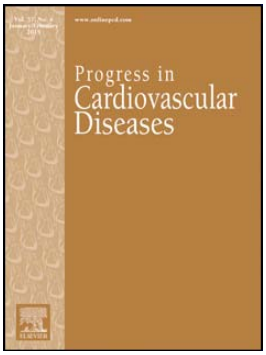
Accepted Manuscript



Use of m-Health Technology for Preventive Interventions to Tackle Cardiometabolic Conditions and Other Non-Communicable Diseases in Latin America- Challenges and Opportunities

Andrea Beratarrechea, Francisco Diez-Canseco, Vilma Irazola, Jaime Miranda, Manuel Ramirez-Zea, Adolfo Rubinstein

PII: S0033-0620(16)30021-4
DOI: doi: 10.1016/j.pcad.2016.03.003
Reference: YPCAD 725

To appear in: *Progress in Cardiovascular Diseases*

Received date: 27 March 2016
Accepted date: 27 March 2016

Please cite this article as: Beratarrechea Andrea, Diez-Canseco Francisco, Irazola Vilma, Miranda Jaime, Ramirez-Zea Manuel, Rubinstein Adolfo, Use of m-Health Technology for Preventive Interventions to Tackle Cardiometabolic Conditions and Other Non-Communicable Diseases in Latin America- Challenges and Opportunities, *Progress in Cardiovascular Diseases* (2016), doi: 10.1016/j.pcad.2016.03.003

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 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.

Use of m-Health Technology for Preventive Interventions to Tackle Cardiometabolic Conditions and Other Non-Communicable Diseases in Latin America- Challenges and Opportunities

Andrea Beratarrechea [1], MD, MSc ;Francisco Diez-Canseco [2,], MPH; Vilma Irazola [1], MD, Msc; Jaime Miranda [2], MD, PhD; Manuel Ramirez-Zea [3], MD, PhD; Adolfo Rubinstein [1], MD, MSc, PhD

[1]South American Center of Excellence for Cardiovascular Health (CESCAS). Institute for Clinical Effectiveness and Health Policy (IECS), [2]CRONICAS Center of Excellence in Chronic Diseases, Universidad Peruana Cayetano Heredia, Peru; [3]INCAP Research Center for the Prevention of Chronic Diseases, Institute of Nutrition of Central America and Panama, Guatemala.

Running Head: mHealth for CVD and other NCDs in Latin America

Disclosures: None

Corresponding author

Andrea Beratarrechea, MD, MSc
South American Center of Excellence for Cardiovascular Health,
Institute for Clinical Effectiveness and Health Policy,
Ravignani 2024
C1414CPV Buenos Aires - Argentina
Tel/Fax: (+54-11) 4777-8767
Email: aberatarrechea@iecs.org.ar

Abstract

In Latin America, cardiovascular disease (CVD) mortality rates will increase by an estimated 145% from 1990 to 2020. Several challenges related to social strains, inadequate public health infrastructure, and underfinanced healthcare systems make cardiometabolic conditions and non-communicable diseases (NCDs) difficult to prevent and control. On the other hand, the region has high mobile phone coverage, making mobile health (mHealth) particularly attractive to complement and improve strategies toward prevention and control of these conditions in low- and middle-income countries. In this article, we describe the experiences of three Centers of Excellence for prevention and control of NCDs sponsored by the National Heart, Lung, and Blood Institute with mHealth interventions to address cardiometabolic conditions and other NCDs in Argentina, Guatemala, and Peru. The nine studies described involved the design and implementation of complex interventions targeting providers, patients and the public. The rationale, design of the interventions, and evaluation of processes and outcomes of each of these studies are described, together with barriers and enabling factors associated with their implementation.

Abbreviations and Acronyms: CVD (cardiovascular disease), NCDs (non-communicable diseases), mHealth (mobile health), CHD (coronary heart disease), HTN (hypertension or hypertensive), LMICs (low-and middle-income countries), BP (blood pressure), SMS (short text message system), T2D (type 2 diabetes), NHLBI (United States National Heart, Lung, and Blood Institute), UHG (United Health Group), COEs (centers of excellence), CESCAS (South American Center of Excellence for Cardiovascular Health), IECS (Institute for Clinical Effectiveness and Health Policy), CIIPEC (Research Centre for the Prevention of Chronic Diseases), INCAP (Institute of Nutrition of Central America and Panama), CRONICAS (Center of Excellence in Chronic Diseases at Universidad Peruana Cayetano Heredia), ICT (information and communication technology), RCT (randomized controlled trial), PCCs (primary care clinics), CHWs (community health workers), apps (applications), mCDSS (mobile clinical

decision support system), MIT/CSAIL (Massachusetts Institute of Technology Computer Science and Artificial Laboratory), WHO (World Health Organization), UNAN (National Autonomous University of Nicaragua), PHCP (primary healthcare providers), CONEMO (control emocional).

Key words: Latin America; mHealth ; cardiometabolic disease.

CARDIOVASCULAR DISEASE BURDEN IN LATIN AMERICA

Coronary heart disease (CHD) and stroke are the leading causes of death worldwide, accounting for 12.9 million, or 1 in 4 deaths, in 2010.[1] Eighty percent of these deaths occur in low- and middle-income countries (LMICs), with almost half in people younger than 70 years of age, compared to only 27% among corresponding age groups in high-income countries.[2] In Latin America, from 1990 to 2020, death from cardiovascular disease (CVD), including CHD, will increase by an estimated 145% in both women and men, compared with increases of 28% in women and 50% in men in developed countries during the same period.[3] The INTERHEART study showed that tobacco use, abnormal lipids, abdominal obesity, and high blood pressure (BP) [4] could explain the majority of CVD risk for myocardial infarction in the Southern Cone. However, responses of most health systems in Latin American countries to CVD and its risk factors are poor in addressing the needs of patients with diseases characterized by long duration and often slow progression.[5] In addition, current primary care systems in the region lack preventive programs targeting people with high CVD risk.[6]

Latin America faces other problems that make CVD more challenging to prevent and control, including socioeconomic factors, inadequate public health infrastructure, lack of preventive programs, underfinanced and fragmented healthcare systems, and low levels of community awareness.[7,8]

MHEALTH TO ADDRESS CARDIOMETABOLIC DISORDERS AND OTHER Non-Communicable Diseases (NCDs) IN LATIN AMERICA

Information and communication technologies represent a potential tool for increasing both the quality and quantity of chronic disease management support in the developing world.[9-11] Overall, Latin America has high population coverage by the mobile phone network, with 112% penetration in 2013. Further, due to widespread adoption of smartphones and the growth of smartphone connections being highest in the

developing world, mobile health (mHealth) interventions are particularly attractive for prevention, management and control of cardiometabolic conditions in the region.[12] Mobile health refers to the use of mobile telecommunication and multimedia technologies for healthcare delivery.[13,14] Mobile phone strategies using phone, short message system (SMS), applications for clinical decision support, or telemedicine have been shown to improve patient-provider communication, promote behavioral changes, and improve chronic disease management and medication adherence in developed countries.[15-17]
With the rapid growth of mobile phone use in LMICs, mHealth is emerging as an opportunity to address several healthcare system constraints in these countries, including a scarce and overburdened health care workforce, limited financial resources, and an increasing prevalence of chronic diseases. However, evidence of the effectiveness of mHealth in relation to its impact and long term effects on prevention and control of chronic diseases in LMICs is limited. The majority of studies in LMICs used text messaging systems to promote behavior change, but the reported impact of these mHealth interventions was mixed, with studies showing only modest benefits for some clinical outcomes.[18,19]

Moreover, one systematic review to address the impact of mHealth on chronic disease outcomes in LMICs published by our group reported 9 trials conducted in LMICs, with only one study, focusing on diabetes management, conducted in Latin America. Another recent review of mHealth in LMICs reported the results of only three studies, two exploratory and one quasi-experimental, addressing CVD and other NCDs in the region,[20,21] which demonstrates that mHealth remains an under-explored topic.

