



# HHS Public Access

Author manuscript

*Cardiol Clin.* Author manuscript; available in PMC 2018 February 01.

Published in final edited form as:

*Cardiol Clin.* 2017 February ; 35(1): 99–115. doi:10.1016/j.ccl.2016.08.010.

## Innovative Approaches to Hypertension Control in Low- and Middle-Income Countries

**Rajesh Vedanthan, MD, MPH<sup>1</sup>, Antonio Bernabe-Ortiz, MD, MPH<sup>2</sup>, Omarys I. Herasme, MPH<sup>1</sup>, Rohina Joshi, MBBS, PhD, MPH<sup>3</sup>, Patricio Lopez-Jaramillo, MD, PhD<sup>4</sup>, Amanda G. Thrift, PhD<sup>5</sup>, Jacqui Webster, PhD<sup>3</sup>, Ruth Webster, PhD, MIPH<sup>3</sup>, Karen Yeates, MD, MPH<sup>6</sup>,**

Corresponding Author: Rajesh Vedanthan, MD, MPH, Icahn School of Medicine at Mount Sinai, One Gustave L. Levy Place, Box 1030, New York, NY 10029, rajesh.vedanthan@mssm.edu.

### Authors Contact Information:

Antonio Bernabe-Ortiz, CRONICAS, Center of Excellence in Chronic Diseases, Universidad Peruana Cayetano Heredia, Lima, Peru, antonio.bernabe@upch.pe

Omarys I. Herasme, Icahn School of Medicine, Mount Sinai Hospital, New York, USA, omarys.herasme@mssm.edu

Rohina Joshi, The George Institute for Global Health, University of Sydney, Sydney, Australia, rjoshi@georgeinstitute.org.au

Patricio Lopez-Jaramillo, Research Institute FOSCAL, Bucaramanga, Colombia, jplopezj@gmail.com

Amanda G. Thrift, Monash University, School of Clinical Sciences at Monash, Health, Melbourne, Australia, amanda.thrift@monash.edu

Jacqui Webster, The George Institute for Global Health, University of Sydney, Sydney, Australia, jwebster@georgeinstitute.org.au

Ruth Webster, The George Institute for Global Health, University of Sydney, Sydney, Australia, rwebster@georgeinstitute.org.au

Karen Yeates, Queens University, School of Medicine, Ontario, Canada, yeatesk@queensu.ca

Joyce Gyamfi, New York University, School of Medicine, New York, USA, joyce.gyamfi@nyumc.org

Merina Ieremia, Samoan Ministry of Health, Apia, Samoa, merinaI@health.gov.ws

Claire Johnson, The George Institute for Global Health, University of Sydney, Sydney, Australia, cjohnson@georgeinstitute.org.au

Jemima H. Kamano, Moi University, School of Medicine, Eldoret, Kenya, shoine.hoine@gmail.com

Maria Lazo-Porras, CRONICAS, Center of Excellence in Chronic Diseases, Universidad Peruana Cayetano Heredia, Lima, Peru, maria.lazo@upch.pe

Felix Limbani, Centre for Health Policy, School of Public Health, University of the Witwatersrand, Johannesburg, South Africa, felix.limbani@wits.ac.za

Peter Liu, University of Ottawa, Ontario, Canada, peter.liu@utoronto.ca

Tara McCready, Population Health Research Institute, Hamilton, Canada, tara.mccready@phri.ca

J. Jaime Miranda, CRONICAS, Center of Excellence in Chronic Diseases, Universidad Peruana Cayetano Heredia, Lima, Peru, jaime.miranda@upch.pe

Sailesh Mohan, Public Health Foundation of India, New Delhi, India, smohan@phfi.org

Brian Oldenburg, University of Melbourne, School of Population and Global Health, Melbourne Australia, brian.oldenburg@unimelb.edu.au

Olugbenga Ogedegbe, New York University, School of Medicine, New York, USA, olugbenga.ogedegbe@nyumc.org

Bruce Ovbiagele, Medical University of South Carolina, Charleston, USA, ovibes@muscc.edu

Mayowa Owolabi, University of Ibadan, Ibadan, Nigeria, mayowaowolabi@yahoo.com

David Peiris, The George Institute for Global Health, University of Sydney, Sydney, Australia, dpeiris@georgeinstitute.org

Vilarmina Ponce-Lucero, CRONICAS, Center of Excellence in Chronic Diseases, Universidad Peruana Cayetano Heredia, Lima, Peru, vilarmina.ponce.l@upch.pe

Devarsetty Praveen, The George Institute for Global Health, Hyderabad, India, dpraveen@georgeinstitute.org.in

Arti Pillay, Fiji National University, Suva, Fiji, arti.pillay@fnu.ac.fj

Jon-David Schwalm, Population Health Research Institute, Hamilton, Canada, schwalj@mcmaster.ca

Sheldon W. Tobe, University of Toronto, Ontario, Canada, sheldon.tobe@sunnybrook.ca

Kathy Trieu, The George Institute for Global Health, University of Sydney, Sydney, Australia, ktrieu@georgeinstitute.org.au

Khalid Yusoff, UCSI University, Kuala Lumpur, Malaysia, khalid@ucsiuniversity.edu.my

Valentin Fuster, Icahn School of Medicine, Mount Sinai Hospital, New York, USA, valentin.fuster@mssm.edu

### Disclosure Statement:

The authors have nothing to disclose.

### Authors' Contributions

All authors were involved in the initial draft of this manuscript, made continual input as the drafts progressed, and approved the final draft for submission. The content within is solely the responsibility of the authors and does not necessarily represent the official views of the Global Alliance for Chronic Diseases funding agencies or affiliates.

**Publisher's Disclaimer:** This is a PDF file of an unedited manuscript that has been accepted for publication. As a service to our customers we are providing this early version of the manuscript. The manuscript will undergo copyediting, typesetting, and review of the resulting proof before it is published in its final citable form. Please note that during the production process errors may be discovered which could affect the content, and all legal disclaimers that apply to the journal pertain.

Joyce Gyamfi, MS<sup>7</sup>, Merina Ieremia, PGDHS<sup>8</sup>, Claire Johnson<sup>3</sup>, Jemima H. Kamano, MBChB, MMed<sup>9</sup>, Maria Lazo-Porras, MD<sup>2</sup>, Felix Limbani, MPH<sup>10</sup>, Peter Liu, MD<sup>11</sup>, Tara McCready, PhD, MBA<sup>12</sup>, J. Jaime Miranda, MD, PhD, MSc<sup>2</sup>, Sailesh Mohan, MD<sup>13</sup>, Olugbenga Ogedegbe, MD, MS, MPH<sup>7</sup>, Brian Oldenburg, PhD, MPsy<sup>14</sup>, Bruce Ovbiagele, MD, MSc<sup>15</sup>, Mayowa Owolabi, MBBS<sup>16</sup>, David Peiris, MBBS, PhD, MIPH<sup>3</sup>, Vilarmina Ponce-Lucero<sup>2</sup>, Devarsetty Praveen, MBBS, MD, PhD<sup>17</sup>, Arti Pillay, PGDPH<sup>18</sup>, Jon-David Schwalm, MD, MSc<sup>12</sup>, Sheldon W. Tobe, MD, MScCH<sup>19</sup>, Kathy Trieu, MPH<sup>3</sup>, Khalid Yusoff, MBBS<sup>20</sup>, and Valentin Fuster, MD, PhD<sup>1</sup>

<sup>1</sup>Icahn School of Medicine at Mount Sinai, New York, USA

<sup>2</sup>CRONICAS Center of Excellence in Chronic Diseases, Universidad Peruana Cayetano Heredia, Lima, Peru

<sup>3</sup>The George Institute for Global Health, University of Sydney, Sydney, Australia

<sup>4</sup>Research Institute FOSCAL, Bucaramanga, Colombia

<sup>5</sup>Monash University School of Clinical Sciences at Monash Health, Melbourne, Australia

<sup>6</sup>Queens University School of Medicine, Ontario, Canada

<sup>7</sup>New York University School of Medicine, New York, USA

<sup>8</sup>Samoa Ministry of Health, Apia, Samoa

<sup>9</sup>Moi University College of Health Sciences, Eldoret, Kenya

<sup>10</sup>University of the Witwatersrand, Johannesburg, South Africa

<sup>11</sup>University of Ottawa, Ontario, Canada

<sup>12</sup>Population Health Research Institute, Hamilton, Canada

<sup>13</sup>Public Health Foundation of India, New Delhi, India

<sup>14</sup>University of Melbourne, School of Population and Global Health, Melbourne Australia

<sup>15</sup>Medical University of South Carolina, Charleston, USA

<sup>16</sup>University of Ibadan, Ibadan, Nigeria

<sup>17</sup>The George Institute for Global Health, Hyderabad, India

<sup>18</sup>Pacific Research Centre for the Prevention of Obesity and Non-Communicable Diseases at Fiji National University, Suva, Fiji

<sup>19</sup>University of Toronto, Ontario, Canada

<sup>20</sup>UCSI University, Kuala Lumpur, Malaysia

## Abstract

Elevated blood pressure, a major risk factor for ischemic heart disease, heart failure, and stroke, is the leading global risk for mortality. Despite global efforts to combat hypertension, it continues to exert a significant health and economic burden on low- and middle-income country (LMIC) populations, thereby triggering the need to address the problem by way of novel approaches. The

Global Alliance for Chronic Diseases has funded 15 research projects related to hypertension control in low-resource settings worldwide. These research projects have developed and evaluated several important innovative approaches to hypertension control, including: community engagement, salt reduction, salt substitution, task redistribution, mHealth, and fixed-dose combination therapies. In this paper, we briefly review the rationale for each of these innovative approaches, as well as summarize the experience of some of the research teams in these respective areas. Where relevant, we also draw upon the wider literature to illustrate how these approaches to hypertension control are being implemented in LMICs. The studies outlined in this report demonstrate innovative and practical methods of implementing for improving hypertension control in diverse environments and contexts worldwide.

