RESEARCH PROPOSAL TITLE:

Implementation of DCP3 based Strategies to Manage and Control Hypertension among Hypertensive Patients in Pakistan: A Randomized Controlled Trial

Submitted by:

Subhana Akber
PhD Public Health (2017)
Health Services Academy, Islamabad

Date of submission: 05th Spetember, 2019.

Supervisor:
Dr. Assad Hafeez
PhD Public Health

1. Introduction

Hypertension is a clinical condition which refers to persistently raised pressure of blood in the vessels.(1) Since 1980s, there has been a reduction in the mean blood pressure (BP) level at population level. By 2010 however; still it was counted as the fourth highest risk factor for cardiovascular diseases (CVD) but then it became the highest risk factor attributable to disability adjusting life years (DALYs).(2) In low and middle-income countries, hypertension disproportionately affects the population which signals the weakness of health system. As hypertension is considered as a silent killer, it often undergoes unrecognized and leads to the development of major cardiovascular events. In addition, it also pertains to dietary and sedentary behaviors including excessive intake of salt in food, obesity and stressful life and environmental factors.(3)

According to the findings of a meta-analysis, the quantifiable rise in lower-middle income countries was primarily due to aging and population growth. Approximately, 80% of global deaths due to cardiovascular deaths occur in lower-middle income countries(4) whereas; a significant decline has been experienced by high-income countries. The decline in high-income countries is mainly accredited to reduction in deaths from coronary heart diseases and stroke. Changes in population-level of risk factors, specific blood pressure control (BP) and effective antihypertensive treatment as well as management of hypercholesterolemia were the major attributable aspects of this success. However; with the exception of some regions of Africa, high blood pressure has been rated among five leading risk factors contributing to worldwide morbidity and mortality.(5)

Globally, 9.4 million deaths per year are accounted for increased blood pressure and due to complications of hypertension alone.(5,6) An increased blood pressure is considered as the leading risk factor of mortality(5,7) however; an estimated 18 million deaths annually are attributed to cardiovascular diseases worldwide.(2,6) Heart diseases, stroke, renal failure, premature death and disability owing to hypertension contributes to the prevailing burden of cardiovascular diseases (CVDs) and therefore pose as an issue of public health concern.(6) The

findings from Global Burden of Disease study (2015) reports the burden from Eastern Mediterranean Region (EMR) due to cardiovascular diseases (CVD) which principally included stroke and ischemic heart disease. One-third of all deaths in 2015 were ascribed to cardiovascular diseases (CVD) alone. Amongst 22 countries of the EMRO region, Pakistan was ranked first for reporting 85.1% of total deaths due to cardiovascular diseases in the country.

Despite the fact that majority of deaths owing to cardiovascular diseases occurred in low and middle-income countries. However; this decline in age standardized mortality rates have been observed since last 25 years which were mainly attributed to public health and preventive interventions.(8) For policy and health system perspective, cost-effective health interventions help to aid budgeting of national healthcare plans and strategies.(9) Some related interventions for the management of hypertension as per Disease Control Priorities (DCP^3) includes initial screening by physicians, monthly visit and training of non-physician healthcare workers. Non-physician healthcare workers can serve in task shifting and can contribute in increasing knowledge about cardiovascular risk, hypertension management and adherence to treatment particularly in low-resource settings.(5)

Table 1: Interventions for the Primary Prevention of Cardiovascular Diseases in Disease Control Priorities 3rd Edition (Adapted)(5)

INTERVENTIONS FOR MANAGEMENT OF HYPERTENSION		
A)	**Modifications of Risk factors through Life Style Changes**	
	i. Cessation of Smoking ii. Exercise/Physical Activity	Smoking Cessation, Weight Loss
	iii. Dietary Modification	Reduction in Salt Intake/Alcohol, DASH diet
B)	**Pharmacological Treatments/Screening/Management**	
	i. Elevated Blood Pressure ii. Hypercholesterolemia iii. Dyslipidemia iv. Diabetes	Regular check-ups, Recommended Target: 140/90 mmHg
C)	**Non-Pharmacological**	
	i. Behavioural Counseling	Awareness, lifestyle modification and changes in diet and pattern

1.1 The Research Problem

Hypertension is a substantial public health concern and among major causes of deaths all over the world. It is a disease which is been termed as a *"silent killer"* that tends to cause premature mortality.(6,10,11) Approximately, more than 7 million deaths are accounted due to increased pressure of blood which reasons 12.8% of all causes of deaths in the world.(12) According to Global Health Observatory (GHO) data, the prevalence of increased blood pressure among men and women of age 18 years and above was 24% and 20%, respectively.(10) Risk of cardiovascular events such as coronary heart disease (CHD), ischemic heart disease (IHD) and stroke results in the presence of hypertension due to positive association. In addition to macrovascular complications, it can also result in number of microvasucular complications such as renal impairment, retinopathy and peripheral vascular diseases.(10)

Managing and treating hypertension can cause a significant reduction in cardiovascular associated complications among hypertensive patients. Globally, a high prevalence of hypertensive patients can be attributed to the increase in population growth and aging. However; hypertension is 40% prevalent in low and middle income countries than in high income countries which is approximately 35% of their total population. Whereas; more men tend to have raised blood pressure as compared to women in all WHO regions.(12–14)

A study was conducted in five countries including Pakistan to assess management of hypertension among 2185 patients in a clinical setting that focused on patient level factors. Rates of controlled hypertension were assessed as per the 2009 Reappraisal of the 2007 European Society of Cardiology/European Society of Hypertension (ESC/ESH) guidelines. Approximately, 40% of the patients had controlled hypertension as per the guidelines. However; poor rates of BP control among patients was primarily linked to non-adherence to treatment, high salt intake and lack of understanding of importance of treatment along with co-morbidity.(15) The results of study recommended promotion of guidelines and implementation of strategies to improve BP control rate.

In addition, non-pharmacological interventions including lifestyle modifications and dietary changes can help to reduce progression of hypertension and onset of cardiovascular diseases.(16)

There is extensive literature available eliciting role of healthcare professionals in hypertension management and control.(15–17) Other numerous studies are also available that focused on behavioural interventions using telemedicine and mhealth.(18,19) But sufficient and relevant evidence on physician's engagement with hypertensive patients on a multi-component hypertension treatment and patients' involvement into their self care and management of hypertension is though limited particularly in context of Pakistan.(20) Hence, this study aims to reduce blood pressure of hypertensive patients in three months to the recommended target of 140/90 mmHg from the baseline at Armed Forces Institute of Cardiology/National Institute of Heart Diseases (AFIC/NIHD), Rawalpindi.

2. Literature Review

Raised or persistent blood pressure level at 140/90mmHg or higher is defined as hypertension.(21) It is a wide known considered risk factor not only for cardiovascular diseases but for renal diseases as well. Hypertension is a risk factor for most, if not all, cardiovascular diseases and renal failure.(20) It is worth to repeatedly measure the blood pressure for the purpose of screening and diagnosis. New techniques of measuring the blood pressure such as self measurement using home or ambulatory blood pressure are bring extensively used for assessments during the treatment. It is however important to focus on blood pressure primarily to detect target organ damage, i.e. left ventricular hypertrophy (LVH) and renal effects.(22)The findings of a meta-analysis (2018) stated that the pooled prevalence of hypertension among Pakistanis was found to be 26.34% with higher prevalence among urban population (26.61%) than among the rural dwellers which was 21.03%.(11)

Table 2: Comparison of Probability (%) of Dying Between Age 30 to 70 Years from any of Cardiovascular Disease, Cancer, Diabetes or Chronic Respiratory Disease from 2010-2016

Year	WHO Global*	Eastern Mediterranean Region
2016	18.3	22.0
2015	18.5	22.3
2010	19.4	23.5

*Global Health Estimates 2016: Deaths by Cause, Age, Sex, by Country and by Region, 2000 2016. Geneva, World Health Organization, 2018; effective date on 05thApril, 2018.

As indicated in Table 2, the probability of dying at the age of 70 years gradually decreased from 2010 to 2016 as compared between WHO global regions versus East Mediterranean Region including Pakistan.(23)This necessitates implementation of effective public health interventions that has been found effective in low and middle income countries including Pakistan such as population-based intervention on hypertensive patients.(24) In this context, Disease Control Priorities, 3rd Edition is a project that is reviewed by policymakers and technical experts. It serves to provide evidence on economical and cost effective strategies in LMICs to address the burden of priorities diseases.(25)In addition, Table 3 shows global mortality from cardiovascular

events such as ischemic stroke, heamorrhagic stroke, hypertensive heart diseases and kidney diseases among both sexes of high income and low-middle income countries from 2000 to 2016.(26) Although deaths from hemorrhagic stroke, hypertensive heart diseases and kidney diseases were reported higher in low-middle income countries during 2000 whereas; only hypertensive heart diseases and kidney diseases were also reported higher among high income countries during 2016. But the global burden of deaths from ischaemic stroke was significantly reduced in both high and low-middle income countries from 2000 to 2016.Worldwide, hypertension is one of the most important cardiovascular risk factor(6) which prevails due to increased longetivity as well as in the presence of contributing factors such as obesity, diabetes, salt intake, smoking, associated clinical conditions and other environmental risk factors. According to World Health Organization (WHO 2016), effective implementation of all of WHO *"best buys"* can help to save more than 169,000 lives.(27) This includes recommended interventions such as drug therapy, treating acute myocardial infarction (MI), acute ischemic stroke, managing diabetes etcetera.(28) Whereas, preventive efforts include regular check-ups, better diet *(*such as *DASH diet),* smoke cessation and physical activity as shown in Table 1.(17,29,30)