The United States National Heart, Lung, and Blood Institute and the United Health Group (NHLBI/UHG) Chronic Disease Initiative have funded a global network of Centers of Excellence (COEs) to help combat chronic diseases in developing countries.[22,23] These COEs developed infrastructure for research and training, and conduct population-based and clinical research to monitor, prevent or control chronic diseases. Some of the COEs have also designed and conducted research projects based on mHealth interventions to prevent or control chronic conditions with a particular focus on cardiometabolic diseases.

In this review, we describe the projects and studies directly linked to developing and/or testing mHealth interventions to address cardiometabolic conditions and other NCDs in which three Latin American COEs funded by NHLBI either were or are currently involved. These COEs are based in Buenos Aires, Argentina (South American Center of Excellence for Cardiovascular Health (CESCAS) at the Institute for Clinical Effectiveness and Health Policy (IECS)); Guatemala City, Guatemala (Research Centre for the Prevention of Chronic Diseases (CIIPEC) at the Institute of Nutrition of Central America and Panama (INCAP)); and Lima, Peru (CRONICAS Center of Excellence in Chronic Diseases at Universidad Peruana Cayetano Heredia).[22]

MHEALTH PROJECTS TO PREVENT AND CONTROL CARDIOMETABOLIC DISORDERS AND OTHER NCDs IN LATIN AMERICA

The following nine studies are either primarily mHealth projects or have incorporated an mHealth component as part of an intervention program to prevent and control cardiometabolic disorders or other NCDs. Most of these studies are ongoing and involve the design and implementation of complex interventions for changing behaviors of providers and high-risk and/or healthy populations. Following Labrique et al. mHealth and information and communication technology (ICT) framework, domains used by these projects are: client education and behavior change communication, registries and vital events tracking, data collection and reporting, electronic decision support, and provider training and education [24]. Mobile functions for these domains include: phone calls, interactive voice responses, text messages, clinical decision support applications, data transfer for health record tracking, one-, two - and multi-way applications, and mobile telemedicine devices for patient monitoring or diagnosis.

The studies conducted by these COEs are described below and are also depicted in (Table 1).

Study conducted collaboratively by the three COEs in Argentina, Guatemala, and Peru

A Randomized Controlled Trial (RCT) of a mobile health intervention to improve cardiometabolic profile in prehypertensive subjects from low resource urban settings in Latin America

Sponsored by NHLBI, this study aimed to promote healthy lifestyle changes (improvements in diet quality and physical activity level) in prehypertensive subjects living in low-income, urban settings in Argentina, Guatemala, and Peru, through an mHealth intervention along a one-year of follow-up. A total of 637 participants were randomly assigned to receive the intervention (n=316) or usual care (n=321). Participants in the intervention arm received counseling on the following target behaviors: reduction of dietary sodium intake, reduction of simple sugars and saturated fat intake, increase of fruit and vegetable intake, and promotion of physical activity . The intervention was led by nutritionists and had three components. First, semi-structured counseling interviews via mobile phones were conducted monthly to promote lifestyle modification in accordance with the motivational interviewing technique. Second, after the counselor's call, participants received a weekly SMS tailored to the state of change of the particular target behavior addressed by the counselor during the call. Both the content and wording of SMS were validated in each of the countries.[25] Third, we developed a web-based application to support the mHealth interventions.[26] Randomization was stratified by country, with minimization by sex and age groups. Primary outcomes were the differences in net changes in systolic and diastolic BP between groups and secondary outcomes were changes in body weight, waist circumference, and self-reported target behaviors from baseline to 12 months of intervention. Data was analyzed using the intention-to-treat approach. Two-hundred and sixty six (84%) participants in the intervention group and 287 (89%) in the control group were assessed at 12 months. The intervention did not result in a change in BP compared with usual care. However, the study showed a significant net reduction in body weight (-0·66 kg; p=0·04)

and intake of high-fat and high-sugar foods (-0·75; p=0·008) in the intervention group compared with the control group. Interestingly, participants in the intervention group who received more than 75% of the calls (nine or more calls) had a much higher reduction of their body weight as well as greater improvement in some eating behaviors.[27]

Studies conducted in Argentina: South American Center of Excellence for Cardiovascular Health, (CESCAS), Institute for Clinical Effectiveness and Health Policy.

A comprehensive approach to hypertension prevention and control in low-resource settings in Argentina

Hypertension (HTN) is a public health challenge because of its high prevalence and concomitant increase in CVD risk.[28] Approximately 80% of the attributable burden of HTN occurs in LMICs.[29] According to the recent CESCAS I study, a large-scale, population-based cohort study conducted in 4 cities of the Southern Cone and led by IECS, the prevalence of hypertension in the adult population aged 35 to 74 years was 43.3%. Overall, 62.2% of HTN patients were aware of their diagnosis, 47.7% were undergoing drug treatment, and only 21.5% had achieved BP control.[30]

This study is an ongoing cluster RCT, sponsored by NHLBI, in 18 primary care clinics (PCCs) of the Argentinian public health network, which has already enrolled almost 2,000 uninsured patients with uncontrolled HTN and their families. The aim of this study is to test an 18-month complex intervention designed to reduce BP and improve HTN control.[31] This intervention includes: 1) periodic home visits driven by community health workers (CHWs) for education and counseling to HTN persons and their families; 2) education, audit, and feed-back to primary care physicians on HTN management; and 3) customized SMS for HTN patients and their families, as boosters to complement the educational sessions

provided by CHWs. SMS are being sent out weekly to intervention participants to promote lifestyle changes, reinforce adherence to antihypertensive medication and promote follow-up visits to the primary care doctor at PCCs. Additionally, a process evaluation is being conducted to assess whether the desired interventions are adopted by participants and healthcare providers and the extent to which they are translated into better outcomes (Table 1).