### Keywords

Hypertension; Low- and middle-income countries; Community engagement; mHealth; Task redistribution; Salt reduction; Salt substitution; Polypill

---

### Introduction

Cardiovascular disease (CVD) is the leading cause of mortality in the world, resulting in 17.3 million deaths annually, with 80% of these deaths occurring in low- and middle-income countries (LMICs).<sup>1</sup> Elevated blood pressure, a major risk factor for ischemic heart disease, heart failure, and stroke,<sup>2</sup> is the leading global risk for mortality.<sup>1</sup> Despite global efforts to combat hypertension, treatment and control rates are very low in LMICs.<sup>3</sup> Given the continued significant health and economic burden on LMIC populations, there is an urgent need to address the problem by way of novel approaches.

Founded in 2009, the Global Alliance for Chronic Diseases (GACD), funds, coordinates, and facilitates global collaborations in implementation research, focusing on the prevention and treatment of chronic non-communicable diseases in LMICs and vulnerable populations in high-income countries.<sup>4</sup> The first round of GACD-sponsored research projects focused on hypertension, and included 15 research teams from around the world.<sup>5</sup> These research projects have involved the development and evaluation of several important innovative approaches to hypertension control, including: community engagement, salt reduction, salt substitution, task redistribution, mHealth, and fixed-dose combination therapies.

In this paper, we briefly review the rationale for each of these innovative approaches, as well as summarize the experience of some of the GACD teams in these respective areas. Where relevant, we also draw upon the wider literature to illustrate how these approaches to hypertension control are being implemented in LMICs.

### Community Engagement

Health care delivery and health systems often fail to meet the needs and expectations of those who need them.<sup>6,7</sup> Community engagement seeks to address this problem by optimizing the appropriateness and alignment of health care to the cultural, social, economic, and environmental setting.<sup>8,9</sup> It encompasses participation, mobilization, and

empowerment (Figure 1).<sup>10</sup> Participation refers to the active or passive engagement of the community in health services.<sup>10, 11</sup> Mobilization furthers this engagement through facilitation by health professionals, while empowerment involves a capacity-building process to engage communities in planning, implementing and/or evaluating activities to achieve more sustainable health improvements.<sup>10, 11</sup> Community engagement has shown promise in supporting interventions to improve health outcomes related to both HIV/AIDS as well as maternal and child health.<sup>12, 13</sup> However, traditional methods for determining efficacy of community engagement are inadequate because there are significant challenges in teasing out the independent effects of the intervention vis a vis the process of community engagement itself.

Four GACD projects described herein have been conducted in Tanzania, Kenya, Colombia, Malaysia, India, and Canada. The investigators of these GACD projects have adopted a diverse range of community engagement activities, targeted at both individuals and systems, in order to identify barriers and facilitators for the care of hypertension, and thereby tailor the intervention to the local context (Table 1). Prior to initiating each of these studies, investigators and research staff met with community leaders, health personnel, and other relevant community stakeholders, to facilitate entry to the communities and to appropriately contextualize their approaches. Components of community engagement included (1) individual interviews with diverse stakeholders; (2) focus group discussions (FGDs) with hypertension patients; (3) workshops with local community health workers (CHWs) and clinicians to refine the intervention and training materials, thus enhancing the capacity of CHWs to deliver the intervention by employing relevant and easy-to-use tools; (4) community social events and gatherings; and (5) *mabaraza* (singular *baraza*), traditional East African community gatherings, conducted among individuals with elevated blood pressure and CHWs to complement the purposive sampling inherent in FGDs.<sup>14</sup> The *baraza* is a unique and novel qualitative research setting which has been used as a form of participatory action research, and allows organization of a diverse and heterogeneous large group of individuals.<sup>15</sup> In Tanzania and Canada, the team used an adapted tool called I-RREACH: Intervention and Research Readiness Engagement and Assessment of Community Health Care.<sup>16</sup> This tool was developed using a community-based consensus method, and is rooted in participatory principles, equalizing the importance of the knowledge and perspectives of researchers and community stakeholders while encouraging respectful dialogue. The I-RREACH tool is an engagement and assessment tool for improving the implementation readiness of researchers, organizations and communities in complex interventions, and consists of three phases: fact finding, stakeholder dialogue, and community member/patient dialogue. Another study being conducted in Canada, Malaysia, and Colombia leveraged non-medical community events for the purposes of screening, recruitment, intervention implementation, and follow-up. Using process evaluation, the GACD projects hope to add to our understanding of how community engagement can be used to support and strengthen programs aimed at improving hypertension control. Such an approach can be applied to more chronic diseases in low-resource settings worldwide.

The need for this research is illustrated by work elsewhere. Although it may seem self-evident that a more participatory approach will improve the acceptability, and thus effectiveness of interventions, this is not fully supported by the evidence. Two projects

conducted in Cape Town, South Africa, and El Paso, Texas, used community-based participatory research approaches to design an intervention to manage hypertension and diabetes.<sup>17, 18</sup> Positive results included: 1) improved self-efficacy to manage hypertension, 2) greater improvements in health behaviours in the intervention group than in the control group,<sup>18</sup> 3) the development of culturally appropriate health education materials specifically developed for low-literacy populations,<sup>18</sup> and 4) inclusion of learnings into local health sector planning for prevention and control of hypertension and diabetes.<sup>17</sup> Although the authors stated that the materials were well received by participants in one study,<sup>18</sup> no evidence for clinical success of community engagement was provided in either study.<sup>17, 18</sup>

## Salt Reduction

Evidence shows that a reduction in the consumption of sodium—found in table salt and naturally occurring foods such as milk, eggs, meat, and shellfish—decreases blood pressure in adults and diminishes the risk of CVD.<sup>19, 20</sup> While there is controversy about the most appropriate target for sodium intake, higher sodium intake in general is associated with poorer outcomes.<sup>21</sup> The World Health Organization (WHO) recommends a reduction in sodium intake to < 2 g/day in adults.<sup>22</sup> In 2013, member states of the United Nations established a target to reduce the average population salt intake by 30% by 2025,<sup>23</sup> and 75 countries now have strategies in place to achieve this target.<sup>24</sup> The majority of these national programs are multifaceted and include initiatives such as industry engagement to lower salt content in foods, consumer education and awareness, establishing front-of-pack labelling schemes and nutrition standards for foods procured in public settings.

Three of the GACD Hypertension programs have implemented innovative salt reduction programs to reduce blood pressure. The first step in any program is to measure existing consumption patterns. These projects measured salt intake using 24-hour urine excretion and tried to understand people's knowledge and eating behaviors through community surveys. Average daily salt excretion at baseline varied from 7 gm (Samoa);<sup>25</sup> 11 gm (Fiji); 9.5 gm and 8.6 gm (Andhra Pradesh and Delhi/Haryana, respectively, India); to 12.6 gm (Shanxi, China). The information on diet was then used to inform the different intervention strategies. Based on the WHO's framework for Creating an Enabling Environment for Salt reduction,<sup>26</sup> the project in Fiji and Samoa used multi-faceted intervention programs to reduce salt in the food supply, while concurrently implementing media and community mobilization campaigns to increase awareness (Figure 2).<sup>27</sup> A parallel project in Andhra Pradesh and Delhi/Haryana, India, used community surveys and stakeholder mapping and established a comprehensive food composition database (based on the George Institute's leading FoodSwitch innovation for monitoring the food supply and identifying healthy choices).<sup>28</sup> This information is being used to inform the development of a government-led salt reduction strategy for India. The Little Emperor project in China trained children to encourage their parents to reduce salt intake. Implemented in the northern province of Shanxi, the researchers taught the children about the harmful effects of a salty diet and asked them to share the messages with adults back home. Innovative children's approaches including hiding the salt pot, making up rhymes or using their status as "Little Emperors" to refuse to eat unhealthy foods, led to a 26% reduction in participants' salt intake in less than 4 months.<sup>29</sup> More than 270 million people currently have hypertension in China; therefore, if

applied nationally, such a strategy could have substantial health and potential economic benefits.