Table 3: Comparative Analysis of Global Mortality due to Cardiovascular Events between High and Low-Middle Income Countries

Cause of Death		High Income Countries (%)		Low-Middle Income Countries (%)	
		2016	**2000**	**2016**	**2000**
1.	Ischaemic stroke	16.8	22.2	16.3	11.2
2.	Haemorrhagic stroke	7.2	10.3	8.4	7.0
3.	Hypertensive heart diseases	1.4	1.0	1.3	1.0
4.	Kidney diseases	2.2	1.6	2.3	1.5

3. Rationale of the Study

The most common single risk factor for cardiovascular diseases is persistently high blood pressure. Incidence of hypertension is escalating in Pakistan with an estimated 18.9 - 29.2% of Pakistani adults are reported to be hypertensive.(11) According to a similar study conducted in Pakistan; almost 33% of individuals of age 45 years and above have hypertension.(20) Gender diversification reveals that an estimated prevalence of hypertension among males in Pakistan is reported to be 24.9% and in females the prevalence is reported to be 24.7%.(11,31) Whereas; among adults (age above 18 years), one in four is reported to be hypertensive along with smoking in Pakistan.(32) Consecutively, evidence also suggest that hypertension is more common among males than in females.(13,14) Furthermore, in Pakistan, every third adult over the age of 40 years is predisposed to a wide range of diseases where; nearly 50% of patients are diagnosed with hypertension, consequently.(33) It is however; essential for hypertension management and control that early screening may be done along with initiation of hypertension treatment and management to reduce incidence of cardiovascular diseases.(34,35) This study will contribute to existing evidence on managing hypertension as no reliable data till date exists on comparative strategies to manage hypertension in Pakistan.(20) Thus, it is substantially important to control blood pressure among hypertensive patients to avert cardiovascular diseases and related complications such as target organ and renal effects among patients.(22) Furthermore, this hospital-based study will serve as a test bed for the intervention's effectiveness to be delivered in the community setting through trained workers.

4. Aims and Objectives

The aim of this study is to reduce systolic blood pressure to the recommended target of (SBP) ≥140 mmHg among hypertensive patients registered in the trial. For primary prevention of cardiovascular diseases among hypertensive patients, it is important to early manage and treat hypertension which also helps to reduce the risk of developing coronary heart disease (CHD). Thus, the objectives of this study are as follows:

4.1. Primary Objectives:

1. To conduct a formative study on hypertension management and control by including subject experts, cardiologists and patients.
2. To test the feasibility, acceptability and adaptability of DCP3 interventions in the cultural context of Pakistan and modify it on the basis of findings of formative phase.
3. To test the effectiveness of DCP3 interventions in reducing systolic blood pressure to the recommended target after three months of delivering the intervention.

4.2. Secondary Objectives:

1. To ascertain proportion of patients with adequate BP control at 03 months in both arms of the study.
2. To calculate cardiovascular risk for each patient according to ACC/AHA 2013 guidelines.
3. To assess each patient's use of number of antihypertensive drugs, compliance to prescribed treatment and their self-rated health before and after the intervention.

4.3. Hypothesis

Hypertensive patients receiving the intervention will have a greater reduction in systolic blood pressure after three months as compared to patients in the control arm receiving the usual medical care. Moreover, patients in the intervention arm will have a higher proportion of controlled blood pressure, a high level of physical activity, weight loss and a greater reduction in salt intake as compared to the control arm at 03 months. The patients will manage and control their blood pressure after the completion of trial at 24 months.

5. Operational Definitions

5.1. Hypertension

It is defined as a condition in which sclerosis of vessels occurs due to persistent and increased pressure of blood. This also results in increased pumping of blood by the heart. Systolic blood pressure of ≥140 mmHg and diastolic blood pressure of ≥ 90 mmHg is termed as hypertension which can affect the overall health and well being of patients.(21)

5.2. Uncontrolled Hypertension

As per International Classification of Diseases (ICD-10 10-CM Diagnosis Code I10) 2019, "persistently high systemic arterial blood pressure. Based on multiple readings (blood pressure determination), hypertension is currently defined as when systolic pressure is consistently greater than 140 mm hg or when diastolic pressure is consistently 90 mm hg or more."(36)

5.3. Blood Pressure (BP) Control

Blood pressure control will be considered when the systolic BP is less than or equal to 140 mm Hg and the diastolic BP is less than or equal to 90 mm of Hg(37) at the end of the intervention and follow up in the intervention arm.

6. PHASE I: SOP (FORMATIVE RESEARCH)

6.1. Study Objectives:

The main objective of the formative phase is to enable the development of intervention comprising of DCP3 strategies for hypertension management and control for hypertensive patients. The specific objectives are as follows:

1. To conduct a desk review on DCP3 interventions for hypertension management and control.
2. To test the feasibility, acceptability and adaptability of DCP3 interventions in the cultural context of Pakistan and modify it on the basis of findings of formative phase.

6.2. Research Questions: (Add RQ to dissertation)

a. Who is the most appropriate healthcare personnel for delivering an intervention based on DCP3 strategies for managing and controlling hypertension among hypertensive patients in Pakistan? (Phase 1)
b. Does a hypertension related intervention based on DCP3 strategies is acceptable among physicians or senior doctors or cardiologists? What are the key challenges in its applicability? Is it feasible in our local context? (Phase 2)

6.3. Methodology:

For the formative study, qualitative research methods will be employed to conduct a desk review analyze and its findings. To explore the feasibility, applicability and acceptance of DCP3 based hypertension intervention, focus group discussion and in depth interviews with selected study participants will be conducted. A prior written and verbal consent will be obtained from the study participants by the principal researcher herself. Data will be collected after obtaining an ethical approval from the Institutional review Board of Health Services Academy (HSA). The following will be the key steps:

A. Desk Review:

A desk review will be conducted using PubMed, CINAHL and Google Scholar and literature available past five years will be selected for the review. The inclusion criteria

will comprise of DCP3 interventions or strategies to manage and control hypertension (Table 1). Specifically, for the non-pharmacological strategy which includes aspects of awareness, counseling, lifestyle modifications and changes in diet pattern to control and manage hypertension among hypertensive patients pattern; systematic reviews and randomized trials will be included for the literature search. The results will be coded into themes and review findings will be reported accordingly.

B. Selection of Study Respondents:

To test the acceptance of DCP3 based intervention on hypertension management and control, potential study respondents will be indentified in a sampling frame (Table 4). The study respondents will be included for qualitative interviews on hypertension, its management and control. Focus group discussion and in-depth interviews will be conducted to determine the feasibility and applicability of intervention among hypertensive patients. Furthermore, patient-focused topic guides will be developed on the non-pharmacological strategy based on DCP3 intervention. Subsequently, content of intervention will be developed based on the findings of qualitative interviews. Evidence suggests that a team-based care model is more effective in preventing CVDs and in reducing blood pressure. In addition, the team-based care model has also been found effective in communities when cost-effective interventions have been deployed im masses. Mainly, the team-based care model includes the patient, healthcare practitioner/ primary health care provider as well as nurses and pharmacists(38). Whereas; certified hypertension specialist, dieticians, medical assistants and social workers have proven contributing role in such team-based care model(39). For developing the intervention, following will be the potential study respondents:

i. Subject experts who have been working for non-communicable diseases and / or involved in policy and decision making for health related priorities.
ii. Cardiologists / physicians / senior doctors.
iii. Pharmacist who are working in the hospital setting.
iv. Nurses who are primarily involved with cardiac patients in OPDS and wards.

v. Patients with uncontrolled hypertension who are able to give consent without any organ damage or serious health condition requiring emergency care.

C. Development of Topic Guides:

A general topic guide on hypertension management and control will be prepared in English language which will be translated into local language Urdu. Initially, the guide will be prepared which will base on the gaps identified in the desk review. The guide will be further modified after collecting data from the identified study respondents for the formative phase. The format of the guide will include the procedure of obtaining consent from the study participants selected through convenience-based sampling technique. Their socio-demographic characteristics and contact details will be documented in information sheets. The topic guide and study tools will be administered by the principal researcher herself. Initially, length of time for each interview will be recorded in the pre-testing phase and an average of time will be settled for consecutive interviews. Common ground rules will be established for the discussion on the topic which will be taken in the form of notes. The guide will be followed by questions concerning hypertension, its management, treatment and self management among hypertensive patients. The study tools will be reviewed by subject experts and will be pre-tested for DCP3 based hypertension intervention's acceptance, feasibility and adaptability into the local context and will be thus modified based on the findings of the formative phase. Furthermore, their awareness, perception, self-rated health and importance of early detection of hypertension will also be assessed. The study questionnaires are adapted from RAND 36-item health survey 1.0. and Health Belief Model. The qualitative interviews will be transcribed into Urdu and will be translated into English language. The interviews will be conducted until saturation is achieved, the results will be coded into themes and findings will be hence reported.