An educational approach to improving physicians' effectiveness in the detection, treatment, and control of hypercholesterolemia and high CVD risk in low-resource settings in Argentina

Despite the existence of clinical practice guidelines and free access to drug treatment for hypercholesterolemia in PCCs in Argentina, uninsured patients with high CVD risk still do not receive adequate care and huge gaps in awareness, treatment and control are observed. In Argentina, CVD represents 34.2% of deaths and 12.6% of years of potential life lost.[32] According to CESCAS I study, the prevalence of dyslipidemia among adults aged 35-74 years in the Southern Cone is 58.4%.[33] Multiple barriers to the appropriate management of hypercholesterolemia at the point of care can be identified, including physicians' competing demands, lack of adherence to clinical practice guidelines, lack of access, medication costs, and patient reluctance to take medication.[34,35] Interventions that have been effective in dealing with barriers related to clinical practice are educational interventions (academic detailing, educational outreach visits, audit and feed-back) and clinical decision support systems (CDSS).[36-38] Mobile phones are recognized as a viable platform for improving health care delivery in low-resource settings in developed countries.[20,39] With the rapid uptake and use of smartphone technology, there has been a surge in the development of mobile applications (apps) for health. Clinical decision support systems in mHealth apps (mCDSS) for patient care can improve clinical decision making.[40,41]

This ongoing study, sponsored by the International Atherosclerotic Society and Pfizer Foundation, aims to evaluate whether a multi-component intervention, lasting 12 months, that incorporates academic detailing through outreach visits and an mCDSS for primary care physicians, as well as educational SMS and reminders for patients, improves the detection, treatment and control of hypercholesterolemia among patients with moderate-high CVD risk in Argentina. This study is a cluster RCT recruiting 350 patients from 10 public PCCs.[42] The mCDSSs on the physicians' smartphones are used to provide evidence-based and guideline-driven decision aids to improve patient management. This app uses the open-source Sana mobile telehealth platform, a highly open telemedicine framework developed by the Massachusetts Institute of Technology Computer Science and Artificial Laboratory (MIT/CSAIL).[43,44] Participants in the intervention group receive SMS for life-style modification and to improve treatment adherence, as well as prompts and reminders for clinic appointments. The main primary outcome measure is the net change of the LDL-c values between baseline and 12 months. As part of the process evaluation, engagement and usability of the mCDSS as well as adherence to clinical practice guidelines will be assessed to explore whether the mHealth component is adopted by physicians (Table 1).

Strengthening diabetes care for underserved populations in the province of Corrientes, Argentina

High rates of physical inactivity, unhealthy diets, overweight and obesity, each of which are related to the epidemiological and nutritional transition, are leading to an increased prevalence of type 2 diabetes (T2D) in developing countries.[45] It is estimated that by 2030, the number of people with T2D in South and Central America will increase from 25 to 39.3 million.[46] In this epidemic, T2D is over-represented among lower socioeconomic groups.[47] According to the National Risk Factor Survey, the prevalence of T2D in Argentina increased from 8.5% to 9.8 % from 2005-2013, reaching epidemic proportions and representing a significant public health problem.[48,49] Creative solutions are necessary to address the

escalating healthcare demands of chronic conditions, especially in low resource settings where public primary care infrastructure is limited and overwhelmed.[50,51]

This study is sponsored by the World Diabetes Foundation and will evaluate whether a multifaceted intervention over a 12 month period, incorporating primary care training in diabetes management and the implementation of an ICT system, improves T2D quality of care at PCCs in low resource settings in the province of Corrientes, Argentina, a poor northeastern province in the Argentinean Mesopotamia. The ICT system uses the Sana mobile telehealth platform and is comprised of a T2D registry and a mCDSS for health care providers in an mHealth app.[43, 44] The app is installed on a tablet and is used to identify T2D patients and to track and monitor T2D care. The recorded information is used as input to generate tailored educational SMS and reminders to improve adherence, treatment, and follow-up of T2D patients. This study, an uncontrolled before-after quasi experimental study, will enroll 1000 T2D patients in 20 public PCCs. Process and outcome measures will include T2D quality of care indicators as well as clinical outcomes. It will also include a qualitative component to assess acceptability and engagement of the ICT system among health care professionals and acceptability and satisfaction with the SMS among T2D patients (Table 1).

mHealth interventions to improve access and coverage of uninsured people with high CVD risk in Argentina

CVD is a major and growing health problem in LMICs and is also a cause of the widening health inequity. Exploring ways to increase screening of persons with high CVD risk in community settings and timely referral to PCCs is a significant priority to reduce the CVD burden in Argentina. The Ministry of Health of Argentina has created a program to reduce inequities by strengthening the primary care model through increased training and technological infrastructure support, and improving control of those

uninsured at high CVD risk through the provision of free essential drugs. The program uses the WHO package for the assessment and management of cardiovascular risk in low-resource settings.[52] Interventions delivered by the program include: 1) identification and enrollment of uninsured populations in the catchment area served by public PCCs; 2) CVD risk stratification and classification of subjects by health care professionals; 3) treatment with generic drugs as needed for subjects with HTN, T2D, or moderate-high CVD risk (≥10%); and, 4) regular follow-up in patients with moderate and high CVD risk. The program operates through financial incentives to providers to increase the enrollment, screening and follow-up of those uninsured at high risk for CVD. Unfortunately, uptake and retention at the PCCs are dismally low; less than a third of moderate-high CVD risk subjects eventually attend the PCCs—only 20% within 2 months. Furthermore, fewer than 15% of all subjects classified as having ≥10% CVD risk actually receive more than one consultation with the primary care doctor in the following year of follow-up (REDES Program-personal communication).

The study was designed as a cluster RCT, sponsored by the Fogarty International Center/ National Institute of Health, to determine whether the use of mHealth tools by CHWs (CVD risk calculator and a PCCs scheduling system) increase the number of persons with high CVD risk who are stratified, referred, and appropriately followed-up at the public PCCs in low resource settings. It will also evaluate the cost-effectiveness of the proposed intervention. Eight PCCs within the public network will be randomized to either apply the integrated mHealth tool or use the usual paper-based CVD screening charts. The study will enroll 740 adults with public coverage and a 10-year CVD risk ≥ 10%.

We will develop an mHealth tool for CHWs that integrates an app to calculate CVD risk and a system synchronized with the PCC's scheduling system in the mobile phone. The app will be built using the Sana mobile telehealth platform and will allow CHWs to make appointments for the identified high-risk individuals at the time of screening.[43,44] Participants will receive SMS messaging as reminders for the first appointments and follow-up visits, as well as educational messages for lifestyle modification.

The primary outcomes will be the proportion of participants with a 10-year CVD risk ≥ 10% who attend the baseline clinical appointment and the proportion of these participants who attend the scheduled follow-up visits to their PCCs within 4 months of the baseline visit (Table 1).

Study conducted in Guatemala –INCAP Research Center for the Prevention of Chronic Diseases (CIIPEC), Institute of Nutrition of Central America and Panama (INCAP).

