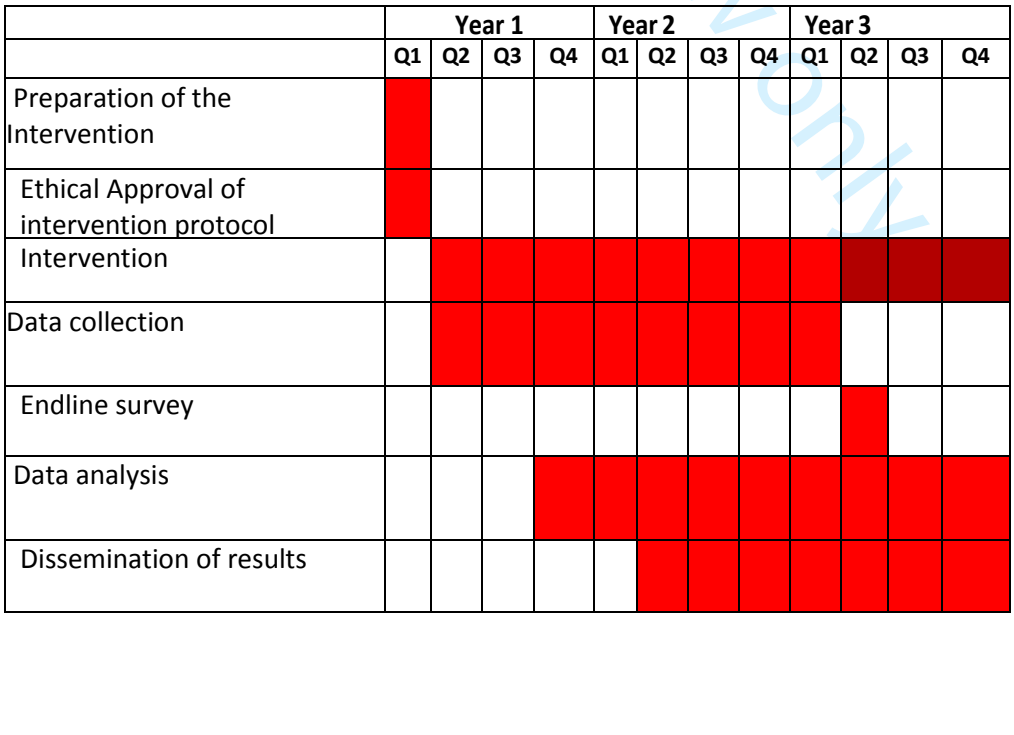
5.3 Insurance

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



 = 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

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Protocol for a controlled before-after quasi-experimental study to evaluate the effectiveness of a multi-component intervention to reduce gaps in hypertension care and control in low-income communes of Medellin, Colombia

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Protocol for a controlled before-after quasi-experimental study to evaluate the effectiveness of a multi-component intervention to reduce gaps in hypertension care and control in low-income communes of Medellin, Colombia

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Abstract

Introduction

Research on public health interventions to improve hypertension care and control in low- and middle-income countries remains scarce. This study aims to evaluate the effectiveness and assess the process and fidelity of implementation of a multi-component intervention to reduce the gaps in hypertension care and control at a population level in low-income communes of Medellin, Colombia.

Methods and analysis

A multi-component intervention was designed based on international guidelines, cross-sectional population survey results, and consultation with the community and institutional stakeholders. Three main intervention components integrate activities related to 1. Health services redesign, 2. Clinical staff training and 3. Patient and community engagement. The effectiveness of the intervention will be evaluated in a controlled before-after quasi-experimental study, with two deprived communes of the city selected as intervention and control arms. We will conduct a baseline and an endline survey two years after the start of the intervention. The primary outcomes will be the gaps in hypertension diagnosis, treatment, follow-up and control. Effectiveness will be evaluated with the difference-in-difference measures. Generalised estimation equation models will be fitted considering the clustered nature of data and adjusting for potential confounding variables. The implementation process will be studied with mixed methods. Implementation fidelity will be documented to assess to which degree the intervention components were implemented as intended.

Ethics and dissemination

The study protocol has been approved by the Ethics Research Committee of Metrosalud in Colombia (reference 1400/5.2), the Medical Ethics Committee of the Antwerp University Hospital (reference 18/40/424), and the Institutional Review Board of the Antwerp Institute of Tropical Medicine (reference 1294/19). We will share and discuss the study results with the community, institutional stakeholders and national health policymakers. We will publish them in national and international peer-reviewed scientific journals.

Trial registration number NCT05011838.

Strengths and limitations of this study

- We respond to exhortations to rigorously evaluate multi-component interventions to improve hypertension care and control in low- and middle-income countries.
- The planned intervention is based on formative research and inspired by guidelines from international hypertension care initiatives and has been adapted to the local environment with the participation of all relevant stakeholders.
- We employ a controlled before-after quasi-experimental study design.
- We will rely on quantitative outcomes and qualitative process assessments, and combine effectiveness and implementation fidelity indicators to better inform subsequent adaptation and scaling up.
- The intervention will be implemented in a low-income area of an industrialised city in a middle-income country, and results may not be generalisable to upper-class urban zones or underserved rural settings.

Introduction

Non-communicable diseases accounted for 73.5% of global deaths in 2017 [1]. Their incidence is disproportionately increasing in developing countries [2], and they constitute the first cause of mortality and disability in the Americas region, generating at least 5.5 million deaths each year [3]. Notwithstanding, most Latin American and Caribbean health systems provide inadequate chronic disease management [4]. Globally, only about one in ten people with chronic conditions are successfully treated [5]. Moreover, most out-of-pocket health payments and catastrophic expenditures are related to such conditions [6, 7].

Uncontrolled hypertension is the main modifiable risk factor for cardiovascular diseases (CVDs) and is associated with more than 10 million deaths worldwide each year [8]. Almost 75% of people suffering from hypertension live in developing countries, where disease awareness is low, and health care access is limited [9, 10]. High disease prevalence and poor hypertension control are pivotal factors in the rising epidemic of CVDs in low- and middle-income countries (LMICs) [11], where they mainly strike the working-age population and further hamper economic growth and social development [10]. Among the 1.6 million people who yearly die from CVDs in Latin America and the Caribbean, half a million are below 70 years old [12]. Nevertheless, limited research in this field has been performed in LMICs [13].

A multi-country cross-sectional study conducted between 2003 and 2009, including 14 LMICs [14], found a prevalence of hypertension of 27.7% in adults, with only 46.5% and 32.5% of hypertension awareness and control, respectively, among the affected. A 2019 review focusing on LMICs [15] pooled individual-level hypertension data on people aged 15 years and older from 44 countries and found a 17.5% hypertension prevalence. Of the hypertensive individuals, 39.2% were aware of their condition, 29.9% received pharmacological treatment, and barely 10% attained controlled blood pressure (BP). These reports provide information on hypertension control internationally and on variations among populations. Most studies assessing patient and health care provider barriers to hypertension care have been conducted at the health facility level and in high-income countries [13]. Research at the population level to document in-depth and to tackle the main gaps and barriers hampering equitable and effective hypertension care and control in LMICs is needed.

The Chronic Care Model [16] and its expanded version [5] aim to guide interventions for improving chronic disease management. It is the basis of the Standardised Hypertension Treatment and Prevention (SHTP) Project [17], developed by the Pan American Health Organization and the Centres

for Disease Control and Prevention. The SHTP Project identified six key elements to strengthen health systems at the primary care level and to improve hypertension control, using evidence-based components: guideline-based standardised treatment protocols; effective drug procurement mechanisms utilising a core set of medications; registries for cohort monitoring and evaluation; patient empowerment; team-based care system and community engagement [17]. This approach was reinforced by the World Health Organization (WHO) Global Hearts Initiative, primarily through the Technical Package for Cardiovascular Disease Management in Primary Health Care [18]. Operational research to assess the impact of this and other similar strategies is urgently advocated.