D. Sample Size:

Using team-based care model(39), purposive sampling will be opted to select study respondents for qualitative interviews in accordance with the sampling matrix as follows:

S. No.	Study Respondent/s	Number of Participants	Total Interviews
For IDI			
1.	Subject Experts	02	02
2.	Cardiologist / Physicians	05	05
For FGD			
3.	Pharmacists	6-8 persons	x2
4.	Nurses	6-8 persons	x2
5.	Patients with uncontrolled hypertension stratified in age groups of 30 years and 30 years above	6-8 persons	x4
Total number of interviews			**15**

Table 4: Sampling Matrix for Qualitative Interviews from Study Respondents (n=55)

As indicated in the sampling matrix (Table 4), the in-depth interviews will be conducted after obtaining consent from the study participants who will be subject experts and cardiologists or physicians. Purposive sampling will be used to identify key subject experts in the field similarly; the physicians will be asked for their contribution to the study. The consent will be taken by the principal investigator herself and they will ensured for anonymity and confidentiality to be protected. The contact details of the study participants will be obtained from relevant authorities, they will be asked to provide a suitable time for the interview. All interviews will be audio recorded as well as notes will be taken which will be transcribed and translated into English language. The focus group interviews with 6-8 participants will be conducted twice or more until the saturation is achieved on the coded themes for the FGDs. However; FGD conducted among hypertensive patients will include equal number of male and female patients which will be stratified into two age groups i.e. less than 30 years and more than 30 years age groups. These FGDs will be conducted at the study site for which a suitable time, day and location will be decided. In FGDs, study assistant will accompany the principal researcher as facilitator and will ensure time and established rules to be followed in the discussion.

E. Analysis Technique:

The interviews will be conducted according to the specified themes which will be coded for the purpose of analysis. All interviews will be audio recorded and will be transcribed and then translated into English language. Thematic analysis will be conducted to interpret the result findings for this study.

F. Development of Intervention:

Subsequent to above mentioned steps the intervention based on DCP3 strategies will be adapted, developed and modified. Following will be main components of the intervention development:

a. Content of Intervention:

The content of intervention will base on the findings of desk review and qualitative interviews. The behavioural intervention will be largely patient-focused which will adhere to aspects of self-management by the patient, compliance to treatment, involvement of family members in reducing the BP of the patient so as to facilitate changes in diet and life style pattern. The characteristics of the participants will be kept in consideration and preferred language as identified in the interviews will be used to develop the training materials to educate hypertensive patients on it. As the intervention based on DCP3 strategies will be deployed to 220 hypertensive patients with 110 patients in intervention and control arm. Minimum two physicians / resident medical officer (RMOs) will be trained by the principal investigator on delivering the intervention among patients recruited in the intervention arm. The physicians will be required to provide an allocated time as identified by the findings of qualitative interviews to counsel the patients on DCP3 defined strategies to reduce BP to the recommended target. Monitoring and supervision of the procedure and collection of data will be done by the principal investigator along with a study assistant.

b. Feedback by Study Respondents:

After completion of data collection, a feedback will be obtained from all study participants of the formative phase particularly the physicians who will deliver the

intervention. Following the formative phase, an evaluative research on effectiveness of intervention based on DCP3 strategies will be conducted using a randomized controlled study design (Phase II) which will adhere to CONSORT guidelines.

7. Proposed Methodology

The following research methodology will be used to conduct this study:

7.1. Study Design

A randomized controlled trial (RCT) study design will be employed (Figure 1) at single study setting. The study will be registered at *clinicaltrial.gov*. Unit of randomization will be the patient and the randomization will be achieved by blinding the subjects.

7.2. Study Area

This study will be conducted at Armed Forces Institute of Cardiology & National Institute of Heart Diseases (AFIC/NIHD), Rawalpindi. It is a 250 bedded major tertiary cardiac care center in Pakistan established in 1953.(40) The researcher will conduct the field work and will visit the study site for data collection after enrolling patients in the trial.

7.3. Duration of Study

The formative phase this study will be initiated in October 2019 and will complete by November 2019. Enrollment of patients will start from November 2019 and simultaneously the pre-testing will be conducted. The trial will be of three months from baseline data collection to the follow up of patients from November 2019 till January 2019. Patients will be enrolled after obtaining their verbal and written consent for participation.

7.4. Data Sources

The formative phase of the study will employ purposive sampling technique which will involve subject experts and physicians to assess the current practices for managing and treating

hypertension. It will also facilitate the adaptation of DCP3 interventions in the local context for primary prevention of cardiovascular diseases. The findings of formative research will help to modify the intervention, its convenience and mode of delivery. The formative survey will assess the current practices for managing and treating hypertension. The study participants will be interviewed using a face to face interview approach and participating patients will be observed for the blood pressure measurements.

7.5. Study Population

For the formative phase, the study population will consists of subject experts, physicians and the hypertensive patients at the study setting. For the intervention phase, hypertensive patients will be screened and recruited into the trial on the basis of pre-defined criteria and the intervention will administered to the patients randomized in the intervention arm. Whereas; patients in the control arm will receive the routine medical care for hypertension. Patients receiving the intervention will required for weekly follow-up and patients in the control arm will be required to follow every two week at the study setting for blood pressure evaluation.

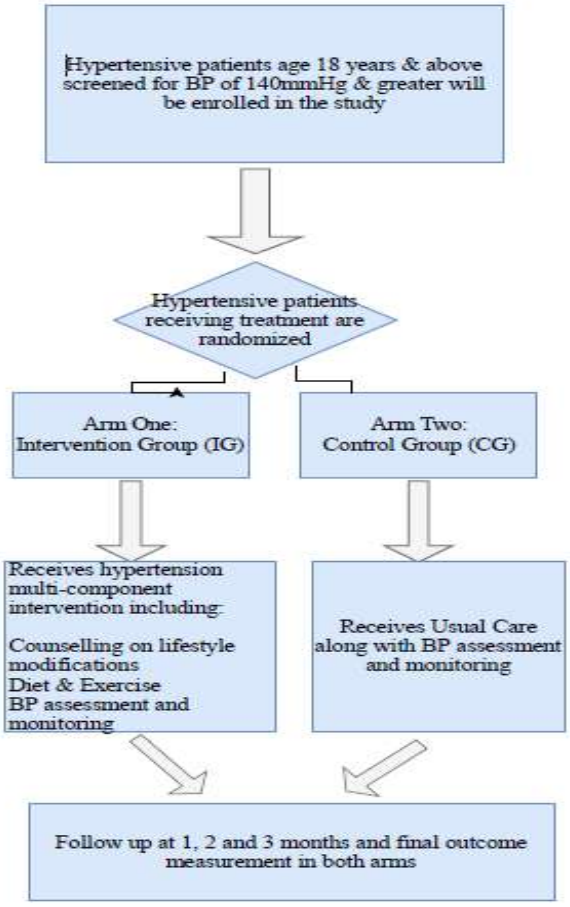

Figure 2: Overview of Study Design

7.5.1. Randomization

For the formative phase, purposive sampling technique will be employed and face to face interviews of subject experts and physicians will be conducted. Similarly, 15% of the patients will be selected using a convenience-based sampling technique. The IDI study tools will be pre-tested for the DCP3 intervention's acceptance, feasibility and adaptability into the local context and will be thus modified based on the findings of the formative phase. Furthermore, their awareness, perception, self-rated health and importance of early detection of hypertension will also be assessed. The IDI study questionnaire will be adapted from RAND 36-item health survey 1.0. and the Health Belief Model. Whereas; for the intervention phase, study tools will be developed and modified on the preference of patients as indicated in the formative research. Study questionnaires will be pre-tested on 15% of patients and then the baseline data will be

collected. All the data will be collected after obtaining an ethical approval from the institutional review board of Health Services Academy and AFIC/NIHD hospital. The data will be kept confidential and will be maintained in the personal computer of the principal investigator which will not be shared in or outside the study setting except with the co-researchers.

First 200 hypertensive patients meeting the eligibility criteria and having systolic blood pressure of ≥140 mmHg in the absence of target organ damage, either on current treatment or been newly diagnosed with hypertension will be invited to participate in the study (Figure 1). After obtaining their written and verbal consent, systolic and diastolic blood pressure of recruited patients will be measured and patients will be assessed for medical history, current therapy, lipids and glucose level in the blood. Using random number technique, randomization will be achieved by selecting every 9^{th} patient at the out-patient department (OPD) of AFIC/NIHD. Patients will be informed about the study purpose and their consent will be obtained for participation. They will be referred to the consulting physician/medical officer/RMO for their routine medical care/physical examination and ECG (if advised). The blood pressure and weight measurements will be assessed at each visit. The laboratory parameters involving routine blood investigations prescribed by the physician such as fasting glucose (RBS and HbA1c), lipids, cholesterol, urea, critinine, calcium will be assessed at the baseline and endline of the trial. Following the routine medical care, patients in the intervention arm will be provided counseling on diet and physical exercise. The key messages will be formulated on the basis of available evidence, literature review and formative research findings. Whereas; timing of each session, provision of awareness/counseling and mode of administering the intervention on DCP3 components will be determined on the preference of patients as specified in the IDIs.

A study assistant / observer independent of the study will assign randomly selected 100 patients into each arm. The patients will be registered into the study with the randomization ID number or CNIC number. Baseline characteristics of all study participants will be recorded. The height of the patient will be measured using stadiometer by a wall and the weight will be measured using a weighing machine for the body mass index (BMI). The patient will be asked to sit in a relaxed position and after 5-10 minutes, the patient will be asked to put left arm at 45 degrees for BP check-up. Using the brachial artery, readings of BP will be taken thrice and an average of three

readings will be recorded. Patients will also be instructed to report any adverse event and will also be provided the contact information of the resident physician/principal investigator in case of emergency. In case of withdrawal from the study, patients will have no liability. Including 10% non-response rate, the total number of study participants included will be 220. To reduce contamination, data will be collected at a point distant to physician's room.