Feasibility and acceptability of an intervention to promote the sale of "healthy eating" in a university campus in Managua, Nicaragua

Health Promoting Universities conduct health education and health promotion for students and staff, integrating health into the culture, processes, and policies of the university.[53] A previous study in the National Autonomous University of Nicaragua (UNAN) at the Managua campus showed that only 8% of university canteens sell healthy food.[54]

The aim of this study, which is sponsored by the International Development Research Centre, is to evaluate the feasibility and acceptability of a 10-week, multi-component intervention that includes: training of owners and employees of university canteens in healthy cooking; implementation of flyers to increase the demand and supply of healthy products; and an e-health intervention to promote the sale of "healthy food" at the university campus of UNAN-Managua.[55] The e-health strategy incorporates a website, social media, and a mobile application for android-running cell phones called "Yo como saludable" (*I eat healthy*). In this application, users will find weekly menus offered by the selected establishments, including healthy dishes of the week, side dishes, and prices. The app will also offer weekly tips to promote a healthy and balanced diet and the user will also be able to share menus through social media and email. This application was created by UNAN staff and is available for free download in

Play Store. In addition, all of this information can be viewed on a website also created by UNAN staff. The study will evaluate six university canteens and 300 users (students and university staff) using a before and after design to assess the number of healthy dishes offered and sold per week and users' food preferences. Other outcome variables will be the number of students/staff who downloaded the app and checked the website, and the mean number of interactions among users of the app (Table 1). Results from this study are expected to be published at the end of 2016.

Studies conducted in Peru – CRONICAS Center of Excellence in Chronic Diseases, Universidad Peruana Cayetano Heredia.

Allillanchu. Integration of mental health into primary health care services in Lima, Peru

Neuropsychiatric disorders affect one in every five Peruvians and are the leading cause of disease burden in the country.[56,57] In Lima, Peru's capital city, almost 20% of the population has suffered depression at one point in their lives.[58] Depression among primary healthcare users can be very high—up to 40% of pregnant women,[59,60] 52% of patients with tuberculosis,[61] and 30% of patients with T2D.[62] Depression is associated with reduced treatment adherence, poorer prognosis, greater disability, and higher mortality among sufferers of non-psychiatric diseases.[63] Despite its high prevalence and impact on patient adherence, depression is largely underdiagnosed and undertreated.[64,65] This context offers an opportunity to address strategies oriented towards the integration of health services.[66]

Allillanchu is a greeting term in Quechua, which means "how are you, how are you feeling?" The Allillanchu project, sponsored by Grand Challenges Canada's Global Mental Health initiative, aims to promote the early detection, opportune referral, and access to treatment for people with common mental disorders who are regular users of PCCs: pregnant women and patients with T2D, HTN, tuberculosis and

HIV/AIDS. To achieve its goal, the project will design, develop, and test an mHealth strategy that comprises (1) a mobile app installed in a tablet for the screening of common mental disorders during the regular consultations of primary healthcare providers (PHCP) and (2) the use of SMS as a reminder and motivational tool for patients identified with the screening app to seek mental health care.

This pragmatic strategy is tested during 2 months with 20 PHCP from 5 public PCCs in Lima, Peru, using a mixed-methods design that includes both qualitative and quantitative methods.[67] The outcomes to be measured include: number of primary health care providers (PHCP) trained, number of PHCP who pass the training evaluation, number of PHCP who implement screening in their daily service routines, number of screened patients, proportion of referred patients who seek mental health care, proportion of referred patients that access mental health care, and proportion of PHCP willing to include the mHealth package in their daily practice. The intervention is preceded by a qualitative study with service users, primary health care providers and mental health specialists, and includes a detailed process evaluation of the implementation (Table 1).

Implementation of foot thermometry and SMS to prevent diabetic foot ulcer

Diabetic foot neuropathy is one of the most important complications of diabetes. Its early diagnosis and treatment can prevent foot ulcers and amputation.[68] The use of thermometry is a promising modality to prevent diabetic foot ulcers.[69,70] However, patient compliance with temperature self-monitoring is a concern because it is difficult to get into a consistent routine of daily monitoring.[71]

This study is a 12-month controlled trial, sponsored by the Fogarty International Center/NIH, that will assess whether the use of SMS and voice messages can remind and motivate diabetic patients to perform daily temperature measurements of their feet in order to prevent diabetic foot ulcers.

A total of 172 patients with type 2 diabetes mellitus at high risk of ulceration, recruited in two public hospitals in Lima, Peru will be randomly assigned to the control or intervention groups. Both arms will receive education and an electronic foot thermometer, but the intervention group will also receive a year of weekly SMS and voice messages to remind and encourage temperature daily measurements.

The main primary outcome will be foot ulceration, as defined by the American Diabetes Association, at any point during the 12-month study (Table 1).

Latin American treatment & innovation network in mental health (Latin-MH)

Worldwide, mental, neurological, and substance-use disorders account for nine out of the 20 leading causes of years lived with disability and 10% of the global burden of disease.[72] Indeed, by 2030, depression is projected to be the world-leading cause of burden of disease.[73] Depression is strongly associated with diabetes and heart disease, non-adherence to medical treatments, and progression of disability across a range of chronic conditions.[74,75] Notwithstanding the public health impact of depression, it often goes unrecognized and untreated.[76-82]

LATIN-MH is one of the 5 hubs awarded by the US-National Institute of Mental Health to increase research capacity and reduce the mental illness treatment gap in resource-poor settings.[83] The research component of the LATIN-MH hub comprises two studies: a cluster RCT that will be conducted in Sao Paulo, Brazil, and a RCT in Lima, Peru, to assess the effectiveness of CONEMO (Control Emocional), a 6-week low-intensity psycho-educational intervention delivered via smartphones and supported by auxiliary nurses. The aim of CONEMO, based on the principles of behavioral activation model, is to reduce depressive symptoms among individuals with T2D and/or HTN who attend to public health care centers in low-resource settings. In Sao Paulo, 20 public PCCs will be randomized to the intervention or

control groups and 851 participants will be included. In Lima, 421 individuals will be randomly assigned to one of the two arms after their recruitment by PCCs of the public health system. Adults with a PHQ-9 score ≥ 10 and a previous diagnosis of hypertension and/or diabetes will be recruited to be part of the studies. The primary outcome will be the proportion of participants whose depressive symptoms have decreased (PHQ-9<10) at 3 months after enrollment into the trial. Each RCT will be preceded by a pilot study. The project includes process and cost-effectiveness evaluations of the intervention in both countries (Table 1).

IMPLICATIONS AND FURTHER RESEARCH

Implementing mHealth interventions in LMICs is a challenge, particularly when these interventions are tested in low-income settings and within a research framework.[84] The barriers to the implementation of research studies in poor settings include the complexity of interventions, multiple components acting on providers, patients, the community, and clinical settings; a limited capacity of local human resources to adopt research methods in a context of a poor evaluative culture; a lack of leadership and management skills at the local level; weak health systems; and a complex social, cultural, and political context.[41] There are several limitations specifically regarding technology use and project implementation, which include but are not limited to: technological illiteracy, health workers' resistance to new technology, different patterns of cell phone usage among underserved populations, shared or lack of mobile phones for personal use, lost or stolen phones, limited connectivity, need of smartphone application updates and lack of standardized data security protocols for the region to assure interoperability and to maximize the full capabilities of mobile devices.[85]

However, to sort out these "barriers," we have identified some specific enabling factors related to mHealth interventions that have proved to extend the following benefits in poor settings:

1) Use of open source software like Sana with intuitive user interfaces to enhance usage and adoption among health care professionals; 2) Frameworks that allow data collection in poor or intermittent connectivity settings and that are compatible with a low grade software; 3) building local capacity to enhance the perceived skills and motivation of the health personnel as an avenue to improve technological literacy and reduce resistance to new technology; 4) include participants who have a cell phone for personal use to assure that they will receive a full dose of intervention; 5) lending, providing, or incentivizing the ownership of smartphones for health care professionals participating in studies that include data collection; 6) training and periodic retraining of study personnel to avoid departure from the protocol and introduce rigorous methods of assessment derived from clinical research, and create an evaluative environment; 7) close monitoring of field work, both on-site and through telephone and e-mail follow-up, is important for auditing, feedback, and, perhaps more important, for supporting the local research team in dealing with the many hurdles that usually arise during implementation; 8) flexibility to respond to changes in local conditions that can affect the study, such as competing activities at the health care centers , lack of personnel, and seasonal jobs; 9) using social media to engage health care professionals or study participants that are involved in the studies; 10) inclusion of process evaluation and qualitative information to assist with interpretation of the outcome results as participating health care professionals explore the implementation, barriers and enablers, reception, and setting of interventions; and 11) design of a data-management workflow to allow efficient and timely data and quality-control measures.

The likelihood of success might be increased by strong leadership and governance and by the active engagement of a broad range of implementers and key stakeholders, including local community organizations and through the collaboration with operators to ensure technical support and scaling-up, and to reduce the costs to drive mHealth demands and innovation.

In LMICs, pilot projects have demonstrated conceptually how mHealth can alleviate specific health system constraints; however, we still need robust evidence to consider mHealth alongside essential health

interventions and guidance about which mHealth interventions should be considered to achieve broader health system goals.[86]

Unfortunately, in Latin America there is limited evidence on the effects of mHealth within healthcare systems. To our knowledge, there is only one RCT, conducted in Argentina, Guatemala and Peru by our COEs, and recently published, evaluating an mHealth intervention to promote healthier behaviors in individuals at higher cardio-metabolic risk in Latin America. As mentioned above our one-year intervention did not result in a change in BP, but it produced a reduction in body weight, as well as an improvement in diet quality.[27]

In conclusion, mHealth, is leveraging an increasingly expanded mobile phone network and looks to be a promising technology in Latin America, which usually deals with weak and fragmented health care systems. However, many questions regarding its effectiveness remain unanswered today such as: which domains and mobile functions (voice, SMS, video, apps, software) are most effective to prevent and control these conditions, whether the effectiveness of interventions is determined by socio-demographic characteristics of populations, user charges, culture or context, local health care systems, and which are the implementation hurdles related to the uptake, ownership, dissemination, and scaling up of these interventions if they prove to be successful.

In this sense, in the majority of studies, selected design will provide strong and unbiased estimations of the impact of mHealth interventions. In addition, proposed mHealth interventions have been integrated into health programs, services, and the community, and formative research and process evaluations will help to identify enablers and barriers to the implementation, how integration works and future uptake. This new technology has considerable potential and these ongoing studies will add evidence to determine if mHealth is effective to prevent and control cardiometabolic diseases and other NCDs and how to integrate these interventions in the Latin America's segmented health systems.

Acknowledgements

The authors would like to thank Maria Lazo-Porras staff from the Hospital Cayetano Heredia for her collaboration and Melissa Amyx and Diana Pham for proof-reading the final manuscript.

References

1. Lozano R, Naghavi M, Foreman K, et al. Global and regional mortality from 235 causes of death for 20 age groups in 1990 and 2010: a systematic analysis for the Global Burden of Disease Study 2010. *Lancet;*380(9859):2095-2128, 2012.
2. Abegunde DO, Mathers CD, Adam T, et al. The burden and costs of chronic diseases in low-income and middle-income countries. *Lancet;*370(9603):1929-1938,2007.
3. Yusuf S, Hawken S, Ounpuu S, et al. Effect of potentially modifiable risk factors associated with myocardial infarction in 52 countries (the INTERHEART study): case-control study. *Lancet;*364(9438):937-952, 2004.
4. Lanas F, Avezum A, Bautista LE, et al. Risk factors for acute myocardial infarction in Latin America: the INTERHEART Latin American study. *Circulation*;115(9):1067-1074, 2007.
5. Maher D, Ford N, Unwin N. Priorities for developing countries in the global response to non-communicable diseases. Globalization and health; 8:14, 2012.
6. Glassman A, Gaziano TA, Bouillon et al. Confronting the chronic disease burden in Latin America and the Caribbean. *Health affairs;*29(12):2142-2148, 2010.
7. Barreto SM, Miranda JJ, Figueroa JP, et al. Epidemiology in Latin America and the Caribbean: current situation and challenges. *International journal of epidemiology;*41(2):557-571, 2012.
8. Ordunez P, Martinez R, Niebylski ML, et al. Hypertension Prevention and Control in Latin America and the Caribbean. *Journal of clinical hypertension;*17(7):499-502, 2015.

9. Car J, Sheikh A. Email consultations in health care: 1--scope and effectiveness. *Bmj;*329 (7463):435-438, 2004.

10. World Health Organization (WHO). *A Health Telematic Policy in support of WHOs Healths-for-All Strategy for Global Health Development.* Geneva, Switzerland,: WHO;1997-1998.

11. Valenzuela JI, Arguello A, Cendales JG, et al. Web-based asynchronous teleconsulting for consumers in Colombia: a case study. *Journal of medical Internet research;*9 (4):e33, 2007.

12. GSMA. *The Mobile Economy. Latin America 2014.* GSM Association; 2014.

13. Istepanian R, Laxminarayan S, CS. P, eds. *M-Health: Emerging Mobile Health Systems.* 2006. Springer, ed.

14. P G, Mourlas C , Samaras G. A Mobile Agent Approach for Ubiquitous and Personalized eHealth Information Systems. Proceedings of the Workshop on 'Personalization for e-Health' of the 10th International Conference on User Modeling (UM'05); July 29, 2005; Edinburgh.

15. Fjeldsoe B.S, Marshall A.L, Miller Y.D. Behavior Change Interventions Delivered by Mobile Telephone Short-Message Service. *Am J Prev Med;*36 (2):165-173, 2009.

16. Krishna S, Boren S A, Balas AE. Healthcare via cell phones: a systematic review.*Telemedicine and E-Health;*15(3):231-240, 2009.

17. Cole-Lewis H, Kershaw T. Text messaging as a tool for behavior change in disease prevention and management. *Epidemiologic Reviews;*32(1):56-69 , 2012.

18. Free C, Phillips G, Galli L, et al. The effectiveness of mobile-health technology-based health behaviour change or disease management interventions for health care consumers: a systematic review. *PLoS medicine;*10(1):e1001362, 2013.

19. Tomlinson M, Rotheram-Borus MJ, Swartz L, et al. Scaling up mHealth: where is the evidence? *PLoS medicine;*10(2):e1001382, 2013.

20. Beratarrechea A, Lee AG, Willner JM, et al. The impact of mobile health interventions on chronic disease outcomes in developing countries: a systematic review. *Telemed J E Health;*20(1):75-82,2014.

21. 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;*7(8):677-691, 2014.