The objective of the present study is to evaluate the effectiveness of a multi-component intervention to reduce the gaps in hypertension care and control in low-income communes of Medellin, Colombia. In addition, we aim to assess the process and fidelity of the intervention's implementation.

Rationale

In 2016, we conducted a cross-sectional survey in a low-income commune of Medellin [19] to estimate the prevalence of hypertension in the adult population and the magnitude and determinants of the main gaps in hypertension care and control. The definitions of those gaps are shown in Table 1. In summary, we found a hypertension prevalence of 43.5%, and 28.2% aware and 15.3% unaware hypertensive individuals. Moreover, among the aware persons, 14.4% presented a follow-up gap, 93.4% were prescribed antihypertensive drugs, 38.9% were not compliant, and 39.0% were uncontrolled. The survey results, the -hypothesised- possible determinants of the identified gaps (Table 2), and potential solutions were discussed with communities, service providers and institutional stakeholders in a series of workshops. Based on the workshops' conclusions, in consultation with the main stakeholders and inspired by the SHTP Project and the WHO Global Hearts Initiative [17, 18], we designed a multi-component intervention to improve hypertension care and control in Medellin.

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

Gap	Numerator	Denominator
Diagnosis gap	Number of Unaware Hypertensive individuals[1]	Number of Unaware Hypertensive individuals plus Number of Aware Hypertensive individuals[2]

Follow-up gap	Number of Aware Hypertensive individuals who did not attend a follow-up consultation during the last year	Number of Aware Hypertensive individuals
Pharmacological treatment gap	Number of Aware Hypertensive individuals who received a prescription but either: -do not take the drugs -or are non-adherent	Number of Aware Hypertensive individuals who received a prescription for antihypertensive medication
Control gap	Number of Aware Hypertensive individuals who did not manifest controlled hypertension[3]	Number of Aware Hypertensive individuals

1 Unaware Hypertensive individual: participant not reporting a previous diagnosis of hypertension but presenting an average BP measurement higher than 140/90 mmHg in the survey

2 Aware Hypertensive individual: participant reporting a previous diagnosis of hypertension

3 Controlled hypertension: see text for precise definition

Table 2. Potential determinants at the health provider, population and health system level of the main gaps in hypertension care and control. Santa Cruz Commune. Medellin, Colombia, 2016.

Gap	Level		
	Health Provider	**Population**	**Health System**
Diagnosis Gap	No measurement of blood pressure during health care contacts High blood pressure is detected, but confirmation of diagnosis fails due to a lack of continuity of care	Low-risk perception of hypertension Mild or no symptoms determine delayed healthcare-seeking	Passive and fragmented health services Limited opening hours of services for hypertension screening
Quality of care (treatment and follow-up gaps)	No pharmacological advice/consultation Limited communication skills of health staff and the poor doctor-patient relationship Interrupted delivery of essential antihypertensive drugs	Low awareness of the importance of non-pharmacological treatment Low educational level hampers communication and treatment compliance	Scarcity of essential antihypertensive drugs Administrative barriers imposed on patients and health providers

Methods and analysis

Overview of study design

The effectiveness of a multi-component intervention in reducing gaps in hypertension care and control will be evaluated in a controlled before-after quasi-experimental study. A graphical summary of the underlying theory of action is depicted in Figure 1. Besides outcomes, the process and implementation fidelity will be studied to assess to which degree the intervention components were implemented as intended. The study will use mixed methods, comprising a baseline and an endline population survey, medical records and health care registers analysis, self-registration forms of intervention activities, non-participant observations, and interviews with key informants such as health care staff, managers, and patients and their caregivers. The intervention will start in the first quarter of 2023 and be evaluated after 24 months.

We checked the completeness and accuracy of our research protocol using the SQUIRE (Standards for Quality Improvement Reporting Excellence) reporting guidelines (online supplementary file 1).

Patient and public involvement

From the onset of the planning phase of the intervention onwards, the main community and institutional stakeholders -the local patient's association, the community representatives to the city council, managers and clinical staff of the city's public health provider (Metrosalud) and public health practitioners from the University of Antioquia- were invited for and participated in a series of workshops to discuss the results of the previous formative research. Hence, patients, community and institutional stakeholders actively proposed pathways to improve hypertension care and control within the community and at the health facility level. We will continuously further involve all local stakeholders in monitoring, analysing and learning from the forthcoming intervention.

Study setting and population

Colombia is a middle-income country with a 2019 per-capita gross domestic product of US$6,429 (current US$) [20]. The mortality from CVDs in 2017 was 150.3 per 100.000 population, and 30.5% of all deaths and 16.7% of Years of Life Lost can be attributed to CVDs [21]. The Colombian health system has two different health insurance schemes run by health insurance companies. People able to contribute and their beneficiaries are compulsorily affiliated to the contributory scheme, which covers the formally employed workers, pensioners and part of the self-employed. The State finances the subsidised scheme, which protects people who cannot afford contributions.

Medellin is the second-largest industrialised city in Colombia. It has 16 Communes, and its total 2016 population was around 2.5 million [22]. The intervention will be implemented in Commune 2, northeast of Medellin. Commune 6, located northwest of Medellin, was selected as the control area to deliver routine care. Both communes are among the most deprived areas of the city [23] and share similar characteristics: urban setting, low-income population, typical functioning of the national health system, and commitment of Metrosalud -the city's public health care provider- to develop improvement programmes based on research results.

Intervention

A multi-component intervention to improve hypertension care and control will integrate activities related to 1. Health services redesign, 2. Clinical staff training, and 3. Patient and community engagement. Each intervention component will be standardised, and its related activities described in detail in a field manual. The intervention will be implemented by health services staff with technical assistance from the investigators. The three components of the intervention are detailed below:

1. **Health services redesign**
   - 1.1. **"Healthy Hearts" service**: A nursing station will be established to provide BP measurement, cardiovascular risk assessment and preventive counselling during extended opening hours. It will secure hypertensive patients' effective follow-up, especially for presumptive hypertensive individuals and those newly diagnosed. The service will facilitate serial, automated, self-measured BP testing to confirm diagnosis within the health facility premises in order to exclude white coat hypertension. It also will administer periodical anonymous exit questionnaires to patients that attended hypertension-related consultations to assess the quality of care. Results will be communicated to the cardiovascular risk team for analysis.
   - 1.2. **Hypertension screening**: The health care flow for patients with a high BP measurement will be standardised using a written procedure. All adults attending health services who did not have their BP measured by a health care provider in the previous year will be referred to the Healthy Hearts service for screening. Furthermore, doctors and nurses fortuitously encountering presumptive hypertensive individuals will refer them to the Healthy Hearts service to confirm the diagnosis.
   - 1.3. **Clinical management**:
     - 1.3.1. **Creation of the cardiovascular risk team**: A group of doctors supervising clinical hypertension management and coordinating action plans for improvement. It will

conduct audits, periodically selecting a representative sample of clinical records of hypertensive patients and use a structured questionnaire to evaluate the fulfilment of the requirements of a complete cardiovascular risk assessment interview and physical examination, doctors' adherence to guidelines and the quality of the provided care. It also will supervise the Healthy Hearts service. This operational body will hold weekly meetings and provide regular feedback and support to health professionals involved in hypertension care.