7.5.1.1. Intervention Arm

Patients in the intervention arm will receive a combination therapy for the management of hypertension for primary prevention of cardiovascular diseases & CHD risk reduction based on DCP^3 recommended strategies (Table 1). Pharmacotherapy will be provided by the physician and the intervention comprising of DCP3 interventions will be administered by the principal investigator. To control BP to the recommended target, at least two hypertensive agents will be required in the treatment regimen according to the hypertension guidelines.(5) Furthermore, patients will be assessed for compliance to medications, follow up and subsequent counseling will be provided for lifestyle modification, stress management and changes in diet such as consuming vegetables and a low fat food.(5) At each appointment, patient will be evaluated for adherence to the aforementioned strategies and therapeutic regimen. The ultimate aim of the intervention will be to reduce the blood pressure and to improve patient's risk factors within recommended goals. Figure 1 provides an overview of the combination therapy based on DCP3 strategies.

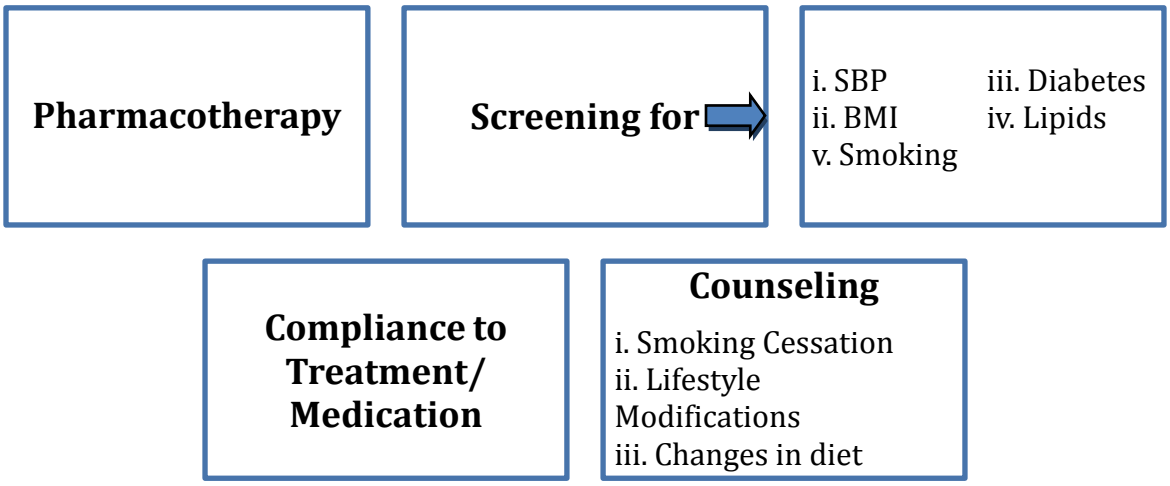

Figure 3: Overview of a Four Component Hypertension Control Intervention based on DCP3 Strategies(5)

7.5.1.2. Control Arm

Patients assigned to the control arm will be expected to receive routine medical care involving pharmacotherapy prescribed by the physician. Patients will be screened for SBP, DBP, lipids, diabetes and smoking. Regular monitoring of patients in improvement seeking care and adherence to medication will be assessed. Patients will be asked for follow up after every two weeks for BP measurements. They will be given awareness about hypertension only at the initial point of recruitment into the study.

7.6. Sampling Technique

7.1. Participants' Selection & Recruitment Procedure

Patients will be enrolled using a convenience-based sampling technique. Study participants will be registered during the study duration. Every 9th patient will be assigned to either intervention or control arm in a 1:1 ratio. The study will be carried out in accordance with CONSORT guidelines.(41) Each patient will serve as a unit of randomization in this study. All

data will be collected after obtaining their consent (both written and verbal). They will be enrolled after explaining them the purpose of the study. The provided information will be kept strictly confidential and their privacy will be protected.

7.2. Sample Size Calculation

First 200 hypertensive patients will be selected through convenience-based sampling technique. The sample size was calculated using a two-tailed alpha level of p=0.05 and power of 0.80 including a non-response rate of 10%, the total sample size calculated was 220 hypertensive patients. Each 110 of patients will be assigned to either intervention arm or control arm into 1:1 ratio.

7.2.1. Sample Recruitment:

7.2.1.1. Inclusion Criteria

- Pakistani nationals both male and female of age 18 years and above will be invited to participate in the study
- Similarly; known hypertensive patients having systolic blood pressure of ≥140 mmHg on current treatment will be included &
- Patients with co-morbidities will also be included such as those suffering from cardiac ailments (angina or transient ischemic attack (TIA) and diabetes

7.2.1.2. Exclusion Criteria

- Patients with compromised neurological or cognitive state who are unable to provide their consent will be excluded
- Patients suffering from non-cardiovascular diseases and life-threatening illnesses such as angiographically proven coronary disease, peripheral or cerebral vascular disease, pulmonary hypertension, having history of myocardial infarction, stroke/PCI/stent or high-risk conditions will be excluded from participation
- Patients with chronic conditions and co-morbidities requiring surgical intervention or treatment such as cardiomyopathies or congenital abnormalities &

- Patients receiving dialysis will also be excluded from the study

7.3. Data Collection Techniques

The data collection will be initiated after obtaining an ethical approval from Health Services Academy (HSA). Open-ended and structured study instruments will be used to collect data for the formative phase (Appendices) which will be adapted from RAND 36-item health survey 1.0. and the Health Belief Model.(42,43) It will be covering the constructs as shown in Figure 3. Initially, it will be drafted in English and will be translated into the local language Urdu and will be then back translated in English language. The study instruments will be pre-tested on the same study population. Purposive sampling technique will be used to collect data from study participants of the formative phase which will include subject experts, physicians and hypertensive patients at the study site. In-depth interviews with the study participants will be conducted by the principal investigator which will last for 40-60 minutes. All interviews will be recorded in a rechargeable audio stick / audio recorder. The collected data will be then transcribed and translated for the purpose of analysis. The questionnaire will be self-administered to the subject experts and physicians while patients will be asked to answer the questions. They will be ensure for comfort and confidentiality. A written and verbal consent for participation will be obtained from all the study participants before the data collection.s

Figure 4: Health Belief Model (Jones, 2015)

For the intervention phase, the study instrument will be adapted based on DCP3 strategies (Figure 1). The intervention will encompass counseling on the components of DCP3 strategies as mentioned in Table 1. The study instrument will be pre-tested and will be then modified accordingly. It will be drafted in English and the principal investigator will record and maintain the database, periodically. Each patient will serve as the unit of randomization and will be systematically assigned to either intervention or control arm of the trial. The principal investigator will collect weekly data from the patients in the intervention arm at the baseline and subsequently at second and third months of delivering the intervention. All researchers involved in this study will assure for the completeness and accuracy of the data collected.

7.4. Procedures for Data Collection and Study Measures

The following will be the method of assessments:

7.4.1. Blood Pressure & Physical Measurements

Five blood pressure readings will be taken of which average will be recorded in the information sheets in the first visit of the patient. The patient will be asked to be seated for 5-10 minutes prior to the assessment using manual sphygmomanometer and in accordance to American Heart Association guidelines.(44) The same procedure will be followed at every visit of patients in intervention and control arm both. Height will be measured using stadiometer /tape rule and weight will be measured using a weighing machine to calculate the body mass index (BMI).

7.4.2. Cardiovascular Risk Scoring

The CV risk score will be evaluated through scoring the indicators of CV risk using American College of Cardiology/American Heart Association ACC/AHA guildelines 2013.(45) It will include laboratory parameters such as fasting blood glucose (FBS), lipid profile, cholesterol and calcium levels.

7.4.3. Patient's Socio-demographics

Socio-demographic data of patients will be collected on selected variables such as age, marital status, educational level, employment status, occupation and total household income. Also, it

will include medical history health insurance coverage, number and cost of medicines, year of diagnosis of hypertension, previous medical history, and adherence to medication(46) will be assessed. Consumption of specified food and restriction on salt intake will be monitored as well as daily physical activity(47,48) will be recorded.

7.5. Data Collection Tool

Study instrument of the formative phase administered to the subject experts and physicians will assess current hypertension guideline being practiced for the treatment and management of hypertension control. Study instrument for hypertensive patients will assess patient's knowledge regarding hypertension, perception about structured care being received, life style practices, follow-up pattern and compliance to treatment. Socio-demographic characteristics of the patients, information on physical activity and diet pattern will be assessed. The study tools will be will be pre-tested and validated. Expert review on study instruments will be obtained and these will be modified accordingly (Appendices). The study tools will be drafted in English, translated into local language Urdu and will be then back translated into English language.

7.5.1. Pre-testing

Study instruments will be pretested on 15% of the patients. For formative phase, the study instrument will be administered to subject experts and physicians sampled through purposive sampling technique.

7.6. Issues of reliability and validity

Concurrent validity will be calculated by administering the study instrument to subject experts, physicians and 15% of hypertensive patients. For the IDIs, construct validity will be opted to ensure generalizability. Study instrument of the intervention phase will be validated using face validity and it will be then modified after expert review. Whereas, Test-Retest Method will be used to ensure reliability of the study instruments.