Post-intervention monitoring in Fiji and Samoa is being finalized and has been supplemented through an in-depth process evaluation to better understand how the interventions have been implemented and potential barriers to effectiveness. Some of the challenges have included the changing political environment, difficulties of multi-sectoral action and limited experience in engaging the food industry. Mainstreaming the agendas with the Health Ministries in the different countries has been key to overcoming some of these problems. The lessons are being documented and will be disseminated widely through the WHO Collaborating Centre for Population Salt Reduction at the George Institute for Global Health, thus supporting rapid and effective translation of research into policy and practice. These and other studies will help to elucidate and clarify the relationship between sodium reduction and CVD.

### Salt substitution

In addition to salt reduction, salt substitution is an innovative, non-pharmacological approach to reduce blood pressure. It involves the partial replacement of sodium chloride with any combination of other salt containing potassium, magnesium, or aluminum. A meta-analysis from six randomized controlled trials using different combinations of salt substitute in comparison to usual salt found, in pooled results, that a salt substitute reduced systolic blood pressure by  $-4.9$  mm Hg (95% CI:  $-7.3, -2.5$ ) and diastolic blood pressure  $-1.5$  mm Hg (95% CI:  $-2.7, -0.3$ ). However, in the subgroup analysis, the effect was significant only among individuals with hypertension.<sup>30</sup>

One of the GACD projects, conducted in Peru,<sup>31</sup> is using a population-wide approach to test the effect on blood pressure of replacing regular salt by an iodine-fortified substitute containing 25% potassium chloride and 75% sodium chloride. This involves a pragmatic stepped wedge trial design, in which the intervention is progressively implemented at random in six villages. The study has been implemented in two phases (Figure 3). The first phase was exploratory and included: (a) formative in-depth interviews and FGDs; (b) a triangle taste test, which found that a salt with 25% of potassium chloride was indistinguishable from regular salt;<sup>32</sup> and (c) the development of the social marketing campaign targeting primarily women responsible for cooking at their home, and focused on promoting consumption and adherence of participants to the potassium-enriched salt. The second phase involved implementation of the intervention. The salt substitute has progressively replaced the common salt used in households, relying heavily on the social marketing/branding campaign as well as educational entertainment delivered by trained community health workers. Salt replacement has been implemented at households, bakeries, community kitchens and restaurants in each village.

Previous salt substitute strategies have focused on delivering the salt substitute product among participants with a diagnosis of hypertension, focusing almost exclusively on the hypertension status of the participant rather than on the product's concept. For instance, the salt substitute used in other studies were no different between intervention and control arms

(i.e. bags were identical in appearance; products were manufactured, packaged, and labeled by the same company).<sup>33–35</sup> The novelty of the Peru study relies on the implementation mechanisms that were developed and put in place, at the community level, aiming to increase the uptake of the salt substitute product as well as ensuring its sustained use over time in populations irrespective of hypertension status. To date, acceptability of the salt substitute to participants has been successful with very low rates of adverse effects related to its use. The study is ongoing and the fourth wedge has been concluded, with expected outcomes in early 2017. If successful, this project's implementation approach may serve as a model for other LMIC settings.

## Task Redistribution

In most countries, primary care physicians are the main providers of healthcare for individuals with CVD. Unfortunately, most LMICs have an inadequate number of physicians, especially in rural and remote regions where a majority of the population reside.<sup>36, 37</sup> According to the WHO Global Health Observatory, there are 0.3 physicians available for every 1000 population in low income countries, 1.2 physicians per 1000 population in lower-middle income countries, and 2.0 per 1000 population in upper-middle income countries.<sup>38</sup> In response to this physician workforce shortage, appropriate strategies for task redistribution—from doctors to a team consisting of doctors and trained non-physician health workers (NPHWs)—have been developed and implemented, especially in the areas of maternal and child health needs,<sup>39, 40</sup> and HIV/AIDS.<sup>41</sup>

Task redistribution describes a situation where a task normally performed by a physician is shared between physicians and other health workers with a different or lower level of education and training (Figure 4).<sup>42</sup> Task redistribution may be aided by technology, clear guidelines, or close supervision by physicians, to help standardize the performance and interpretation of certain tasks, therefore allowing them to be performed by NPHWs.<sup>43</sup> Systematic reviews on task-redistribution for CVD management,<sup>44, 45</sup> indicate that not many studies have been conducted to test the effectiveness of task redistribution, and that further operational research, including detailed process evaluation, is required to understand the complexity, effectiveness, and cost-effectiveness of task-redistribution within different country contexts. Recent studies involving task-redistribution have shown that NPHWs can be effectively trained in the implementation of CVD prevention and management guidelines,<sup>46, 47</sup> successfully screen individuals at high-risk of CVD,<sup>48, 49</sup> provide lifestyle education and adherence to patients,<sup>50</sup> and support patients with acute coronary syndrome.<sup>51</sup> This approach has also been shown to be cost-effective for chronic disease care in the LMIC context.<sup>52, 53</sup> While there are now some published studies concerning the effectiveness of task-redistribution, there remain large evidence gaps and obstacles regarding the translation of positive research findings into routine health care delivery in LMICs, while also ensuring quality of care, safety, and patient acceptability. These shortcomings notwithstanding, task redistribution for the prevention and control of hypertension and other chronic diseases presents a great opportunity that could increase access to care, reduce health care costs, free up physician time for other tasks, and increase system efficiency in the long-term.

Eight of the GACD projects included a component of task redistribution for the detection and management of hypertension. These include the redistribution of tasks related to hypertension screening, referral to clinicians, providing lifestyle advice, and support for adherence to medications to NPHWs. All the studies supported NPHWs by training them for two to six days, followed by re-training where required.<sup>14, 54, 55</sup> Some studies facilitated task redistribution by using mHealth technology,<sup>14, 56</sup> whereby NPHWs used electronic decision support tools to screen individuals in the community and link them to hypertension care. Process and interim evaluations have identified that the main barriers to task-redistribution include resistance from other health professionals; increasing NPHW workload due to additional tasks; complexity of training materials; health system-related issues such as non-availability or non-functioning BP machines, poor drug supply, lack of physician availability for referral; regulatory restrictions including the inability to prescribe medications; and low remuneration of NPHWs.<sup>57</sup> The key enablers included an increase in the enthusiasm and motivation of NPHWs to be trained and take on new roles, as well as a reduction in the physician workload leading to improved performance. All of these studies are currently in progress and will have effectiveness and cost-effectiveness results in the near future.

## mHealth

mHealth is the use of mobile phones to improve and support health, and can be used for a variety of purposes to connect clinicians, other health workers including CHWs, and patients or patient caregivers (Figure 6). mHealth can be used to provide health education, promote behavior change, facilitate decision support in diagnosis and management of a wide variety of conditions, support diagnostic testing, or link medical records.<sup>58</sup> Evidence for benefits of mHealth is widespread among a variety of high-income country settings, and further data are emerging on the use of mHealth in LMICs with respect to the impact on clinical outcomes, processes of care, health care costs and health related quality of life.<sup>59–61</sup> There is great potential for the use of mHealth for hypertension management in LMICs as mobile phone ownership is high and growing rapidly, even among the poor.<sup>62</sup> However, there still remain research gaps with a relatively limited number of studies in this area, particularly in hypertension.

Five projects within the GACD research network have a mHealth component at their core, or in conjunction with other innovations, in order to address barriers within health systems and to optimize opportunities for the detection and management of hypertension. The projects are taking place in communities in rural Kenya,<sup>14</sup> rural Tanzania, both urban and rural Colombia and Malaysia, rural and remote Aboriginal communities in Canada, Nigeria,<sup>63</sup> and rural India. All of the projects are utilizing either a smartphone- or tablet-based tool designed for use by community health workers (CHWs) to improve hypertension care; facilitate improved identification, follow-up, and tracking of patients; promote adherence to medications; and improve education of patients and CHWs. All of the programs have a component of real-time decision support. In addition, the Nigerian and Tanzanian/Canada program also send educational, behaviour change communication messages via text message directly to patients' mobile phones, while the India project uses interactive voice response messaging because text messaging was not acceptable in this setting. The Kenya and India



projects embed educational messaging in novel audio-visual formats, so that CHWs can share these audio-visual materials to patients during home visits.