1.3.2. **Guideline-based standardised diagnostic and treatment protocols**: A simplified diagnostic and treatment algorithm based on the national clinical guidelines and in line with the Global Hearts Initiative will be agreed upon with the general direction of Metrosalud, the direction of the health area and the clinical staff. It will identify a core set of primary and secondary options within each of the major classes of antihypertensive medication.

1.3.3. **Availability of antihypertensive medications**: It will be assured through procurement mechanisms agreed with the central drug store of Metrosalud. To timely inform on the possible need for alternative prescriptions, the availability of antihypertensive medications will be communicated to clinicians at the beginning of each week and *ad hoc* in case of stock-out.

2. Clinical staff training

2.1. **Training on good clinical management of hypertension**: It will be focused on correct BP measurement, use of evidence-based guidelines, cardiovascular risk assessment, a standardised diagnostic and treatment algorithm, correct prescription of pharmacological and non-pharmacological treatment, patient counselling, and prevention of clinical inertia.

2.2. **Training on communication skills and patients' needs assessment:** This training will be designed under the "patient-centred medicine" framework [24], aiming to equip all health workers involved in hypertension care with tools for understanding patients' feelings and experiences of illness and improving their capacity to address social, psychological, and behavioural dimensions of hypertension care.

3. Patient and community engagement

3.1. **Patients' empowerment**: "Expert hypertensive patients", under the supervision of a social worker, will provide support and transmit their know-how to other patients in need,

particularly those newly diagnosed or non-adherent to treatment or presenting uncontrolled hypertension.

3.2. **Community engagement**: a Community Hypertension Outreach Group will be set up, composed of existing voluntary community health workers, who will be trained and certified. This group will conduct BP measurements in selected public areas of the commune, referring those with positive screening to the nearest health facility for diagnosis confirmation. It will also provide health information with an emphasis on healthy lifestyles. Additionally, local communication channels such as the community radio and the local newspaper will be engaged.

Effectiveness assessment

The primary outcome will be the control gap in the total hypertensive population (aware and unaware hypertensive individuals). The secondary outcomes will be the diagnostic, treatment, follow-up and control gaps defined in Table 1.

Inclusion and exclusion criteria for the baseline and endline surveys

Eligible persons will be all 35 years or older permanent inhabitants of the selected communes, willing and able to provide written informed consent. Potential participants with a mental disability or unable to answer the questionnaire will be excluded.

Sample size and sampling procedures for the surveys

Expecting at baseline 60% non-control in the 35 years or older hypertensive population and at endline 10% difference in difference (baseline minus endline) between the intervention and control arms, a sample of 385 hypertensive individuals per arm is required for 80% power and a 95% confidence level. Given a 45% prevalence of hypertension in individuals aged 35 years or older, screening 856 individuals will allow finding the needed number of hypertensive individuals. We will increase the number screened to 1190 individuals, assuming 10% non-response and, based on previous observations, a design effect of 1.25 for our sampling scheme.

A cluster sample will be drawn from a sampling frame consisting of the addresses of all premises provided by the municipality and using maps of Medellin detailing house blocks. Given an average of 1.5 individuals ≥35 years old per household, 795 households will be sampled per study arm by selecting 53 clusters of 15 households from the different neighbourhoods of the Communes, with an allocation of the number of clusters proportional to neighbourhood size. A group of trained

interviewers will make up to two repeat door-to-door visits to every selected household to include all identified eligible household members aged 35 years or older in the surveys.

Data collection

Using a structured questionnaire, participants will be interviewed on socio-demographic characteristics, health-seeking behaviour, cardiovascular risk factors and previous hypertension diagnosis. In addition, participants aware of being hypertensive will be questioned on their follow-up, antihypertensive pharmacological and non-pharmacological treatment, and treatment compliance. BP will be measured using a digital manometer, following international recommendations for standardised BP measurement in population surveys [25, 26].

Operational definitions for the surveys

Hypertensive individual: self-report of previously diagnosed hypertension or without a previous diagnosis but presenting an average repeat BP measurement equal to or higher than 140/90 mm Hg. [14, 27].

Controlled hypertensive individual: self-report of previously diagnosed hypertension and an average repeat BP measurement of less than 140/90 mm Hg for patients between 35 and 59 years old or diabetic patients and below 150/90 mm Hg for patients aged 60 years or older [28].

Data analysis

The difference-in-difference measures [29, 30] will be calculated (endline-baseline changes in the intervention minus endline-baseline changes in the control commune) for the primary and secondary outcomes. Where relevant, we will stratify on affiliation to subsidised or contributory insurance schemes. Generalised estimation equation models will be fitted, considering the clustered nature of the data, and adjusting for potential confounding variables. Unadjusted and adjusted odds ratios and their 95% confidence interval will be calculated. The Statistical Package for Social Sciences V.24 (SPSS Inc., Chicago, IL, USA) will be used for data analysis.

Assessment of the implementation process and fidelity

The indicators to measure results at the health service level are shown in Table 3. They were elaborated considering the performance indicators proposed by the SHTP Project, the Global Hearts initiative and other propositions to improve the global prevention and control of cardiovascular diseases [17, 18, 31, 32]. The indicators we constructed for monitoring implementation are listed in

Table 4. The needed data will be collected in the intervention and control areas, at baseline, during implementation, and at the endline. Electronic clinical and billing records of Metrosalud, registers of the "Healthy Hearts" service, exit interviews, and clinical audits will be the data sources.

Table 3. Performance indicators at the health facility level.

Indicator	Operational Definition
Number of hypertensive patients enrolled in the Cardiovascular Risk Program (CVRP)	Number of hypertensive patients enrolled in the CVRP
Prevalence of diagnosed hypertension in the catchment area	Number of hypertensive patients enrolled in the CVRP/Total catchment population.
Ratio of the 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
New hypertensive patients enrolled in the CVRP	Total number of new hypertensive patients enrolled in the CVRP per month
Cardiovascular risk assessment	Hypertensive patients with a recorded cardiovascular assessment in the last year/ Number of hypertensive patients enrolled in the CVRP
Prevalence of 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 the last BP measurement during the previous year/ Number of hypertensive patients enrolled in the CVRP
Prevalence of controlled hypertension	Hypertensive patients with documented systolic BP <140 mm Hg and diastolic BP <90 mm Hg in the most recent BP measurement during the last year/ Number of hypertensive patients enrolled in the CVRP
Prevalence of controlled hypertension six months after enrolment in the CVRP	Hypertensive patients who started treatment six months before and had systolic BP <140 mm Hg and diastolic BP <90 mm Hg at follow-up visit / Number of hypertensive patients enrolled in the CVRP during the last six months.
Uncontrolled hypertension in patients with cardiovascular disease, renal disease or diabetes	Hypertensive patients diagnosed ≥ six 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

Indicator	Operational Definition
	year/ Number of hypertensive patients enrolled in the CVRP ≥ six months before the start of the reporting period
Uncontrolled hypertension	Hypertensive patients diagnosed ≥ six 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 ≥ six months before the start of the reporting period
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 ≥ six months before the start of the reporting period
Six-monthly control of blood pressure among people who started pharmacological treatment for hypertension	Number of patients who began pharmacological treatment for hypertension during the quarter that ended six 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)/ Number of patients started on the pharmacological treatment of hypertension during the quarter that ended six months before.