22. UnitedHealth Group/National Heart L, Blood Institute Centres of Excellence. A global research network for non-communicable diseases. *Lancet;*383(9927):1446-1447, 2014.

23. UnitedHealth National Heart, Lung, and Blood Institute Centers of Excellence, Cerqueira MT, Cravioto A, et al. Global response to non-communicable disease. *Bmj;*342:d3823, 2011.

24. Labrique AB, Vasudevan L, Kochi E, et al. mHealth innovations as health system strengthening tools: 12 common applications and a visual framework. *Global health, science and practice;*1(2):160-171, 2013.

25. Diez-Canseco F, Zavala-Loayza JA, Beratarrechea A, et al. Design and Multi-Country Validation of Text Messages for an mHealth Intervention for Primary Prevention of Progression to Hypertension in Latin America. *JMIR mHealth and uHealth;*3(1):e19, 2015.

26. Beratarrechea A, Diez-Canseco F, Fernandez A, et al. Acceptability of a Mobile Health based intervention to modify lifestyles in prehypertensive patients in Argentina, Guatemala and Peru: a pilot study]. *Revista peruana de medicina experimental y salud publica;*32(2):221-229, 2015.

27. Rubinstein A, Miranda J, Beratarrechea A, et al. Effectiveness of an mHealth intervention to improve the cardiometabolic profile of people with prehypertension in low-resource urban settings in Latin America: a randomised controlled trial. Lancet Diabetes Endocrinol. 4(1):52-63, 2016.

28. Danaei G, Finucane MM, Lin JK, et al. National, regional, and global trends in systolic blood pressure since 1980: systematic analysis of health examination surveys and epidemiological studies with 786 country-years and 5.4 million participants. *Lancet;*377(9765):568-577, 2011.

29. Lawes CM, Vander Hoorn S, Rodgers A, International Society of H. Global burden of blood-pressure-related disease, 2001. *Lancet;*371(9623):1513-1518, 2008.

30. Rubinstein AL, Irazola VE, Poggio R, et al. Detection and follow-up of cardiovascular disease and risk factors in the Southern Cone of Latin America: the CESCAS I study. *BMJ open;*1(1):e000126, 2011.

31. Mills KT, Rubinstein A, Irazola V, et al. Comprehensive approach for hypertension control in low-income populations: rationale and study design for the hypertension control program in Argentina. *The American journal of the medical sciences;*348(2):139-145, 2014.

32. Rubinstein A, Colantonio L, Bardach A, et al. Estimation of the burden of cardiovascular disease attributable to modifiable risk factors and cost-effectiveness analysis of preventative interventions to reduce this burden in Argentina. *BMC public health;*10:627, 2010.

33. Rubinstein AL, Irazola VE, Calandrelli M, et al. Multiple cardiometabolic risk factors in the Southern Cone of Latin America: a population-based study in Argentina, Chile, and Uruguay. *International journal of cardiology;*183:82-88, 2015.

34. Hickling J, Rogers S, Nazareth I. Barriers to detecting and treating hypercholesterolaemia in patients with ischaemic heart disease: primary care perceptions. *The British journal of general practice : the journal of the Royal College of General Practitioners;*55(516):534-538, 2005.

35. Jaen CR, Stange KC, Nutting PA. Competing demands of primary care: a model for the delivery of clinical preventive services. *The Journal of family practice;*38(2):166-171,1994.

36. Shea S, DuMouchel W, Bahamonde L. A meta-analysis of 16 randomized controlled trials to evaluate computer-based clinical reminder systems for preventive care in the ambulatory setting. *Journal of the American Medical Informatics Association : JAMIA;*3(6):399-409, 1996.

37. Johnston ME, Langton KB, Haynes RB, et al. Effects of computer-based clinical decision support systems on clinician performance and patient outcome. A critical appraisal of research. *Annals of internal medicine;*120(2):135-142, 1994.

38. Heselmans A, Aertgeerts B, Donceel P, et al. Human computation as a new method for evidence-based knowledge transfer in Web-based guideline development groups: proof of concept randomized controlled trial. *Journal of medical Internet research;*15(1):e8, 2013.

39. Donner J. Research approaches to mobile use in the developing world: a review of the literature. *Inf Soc;*24 (3):140-159, 2008.

40. Bates DW, Kuperman GJ, Wang S, et al. Ten commandments for effective clinical decision support: making the practice of evidence-based medicine a reality. *Journal of the American Medical Informatics Association : JAMIA*;10(6):523-530, 2003.

41. Grimshaw J, Eccles M, Tetroe J. Implementing clinical guidelines: current evidence and future implications. *The Journal of continuing education in the health professions;*24 Suppl 1:S31-37, 2004.

42. Rubinstein AL, Irazola VE, Poggio R, et al. Challenges and opportunities for implementation of interventions to prevent and control CVD in low-resource settings: a report from CESCAS in Argentina. *Global heart*;10 (1):21-29, 2015.

43. Celi LA, Sarmenta L, Rotberg J, et al. Mobile Care (Moca) for Remote Diagnosis and Screening. *Journal of health informatics in developing countrie;*3(1):17-21, 2009.

44. Depasse J, Celi LA. Collaboration, capacity building and co-creation as a new mantra in global health. Int J Qual Health Care. Nov 13 2013.

45. Guariguata L, Whiting DR, Hambleton I, et al. Global estimates of diabetes prevalence for 2013 and projections for 2035. *Diabetes research and clinical practice;*103 (2):137-149, 2014.

46. Whiting DR, Guariguata L, Weil C, et al. IDF diabetes atlas: global estimates of the prevalence of diabetes for 2011 and 2030. *Diabetes research and clinical practice;*94 (3):311-321, 2011.

47. Eakin EG, Bull SS, Glasgow RE, et al. Reaching those most in need: a review of diabetes self-management interventions in disadvantaged populations. *Diabetes/metabolism research and reviews;*18(1):26-35, 2002.

48. Ferrante D, M V. National Risk Factor Survey 2005: Main Results. Prevalence of Cardiovascular Risk Factors in Argentina. *Rev Argent Cardiol*;75:20-29, 2007.

49. Minsterio de Salud de la Nacion INdEyC. *Tecera Encuesta Nacional de Factores de Riesgo para Enfermedades No Trasmisibles.* 2015.

50. Wagner EH. Population-based management of diabetes care. *Patient education and counseling;*26(1-3):225-230, 1995.

51. McCulloch DK, Price MJ, Hindmarsh M, et al. A population-based approach to diabetes management in a primary care setting: early results and lessons learned. *Effective clinical practice : ECP;*1(1):12-22, 1998.

52. (WHO) WHO. *CVD-Risk Management Package for low- and medium-resource settings.* Geneva 2002.

53. Dooris M, Doherty S. Healthy Universities: current activity and future directions--findings and reflections from a national-level qualitative research study. *Global health promotion;*17(3):6-16, 2010.

54. Ahlers N. *Estudio sobre oferta alimentaria y preferencias de consumo de la comunidad universitaria en tres universidades de Managua, en el marco de la estrategia de "Universidades Saludables" (Universidad Americana).* 2013.