Some unique features among the mHealth innovations and programs should be highlighted. The programs in Kenya and India use an open-source platform called Open Data Kit, which has been utilized successfully to provide clinical decision source tools for HIV care. The Indian program also provides access to a mobile device that allows primary care physicians in government health clinics to access the health information of participants screened by CHWs; the device offers decision support for those participants identified at high CVD risk. This feature is also a component of the Tanzania-Canada program, whereby health center nurses and clinical officers can access all BP measurements taken for a patient by CHWs. A substudy of the Tanzania project is also evaluating the effectiveness of a phone-based drug voucher program to ensure the authenticity of drug supply and adherence factors in hypertension control. The Nigerian program is targeting patients who have experienced a stroke, who are at high risk for another stroke. Across the programs there have been common challenges, which include both technical and human factors. Technical factors have included mobile network coverage and server issues. Human factors have included overcoming end-user challenges with the new technology, as well as implementation delays due to government approval processes, equipment procurement delays, misalignment of incentives, competing obligations, and excessive workload for the health providers who are utilizing these new systems.

### **Polypill – Fixed-dose Combination Therapy**

Most patients with hypertension generally require blood pressure (BP) lowering medication from multiple classes to achieve adequate control.<sup>64</sup> The need for titration of medication and addition of multiple classes of drug requires multiple physician visits and this in itself can lead to poor adherence to prescribed medication and poor attendance at scheduled visits.<sup>65</sup> The requirement to take multiple medications in complex regimes also encourages poor adherence.<sup>66</sup> For physicians, the need for repeated up-titrating or adding extra medications can lead to inertia and tacit acceptance of inadequate BP control.<sup>67, 68</sup> Initiating anti-hypertensive treatment with dual combination therapy not only accelerates the time taken to achieve control but also attains a lower final target.<sup>69, 70</sup> For the patient, improved adherence has also been demonstrated without worsening the side effect profile.<sup>71</sup> Further benefits in BP control can also result from simplifying up-titration regimes.<sup>70</sup>

Use of multi-modal fixed-dose combination pills (FDCs)—also known as ‘polypills’—containing not only multiple low-dose blood pressure-lowering drugs, but also statins and aspirin, has the potential to reduce a person’s cardiovascular risk beyond that achieved by simply lowering their blood pressure, by addressing multiple risk factors concurrently in a single pill. Multiple large clinical trials have shown that use of ‘polypills’ in patients at high risk of CVD improves adherence to long-term medication with consequent improvements in cholesterol and blood pressure measurements, and are highly acceptable to patients and physicians alike (Figure 5).<sup>72, 73</sup> The recently published HOPE-3 study utilized a polypill type strategy in patients at moderate CVD risk and showed a significant reduction in CV events in patients with hypertension.<sup>74</sup> While reducing BP was a benefit only in those in the

hypertensive range, lowering cholesterol had beneficial effects in reducing fatal and non-fatal cardiovascular events overall.<sup>75</sup> Evidence is needed, however, on the implementation of such a strategy in real-life clinical contexts rather within the constraints of a highly regulated clinical trial.

The GACD has funded two projects looking at whether use of FDCs will improve management of hypertension, and also overall CVD risk, in real-life clinical contexts in several LMICs. The **TRI**ple Pill vs. **U**sual care **M**anagement for **P**atients with mild-to-moderate **H**ypertension (TRIUMPH) study,<sup>76</sup> is a prospective, open, randomized controlled clinical trial (n=700) of a fixed dose combination blood pressure-lowering pill (“Triple Pill”)-based strategy compared to usual care among individuals with persistent mild-to-moderate hypertension on no or minimal drug therapy. The aim is to see whether early use of low dose FDC medications will result in faster and better control of blood pressure. The HOPE-4 study, being conducted in 50 urban and rural communities in Canada, Colombia, and Malaysia, is implementing and evaluating (compared to usual care) an evidence-based, contextually-appropriate program for CVD risk assessment, treatment and control involving simplified algorithms implemented by NPHWs, supported by e-health technologies; initiation of FDC of two antihypertensive drugs plus one statin; and use of treatment supporters to optimize long-term medication and lifestyle adherence. Both studies are ongoing with outcomes anticipated in the near future.

The use of a simplified strategy utilizing early introduction of inexpensive generic FDC pills (or ‘polypills’) is an approach with important potential to impact on what are currently exceedingly poor blood pressure control rates in LMICs. If found to be effective, cost-effective, and acceptable, this approach has the potential to impact the cardiovascular health of significant numbers of individuals around the world.

## Discussion

Elevated blood pressure is the leading global risk for mortality,<sup>1</sup> and novel approaches for improving hypertension control are urgently required for LMICs. The GACD hypertension studies described here are beginning to disseminate outcomes, results, and lessons in relation to several different innovative approaches. In addition, they are well-poised to develop post-study knowledge translation strategies. Finally, the GACD researchers have the potential to engage policy makers, payers, and other stakeholders, to translate the findings of individual research studies into sustainable and scalable interventions. Each GACD-funded project has designed one or more innovative approaches to enable the implementation and evaluation of interventions within local contexts, in order to improve care without significant disruption to, and increased workload of, already over-burdened health workers and health care systems.

All of the approaches described here have the potential to improve the cardiovascular health of populations in low-resource settings worldwide. Community engagement is a critical part of developing and introducing any new program, and increases the likelihood of successful uptake and implementation. Salt reduction and salt substitutes can reduce blood pressure and improve cardiovascular health, especially if combined with improved dietary intake of fresh

fruits and vegetables. Task redistribution expands the reach of delegated medical acts, empowers and engages community members, improves health literacy of communities, and improves the efficiency of the existing pool of health care providers. mHealth can additionally provide decision support, remote medical record access, and novel educational interfaces, all of which can enhance care delivery in resource-limited settings. Finally, FDC pills have the potential to transform the landscape of medical management of hypertension and CVD. The studies outlined in this report demonstrate innovative and practical methods of implementing all of these strategies for hypertension control in diverse environments and contexts worldwide.

## Acknowledgments

The writing group would like to thank Gary Parker from the GACD Secretariat for invaluable logistical and administrative support, and Drs. Clara Chow, Pallab Maulik, and Martin McKee for critical review of the manuscript. They would also like to thank all members of the GACD Hypertension Research Program for their support and input throughout the preparation of this manuscript. Funding for the studies described and for manuscript submission was provided by the following GACD Hypertension Program funding agencies: Canadian Institutes of Health Research (Grant No. 120389); Grand Challenges Canada (Grant Nos. 0069-04, and 0070-04); International Development Research Centre; Canadian Stroke Network; Australian National Health and Medical Research Council (Grant Nos. ID 1040147, and 104018); the US National Institutes of Health (National Heart, Lung and Blood Institute and National Institute of Neurological Disorders and Stroke) (Grant Nos. U01 HL114200, U01 NS079179, and U01 HL114180); the United Kingdom Medical Research Council (Grant Nos. APP 1040179, APP 1041052, and J01 60201); the Malaysian Ministry of Higher Education (Long-term Research Grants Scheme); and the South African Medical Research Council. This report does not represent the official view of the National Institute of Neurological Disorders and Stroke, the National Institutes of Health, or any part of the US Federal Government. No official support or endorsement of this article by the National Institutes of Health is intended or should be inferred.

## Abbreviations

<b>BP</b>	Blood Pressure
<b>CHW</b>	Community Health Workers
<b>CVD</b>	Cardiovascular Disease
<b>FDC</b>	Fixed-Dose Combination Pills
<b>FGD</b>	Focus Group Discussions
<b>GACD</b>	Global Alliance for Chronic Diseases
<b>I-RREACH</b>	Intervention and Research Readiness Engagement and Assessment of Community Health Care
<b>LMIC</b>	Low- and Middle-Income Countries
<b>NPHW</b>	Non-physician Health Workers
<b>TRIUMPH</b>	<b>TRI</b> ple Pill vs. Usual care <b>M</b> anagement for <b>P</b> atients with mild-to- moderate <b>H</b> ypertension
<b>WHO</b>	World Health Organization