For assessing implementation fidelity [33, 34], we will use self-registration forms for specific intervention activities, alongside non-participant observations and semi-structured key informant interviews. Self-registration forms will be collected monthly to determine whether actual implementation is done as intended. We will also select a heterogeneous sample of activities to be observed purposively and actors to be interviewed. Observations will provide real-time information on implementation, while interviews will throw light on observed practices and reasons for non-adherence. Additionally, overall experience with the intervention will be explored through in-depth interviews with stakeholders and patients. Data saturation will be considered to determine the frequency of observations and the number of interviews. A local social scientist will analyse data with NVivo 10 (QSR International Pty LTD, Melbourne, Australia, 2010). A senior sociologist not involved in data collection will review the coding consistency.

Table 4. Quantitative indicators for monitoring implementation.

Indicators related to BP screening and hypertension diagnosis.	
Indicator	**Operational definition**
Adequate 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
Effective referral to the Healthy Hearts service and BP screening	Number of people without BP measurement in the last year and referred for BP measurement that reaches and receive BP screening at the Healthy Hearts service/ Total number of people without BP measurement in the previous year referred for BP measurement to the Healthy Hearts service
Referral for serial BP measurement to the Healthy Hearts service	Number of patients not previously enrolled in the CVRP with high BP detected at the doctor or nurse consultation who are referred for serial BP measurement to the Healthy Hearts service during the reporting month/ Total number of patients not previously enrolled in the CVRP with high BP detected at the doctors or nurses consultation during the reporting month
Implementation 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 (>=3) BP measurements/ Total number of individuals with high BP detected by BP screening at the Healthy Hearts service.
Result of serial BP measurement	Number of patients with average systolic BP ≥140 mm Hg or diastolic BP ≥90 mm Hg at serial (>=3) BP measurement/ Number of individuals receiving serial BP measurements
Implementation 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
Result of serial self-measured BP monitoring	Number of patients with average systolic BP ≥140 mm Hg or diastolic BP ≥90 mm Hg as a result of a serial self-measured BP monitoring/ Number of patients with serial self-measured BP monitoring.
Indicators related to the hypertension management program.	
Indicator	**Operational definition**
Implementation of BP measurements by medical and nursing staff	Number of interviewed individuals referring that they had a BP measurement/ Total number of exit-interviews
Missed hypertension-related appointment	Number of patients who missed their last hypertension-related appointment during the reporting week/ Patients with scheduled hypertension follow-up visits during the reporting week
Correct prescription of pharmacological treatment	Number of patients who received a proper prescription of pharmacological treatment according to the clinical condition and defined algorithm / Total number of audited clinical records
Use of recommended antihypertensive drugs	Number of patients who received a prescription of antihypertensive drugs included in the standardised algorithm/ Total number of hypertensive patients receiving pharmacological treatment in the audited clinical records
Pharmacological advice by the medical doctor during the consultation	Number of interviewed hypertensive patients who referred they received pharmacological advice by the medical doctor/ Total number of exit interviews

Percentage of hypertensive patients who received prescription of non-pharmacological treatment.	Number of interviewed who refer they received a prescription of non-pharmacological treatment by the doctor/ Total number of exit interviews

Indicators related to the training of health care staff.	
Indicator	**Operational Definition**
Trained health care professionals	Number of trained professionals
Effectiveness of training in improving clinical knowledge	Average post-test score minus average pre-test score
Effectiveness of training on acquiring BP measurement skills	Number of trained professionals passing the post-training practical test/ Total number of trained professionals

Indicators related to (stock management and availability of the essential antihypertensive medication.	
Indicator	**Operational Definition**
Number of weeks without availability of essential antihypertensive drugs	Number of weeks without availability of one or more essential antihypertensive drugs

Indicators related to patients and community engagement.	
Indicator	**Operational Definition**
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
BP screening in the population by the Community Hypertension Outreach Group (CHOG)	Number of people screened and prevalence of high BP readings during the screening
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

We will determine whether intervention components were implemented as planned or were modified, deleted, or added [35] and assess adherence to the content and dose (i.e., frequency, duration, and coverage) of components and the influence of moderating factors such as comprehensiveness of intervention description, facilitation strategies, quality of delivery, recruitment, participant responsiveness, and context. Factors influencing implementation will be classified using these pre-established categories, and aspects not matching this coding will be categorised as intervention-specific moderating factors [36]. Finally, reasons for adapting intervention components will be identified through an inductive thematic analysis of key informants' interview responses.

Finally, we will contrast outcome data with implementation data and triangulate quantitative and qualitative results obtained from different information sources to validate and complement our findings.

Data Management

Databases will be electronically encrypted, and, when relating to individuals, a single study code will be assigned to each participant. The log of participant names and their assigned codes will be stored in a separate database with restricted access. For the surveys, questionnaires will be filled in employing tablets, and the information will be consolidated using an electronic platform. We will develop checks for data entry with built-in filters and logical constraints to assess the completeness and accuracy of our data. Recorded qualitative information will be transcribed *verbatim* by a local social scientist. Transcripts will be anonymised. Study-related material will be securely stored. Paper documents and tapes will be locked, and electronic databases and backup copies will be password protected. Data will be retained following local legislation.

Ethics and dissemination

The study will be conducted in accordance with the Helsinki declaration of research ethics. All field staff will be trained in responsible conduct of research. Informed consent will be obtained from survey participants and partakers in the qualitative research components (online supplementary file 2). A convenient place and time for interviews will be assured. Confidentiality will be guaranteed throughout. In particular, exit interviews will be anonymous and will not inquire into the identity of the health personnel the interviewee consulted with. Patients who are hypertensive in the survey and without follow-up or treatment will be referred for care to a provider of their health insurance scheme.

The planned intervention is based on formative research and inspired by guidelines from international hypertension care initiatives and has been adapted to the local environment with the participation of all relevant stakeholders. It does not pose health risks to beneficiaries as it implies implementing evidence-based best practices in the standard health setting. The local patients' association, study site health staff and Metrosalud central authorities have agreed upon any new patient care procedure. All activities are implemented conditional on adjustment when needed and planned to be continued beyond the study period.

The study protocol (online supplementary file 3) has been reviewed and approved by the Ethics Research Committee of Metrosalud in Colombia (reference 1400/5.2), the Medical Ethics Committee of the Antwerp University Hospital (reference 18/40/424), and the Institutional Review Board of the Antwerp Institute of Tropical Medicine (reference 1294/19).

The study findings will be shared and discussed in workshops with the local health authorities, health staff, representatives of Metrosalud and patient organizations in view of adjusting activities where needed, strengthening sustainability and preparing to scale up the intervention. Finally, results will be further disseminated through the media, presented at national and international conferences and published in peer-reviewed scientific journals.

Implications of this research

There is an urgent need, particularly in LMICs, to develop and test public health approaches that tackle the rising burden of non-communicable diseases [37]. Doing so within an integrated framework of care will benefit all patients [5]. When developing our proposal, we started with the international hypertension initiatives' guidelines [17, 18, 31, 32] and stepped them up considering the local context. We will thus implement and evaluate a comprehensive multi-component strategy involving stakeholders from community members to health program administrators, who all participated in the protocol's design. We believe this ensures social relevance and will increase intervention uptake at the health service and community levels.

The quasi-experimental nature of our design will provide solid evidence regarding the outcome of the intervention, which can form the basis for further economic evaluation. Relevant lessons will also be learned on what functioned, for whom, and why within a specific national health system's complex dynamics. While findings should not be extrapolated to upper-class urban zones or underserved rural areas, over half of the Colombian population lives in low-income urban environments, to which the results may be readily generalizable.