7.7. Data Analysis Plan

The average of blood pressure measurements will be taken for each of the study participant at the baseline and follow-up visits. Repeated ANOVA measure will applied to calculate the changes in mean scores of BP measurements at baseline, second and third month of trial. Paired t-test will be used to test the significance between the baseline and follow-up blood pressure measurements within each study arm. Chi-square test will be used to analyze the difference in blood pressure control rate between the intervention and control arm and with other co-variates. A p-value of ≤ 0.05 will be considered as significant. Predictors of blood pressure control at the patient level will be identified at the follow up where covariates will be included in the analysis. Whereas; the effect size will be reported in odds ration with 95% CI. Data will be double entered for the purpose of cleaning and will be analyzed using SPSS version 21.

7.7.1. OUTCOME MEASURES

7.7.1.1. Primary Endpoint

The primary endpoint of the study will be control and reduction in systolic blood pressure below recommended target of 140/90 mm Hg from baseline to 03 months after intervention. Adequate BP control will be assessed by taking BP measurement and BMI of the patients in the intervention arm and it will be compared with the control arm.

7.7.1.2. Secondary Endpoint

The secondary endpoint will be to determine proportion of patients with adequate BP control at 03 months. Secondary outcomes for BP reduction will be assessed through use of number of antihypertensive drugs, compliance to treatment, self-rated health before and after the intervention. Moreover, cardiovascular risk score will also be calculated.

7.8. Ethical Considerations

Ethical approval will be obtained from the Institutional Review Board (IRB) of Health Services Academy (HSA) and Armed Forces Institute of Cardiology/National Institute of Heart Diseases (AFIC/NIHD), Rawalpindi. After obtaining an ethical approval, the study will be

carried out as per the institutional and ethical guidelines for research studies involving human subjects.(49) The data will be collected after obtaining an informed consent (both verbal and written) from each of the study participant. All participants will be enrolled after explaining them the purpose of the study. Their provided information will be kept strictly confidential and their privacy will be protected.

8. & 9.Timeline and Budget

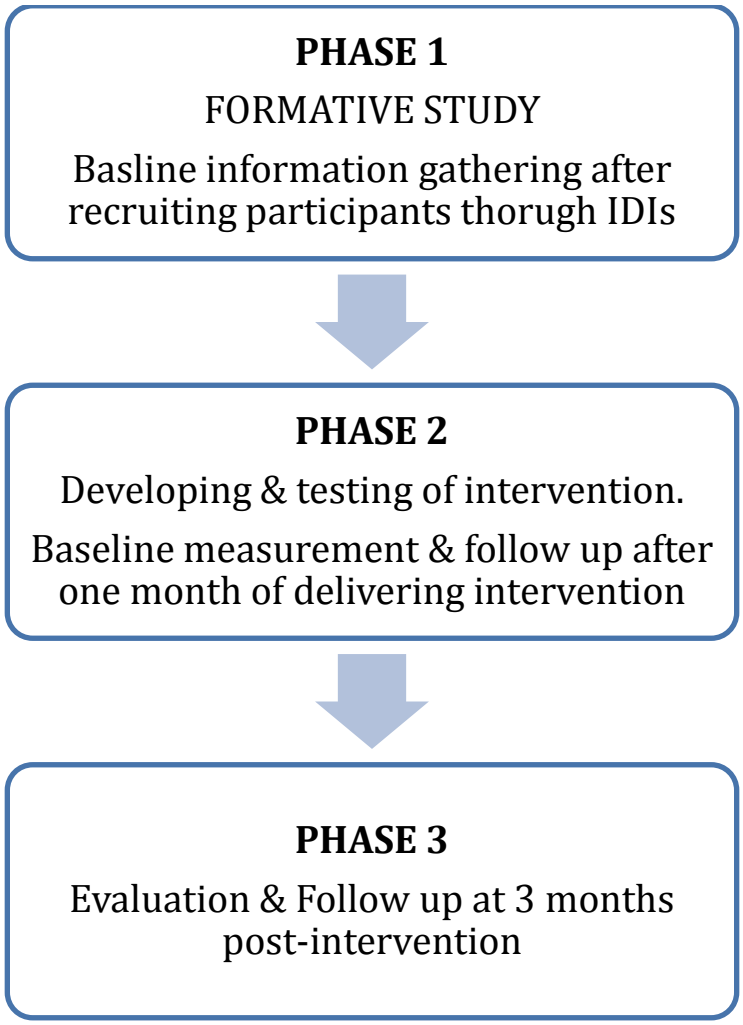

Figure 5: Study Phases from Baseline to Follow Up

References

1. WHO | Hypertension. WHO [Internet]. 2017 [cited 2018 Dec 30]; Available from: https://www.who.int/topics/hypertension/en/
2. Murray CJL, Vos T, Lozano R, Naghavi M, Flaxman AD, Michaud C, et al. Disability-adjusted life years (DALYs) for 291 diseases and injuries in 21 regions, 1990–2010: a systematic analysis for the Global Burden of Disease Study 2010. Lancet [Internet]. 2012 Dec 15 [cited 2018 Dec 31];380(9859):2197–223. Available from: http://www.ncbi.nlm.nih.gov/pubmed/23245608
3. Batool A, Gilani P, Javed T. Risk factors, pathophysiology and management of hypertension. Int J Pharma Sci Sci Res [Internet]. 2018 [cited 2019 Feb 11];4(5):49–61. Available from: https://biocoreopen.org/ijpsr/Risk-factors-pathophysiology-and-management-of-hypertension.pdf
4. Yusuf S, Rangarajan S, Teo K, Islam S, Li W, Liu L, et al. Cardiovascular Risk and Events in 17 Low-, Middle-, and High-Income Countries. N Engl J Med [Internet]. 2014 Aug 28 [cited 2018 Dec 31];371(9):818–27. Available from: http://www.nejm.org/doi/10.1056/NEJMoa1311890
5. Jeemon P, Gupta R, Onen C, Adler A, Gaziano TA, Prabhakaran D, et al. Management of Hypertension and Dyslipidemia for Primary Prevention of Cardiovascular Disease [Internet]. [cited 2018 Dec 31]. Available from: http://dcp-3.org/sites/default/files/chapters/DCP3 CVRD_Ch 22.pdf
6. WHO | A global brief on hypertension. WHO [Internet]. 2013 [cited 2018 Dec 31]; Available from: https://www.who.int/cardiovascular_diseases/publications/global_brief_hypertension/en/
7. Lim SS, Vos T, Flaxman AD, Danaei G, Shibuya K, Adair-Rohani H, et al. A comparative risk assessment of burden of disease and injury attributable to 67 risk factors and risk factor clusters in 21 regions, 1990–2010: a systematic analysis for the Global Burden of Disease Study 2010. Lancet [Internet]. 2012 Dec 15 [cited 2018 Dec 31];380(9859):2224–60. Available from: http://www.ncbi.nlm.nih.gov/pubmed/23245609
8. GBD 2015 Eastern Mediterranean Region Cardiovascular Disease Collaborators G 2015 EMRCD. Burden of cardiovascular diseases in the Eastern Mediterranean Region, 1990-2015: findings from the Global Burden of Disease 2015 study. Int J Public Health [Internet]. 2018 May [cited 2019 Jan 8];63(Suppl 1):137–49. Available from: http://www.ncbi.nlm.nih.gov/pubmed/28776245
9. Horton S, Gelband H, Jamison D, Levin C, Nugent R, Watkins D. Ranking 93 health interventions for low- and middle-income countries by cost-effectiveness. 2017 [cited 2019 Feb 12]; Available from: https://doi.org/10.1371/journal.pone.0182951
10. WHO | Raised blood pressure. WHO [Internet]. 2016 [cited 2019 Jan 11]; Available from: https://www.who.int/gho/ncd/risk_factors/blood_pressure_text/en/
11. Shah N, Shah Q, Shah AJ. The burden and high prevalence of hypertension in Pakistani adolescents: a meta-analysis of the published studies. [cited 2019 Jan 11]; Available from: https://doi.org/10.1186/s13690-018-0265-5
12. WHO | Raised blood pressure. WHO [Internet]. 2015 [cited 2019 Jan 11]; Available from:

https://www.who.int/gho/ncd/risk_factors/blood_pressure_prevalence_text/en/
13. Singh S, Shankar R, Singh GP. Prevalence and Associated Risk Factors of Hypertension: A Cross-Sectional Study in Urban Varanasi. Int J Hypertens [Internet]. 2017 [cited 2019 Jul 27];2017:5491838. Available from: http://www.ncbi.nlm.nih.gov/pubmed/29348933
14. EVERETT B, ZAJACOVA A. Gender Differences in Hypertension and Hypertension Awareness Among Young Adults. Biodemography Soc Biol [Internet]. 2015 [cited 2019 Jul 27];61(1):1. Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4896734/
15. Ragot S, Beneteau M, Guillou-Bonnici F, Herpin D. Prevalence and management of hypertensive patients in clinical practice: Cross-sectional registry in five countries outside the European Union. Blood Press [Internet]. 2016 Mar 3 [cited 2019 Jul 31];25(2):104–16. Available from: http://www.ncbi.nlm.nih.gov/pubmed/26873621
16. Mahmood S, Shah KU, Khan TM, Nawaz S, Rashid H, Baqar SWA, et al. Non-pharmacological management of hypertension: in the light of current research. Irish J Med Sci (1971 -) [Internet]. 2019 May 22 [cited 2019 Jul 31];188(2):437–52. Available from: http://link.springer.com/10.1007/s11845-018-1889-8
17. Bazzano LA, Green T, Harrison TN, Reynolds K. Dietary approaches to prevent hypertension. Curr Hypertens Rep [Internet]. 2013 Dec [cited 2018 Dec 30];15(6):694–702. Available from: http://www.ncbi.nlm.nih.gov/pubmed/24091874
18. Brokmann JC, Rossaint R, Müller M, Fitzner C, Villa L, Beckers SK, et al. Blood pressure management and guideline adherence in hypertensive emergencies and urgencies: A comparison between telemedically supported and conventional out-of-hospital care. J Clin Hypertens [Internet]. 2017 Jul [cited 2019 Jul 31];19(7):704–12. Available from: http://www.ncbi.nlm.nih.gov/pubmed/28560799
19. Siddiqui M, Islam MY ul, Mufti BAI, Khan N, Farooq MS, Muhammad MG, et al. Assessing acceptability of hypertensive/diabetic patients towards mobile health based behavioral interventions in Pakistan: A pilot study. Int J Med Inform [Internet]. 2015 Nov 1 [cited 2019 Jul 31];84(11):950–5. Available from: https://www.sciencedirect.com/science/article/abs/pii/S1386505615300332?via%3Dihub
20. Tazeen Jafar. AKU Launches Largest Study on Hypertension in Pakistan | The Aga Khan University News [Internet]. [cited 2019 Jul 28]. Available from: https://clinicaltrials.gov/ct2/show/record/NCT00327574
21. WHO EMRO | High blood pressure: a public health problem | World Health Day 2013 | World Health Days [Internet]. [cited 2019 Jan 8]. Available from: http://www.emro.who.int/media/world-health-day/public-health-problem-factsheet-2013.html
22. Kjeldsen SE, Aksnes TA, Fagard RH, Mancia G. Hypertension. In: The ESC Textbook of Cardiovascular Medicine [Internet]. Oxford University Press; 2009 [cited 2019 Jul 19]. p. 437–63. Available from: http://oxfordmedicine.com/view/10.1093/med/9780199566990.001.0001/med-9780199566990-chapter-13
23. GHO | By category | Risk of premature death from the four target NCDs - Data by WHO Region. WHO [Internet]. [cited 2019 Jan 11]; Available from: http://apps.who.int/gho/data/view.main.2485REG?lang=en
24. Afshin A, Micha R, Webb M, Capewell S, Whitsel L, Rubinstein A, et al. Effectiveness of Dietary Policies to Reduce Noncommunicable Diseases [Internet]. [cited 2019 Jan 11].

Available from: http://dcp-3.org/sites/default/files/chapters/DCP3 CVRD_Ch 6.pdf
25. About the Project | DCP3 [Internet]. [cited 2019 Jul 28]. Available from: http://dcp-3.org/about-project
26. GHO | By category | Risk of premature death from the four target NCDs - Data by MDG Region. WHO [Internet]. [cited 2019 Jan 11]; Available from: http://apps.who.int/gho/data/view.main.2485MDG?lang=en
27. Pakistan Risk of Prematre Death to NCDs (%)*. [cited 2019 Jan 12]; Available from: https://www.who.int/nmh/countries/2018/pak_en.pdf?ua=1
28. Best Buys. Tackling NCDs [Internet]. 2009 [cited 2019 Jan 12]. Available from: http://apps.who.int/iris/bitstream/handle/10665/259232/WHO-NMH-NVI-17.9-eng.pdf?sequence=1
29. World Health Organization. Men's health checklist [Internet]. [cited 2019 Jan 12]. Available from: https://www.who.int/news-room/feature-stories/detail/men's-health-checklist
30. DASH Eating Plan | National Heart, Lung, and Blood Institute (NHLBI) [Internet]. [cited 2018 Dec 30]. Available from: https://www.nhlbi.nih.gov/health-topics/dash-eating-plan
31. Ishtiaq S, Ilyas U, Naz S, Altaf R, Afzaal H, Muhammad SA, et al. Assessment of the risk factors of hypertension among adult & elderly group in twin cities of Pakistan [Internet]. Vol. 67. 2017 [cited 2019 Jul 27]. Available from: https://jpma.org.pk/PdfDownload/8428
32. HEALTH SITUATION [Internet]. 2018 [cited 2019 Jul 20]. Available from: http://apps.who.int/gho/data/node.cco
33. Saleem F, Dua JS, Hassali AA, Shafie AA. Hypertension in Pakistan: time to take some serious action. Br J Gen Pract [Internet]. 2010 Jun [cited 2019 Jul 27];60(575):449–50. Available from: http://www.ncbi.nlm.nih.gov/pubmed/20529498
34. Lippincott Williams & Wilkins. 2003 World Health Organization (WHO)/International Society of Hypertension (ISH) statement on management of hypertension. [cited 2019 Jan 11]; Available from: https://www.who.int/cardiovascular_diseases/guidelines/hypertension_guidelines.pdf?ua=1
35. WHO | WHO/ISH Hypertension guidelines. WHO [Internet]. 2013 [cited 2019 Jan 11]; Available from: https://www.who.int/cardiovascular_diseases/guidelines/hypertension/en/
36. 2019 ICD-10-CM Diagnosis Code I10: Essential (primary) hypertension [Internet]. [cited 2019 Jan 12]. Available from: https://www.icd10data.com/ICD10CM/Codes/I00-I99/I10-I16/I10-/I10
37. Ogedegbe G, Plange-Rhule J, Gyamfi J, Chaplin W, Ntim M, Apusiga K, et al. A cluster-randomized trial of task shifting and blood pressure control in Ghana: study protocol [Internet]. 2014 [cited 2019 Jul 19]. Available from: http://www.implementationscience.com/content/9/1/73
38. Control High Blood Pressure | 6|18 Initiative | CDC [Internet]. [cited 2019 Oct 18]. Available from: https://www.cdc.gov/sixeighteen/bloodpressure/index.htm
39. Community Preventive Services Task Force T. Cardiovascular Disease Prevention: Team-Based Care to Improve Blood Pressure Control Task Force Finding and Rationale Statement.
40. AFIC / NIHD [Internet]. [cited 2019 Jul 14]. Available from: http://afic.gov.pk/?page_id=126

41. Consort - Welcome to the CONSORT Website [Internet]. [cited 2019 Jul 15]. Available from: http://www.consort-statement.org/
42. Jones CL, Jensen JD, Scherr CL, Brown NR, Christy K, Weaver J. The Health Belief Model as an explanatory framework in communication research: exploring parallel, serial, and moderated mediation. Health Commun [Internet]. 2015 [cited 2019 Sep 15];30(6):566–76. Available from: http://www.ncbi.nlm.nih.gov/pubmed/25010519
43. RAND. The RAND 36-Item Health Survey The RAND 36-Item Health Survey. Heal (San Fr. 1992;2(March):91–7.
44. 2017 ACC/AHA/AAPA/ABC/ACPM/AGS/APhA/ASH/ASPC/NMA/PCNA Guideline for the Prevention, Detection, Evaluation, and Management of High Blood Pressure in Adults - Health Metrics [Internet]. [cited 2019 Jul 15]. Available from: https://healthmetrics.heart.org/2017-guideline-for-the-prevention-detection-evaluation-and-management-of-high-blood-pressure-in-adults/
45. Lloyd-Jones DM, Bennett G, Coady S, D RB, Gibbons R, Greenland P, et al. 2013 ACC/AHA Guideline on the Assessment of Cardiovascular Risk. S49 (Circulation [Internet]. 2014 [cited 2019 Jul 27];129:49–73. Available from: http://circ.ahajournals.org/lookup/suppl/doi:10.1161/01.cir.0000437741.48606.98/-/DC1.
46. Plank T. 41 to improve hypertension control [Internet]. [cited 2019 Jul 17]. Available from: http://www.measureuppressuredown.com/HCProf/Find/Toolkit/Plank4Tool1.pdf
47. WHO Global Recommendations on Physical Activity for Health [Internet]. 2010 [cited 2019 Jul 17]. Available from: https://www.who.int/dietphysicalactivity/global-PA-recs-2010.pdf
48. Global Physical Activity Questionnaire (GPAQ) WHO STEPwise approach to NCD risk factor surveillance Surveillance and Population-Based Prevention Prevention of Noncommunicable Diseases Department World Health Organization [Internet]. [cited 2019 Jul 17]. Available from: www.who.int/chp/steps
49. International Ethical Guidelines for Health-related Research Involving Humans Prepared by the Council for International Organizations of Medical Sciences (CIOMS) in collaboration with the World Health Organization (WHO). 2016 [cited 2018 Apr 9]; Available from: https://cioms.ch/wp-content/uploads/2017/01/WEB-CIOMS-EthicalGuidelines.pdf

10. Appendix

Appendice A. Informed Consent for Participation into the Research Study

Informed Consent Form

[YOUR INSTITUTIONAL LETTER HEAD]

[Informed Consent Form for participation in formative study (Phase 1)]

This informed consent form is for cardiologists, subject experts, nurses and patients.

[Name of Principle Investigator]	Subhana Akber, PhD Fellow 2017
[Name of Organization]	Health Services Academy, Islamabad Pakistan
[Name of Project]	Implementation of DCP3 Strategies to Manage and Control Hypertension among Hypertensive Patients in Pakistan: A Randomized Controlled Trial

Part I: Information Sheet

Introduction

I am Subhana Akber, doctoral student at HSA, Islamabad. I am conducting a research on hypertensive patients which comprises of an intervention on reducing blood pressure. The study duration is of 03 months. Hence, I would like to invite you for participation in this study. I shall be having your interview which will require less than 10 minutes of your time. Your participation is entirely voluntary. Read the information below, and please feel free to ask any question before participation.