## References

1. Lim SS, Vos T, Flaxman AD, 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*. 2012; 380(9859):2224–2260. [PubMed: 23245609]
2. Lewington S, Clarke R, Qizilbash N, et al. Age-specific relevance of usual blood pressure to vascular mortality: a meta-analysis of individual data for one million adults in 61 prospective studies. *Lancet*. 2002; 360(9349):1903–1913. [PubMed: 12493255]
3. Chow CK, Teo KK, Rangarajan S, et al. Prevalence, awareness, treatment, and control of hypertension in rural and urban communities in high-, middle-, and low-income countries. *JAMA : the journal of the American Medical Association*. 2013; 310(9):959–968. [PubMed: 24002282]
4. [Accessed 5/20/2016] Disease GAfC. <http://www.gacd.org/about/history/howeare>
5. Tobe W. S, the Global Alliance for Chronic Diseases Hypertension Research Teams With the World Hypertension L. The Global Alliance for Chronic Diseases Supports 15 Major Studies in Hypertension Prevention and Control in Low- and Middle-Income Countries. *The Journal of Clinical Hypertension*. 2016 n/a-n/a.
6. Khatib R, Schwalm JD, Yusuf S, et al. Patient and healthcare provider barriers to hypertension awareness, treatment and follow up: a systematic review and meta-analysis of qualitative and quantitative studies. *PLoS One*. 2014; 9(1):e84238. [PubMed: 24454721]
7. Maimaris W, Paty J, Perel P, et al. The influence of health systems on hypertension awareness, treatment, and control: a systematic literature review. *PLoS Med*. 2013; 10(7):e1001490. [PubMed: 23935461]
8. Digiacomio M, Abbott P, Davison J, et al. Facilitating uptake of Aboriginal Adult Health Checks through community engagement and health promotion. *Quality in primary care*. 2010; 18(1):57–64.
9. National Institute for Health and Care Excellence. Community engagement to improve health. United Kingdom: National Institute for Health and Care Excellence; 2014. (downloaded from <https://www.nice.org.uk/guidance/Igb16/resources/communityengagement-to-improve-health-60521149786309> 14 May 2016).
10. Rosato M, Laverack G, Grabman LH, et al. Community participation: lessons for maternal, newborn, and child health. *Lancet*. 2008; 372(9642):962–971. [PubMed: 18790319]
11. Joint United Nations Programme on HIV/AIDS (UNAIDS). Promising practices in community engagement for elimination of new HIV infections among children by 2015 and keeping their mothers alive. Geneva, Switzerland: UNAIDS; 2012. (dowbloaded from [http://www.unaids.org/sites/default/files/media\\_asset/20120628\\_JC2281\\_PromisingPracticesCommunityEngagements\\_en\\_0.pdf](http://www.unaids.org/sites/default/files/media_asset/20120628_JC2281_PromisingPracticesCommunityEngagements_en_0.pdf) 15 May 2016)
12. Rifkin SB. Examining the links between community participation and health outcomes: a review of the literature. *Health policy and planning*. 2014; 29(Suppl 2):ii98–106. [PubMed: 25274645]
13. Marston C, Renedo A, McGowan CR, et al. Effects of community participation on improving uptake of skilled care for maternal and newborn health: a systematic review. *PloS one*. 2013; 8(2):e55012. [PubMed: 23390509]
14. Vedanthan R, Kamano JH, Naanyu V, et al. Optimizing linkage and retention to hypertension care in rural Kenya (LARK hypertension study): study protocol for a randomized controlled trial. *Trials*. 2014; 15(1):143. [PubMed: 24767476]
15. Naanyu V, Vedanthan R, Kamano JH, et al. Barriers Influencing Linkage to Hypertension Care in Kenya: Qualitative Analysis from the LARK Hypertension Study. *Journal of general internal medicine*. 2016; 31(3):304–314. [PubMed: 26728782]
16. Maar M, Yeates K, Barron M, et al. I-RREACH: an engagement and assessment tool for improving implementation readiness of researchers, organizations and communities in complex interventions. *Implement Sci*. 2015; 10:64. [PubMed: 25935849]
17. Bradley HA, Puoane T. Prevention of hypertension and diabetes in an urban setting in South Africa: participatory action research with community health workers. *Ethnicity & disease*. 2007; 17(1):49–54. [PubMed: 17274209]

18. Balcazar HG, Byrd TL, Ortiz M, et al. A randomized community intervention to improve hypertension control among Mexican Americans: using the promotoras de salud community outreach model. *Journal of health care for the poor and underserved*. 2009; 20(4):1079–1094. [PubMed: 20168020]
19. He FJ, Li J, Macgregor GA. Effect of longer term modest salt reduction on blood pressure: Cochrane systematic review and meta-analysis of randomised trials. *Bmj*. 2013; 346:f1325. [PubMed: 23558162]
20. Aburto NJ, Ziolkovska A, Hooper L, et al. Effect of lower sodium intake on health: systematic review and meta-analyses. *Bmj*. 2013; 346:f1326. [PubMed: 23558163]
21. Reducing salt intake in populations: report of a WHO forum and technical meeting. Geneva: World Health Organization; 2007.
22. Guideline: Sodium intake for adults and children. Geneva: World Health Organization; 2012.
23. WHO. [accessed February 17, 2013] Monitoring framework and targets for the prevention and control of NCDs. Revised WHO discussion paper on the development of a comprehensive global monitoring framework, including indicators, and a set of voluntary global targets for the prevention and control of NCDs. Jul 25. 2012 [http://www.who.int/nmh/events/2012/discussion\\_paper3.pdf](http://www.who.int/nmh/events/2012/discussion_paper3.pdf)
24. Trieu K, Neal B, Hawkes C, et al. Salt Reduction Initiatives around the World - A Systematic Review of Progress towards the Global Target. *PloS one*. 2015; 10(7):e0130247. [PubMed: 26201031]
25. Webster J, Su'a SA, Ieremia M, et al. Salt Intakes, Knowledge, and Behavior in Samoa: Monitoring Salt-Consumption Patterns Through the World Health Organization's Surveillance of Noncommunicable Disease Risk Factors (STEPS). *Journal of clinical hypertension*. 2016
26. The World Health Organization. Creating an enabling environment for population-based salt reduction strategies. World Health Organization; 2011.
27. Webster J, Snowdon W, Moodie M, et al. Cost-effectiveness of reducing salt intake in the Pacific Islands: protocol for a before and after intervention study. *BMC public health*. 2014; 14:107. [PubMed: 24495646]
28. Dunford E, Trevena H, Goodsell C, et al. FoodSwitch: A Mobile Phone App to Enable Consumers to Make Healthier Food Choices and Crowdsourcing of National Food Composition Data. *JMIR mHealth and uHealth*. 2014; 2(3):e37. [PubMed: 25147135]
29. He FJ, Wu Y, Feng XX, et al. School based education programme to reduce salt intake in children and their families (School-EduSalt): cluster randomised controlled trial. *Bmj*. 2015; 350:h770. [PubMed: 25788018]
30. Peng YG, Li W, Wen XX, et al. Effects of salt substitutes on blood pressure: a meta-analysis of randomized controlled trials. *The American journal of clinical nutrition*. 2014; 100(6):1448–1454. [PubMed: 25411279]
31. Bernabe-Ortiz A, Diez-Canseco F, Gilman RH, et al. Launching a salt substitute to reduce blood pressure at the population level: a cluster randomized stepped wedge trial in Peru. *Trials*. 2014; 15:93. [PubMed: 24667035]
32. Saavedra-Garcia L, Bernabe-Ortiz A, Gilman RH, et al. Applying the Triangle Taste Test to Assess Differences between Low Sodium Salts and Common Salt: Evidence from Peru. *PloS one*. 2015; 10(7):e0134700. [PubMed: 26225848]
33. Salt substitution: a low-cost strategy for blood pressure control among rural Chinese. A randomized, controlled trial. *J Hypertens*. 2007; 25(10):2011–2018. [PubMed: 17885542]
34. Zhou X, Liu JX, Shi R, et al. Compound ion salt, a novel low-sodium salt substitute: from animal study to community-based population trial. *American journal of hypertension*. 2009; 22(9):934–942. [PubMed: 19661926]
35. Zhao X, Yin X, Li X, et al. Using a low-sodium, high-potassium salt substitute to reduce blood pressure among Tibetans with high blood pressure: a patient-blinded randomized controlled trial. *PloS one*. 2014; 9(10):e110131. [PubMed: 25338053]
36. World Health Organization. World Health Report 2006: Working together for health. Geneva: WHO; 2006.