Our research closely involves Metrosalud, the most significant public health care provider of Medellin. This major stakeholder in the Colombian health system intends to further explore the effectiveness of the multi-component hypertension care and control intervention in other health areas of its network. Based on the results of the present trial, replication studies will be set up to evaluate and contrast, using routine data, the outcomes of the strategy in rural and urban settings and health areas with different socioeconomic levels. Study findings can also inform and inspire other initiatives for better

chronic care in LMICs, particularly in Latin America. Finally, assessing the implementation fidelity of the intervention and its determinants may provide valuable insights into the scalability of the WHO Global Hearts Initiative.

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Contributors: Esteban Londoño-Agudelo and Tullia Battaglioli contributed equally to this paper. Armando Rodríguez and Patrick Van der Stuyft are guarantors for the overall content. Patrick Van der Stuyft, Esteban Londoño, Tullia Battaglioli and Armando Rodriguez conceived the study and took the lead in conceptualising and designing the intervention, with contributions from Alonso Soto, Rubén Gómez and Patricia Ortiz. José Vásquez, Hernán Aguilar, Viviana Pérez, Rubén Gómez and Esteban Londoño coordinated different facets of the stakeholder involvement and engaged in the workshops in which the content of the intervention activities and operational procedures were defined. Dennis Pérez developed qualitative aspects of the process assessment and the evaluation of the implementation fidelity, with support of Patrick Van der Stuyft. All authors significantly contributed to refining the research protocol and the data collection tools. Alonso Soto, Esteban Londoño, Patrick Van der Stuyft, and Tullia Battaglioli drafted the manuscript, with involvement of Armando Rodriguez. All authors commented on subsequent versions of the paper and read and approved the final manuscript.

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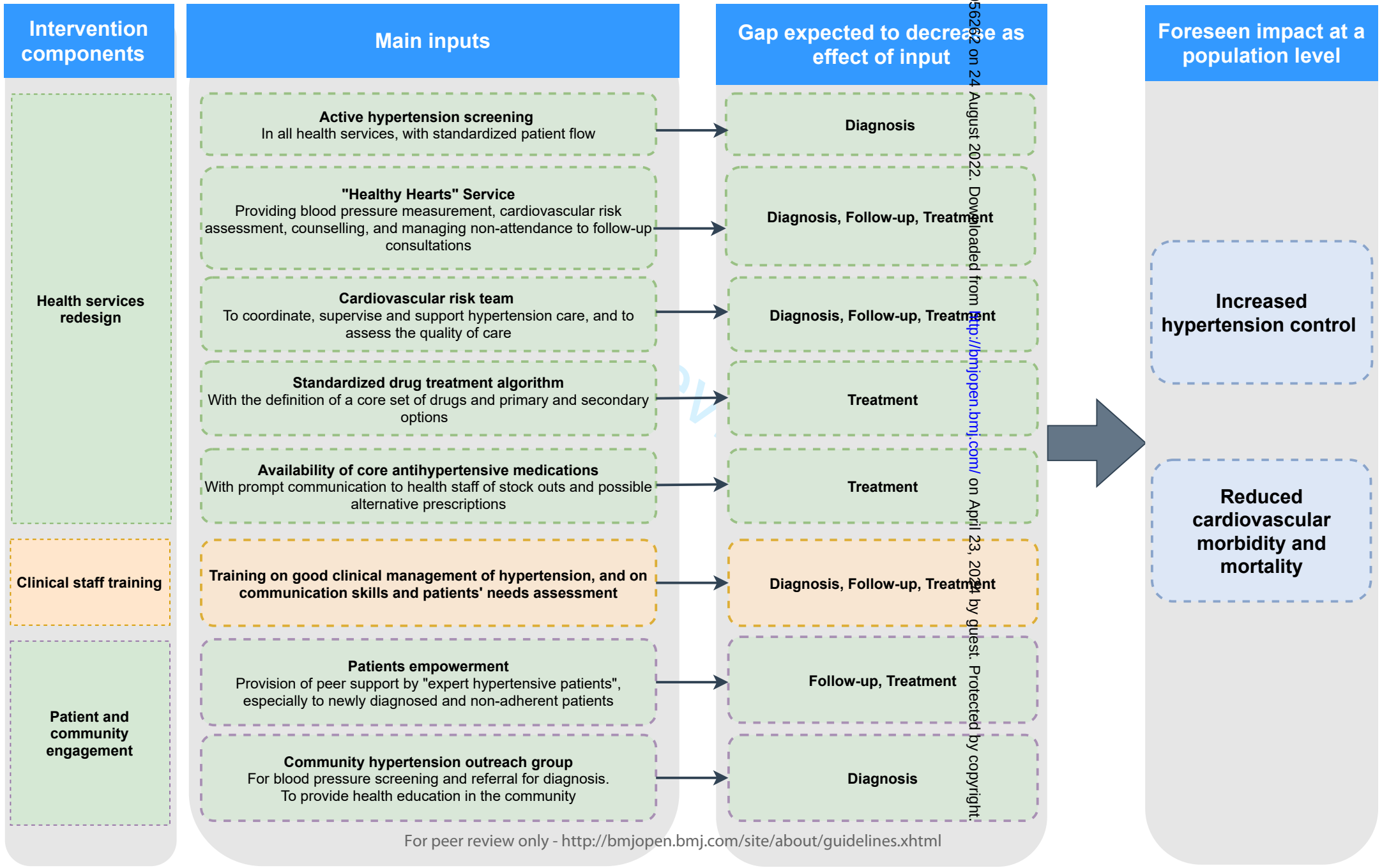
Competing interests: None declared.

Figure legend

Figure 1. Model conceptualizing the theory of action of a multi-component intervention to improve hypertension care and control in low-income Medellin, Colombia.



Reporting checklist for quality improvement in health care.

Based on the SQUIRE guidelines.

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Complete this checklist by entering the page numbers from your manuscript where readers will find each of the items listed below.

Your article may not currently address all the items on the checklist. Please modify your text to include the missing information. If you are certain that an item does not apply, please write "n/a" and provide a short explanation.

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		Reporting Item	Page Number
Title			
	#1	Indicate that the manuscript concerns an initiative to improve healthcare (broadly defined to include the quality, safety, effectiveness, patientcenteredness, timeliness, cost, efficiency, and equity of healthcare)	1
Abstract			3
	#02a	Provide adequate information to aid in searching and indexing	
	#02b	Summarize all key information from various sections of the text using the abstract format of the intended publication or a structured summary such as: background, local problem, methods, interventions, results, conclusions	
Introduction			

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	#13c	Contextual elements that interacted with the intervention(s)	n/a (it is a protocol)
	#13d	Observed associations between outcomes, interventions, and relevant contextual elements	n/a (it is a protocol)
	#13e	Unintended consequences such as unexpected benefits, problems, failures, or costs associated with the intervention(s).	n/a (it is a protocol)
	#13f	Details about missing data	n/a (it is a protocol)
Discussion			
Summary	#14a	Key findings, including relevance to the rationale and specific aims	n/a (it is a protocol)
Summary	#14b	Particular strengths of the project	4, 18-19
Interpretation	#15a	Nature of the association between the intervention(s) and the outcomes	n/a (it is a protocol)
Interpretation	#15b	Comparison of results with findings from other publications	n/a (it is a protocol)
Interpretation	#15c	Impact of the project on people and systems	18-19
Interpretation	#15d	Reasons for any differences between observed and anticipated outcomes, including the influence of context	n/a (it is a protocol)
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Other information			
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A Multi-component Intervention to Reduce Gaps in Hypertension Care and Control in Medellin, Colombia

INFORMED CONSENTS V.2.0. dated: 29-Apr-2019

Annex 10. Informed consent for endline survey

Study title: Gaps in hypertension care and control in Medellin, Colombia: cross-sectional survey in two Communes.