Purpose of the research

Hypertension is a substantial public health concern and among major causes of deaths all over the world. It is a disease which is been termed as a *"silent killer"* that tends to cause premature

mortality. Incidence of hypertension is escalating in Pakistan with an estimated 18.9 - 29.2% of Pakistani adults are reported to be hypertensive. It is however; essential for hypertension management and control that early screening may be done along with initiation of hypertension treatment and management to reduce incidence of cardiovascular diseases. Therefore, we want to learn about the current practices of physicians and awareness among patients about hypertension.

Type of Research Intervention

The study is a randomized controlled trial which involves non-invasive blood pressure measurements. Moreover, IDI interviews are a component of qualitative research. Your answers will help to contribute to the formative phase of our study and in the deployment of intervention to hypertensive patients. This will require less than 10 minutes of your valuable time.

Participant Selection

You have been randomly selected and invited to participate in this study on the basis of your experience and knowledge. If case, if you are a patient, we would like to know about your understanding on this public health priority.

Voluntary Participation

Your participation in this research is entirely voluntary. It is your choice whether to participate or not. However; you can withdraw only in case you report serious adverse events during the study period.

Procedures

After obtaining your verbal and signed consent form, you will be required to answer a few set of questions that will assess your knowledge about hypertension. Whereas; participation into the trial will require you to visit the health facility where twice a weekly your blood pressure will be measured and record will be kept. All information will be kept save in the personal computer of the principal investigator.

.

Duration

The research will take place for a period of four months. Recruited patients will be required to visit the health facility twice a month for measuring their BP readings and baseline characteristics.

Risks

Since, the study bears no clinical procedure or clinical testing of medicine. However; still you will be provided contact information of physician in case of emergency.

Benefits

There will be no direct benefit to you, but your participation is likely to help us find out more about how to manage and control high bold pressure among hypertensive patients.

Reimbursements

You will not be provided any incentive to take part in the research or for your time, and travel expenses.

Confidentiality

It is to assure that all your information will be kept highly confidential and in strict privacy. No data will shared with anyone except with the co-investigators.

Sharing the Results

Nothing that you tell us today will be shared with anybody outside the research team, and nothing will be attributed to you by name. The knowledge that we get from this research will be shared with you (upon request) before it is made widely available to the public. Each participant will receive a summary of the results. Small meetings will be held at hospitals to ensure that the gap of knowledge is fulfilled by the results of this research.

Right to Refuse or Withdraw

This is a reconfirmation that participation is voluntary and includes the right to withdraw. Participants will have an opportunity to review their remarks in individual interviews.

Who to Contact

If you have any questions, you can ask them now or later. If you wish to ask questions later, you may contact any of the following: **[Subhana Akber, Contact No. 0312-8661755, email: subhanaakber@gmail.com**. This proposal has been reviewed and approved by IRB of Health Services Academy which is a committee whose task it is to make sure that research participants are protected from harm.

Part II: Certificate of Consent

I have read the foregoing information, or it has been read to me. I have had the opportunity to ask questions about it and any questions I have been asked have been answered to my satisfaction. I consent voluntarily to be a participant in this study. My participation is entirely voluntary in this research and I agree to the terms of research and the principal investigator.

Name of Participant/Thumb Impression _____

Signature of Participant _____

Date _____

Day/month/year

Thumb print of participant

.

Statement by the Researcher/Person Taking Consent

I have accurately read out the information sheet to the potential participant, and to the best of my ability made sure that the participant understands that the following will be done:

1. It is a non-invasive study that bears no clinical testing except measuring the blood pressure of the patients.
2. The participation of the patient is entirely voluntary and bears no benefit, risk or harm.
3. Participating patient has been provided the complete contact information of the physician and principal investigator in terms of emergency or adverse event.

I confirm that the participant was given an opportunity to ask questions about the study, and all the questions asked by the participant have been answered correctly and to the best of my ability. I confirm that the individual has not been coerced into giving consent, and the consent has been given freely and voluntarily.

A copy of this ICF has been provided to the participant.

Name of Researcher/person taking the consent: **Subhana Akber**

Signature of Researcher /person taking the consent: _____

Date _____

Day/month/year

Appendice B: IDI: PATIENTS

Ground Rules

- The interviewer and the note taker shall turn off their cell phones
- Remain as neutral or impartial as possible
- Use probes and clarifying questions where required
- Avoid asking leading questions
- Ensure all sections are covered

Introduction:

Asalam-o-Alaikum.Mr/Ms: _____s/d/w/o_____

I am Subhana Akber, PhD Scholar at Health Services Academy, Islamabad. My purpose to meet you today is for an in-depth interview regarding hypertension management and control. I thank you for providing me your valuable time to talk on the topic. You are requested to provide us your detailed information and your relevant experiences with the health care services in the hospital. I would like to know about your knowledge regarding hypertension and your health seeking behavior to manage it. I assure that your all information will be kept confidential and anonymous. Your interview and answers to the questions asked for this interview will be recorded after obtaining your consent. I thank you for your contribution to this study and for taking out few minutes from you precious time. Please provide your signed consent below:

Time for discussion: One hour

Interviewer's Name & Signature:	
Affiliation:	
Email & Contact:	
Study participant's signature for consent:	
Day & Date:	

.

I. PATIENTS'S PROFILE			
Socio-Demographic History of the Patient:			
Name:		**s/d/w**	
Age:		**Gender:**	
Marital Status:		**Ethnicity:**	
Number of Children:		**Family Type:**	
Current Diagnosis:		**Duration (years):**	
Address:			
Contact No.			
Highest Educational Level:		**Total Household Income (monthly):**	
Occupation:		**Occupation Type:**	
Regular Medical Care:	Yes ☐ No ☐	**Provider:**	
Any health insurance	Yes ☐ No ☐	**Height:**	**Weight:**
Cardiovascular risk factors:		**Smoking Status:**	Yes ☐ No ☐
BMI:		**Duration (Years):**	
Diabetes:	Yes ☐ No ☐	**Other co-morbidities:**	
Since Years:		**Duration (Years):**	
Medical Prescription Advised by:		**Cost of Medicines Purchased (in PKR):**	
Name of Medicines:			
Recommendation:			**Next follow-up:**

II. INTERVIEW

1. In general, would you say your health is [Self-rated health]: (Circle One)

   i. Excellent ……1
   ii. Very good……2
   iii. Good……3
   iv. Fair……..…..4
   v. Poor……..5

2. Have you ever been part of any hypertension control program? If please share the details.
3. In your opinion, what is hypertension?
4. How early detection of hypertension is important? (Circle One)
   Not Important ←----------Moderately Important ----------→Most Important
   0 1 2 3 4 5 6 7 8 9 10

5. How do you perceive your satisfaction level with the provided healthcare services at this hospital for hypertension? (Circle One)

   Not Satisfied ←---------- Moderate/Likely ----------→Most Satisfied
   0 1 2 3 4 5 6 7 8 9 10

6. How do you perceive your satisfaction level as a patient with your healthcare provider for managing and treating hypertension? (Circle One)

   Not Satisfied ←---------- Moderate/Likely ----------→Most Satisfied
   0 1 2 3 4 5 6 7 8 9 10

7. Please describe your diet pattern or the diet changes that you have adopted for managing hypertension? (e.g. food and restriction on salt intake)
8. Do you regularly follow up with the doctor for BP check-up? (Circle One)
   i. Yes ii. No

9. [Probe: Since your current diagnosis is of _____. Then ask the following questions:]
   i. How many years it's been for seeking health care for hypertension: _____
   ii. How many years have been of seeking health care from this facility: _____

10. How do you rate the health care services in this healthcare facility:

Not Satisfactory ←---------- Moderate/Likely ----------→Most Satisfactory

0 1 2 3 4 5 6 7 8 9 10

11. What procedure you follow to get to a doctor for BP check up? Provide the details.
12. Have you visited some other doctor for treating HTN before? If yes, then please provide details why the follow-up has been discontinued?
13. Do you comply with the medicines? If yes, then how much? If no, they state the reasons. Please provide details.
14. How do you manage hypertension yourself? Provide details.
15. What type of life style pattern do you follow?

    i. Sedentary ii. Non-Sedentary

16. What about lifestyle changes you have adopted and why? Concerning the aspects of exercise, diet, lifestyle modifications?
17. Did your family members contribute towards managing hypertension? If yes then explain how? Who advised them?
18. During the past 4 weeks, to what extent has your physical health or emotional problems interfered with your normal social activities with family, friends, neighbors, or groups? (Circle One)

    i. Not at all…….……1
    ii. Slightly……....2
    iii. Moderately……..3
    iv. Quite a bit……4
    v. Extremely……5

19. Do you think family members are integral to manage hypertension of the patient? How much likely:

Not Likely ←---------- Moderate/Likely ----------→Most Likely

0 1 2 3 4 5 6 7 8 9 10

20. What measures do you take for diet in relation to manage and treat hypertension?
21. Do you do physical exercise for controlling hypertension?

    i. Yes ii. No

22. Kindly give details how you do exercise and who advised it? Give details for complete timing of the way the physical exercise you do?