37. Ministry of Health and Family Welfare. Rural Health Statistics Bulletin, March 2010. New Delhi: Government of India; 2010.
38. World Health Organisation. [Accessed 13.5.16, 2016] Density of physicians (total number per 1000 population, latest available year). Global Health Observatory Data. [http://www.who.int/gho/health\\_workforce/physicians\\_density\\_text/en/](http://www.who.int/gho/health_workforce/physicians_density_text/en/)
39. Deller B, Tripathi V, Stender S, et al. Task shifting in maternal and newborn health care: Key components from policy to implementation. *International Journal of Gynecology & Obstetrics*. 2015; 130(Supplement 2):S25–S31. [PubMed: 26115853]
40. Dawson AJ, Buchan J, Duffield C, et al. Task shifting and sharing in maternal and reproductive health in low-income countries: a narrative synthesis of current evidence. *Health policy and planning*. 2013
41. World Health Organization. Task shifting to tackle health worker shortages. 2007.
42. Lekoubou A, Awah P, Fezeu L, et al. Hypertension, Diabetes Melitus and task shifting and their management in Sub-saharan Africa. *Int J Environ Res Public Health*. 2010; 7:353–363. [PubMed: 20616978]
43. 60th WMA General Assembly. WMA Resolution on Task Shifting from the Medical Profession. New Delhi: World Medical Association; 2009.
44. Joshi R, Alim M, Kengne AP, et al. Task Shifting for Non-Communicable Disease Management in Low and Middle Income Countries? A Systematic Review. *PloS one*. 2014; 9(8):e103754. [PubMed: 25121789]
45. Ogedegbe G, Gyamfi J, Plange-Rhule J, et al. Task shifting interventions for cardiovascular risk reduction in low-income and middle-income countries: a systematic review of randomised controlled trials. *BMJ open*. 2014; 4(10):e005983.
46. Gaziano TA, Abrahams-Gessel S, Denman CA, et al. An assessment of community health workers' ability to screen for cardiovascular disease risk with a simple, non-invasive risk assessment instrument in Bangladesh, Guatemala, Mexico, and South Africa: an observational study. *The Lancet Global Health*. 2015; 3(9):e556–e563. [PubMed: 26187361]
47. Akinyemi RO, Owolabi MO, Adebayo PB, et al. Task-shifting training improves stroke knowledge among Nigerian non-neurologist health workers. *Journal of the neurological sciences*. 2015; 359(1–2):112–116. [PubMed: 26671098]
48. Joshi R, Chow C, Raju PK, et al. The Rural Andhra Pradesh Cardiovascular Prevention Study. *JACC*. 2012; 59(13):1188–1196. [PubMed: 22440219]
49. Kar SS, Thakur JS, Jain S, et al. Cardiovascular disease risk management in a primary health care setting of north India. *Indian heart journal*. 2008; 60(1):19–25. [PubMed: 19212017]
50. Jafar TH, Islam M, Hatcher J, et al. Community based lifestyle intervention for blood pressure reduction in children and young adults in developing country: cluster randomised controlled trial. *Bmj*. 2010:340.
51. Xavier D, Gupta R, Kamath D, et al. Community health worker-based intervention for adherence to drugs and lifestyle change after acute coronary syndrome: a multicentre, open, randomised controlled trial. *The Lancet Diabetes & Endocrinology*. 4(3):244–253.
52. Gaziano T, Abrahams-Gessel S, Surka S, et al. Cardiovascular Disease Screening By Community Health Workers Can Be Cost-Effective In Low-Resource Countries. *Health affairs (Project Hope)*. 2015; 34(9):1538–1545. [PubMed: 26355056]
53. Buttorff C, Hock RS, Weiss HA, et al. Economic evaluation of a task-shifting intervention for common mental disorders in India. *Bull World Health Organ*. 2012; 90:813–821. [PubMed: 23226893]
54. Thorogood M, Goudge J, Bertram M, et al. The Nkateko health service trial to improve hypertension management in rural South Africa: study protocol for a randomised controlled trial. *Trials*. 2014; 15:435. [PubMed: 25380994]
55. Ogedegbe G, Plange-Rhule J, Gyamfi J, et al. A cluster-randomized trial of task shifting and blood pressure control in Ghana: study protocol. *Implementation science : IS*. 2014; 9:73. [PubMed: 24923300]
56. Praveen D, Patel A, McMahon S, et al. A multifaceted strategy using mobile technology to assist rural primary healthcare doctors and frontline health workers in cardiovascular disease risk

management: protocol for the SMARTHealth India cluster randomised controlled trial. *Implementation science* : IS. 2013; 8:137. [PubMed: 24274431]

57. Praveen D, Patel A, Raghu A, et al. SMARTHealth India: Development and Field Evaluation of a Mobile Clinical Decision Support System for Cardiovascular Diseases in Rural India. *JMIR mHealth and uHealth*. 2014; 2(4):e54. [PubMed: 25487047]
58. Piette JD, List J, Rana GK, et al. Mobile Health Devices as Tools for Worldwide Cardiovascular Risk Reduction and Disease Management. *Circulation*. 2015; 132(21):2012–2027. [PubMed: 26596977]
59. Peiris D, Praveen D, Johnson C, et al. Use of mHealth systems and tools for non-communicable diseases in low- and middle-income countries: a systematic review. *Journal of cardiovascular translational research*. 2014; 7(8):677–691. [PubMed: 25209729]
60. Bloomfield GS, Vedanthan R, Vasudevan L, et al. Mobile health for non-communicable diseases in Sub-Saharan Africa: a systematic review of the literature and strategic framework for research. *Globalization and health*. 2014; 10:49. [PubMed: 24927745]
61. Beratarrechea A, Lee AG, Willner JM, et al. The impact of mobile health interventions on chronic disease outcomes in developing countries: a systematic review. *Telemedicine journal and ehealth* : the official journal of the American Telemedicine Association. 2014; 20(1):75–82.
62. Okoro E, Sholagberu H, Kolo P. Mobile phone ownership among Nigerians with diabetes. *African Health Sciences*. 2010; 10(2):183–186. [PubMed: 21326973]
63. Owolabi MO, Akinyemi RO, Gebregziabher M, et al. Randomized controlled trial of a multipronged intervention to improve blood pressure control among stroke survivors in Nigeria. *International journal of stroke* : official journal of the International Stroke Society. 2014; 9(8): 1109–1116. [PubMed: 25042605]
64. Cushman WC, Ford CE, Einhorn PT, et al. Blood pressure control by drug group in the Antihypertensive and Lipid-Lowering Treatment to Prevent Heart Attack Trial (ALLHAT). *Journal of clinical hypertension*. 2008; 10(10):751–760. [PubMed: 19090876]
65. Johnston A, Stafylas P, Stergiou GS. Effectiveness, safety and cost of drug substitution in hypertension. *British journal of clinical pharmacology*. 2010; 70(3):320–334. [PubMed: 20716230]
66. Shaw E, Anderson JG, Maloney M, et al. Factors associated with noncompliance of patients taking antihypertensive medications. *Hosp Pharm*. 1995; 30(3):201–203. [PubMed: 10140764]
67. Faria C, Wenzel M, Lee KW, et al. A narrative review of clinical inertia: focus on hypertension. *Journal of the American Society of Hypertension* : JASH. 2009; 3(4):267–276. [PubMed: 20409968]
68. Okonofua EC, Simpson KN, Jesri A, et al. Therapeutic inertia is an impediment to achieving the Healthy People 2010 blood pressure control goals. *Hypertension*. 2006; 47(3):345–351. [PubMed: 16432045]
69. Brown MJ, McInnes GT, Papst CC, et al. Aliskiren and the calcium channel blocker amlodipine combination as an initial treatment strategy for hypertension control (ACCELERATE): a randomised, parallel-group trial. *Lancet*. 2011; 377(9762):312–320. [PubMed: 21236483]
70. Feldman RD, Zou GY, Vandervoort MK, et al. A Simplified Approach to the Treatment of Uncomplicated Hypertension: A Cluster Randomized, Controlled Trial. *Hypertension*. 2009; 53(4):646–653. [PubMed: 19237683]
71. Gupta AK, Arshad S, Poulter NR. Compliance, safety, and effectiveness of fixed-dose combinations of antihypertensive agents: a meta-analysis. *Hypertension*. 2010; 55(2):399–407. [PubMed: 20026768]
72. Webster R, Patel A, Selak V, et al. Effectiveness of fixed dose combination medication ('polypills') compared with usual care in patients with cardiovascular disease or at high risk: A prospective, individual patient data meta-analysis of 3140 patients in six countries. *International journal of cardiology*. 2016; 205:147–156. [PubMed: 26736090]
73. Castellano JM, Sanz G, Penalvo JL, et al. A polypill strategy to improve adherence: results from FOCUS (Fixed-dose Combination Drug for Secondary Cardiovascular Prevention) Project. *Journal of the American College of Cardiology*. 2014

74. Lonn EM, Bosch J, López-Jaramillo P, et al. Blood-Pressure Lowering in Intermediate-Risk Persons without Cardiovascular Disease. *New England Journal of Medicine*. 0(0):null.
75. Yusuf S, Lonn E, Pais P, et al. Blood-Pressure and Cholesterol Lowering in Persons without Cardiovascular Disease. *The New England journal of medicine*. 2016
76. Salam A, Webster R, Singh K, et al. TRIple pill vs Usual care Management for Patients with mildto- moderate Hypertension (TRIUMPH): Study protocol. *American heart journal*. 2014; 167(2):127–132. [PubMed: 24439972]
77. World Health Organization, PEPFAR, UNAIDS. Task shifting: rational redistribution of tasks among health workforce teams : global recommendations and guidelines. 2016. <http://www.who.int/healthsystems/TTR-TaskShifting.pdf>
78. Thom S, Poulter N, Field J, et al. Effects of a fixed-dose combination strategy on adherence and risk factors in patients with or at high risk of cvd: The umpire randomized clinical trial. *JAMA*. 2013; 310(9):918–929. [PubMed: 24002278]
79. Patel A, Cass A, Peiris D, et al. A pragmatic randomized trial of a polypill-based strategy to improve use of indicated preventive treatments in people at high cardiovascular disease risk. *European journal of preventive cardiology*. 2015; 22(7):920–930. [PubMed: 24676715]
80. Selak V, Elley CR, Bullen C, et al. Effect of fixed dose combination treatment on adherence and risk factor control among patients at high risk of cardiovascular disease: randomised controlled trial in primary care. *Bmj*. 2014; 348:g3318. [PubMed: 24868083]



### Key Points

- Elevated blood pressure is a major risk factor for cardiovascular disease, and it is the leading global risk for mortality.
- There is a need for novel approaches when addressing hypertension due to its growing health and economic burden on LMIC populations.
- The Global Alliance for Chronic Diseases sponsored 15 research projects focused on hypertension.
- These research projects have involved the development and evaluation of several important innovative approaches to hypertension control, including: community engagement, salt reduction, salt substitution, task redistribution, mHealth, and fixed-dose combination therapies.