Principal Investigator: Dr. Esteban Londoño Agudelo, MD. MPH. Institution: ITM, Belgium – University of Antioquia, Colombia.

Metrosalud E.S.E. (Medellin, Colombia), the University of Antioquia (Medellin, Colombia) and the Institute of Tropical Medicine (Antwerp, Belgium) are conducting a study on the gaps in the process of care and control of hypertension at population level in Medellin city, Colombia.

This informed consent form has two parts:

Part I: Information sheet (to share information about the study with you)
Part II: Signature of Consent (for signature if you choose to participate)

You will be given a copy of both parts.

Part I: Information sheet

Introduction: We invite you to participate in this research study on how to improve the medical care and treatment for high blood pressure in the city. It is important that you understand the information given in this sheet before you decide to be part of this study. This sheet explains your rights and our responsibilities to you. We are going to give you information on the study and invite you to be part of this research. This sheet is asking for your consent. It may contain words that you do not understand, so please feel free to ask any question regarding this study before you decide to participate. If you have questions later, you can ask them to the study responsible, **Dr. Esteban Londoño** or to any member of the team. You can also go directly to the Direction of the Hospital of Metrosalud in Santa Cruz, asking for Dr. Hernán Aguilar; or to the Direction of the Hospital of Metrosalud in Doce de Octubre, asking for Dr. Valentina Sossa.

Purpose and description of the research:
People with high blood pressure readings (that is, hypertension), who are still not detected or not properly treated by a doctor can suffer from serious health problems. Uncontrolled high blood pressure can lead to serious problems like heart attacks, strokes, heart failures, and renal failures. If a community has a lot of people with uncontrolled high blood pressure, we can expect to find a lot of individuals suffering from serious health problems or prematurely dying. We want to find out how many people have high blood pressure readings among individuals 35 years or older in your Commune and what are the main problems that prevent the health personnel to detect people suffering from high blood pressure and to properly treat them. The results of this study can help to detect the main problems for the people of this Commune to receive timely and good health care for high blood pressure. We will use the results of this research to design strategies to improve the quality of health care for people living with high blood pressure.

Participants selection: People aged 35 years or older who live in the Commune can join this study. Using a computerized program, we have randomly selected a group of homes in each neighborhood, which will take part in this study. Then, in each selected home we will interview all the inhabitants aged 35 years or older.

Voluntary participation: Your decision to join this study is totally voluntary. It is your choice whether to participate or not. On the other hand, if you decide to join, you can choose to answer only the questions that you like. You can also leave the study at any time, even after you have signed this Informed Consent Form.

Procedures: Using a questionnaire, we will ask questions about your health, how often you use health services, what are your health problems and general health. We will especially ask you if you suffer from high blood pressure. In case you do, we will ask you about your treatment and how often you get follow-up consultations. This won't take much time, approximately 60 minutes, a professional survey taker for this study, will carry out the interview. The survey taker will also measure your blood pressure readings three times during the interview.

Risks and discomforts: There is no physical risk. You will only share personal information and if you feel any question too personal or you feel uncomfortable you do not have to answer. The study will not interfere with the health care that you receive.

Benefits: You will not receive direct benefits from this study, neither incentives to participate. With no doubt you will

obtain more information on what high blood pressure is, what are the measures you can take to prevent the disease and also how to get medical control. If during the interview the survey taker finds out that you have high blood pressure or any medical complication, you will be informed and referred to the health center where you are subscribed. Furthermore, the results of this study can help to improve how to provide health care to people with high blood pressure in Medellin and in Colombia.

Confidentiality: The information that you provide us will be kept confidential and will be accessed only by the study investigators. All formats in the study will be recognized by a number code, not by your name. Your name or any data that could identify you will not be revealed by the research team. Your identity will never be revealed in any report or publication resulting from this study.

Sharing the results: The results of this study will be shared with the managers of Metrosalud E.S.E. and of the health insurance companies of the Contributory Regimen; and may be published in national and or international scientific journals.

Right to Refuse or Withdraw from the study: The participation in this study is voluntary and you are not obliged to participate. If you prefer not to participate this won't influence the medical care and treatment that you receive. You can withdraw from the study at any time. You can refuse to answer any question that you feel uncomfortable. Should you have any question on the study, you can ask all questions that you want, either now or at any other time. In this case you can contact the principal investigator of this study, *Dr.* Esteban Londoño Agudelo (see below).

Part II: Signature of the consent.

Part for the participant

I declare that I have been informed about this study and that I have received a copy of the Informed Consent. I have been explained and read the information and I understand the objectives and procedures of the study, and that the collected data will be used only for this investigation. I had the chance to ask questions on the study and clarify doubts.
I freely consent to participate in this study and understand that I have the right to withdraw from the study at any time, without any consequence for me.

In consideration of the above, I sign this document on

Date: day ____ month _____ year _____

Name and surnames of the participant

_____

Signature: _____

Part for the investigator: I duly read the informed consent form to the potential participant, and the person had the opportunity to ask questions. I confirm that the person has given his/her consent voluntarily.

Date: day ____ month _____ year _____

Name and surnames of the Investigator: _____ **Signature**:

_____

Any question on the study can be addressed to the study responsible: **Dr. Esteban Londoño Agudelo, Facultad Nacional de Salud Pública, Universidad de Antioquia. Calle 62 No. 52-59. Phone: +57(4) 2196822, email:** estebanlondonoag@gmail.com

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Part for the participant I declare that I have been informed about this study and that I have received a copy of the Informed Consent. I have been explained and read the information and I understand the objectives and procedures of the study, and that the collected data will be used only for this investigation. I had the chance to ask questions on the study and clarify doubts.

I freely consent to participate in this study and understand that I have the right to withdraw from the study at any time, without any consequence for me.
In consideration of the above, I sign this document on
Date: day ____ month _____ year _____

Name and surnames of the participant

_____

Signature_____

Part for the investigator: I duly read the informed consent form to the potential participant, and the person had the opportunity to ask questions. I confirm that the person has given his/her consent voluntarily

Date: day ____ month _____ year _____ **Signature**:

Name and surnames of the Investigator: _____ _____

Study title: "A multi-component intervention to reduce gaps in hypertension care and control in Medellin, Colombia"
(Qualitative data collection of process evaluation in the intervention commune).

Principal Investigator: Dr. Esteban Londoño Agudelo, MD. MPH.
Institution: ITM, Belgium – University of Antioquia, Colombia.

Metrosalud E.S.E. (Medellin, Colombia), the University of Antioquia (Medellin, Colombia) and the Institute of Tropical Medicine (Antwerp, Belgium) are conducting a study on the gaps in the process of care and control of hypertension at population level in Medellin city, Colombia.

This informed consent form has two parts:

Part I: Information sheet (to share information about the study with you)
Part II: Signature of Consent (for signature if you choose to participate)

You will be given a copy of both parts.

Part I: Information sheet

Introduction: We invite you to participate in this research study on the improvement of hypertension care and control in the Commune. It is important that you understand the information given in this sheet before you decide to be part of this study. This sheet explains your rights and our responsibilities to you. We are going to give you information on the study and invite you to be part of this research. This sheet is asking for your consent. It may contain words that you do not understand, so please feel free to ask any question regarding this study before you decide to participate. If you have questions later, you can ask them to the study responsible, **Dr. Esteban Londoño** or to any member of the team. You can also go directly to the Direction of the Hospital Unit of Metrosalud in Santa Cruz, asking for Dr. Hernán Aguilar.