23. During the past 4 weeks, have you had any of the following problems with your work or other regular daily activities as a result of your physical health? (Circle One)

		Yes	No
i.	Cut down the amount of time you spent on work or other activities…	1	2
ii.	Accomplished less than you would like…….…….	1	2
iii.	Were limited in the kind of work or other activities……	1	2
iv.	Had difficulty performing the work or other activities (For example, it took extra effort)…….……	1	2

24. During the past 4 weeks, have you had any of the following problems with your work or other regular daily activities as a result of any emotional problems (such as feeling depressed or anxious)? (Circle One)

		Yes	No
i.	Cut down the amount of time you spent on work or other activity…..	1	2
ii.	Accomplished less than you would like…….	1	2
iii.	Were limited in the kind of work or other activities……..	1	2
iv.	Had difficulty performing the work or other activities (For example, it took extra effort)……	1	2

25. How do you adhere to the prescribed medicines and if not, then provide the reasons for non-adherence to the prescribed treatment?
26. [Probe about the smoking status and ask the following question] Have you taken any steps to quit smoking? If you have successfully quit smoking, what were the facilitators and barriers?
27. How do you manage other co-morbidities along with hypertension?
28. What alone as a component have helped to manage your blood pressure more?
29. How TRUE or FALSE is each of the following statements for you. (Give one number on each line)

Definitely true -------Mostly true------Don't know-------Mostly false--------Definitely false

1←----------2----------3----------4----------5----------→

i.	I seem to get sick a little easier than other people……..	_____
ii.	I am as healthy as anybody I know…….	_____
iii.	I expect my health to get worse……..	_____
iv.	My health is excellent……	_____

Adapted from:

1. Hays RD, Sherbourne CD, Mazel RM. The rand 36-item health survey 1.0. Health economics. 1993 Oct;2(3):217-27.
2. Young DR, Coughlin J, Jerome GJ, Myers V, Chae SE, Brantley PJ. Effects of the PREMIER interventions on health-related quality of life. Annals of Behavioral Medicine. 2010 Aug 27;40(3):302-12.
3. De Villiers MR. Three Approaches as Pillars for Interpretive Information Systems Research: Development Research. Action Research and Grounded Theory. In Bishop, J & D Konrie. Research for a Changing World." Proceedings of SAICSIT. 2005 Sep;2005:l42-5l.
4. Abdel-Fattah MA. Grounded theory and action research as pillars for interpretive information systems research: A comparative study. Egyptian Informatics Journal. 2015 Nov 1;16(3):309-27.
5. Jones CL, Jensen JD, Scherr CL, Brown NR, Christy K, Weaver J. The Health Belief Model as an explanatory framework in communication research: exploring parallel, serial, and moderated mediation. Health Commun. 2015;30(6):566–76. Available from: http://www.ncbi.nlm.nih.gov/pubmed/25010519

Appendice C: IDI: PHYSICIAN & SUBJECT EXPERTS

- **Time Allocation:** The interview will last about 30-40 minutes

Ground Rules

- The interviewer and the note taker shall turn off their cell phones
- Remain as neutral or impartial as possible
- Use probes and clarifying questions where required
- Avoid asking leading questions
- Ensure all sections are covered

Introduction:

Asalam-o-Alaikum. Dear Dr. _____

I am Subhana Akber, PhD Scholar at Health Services Academy, Islamabad. My purpose to meet you today is for an in-depth interview regarding hypertension management and control. I thank you for providing me your valuable time to talk on the topic. You are requested to provide us your detailed information. I assure that your all information will be kept confidential and anonymous. Your interview and answers to the questions asked for this interview will be recorded after obtaining your consent. I thank you for your contribution to this study and for taking out few minutes from you precious time. You are requested to provide detailed information where deemed necessary and to give us your signed consent below:

I. INTERVIEWEE'S PROFILE:

Name:		**s/d/w**	
Age:		**Gender:**	
Qualifications:		**Current Designation:**	
Affiliation:			
Total years of service:		**Email & Contact:**	
Signature for Consent:			

Date: _____

IDI INTERVIEW

SECTION 1: RAPPORT BUILDING 5 minutes

1. Kindly inform us what criteria or protocol is followed for diagnosing hypertension?
2. How hypertension is managed among hypertensive patients?
3. How hypertensive patients are treated and what protocol is followed to treat hypertensive patients in your hospital?
4. How much do you think it is important to screen patients for hypertension? What are the main reasons?

SECTION 2: HYPERTENSION GUIDELINESS & POLICY CONTEXT 10 minutes

5. Are you aware of any national or international policy regarding hypertension or its management?
6. What guidelines are recommended? What guidelines are followed in practice? (e.g. NICE)

SECTION 3: PRACTICES REGARDING HYPERTENSION Rx & MANAGEMENT 15 minutes

7. How the record of the patient's follow up is maintained and kept? How often:
    a. Every week
    b. Every two weeks
    c. Other: _____
8. How you measure the blood pressure of your patient?
9. What is the recommended procedure to measure the blood pressure?
10. How regularly your patients comply with your advice? What an average is the compliance rate?
11. Do you provide awareness regarding hypertension to your patients? If not, then who is responsible to provide the awareness in your hospital?
12. What measures do you take to counsel the hypertensive patients and provide them awareness? What awareness is provided to the patients? Kindly inform in detail:
13. What are the facilitators & barriers:
    - In screening hypertension:
    - Prevention:
    - Diagnosis and Management:
    - Treating:
14. Do you use any tools for predicting cardiovascular risk?

SECTION 4: CONCLUSION 5 minutes

15. How do you think hypertension can be prevented considering primary, secondary and tertiary levels of prevention?
16. What benefits are gained by early detection of hypertension among patients?
17. Do you have any recommendation? Or if you like to add something to the topic?

WRAP UP INTERVIEW:

Finally, I would like to thank you for providing us your valuable time. Your contribution is highly appreciated for this research work.

C. Appendix

Study Questionnaire

REGISTRATION OF BASIC DEMOGRAPHIC & CLINICAL DATA TO BE USED FOR RAPID ASSESSMENT AND FOLLOW-UP

Patients Registration ID: _____ **Date:** _____

Sr. Q#	Participant's Baseline Characteristics				
2.	**Age (years):** _____ Less than ≤30 years ☐ More than ≥60 years ☐	**3.**	**Marital Status:** Unmarried ☐ Married ☐ Separated/divorced/prefer not to mention ☐	**4.**	**Highest Education Level:** No education ☐ Matric/Intermediate ☐ Graduate ☐ Postgraduate & higher ☐
5.	**Total household income (monthly):** **PKR:** _____	**6.**	**Regular medical care provider:** Public ☐ Private ☐ Specify: _____	**7.**	**Regular Provider:** Doctor/GP ☐ Consultant/Specialist ☐

8.	**Any health insurance:** Yes ☐ No ☐ **If yes, please specify:** _____	**9.**	**Cardiovascular risk assessment for high risk group:** Family Hx ☐ years: _____ High BP ☐ years: _____ High Lipid profile ☐ years: _____ *Mark unknown if patient does not knows	**10.**	**Anthropometric Measures:** a. Height: _____ b. Weight: _____ c. **BMI:** _____ *Reference Categories: Underweight: BMI is less than 18.5. Normal weight: BMI is 18.5 to 24.9. Overweight: BMI is 25 to 29.9. Obese: BMI is 30 or more.
11.	**Smoking Status:** Currently ☐ Ex-Smoker ☐ Occasionally ☐	**12.**	a. **Years:** _____ b. **Cigarettes per day:** _____	**13.**	**Family Size:** *Total household members* _____
14.	**Co-morbidities:** Diabetes ☐ Cancer ☐ Congenital Abnormalities ☐ Others: _____	**15.**	**Life Style pattern** Sedentary ☐ Non-Sedentary ☐	**16.**	**Physical Exercise** Yes ☐ No ☐ If yes, specify minutes per day:_____

17.	**Pattern of Exercise:** Walk Jogging/Running Yoga Others: _____	**18.**	**Category of regimen prescribed:** Antihypertensive Cholesterol-lowering therapies Use of Aspirin Other, please specify: _____	**19.**	**a. Total number of medicines taken:** _____ **b. Dosage:** OD ☐ BD ☐ TDS ☐
20.	**Cost of medicines purchased (monthly):** **PKR:** _____	**21.**	**Occupation:** Public Servant Private employee Laborer/Worker Other _____	**2.**	**Years of HTN being diagnosed:** Recently ☐ Less than five years ☐ 5-10 years ☐ More than 10 years ☐
23.	**Hematological Findings:** **Lipid Profile (at baseline, 3 & 6 months):** HDL _____, _____, _____ LDL _____, _____, _____ Triglycerides _____, _____, _____		Urea _____ Critenine _____ Electrolytes: _____ **FBS Follow-up:** At baseline _____ At 1 months _____ At 3 months	**24.**	**Disability due to HTN:** CHD ☐ Hypercholesterolemia ☐ Blindness ☐ Stroke/Paralysis ☐ Depression ☐ Any other: _____
25.	**Presenting complaint/s:**				

26.	**Adverse Event (any reported)** Yes ☐ No ☐	**27.**	**AE Type (ever):** IHD ☐ Cardiac Arrest ☐ CHD/Angina ☐ Stroke ☐ Hemorrhage ☐ Other ☐	**28.**	**Food Intake** Salt intake Yes ☐ No ☐ Red Meat Yes ☐ No ☐ Sugary items Yes ☐ No ☐ Beverages Yes ☐ No ☐ Sweets Yes ☐ No ☐ Caffeine/Tea Yes ☐ No ☐