### Synopsis

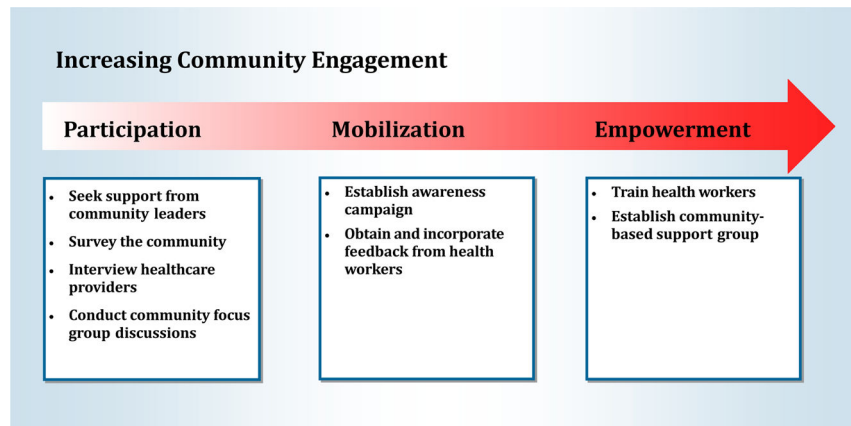
Elevated blood pressure, a major risk factor for ischemic heart disease, heart failure, and stroke, is the leading global risk for mortality. Despite global efforts to combat hypertension, treatment and control rates are very low in LMICs. Given the continued significant health and economic burden on LMIC populations, there is an urgent need to address the problem by way of novel approaches. The Global Alliance for Chronic Diseases sponsored 15 research projects focused on hypertension, which have involved the development and evaluation of several important innovative approaches to hypertension control, including: community engagement, salt reduction, salt substitution, task redistribution, mHealth, and fixed-dose combination therapies.

Author Manuscript

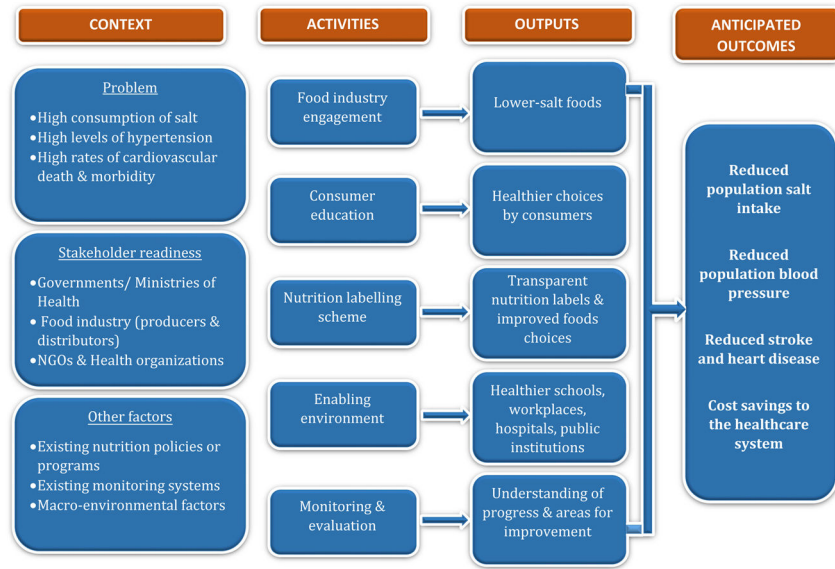
Author Manuscript

Author Manuscript

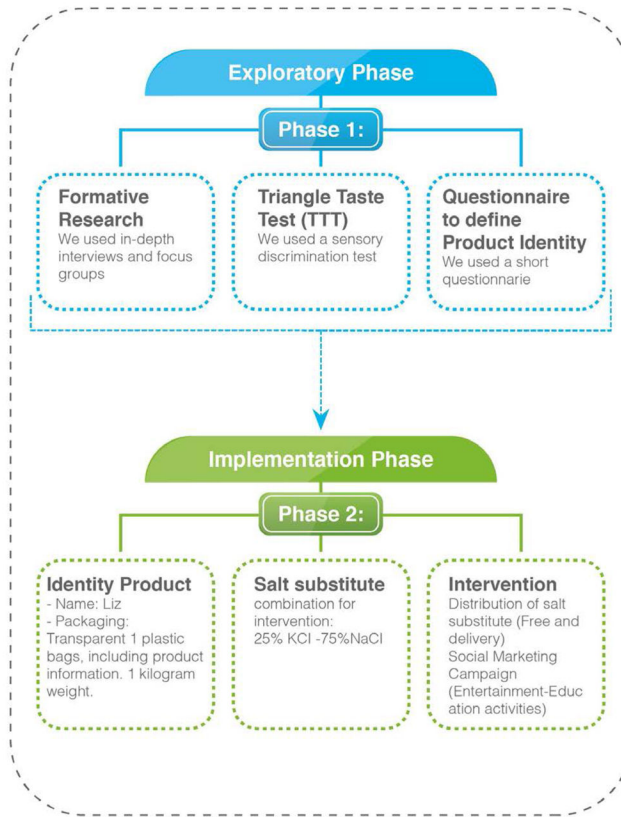
Author Manuscript



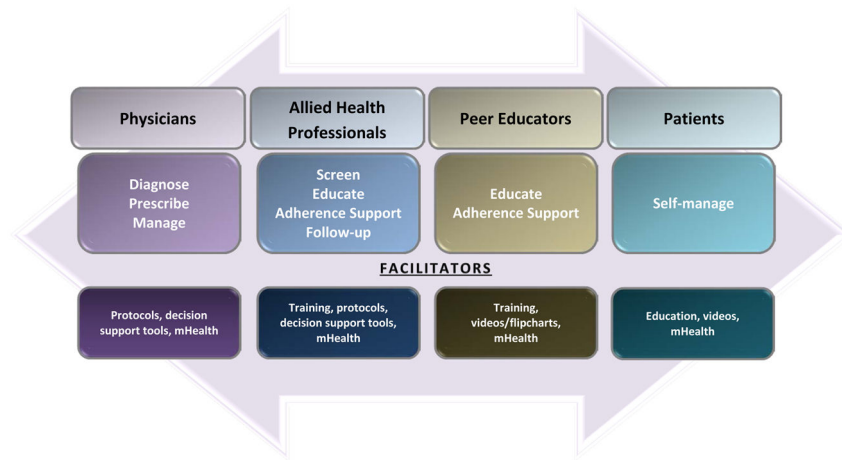
**Figure 1.** Community engagement activities undertaken within GACD Projects. Participation activities denote the least level of engagement while empowerment activities denote the greatest level of engagement.



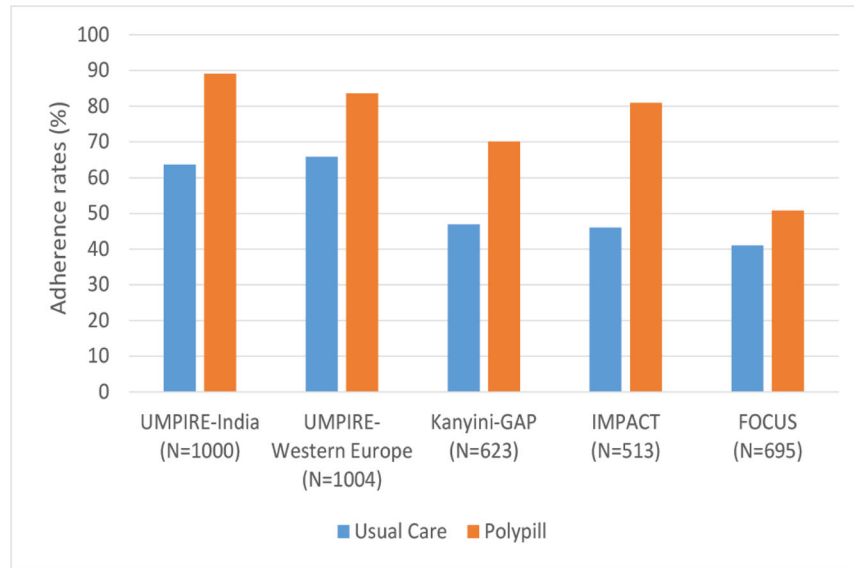
**Figure 2.** Framework for salt reduction strategies, including context, activities, outputs, and anticipated outcomes.