Purpose and description of the research:

People with hypertension, who are still not detected or not properly treated can suffer from serious health problems. Uncontrolled high blood pressure can lead to serious problems like heart attacks, strokes, heart failures, and renal failures. If a community has a lot of people with uncontrolled high blood pressure, we can expect to find a lot of young people (under 70 years of age) suffering from serious health problems or prematurely dying. We want to contribute to address the main problems that prevent the timely detection and adequate treatment of people with hypertension in the Commune. To achieve this, we have implemented a number of improvement interventions in the Commune's Metrosalud health services and in the community. For this purpose, a few months ago, you were explained about the intervention activities and invited to implement them. You were provided with the skills, guidelines and all the resources required to improve hypertension care and control actions within your health service. As part of the study, we are going to monitor and evaluate the implementation of the activities assigned to you and the rest of the involved health workers. We will use the results of this research to identify the main difficulties and to improve the implementation of the different components of the intervention. The results of this study can contribute to improve the quality of the health care provided to people living with hypertension.

Participants selection: Health providers involved in implementation of the different components of the intervention to improve hypertension care and control in the intervention commune.

Voluntary participation: Your decision to join this study is totally voluntary. It is your choice whether to participate or not. On the other hand, if you decide to join, you can choose to answer only the questions that you like. You can also leave the study at any time, even after you have signed this Informed Consent Form.

Procedures: If you agree to participate in the research, you could be subject of observation of your activities and semi-structured interviews. Observations will be conducted by research staff ("observers") in a systematic way and at different points in time. The exact moment of the observation will not be communicated not to interfere with your activities and not to influence or bias your performance. The observer will take notes of the activities you conduct as part of the intervention. Based on those notes you could be further interviewed by the research staff. The time and the place of the interview will be arranged with you in advance. The interview could take between 45 minutes and one hour. The interviewer will ask you some questions. If you do not wish to answer any of the questions during the interview, you may say so and the interviewer will move on to the next question. We foresee to tape-record the entire interview unless you do not allow us doing so. Your name will not be identified on the tape. The recorded information will be confidential and the tapes will be destroyed after three months.

Risks and discomforts: The risks related to observation and interview are minimal. There is no physical risk. You will only share personal information and if you feel any question too personal or you feel uncomfortable you do not have to answer. The study will not represent an evaluation or report of your performance.

Benefits: You will not receive direct benefits from this study, neither incentives to participate. The results of this study can help to improve how to provide health care to people with hypertension in Medellin and in Colombia.

Confidentiality: The information that you provide us will be kept confidential and will be accessed only by the study investigators. All formats of the study will be recognized by a number code, not by your name. Your name or any data that could identify you will not be revealed by the research team. Your identity will never be revealed in any report or publication resulting from this study.

Sharing the results: The results of this study will be shared with the managers of Metrosalud E.S.E. and of the health insurance companies of the Contributory Regimen; and may be published in national and or international scientific journals.

Right to Refuse or Withdraw from the study: The participation in this study is voluntary and you are not obliged to participate. If you prefer not to participate this won't have any implication for your job or work-related evaluation. You can withdraw from the study at any time. You can refuse to answer any question that you feel uncomfortable. You can also stop the interview at any time if you decide to do so.

Should you have any question on the study, you can ask all questions that you want, either now or at any other time. In this case you can contact the principal investigator of this study, *Dr.* Esteban Londoño Agudelo (see below).

Annex 11. Informed Consent for semi-structured interviews on health providers. Version 2.0, dated 18-APR-2019

Reducing gaps in hypertension care and control in Colombia

Part II: Signature of the consent.

Part for the participant

I declare that I have been informed about this study and that I have received a copy of the Informed Consent. I have been explained and read the information and I understand the objectives and procedures of the study, and that the collected data will be used only for this investigation. I had the chance to ask questions on the study and clarify doubts.
I freely consent to participate in this study and understand that I have the right to withdraw from the study at any time, without any consequence for me.

I agree that the interview can be recorded: Yes No

In consideration of the above, I sign this document on **Date:** day ____ month _____ year _____

Name and surnames of the participant

_____ **Signature**: _____

Part for the investigator: I duly read the informed consent form to the potential participant, and the person had the opportunity to ask questions. I confirm that the person has given his/her consent voluntarily.

Date: day ____ month _____ year _____ **Signature**:

Name and surnames of the Investigator: _____ _____

Any question on the study can be addressed to the study responsible: **Dr. Esteban Londoño Agudelo, Facultad Nacional de Salud Pública, Universidad de Antioquia. Calle 62 No. 52-59. Phone: +57(4) 2196876, email:** elondono@ext.itg.be

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Part for the participant: I declare that I have been informed about this study and that I have received a copy of the Informed Consent. I have been explained and read the information and I understand the objectives and procedures of the study, and that the collected data will be used only for this investigation. I had the chance to ask questions on the study and clarify doubts.

I freely consent to participate in this study and understand that I have the right to withdraw from the study at any time, without any consequence for me.

I agree that the interview can be recorded: Yes No
In consideration of the above, I sign this document on **Date**: day ____ month _____ year _____
Name and surnames of the participant

_____ **Signature**: _____

Part for the investigator: I duly read the informed consent form to the potential participant, and the person had the opportunity to ask questions. I confirm that the person has given his/her consent voluntarily
Date: day ____ month _____ year _____ **Signature**:

Annex 11. Informed Consent for semi-structured interviews on health providers. Version 2.0, dated 18-APR-2019

Reducing gaps in hypertension care and control in Colombia

Name and surnames of the Investigator: _____

_____

Annex 11. Informed Consent for semi-structured interviews on health providers. Version 2.0, dated 18-APR-2019

Reducing gaps in hypertension care and control in Colombia

Study title: A multi-component intervention to reduce gaps in hypertension care and control in Medellin, Colombia
(Qualitative data collection of process evaluation in the intervention commune)

Principal Investigator: Dr. Esteban Londoño Agudelo, MD. MPH.
Institution: ITM, Belgium – University of Antioquia, Colombia.

Metrosalud E.S.E. (Medellin, Colombia), the University of Antioquia (Medellin, Colombia) and the Institute of Tropical Medicine (Antwerp, Belgium) are conducting a study on the gaps in the process of care and control of hypertension at population level in Medellin city, Colombia.

This informed consent form has two parts:

Part I: Information sheet (to share information about the study with you)
Part II: Signature of Consent (for signature if you choose to participate)

You will be given a copy of both parts.

Part I: Information sheet

Introduction: We invite you to participate in this research study on how to improve the medical care and treatment for persons with high blood pressure. It is important that you understand the information given in this sheet before you decide to be part of this study. This sheet explains your rights and our responsibilities to you. We are going to give you information on the study and invite you to be part of this research. This sheet is asking for your consent. It may contain words that you do not understand, so please feel free to ask any question regarding this study before you decide to participate. If you have questions later, you can ask them to the study responsible, **Dr. Esteban Londoño** or to any member of the team. You can also go directly to the Direction of the Hospital of Metrosalud in Santa Cruz, asking for Dr. Hernán Aguilar.

Purpose and description of the research:

People with high blood pressure readings (that is, hypertension), who are still not detected or not properly treated can suffer from serious health problems. Uncontrolled high blood pressure can lead to serious problems like heart attacks, strokes, heart failures, and renal failures. If a community has a lot of people with uncontrolled high blood pressure, we can expect to find a lot of young people (under 70 years of age) suffering from serious health problems or prematurely dying. We want to contribute to solve the main problems that prevent the health personnel from detecting people suffering from high blood pressure and to properly treat them in your Commune. In order to do so, we have implemented a number of improvement interventions in the Commune's Metrosalud health services and in the community. The results of this study can help to improve the quality of the health care provided for people living with high blood pressure.