55. Tercero RTI. Factibilidad y aceptabilidad de una intervención para promover la venta de "alimentación saludable" en el Recinto Universitario Rubén Darío, Universidad Nacional Autónoma de Nicaragua, UNAN-Managua 2015. Nicaragua2015.

56. Velasquez A. The burden of disease and injuries in Peru and the priorities of the universal assurance essential plan. *Rev. perú. med. exp. salud publica;*26(2):222-231, 2009.

57. Henriquez-Camacho C, Losa J, Miranda JJ, et al. Addressing healthy aging populations in developing countries: unlocking the opportunity of eHealth and mHealth. *Emerging themes in epidemiology;*11(1):136, 2014.

58. Instituto Especializado de Salud Mental. *Estudio epidemiológico metropolitano en salud mental 2002.* Lima: Instituto Especializado de Salud Mental "Honorio Delgado - Hideyo Noguchi";2002.

59. Luna Matos ML, Salinas Pielago J, Luna Figueroa A. Major depression in pregnant women served by the National Materno-Perinatal Institute in Lima, Peru. *Pan American journal of public health*;26(4):310-314., 2009.

60. Cripe SM, Sanchez S, Lam N, et al. Depressive symptoms and migraine comorbidity among pregnant Peruvian women. *Journal of affective disorders;*122(1-2):149-153, 2010.

61. Vega P, Sweetland A, Acha J, et al. Psychiatric issues in the management of patients with multidrug-resistant tuberculosis. *The international journal of tuberculosis and lung disease: the official journal of the International Union against Tuberculosis and Lung Disease;*8(6):749-759, 2004.

62. Anderson RJ, Freedland KE, Clouse RE, et al. The prevalence of comorbid depression in adults with diabetes: a meta-analysis. *Diabetes Care;*24(6):1069-1078, 2001.

63. Rayner L, Price A, Evans A, et al. Antidepressants for depression in physically ill people. *The Cochrane database of systematic reviews.* (3):CD007503, 2010.

64. Sorkin DH, Ngo-Metzger Q, Billimek J, et al. Underdiagnosed and undertreated depression among racially/ethnically diverse patients with type 2 diabetes. *Diabetes Care*;34(3):598-600, 2011.

65. Wu DY, Munoz M, Espiritu B, et al. Burden of depression among impoverished HIV-positive women in Peru. *Journal of acquired immune deficiency syndromes (1999);*48(4):500-504 , 2008.

66. Diez-Canseco F, Ipince A, Toyama M, et al. Integration of mental health and chronic non-communicable diseases in Peru: challenges and opportunities for primary care settings. *Revista peruana de medicina experimental y salud publica;* 31(1):131-136, 2014.

67. Peters DH, Adam T, Alonge O, et al. Implementation research: what it is and how to do it. *Bmj;*347: f6753, 2013.

68. Singh N, Armstrong DG, Lipsky BA. Preventing foot ulcers in patients with diabetes. *JAMA;*293(2):217-228, 2005.

69. Lavery LA, Higgins KR, Lanctot DR, et al. Home monitoring of foot skin temperatures to prevent ulceration. *Diabetes Care*;27(11):2642-2647, 2004.

70. Armstrong DG, Holtz-Neiderer K, Wendel C, et al. Skin temperature monitoring reduces the risk for diabetic foot ulceration in high-risk patients. *The American journal of medicine;*120(12):1042-1046, 2007.

71. Lavery LA, Higgins KR, Lanctot DR, et al. Preventing diabetic foot ulcer recurrence in high-risk patients: use of temperature monitoring as a self-assessment tool. *Diabetes Care;*30(1):14-20, 2007.

72. World Health Organization. *Investing in Mental Health: Evidence for Action.* Geneva: WHO; 2013.

73. World Health Organization. *Mental Health and Development: Targeting People with Mental Health Conditions as a Vulnerable Group.* Geneva: WHO; 2010.

74. Moussayi S, Chatterji S, Verdes E, et al. Depression, chronic diseases, and decrements in health: results from the World Health Surveys. *Lancet;*370 (9590):851-858, 2007.

75. Patel V, Araya R, Chatterji S, et al. Treatment and prevention of mental disorders in low-income and middle-income countries. *Lancet*;370(9591):991-1005, 2007.

76. Prevalence, Severity, and Unmet Need for Treatment of Mental Disorders in the. *World Health Organization World Mental Health Surveys;*291:2581-2590, 2004.

77. Wang PS, Angermeyer M, Borges G, et al. Delay and failure in treatment seeking after first onset of mental disorders in the World Health Organization's World Mental Health Survey Initiative. *World Psychiatry;*6(3):177-185, 2007.

78. Wang PS, Guilar-Gaxiola S, Alonso J, et al. Use of mental health services for anxiety, mood, and substance disorders in 17 countries in the WHO world mental health surveys. *Lancet.* ;370(9590), 2007.

79. Araya R, Rojas G, Fritsch R, et al. Inequity in mental health under the reform mental health system in Chile. *American Journal of Publiic Health;*96:109-113, 2006.

80. Ormel J, Petukhova M, Chatterji S, et al. Disability and treatment of specific mental and physical disorders across the world. *British Journal of Psychiatry;*192(5):368-375, 2008.

81. Posada-Villa J, Rodríguez M, Duque P, et al. Mental disorders in Colombia: Results from the World Mental Health Survey. *The WHO World Mental Health Surveys: Global Perspectives on the Epidemiology of Mental Disorders*. New York: Cambridge University Press; 2008:131-143.

82. Demyttenaere K, Bruffaerts R, Posada-Villa J, et al. Prevalence, severity, and unmet need for treatment of mental disorders in the World Health Organization World Mental Health Surveys. *JAMA;*291 (21):2581-2590, 2004.

83. Menezes PM, Araya R, Miranda JJ, et al. The Latin American Treatment and Innovation Network in Mental Health (LATIN-MH): Rationale and Scope. *Rev Fac Cien Med Univ Nac Cordoba (in press).*

84. Gwatkin DR. IMCI: what can we learn from an innovation that didn't reach the poor? *Bulletin of the World Health Organization*;84(10):768., 2006.

85. Nelson LA, Zamora-Kapoor A. Challenges in conducting mHealth research with underserved populations: Lessons learned. *Journal of telemedicine and telecare.* 2015.

86. World Health Organization. *mHealth: new horizons for health through mobile technologies: based on the findings of the second survey on eHealth.* Geneva2011.