**Figure 3.** Launching a salt substitute to reduce blood pressure at the population level in Peru, divided into two phases.

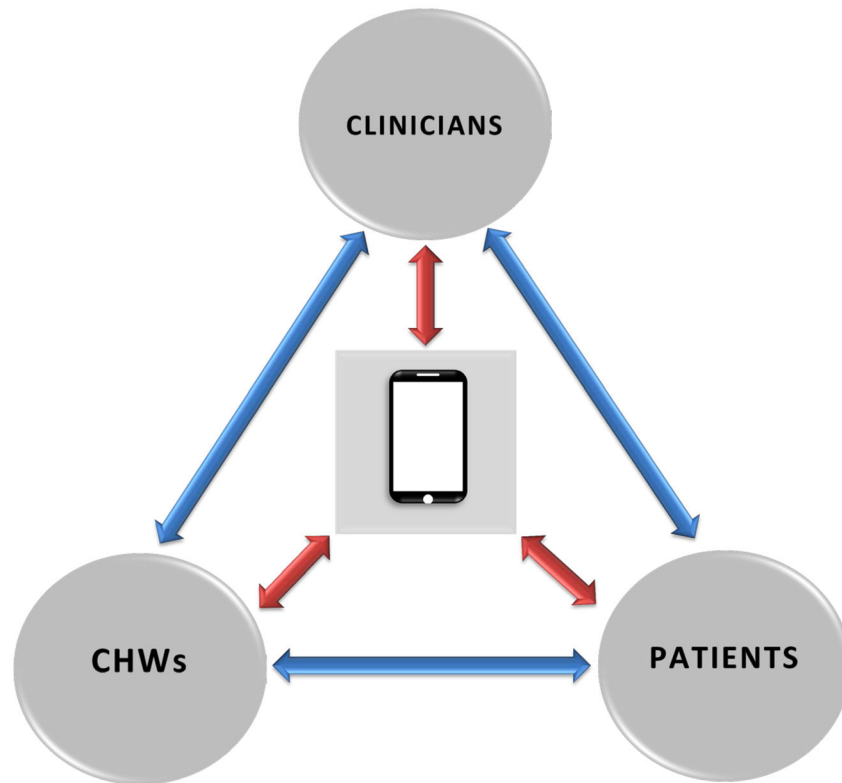


**Figure 4.** The process of task-redistribution for the management of hypertension adapted from the WHO’s recommendations on task-shifting. From World Health Organization, PEPFAR, UNAIDS. Task shifting: rational redistribution of tasks among health workforce teams : global recommendations and guidelines. <http://www.who.int/healthsystems/TTR-TaskShifting.pdf>, 2016, with permission.



**Figure 5.**

Proportion of participants adherent to combination therapy at end of study in patients either with established CVD or at high calculated risk. Adherence is defined as taking antiplatelet, statin and 2 BP-lowering drugs at least 4 days of the last 7 at end of study in UMPIRE,<sup>78</sup> Kanyini-GAP<sup>79</sup> and IMPACT.<sup>80</sup> Adherence in the FOCUS<sup>73</sup> trial was defined as pill count between 80 and 110% at end of study plus a score of 20/20 on the Morisky-Green questionnaire. Data from references 73, 78, 79, 80.



**Figure 6.** Schematic illustrating the potential for mHealth to connect clinicians, community health workers (CHWs), and patients. Blue arrows indicate direct interactions among individuals. Red arrows indicate interactions that are facilitated by mHealth.



**Table 1** Type and target group of community engagement activities undertaken within GACD projects, including timing of engagement and materials developed through each activity.

Region	Type	Target Group	Timing of Engagement	Rationale for Activity	Materials Developed
INDIA	Community Entry	Community leaders	Prior to the initiation of study activities within each cluster/community unit	To gain entry into the community	Protocol, specific aims, abstract
	Survey of community members	Individuals	Once at study initiation Length: 60–90 minutes	To identify barriers to seeking health care and/or treatment	Survey
	Community Focus Group Discussions	Individuals with hypertension	Up to 12 focus groups, each comprising up to 10 people Length: 60–90 minutes	To identify barriers to seeking health care and/or treatment	Structured guide for discussions
	In-depth interviews	Health care providers	23 interviews with doctors, nurses, and CHWs	To identify barriers to providing health care and/or treatment	Structured guide for interviews
	Survey of medicines	Public, private and other medicine outlets	20 public outlets 16 private outlets 2 other outlets selling medicines at subsidized rates to all patients	To determine availability, affordability and acceptability of medications	Structured list of essential medicines for audit
	Consultation via a planning day	Local, and state government health officials, and local experts	Once at a 4-hour planning session	To ensure that the design of the intervention fit into the health system	Final design of intervention
	Working group testing of intervention materials	CHWs and local doctors	Over 5 days, CHWs and doctors participated in a pilot training program	To develop educational materials for training CHWs and to educate people with hypertension	Educational materials for training CHWs and for people with hypertension
	Training	CHWs	5 full days of training delivered by doctors and researchers	To provide skills to CHWs to enable them to conduct a peer support group and educate people with hypertension	Education materials for CHWs
	Community-based support group of people with hypertension	Letter of support and encouragement from head of village (Sarpanch)	3-month intervention comprising 6 fortnightly education sessions delivered by CHWs, locally sourced expert advisers, health care providers, and researchers	Self-management and education support group of people with hypertension	Education materials for people with hypertension, including handouts

Region	Type	Target Group	Timing of Engagement	Rationale for Activity	Materials Developed
KENYA	Dissemination of study results	Communities, local health providers, medicines outlets, Ministry of Health & Welfare, National Health Mission	At end of study	To build capacity and sustainability	Development of resources for use by health care providers for assessing and treating hypertension
	Community Entry	Community leaders, health personnel, community stakeholders	Prior to the initiation of study activities within each cluster/community unit	To gain entry into the community	Protocol, specific aims, abstract, and PowerPoint summary
	Community Gatherings (Mabaraza)	Community	Six in total (until content saturation achieved) Length: 1–2 hours	To identify the barriers and facilitators to linkage to care for hypertension and retention to care	Structured discussion guides for mabaraza
	Focus Group Discussions	Individuals with hypertension and CHWs	17 total (until content saturation achieved) Length: 1–2 hours	To identify barriers to seeking and delivering health care and/or treatment	Moderator guides
	Human-Centered Design	Design team with diverse stakeholders; content validity testing with diverse stakeholders	Occurrence: Approximately 10 design team meetings; nine content validity focus group discussions with patients, community health workers, and clinicians Length: 60 min	Design of behavioral assessment and tailored communication strategy	Final design of intervention
TANZANIA & CANADA	Community Entry	Community leaders/stakeholders	Prior to the initiation of study activities within each of the 2 selected communities	To gain entry into the community and gauge interest	Framework for development of the I-RREACH Tool
	Completion of 3 'consensus' cycles	Stakeholders and community-based researchers in Canada and Tanzania	At project initiation moving forward over a 1 year period in 3 cycles	To test theoretical frameworks regarding researcher's practice-based knowledge, community readiness, indigenous approaches to research, empowerment approaches	Development of the I-RREACH Tool (insert Ref)
	Community Focus Group Discussions	Individuals with hypertension and their families as well as local health care providers	3 focus groups were held in participating Indigenous communities in Canada and 1 in Tanzania of varying length with a total of 45 participants	To identify major factors that may impact on the effectiveness of evidence-based educational SMS messages for people with hypertension and reduce health inequalities	Content from focus groups informed the development of the SMS messages to be used for the intervention in each country

Region	Type	Target Group	Timing of Engagement	Rationale for Activity	Materials Developed
	Training	CHWs and local health providers	In the second year, CHWs and doctors participated in country specific training programs on hypertension and cardiovascular disease as well as use of the mHealth tools/equipment. In Tanzania there was also a pre-post evaluation of knowledge gained and an observed standardized clinical exam	To prepare CHWs and health providers to provide educational support to their communities (people with hypertension and their families)	Educational materials for training CHWs and health providers
	Training	Local health providers (Tanzania only)	5 full days of training delivered by doctors and researchers in year 3 to evaluate the appropriateness of the treatment algorithm for management of hypertension (adapted from the existing Tanzanian hypertension guideline)	To provide skills to health providers to enable them to manage hypertension effectively	Treatment algorithm for hypertension that is specific to low-resource rural setting in sub-Saharan Africa
	Dissemination of study results	Communities, local health providers, medicines outlets, Ministry of Health & Social Welfare, National health Mission	Will occur at end of study	To build capacity and sustainability	Dissemination of resources for use by health care providers for assessing and treating hypertension
COLOMBIA, MALAYSIA, & CANADA	Community social events or other non-clinical gatherings	Non-physician health workers attend the community events	NPHW attend events opportunistically with the permission of event organizers	Posters explaining the NPHW attendance; curated collections of local government brochures regarding CV health and other available health services; personalized healthy lifestyle counselling based on WHO recommendations (Intervention-only).	