Participants selection: you have been selected to participate because you are aged 35 years or older and live in the Commune.

Voluntary participation: Your decision to join this study is totally voluntary. It is your choice whether to participate or not. On the other hand, if you decide to join, you can choose to answer only the questions that you like. You can also leave the study at any time, even after you have signed this Informed Consent Form.

Procedures: If you agree to participate in the research, we will conduct an in-depth interview with you, once you have signed this document. The interview could last for one or more sessions of about one hour each. During the first session, we will agree with you themost comfortable pace for you. If after the first session additional information is required we will ask you to arrange new sessions. In each interview session, the interviewer will ask you some questions on your knowledge, opinion and experience with hypertension and the health care you receive for it. If you do not wish to answer any of the questions, you may say so and the interviewer will move on to the next question. We foresee to tape-record the entire interview unless you do not allow us doing so. Your name will not be identified on the tape. The information recorded will be confidential and the tapes will be destroyed after three months.

Risks and discomforts: The risk related to the interview is minimal. There re is no physical risk. You will only share personal information and if you feel any question too personal or you feel uncomfortable you do not have to answer. The study will not interfere with the health care that you receive.

Benefits: You will not receive direct benefits from this study, neither incentives to participate. With no doubt you will obtain more information on what high blood pressure is, what are the measures you can take to prevent the disease and also how to get medical care. The results of this study can help to improve how to provide health care to people with high blood pressure in Medellin and in Colombia.

Confidentiality: The information that you will provide us will be kept confidential and will be accessed only by the study investigators. All formats in the study will be identified by a code, not by your name. Your name or any data that could identify you will not be revealed by the research team. Your identity will never be revealed in any report or publication resulting from this study.

Sharing the results: The results of this study will be shared with the managers of Metrosalud E.S.E. and of the health insurance companies of the Contributory Regimen; and may be published in national and international scientific journals.

Right to Refuse or Withdraw from the study: The participation in this study is voluntary and you are not obliged to participate. If you prefer not to participate this won't influence the medical care and treatment that you receive. You can withdraw from the study at any time. You can refuse to answer any question that you feel uncomfortable. You can also stop the interview at any time if you decide to do so.

Should you have any question on the study, you can ask all questions that you want, either now or at any other time. In this case you can contact the principal investigator of this study, *Dr.* Esteban Londoño Agudelo (see below).

Annex 12. Informed consent for in-depth interview with patients, version 2.0, dated 18-APR-2019

Reducing gaps in hypertension care and control in Colombia

Part II: Signature of the consent.

Part for the participant

I declare that I have been informed about this study and that I have received a copy of the Informed Consent. I have been explained and read the information and I understand the objectives and procedures of the study, and that the collected data will be used only for this investigation. I had the chance to ask questions on the study and clarify doubts.
I freely consent to participate in this study and understand that I have the right to withdraw from the study at any time, without any consequence for me.

I agree that the interview can be recorded: Yes No

In consideration of the above, I sign this document on **Date:** day ____ month _____ year _____

Name and surnames of the participant

_____ **Signature**: _____

Part for the investigator: I duly read the informed consent form to the potential participant, and the person had the opportunity to ask questions. I confirm that the person has given his/her consent voluntarily.

Name and surnames of the Investigator: _____

Date: day ____ month _____ year _____ **Signature**: _____

Any question on the study can be addressed to the study responsible: **Dr. Esteban Londoño Agudelo, Facultad Nacional de Salud Pública, Universidad de Antioquia. Calle 62 No. 52-59. Phone: +57(4) 2196876,**
email: elondono@ext.itg.be

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Part for the participant: I declare that I have been informed about this study and that I have received a copy of the Informed Consent. I have been explained and read the information and I understand the objectives and procedures of the study, and that the collected data will be used only for this investigation. I had the chance to ask questions on the study and clarify doubts.

I freely consent to participate in this study and understand that I have the right to withdraw from the study at any time, without any consequence for me.
I agree that the interview can be recorded: Yes No
In consideration of the above, I sign this document on **Date**: day ____ month _____ year _____**Name and surnames of the participant**

_____ **Signature**: _____

Part for the investigator: I duly read the informed consent form to the potential participant, and the person had the opportunity to ask questions. I confirm that the person has given his/her consent voluntarily

Name and surnames of the Investigator: _____

Date: day ____ month _____ year _____ **Signature**: _____

Annex 12. Informed consent for in-depth interview with patients, version 2.0, dated 18-APR-2019

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
Principal Investigator:	Esteban Londoño. MD. MPH. ITM PhD Student

Title:	A multi-component intervention to reduce gaps in hypertension care and control in Medellin, Colombia
Version:	Version 2.0 dated 29 APRIL 2019
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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.

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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. Improvement of clinical management of patients with hypertension

A.3.1. Creation of the cardiovascular risk team (CVRT), 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. Guideline-based standardized diagnostic and treatment protocols: 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. Availability of antihypertensive medications: 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:

The 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 pharmacological 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

	serial BP measurement			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	

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.

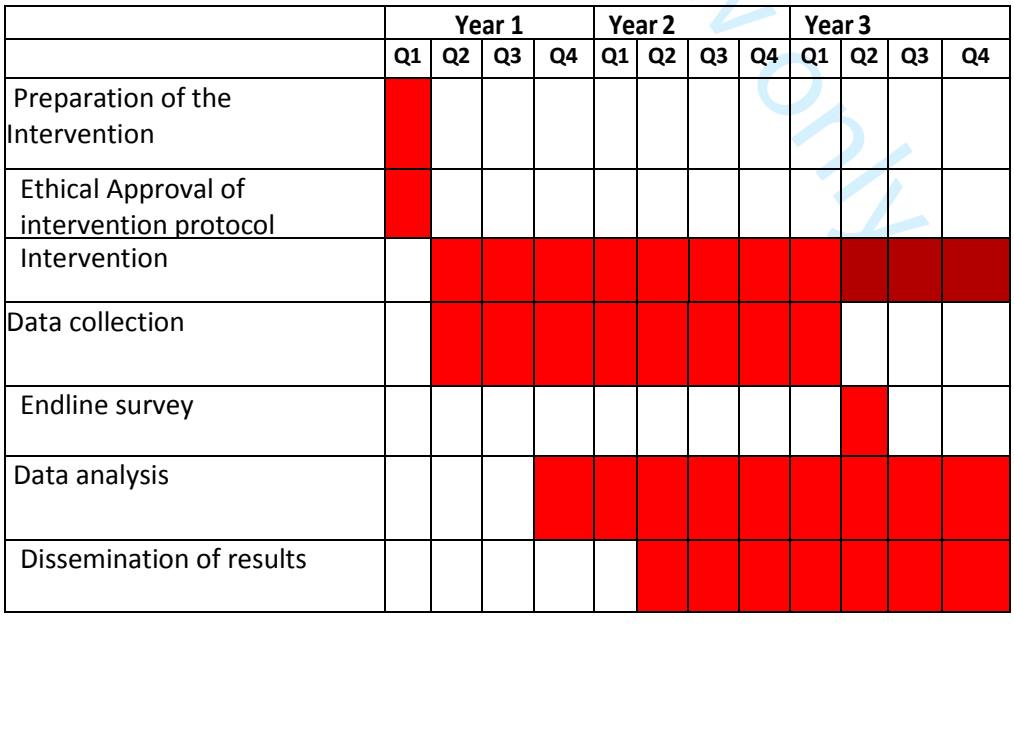
5.3 Insurance

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



 = 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.

10. REFERENCES

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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