Table 1. Summary of the studies conducted in the three Latin American COEs

Center of Excellence	Study	Study Design	Target Population and Sample size	Duration	mHealth Intervention component	Other Intervention components	Outcome Measures
Argentina (CESCAS), Guatemala (CIIPEC), Perú (CRONICAS)	A Randomized Controlled Trial of a mobile health intervention to improve cardiometabolic profile in prehypertensive subjects from low resource urban settings in Latin America	Individual RCT	637 pre-hypertensive individuals randomized: 316 allocated to the intervention and 321 to the control arm.	12 months	1) Monthly motivational counseling calls to their mobiles along one year. 2) Weekly boosters of individualized short		1) Mean difference of change in systolic (SBP) and diastolic (DBP) blood pressure. 2) Other secondary outcomes: changes in body weight, waist circumferen

					message services (SMS) targeted to improve ment of diet quality and physical activity, or usual care.		ce, and self-reported target behaviors between the intervention and control arm from baseline to 12 months.
Argentina (CESCAS), Institute for Clinical Effectiveness and Health Policy	A Comprehensive Approach to Hypertension Prevention and Control in Low-resource settings in Argentina	Cluster RCT	18 PCCs and 1950 uninsured hypertensive adults and their families	18 months	1) Educational SMS and reminders to promote healthy lifestyle habits	1) Primary care physicians training on HTN management. 2) Physician Audit and feed-back. 3) Home visits	1) Net change in the SBP and DBP value at baseline, 6, 12 and 18 months of follow-up. 2) Proportion

					and adherenc e to HTN drugs and doctor appointm ents at the PCCs.	driven by CHWs to hypertensive individuals and their families to promote lifestyle modification, and adherence to HTN medication and follow-up at PCCs.	of HTN control at baseline, 6, 12 and 18 months of follow-up. 3) Self-reported medication adherence among hypertensiv e patients at baseline, 6, 12 and 18 months of follow-up. 4) Net change in body weight and waist circumferen ce at baseline, 6,

							12 and 18 months of follow-up. 5) Cost-effectiveness and process evaluation outcomes.
	An Educational Approach to Improving Physicians' Effectiveness in the Detection, Treatment, and Control of hypercholesterolemia and high CVD risk in low-resource	Cluster RCT	10 public PCCs and 350 patients with moderate-to-high cardiovascular risk	12 months	1) a mCDSS to guide lipid management. 2) Educational SMS and reminders to promote adherence to	1) Primary care physician training in hypercholesterolemia and high CVD risk management. 2) Educational outreach visits to physicians.	1) Net change of LDL-c values at baseline, 6 and 12 months of follow-up. 2) Net change in 10-year-CVD Framingham risk score before and

	settings in Argentina				treatment.		after the implementation of the program at baseline, 6 and 12 months of follow-up. 3) Proportion of patients with moderate-high CVD risk who have reduced 30% and 50% of their LDL-C at baseline, 6 and 12 months of follow-up.

							4) Proportion of patients with high CVD risk who are on statins, and are receiving an appropriate dose according to the CPG at baseline, 6 and 12 months of follow-up.
	Strengthening Diabetes Care for Underserved in the province of Corrientes, Argentina	Before-after quasi-experimental	20 PCCs and 1000 diabetic patients	12 months	1) An ICT system: electronic diabetes registry associate	1) Primary care team training in diabetes management and education.	1) Proportion of diabetics with an annual A1c value, eye and foot

					d with a mCDSS for health care professionals to guide diabetes care. 2) Educational SMS and reminders for diabetic patients.		exam. 2) Proportion of diabetics with poor metabolic control (HbA1c>9 %) at baseline, 6 and 12 months of follow-up. 2) Proportion of diabetics with HTN control (BP≤140/90 mmHg) at baseline, 6 and 12 months of follow-up.

	mHealth Interventions to improve access and coverage of uninsured people with high cardiovascular risk in Argentina	Cluster RCT	8 public PCCs and 350 patients with a 10 year CVD risk ≥ 10%	6 months	1) mCDSS for CHWs to calculate CVD risk associated with a scheduling systems in a mobile phone to refer and make clinical appointment to PCCs in patients a 10 year CVD risk ≥ 10%. 2)		1) Proportion of participants with a10 - year CVD risk ≥ 10% who have successfully completed the baseline (first) visit to a clinic out of all those classified as having risk >10% within the prior 6 weeks in the community. 2) Proportion

					Educational SMS and reminders for participants to attend appointments.		of participants with a10 - year CVD risk ≥ 10% who attend follow-up visits at PCCs within 4 months of the baseline visit. 3) Cost effectiveness and process evaluation outcomes.
INCAP Research Center for the Preventio	Feasibility and acceptability of an intervention to promote the	Quasi-experimental (pre-post with no-	6 Food establishments and 300 users (universit	10 weeks	1) A mobile phone app and a website	1) Healthy cooking training for staff of university	1) Number of students/staff who downloaded

n of Chronic Diseases	sale of "healthy eating" in the university campus Ruben Dario National Autonomous University of Nicaragua, UNAN-Managua	treatmen t control group)	y students and staff)		that show daily menus, healthy dishes, prices, and promote healthy eating through education al tips.	canteens. 2) on-site advertisement strategy and through the university social media and website	the app and checked the website. 1) Mean number of interactions among users of the mHealth app. 2) Number of new healthy dishes offered and sold per week. 3) Users' food preference.
CRONIC AS, Universid	Allillanchu. Integration of Mental Health	Quasi-experim ental and	20 PHCP of 5 public	2 mont hs	1) an app installed in a tablet		1) Number PHCP trained.

ad Peruana Cayetano Heredia	into Primary Health Care Services in Lima, Peru	qualitative study	PCCs Pregnant women and patients with diabetes, hypertension, tuberculosis and HIV/AIDS who are regular users of 5 public PCCs.		for the screening of common mental disorders during the regular consultations of PHCP. 2) Use of SMS to remind and motive patients to seek mental health care.		2) Number of PHCP who pass the training evaluation. 3) Number of PHCP who implement screening in their daily service routines. 4) Number of screened patients. 5) Proportion of patients who seek mental health care after being identified

							and referred by a PHCP. 6) Proportion of patients who access mental health care after being identified and referred by a PHCP. 7) Proportion of PHCP willing to include the mHealth package in their daily practice after the end of the 2-month

							intervention
	Implementation of foot thermometry and SMS to prevent diabetic foot ulcer	RCT	172 patients with type 2 diabetes at high risk of ulceration who receive care at 2 public hospitals (86 in each group)	12 months	1) SMS and voice messages to remind and promote the use of the foot thermometer, during one year. First two weeks participants will receive daily reminders and for the remaining 50		1) Proportion of patients with foot ulceration (at least one ulcer) along a 1-year follow-up. 2) Proportion of patients who adherence to daily temperature measurements (at least 50% of daily measurements during a 1 year

					weeks, patients will receive two messages per week, one SMS and one voice message, alternating content.		period).
Peru (Lima) & Brazil (Sao Paulo) CRONICAS Center of Excellence in Chronic	Latin America Treatment & Innovation Network in Mental Health (LATIN-MH)	Cluster RCT & RCT	Adults with hypertension and/or diabetes attending ambulatory clinics, and who present depressiv	3 months	1) Control Emocional (CONEMO), a 6 - week low-intensity psycho-education		1) Proportion of participants whose depressive symptoms have "recovered" (PHQ-9<10) at

Diseases, Universidad Peruana Cayetano Heredia University of Sao Paulo Northwestern University London School of Hygiene and Tropical Medicine			e symptoms (PHQ-9 ≥ 10). 421 participants in Peru and 20 PCCs , 851 participants in Brazil (50% in each arm).		al intervention, based on behavioral activation model, delivered via smartphones phones assisted by an auxiliary nurse for reducing depressive symptoms.		baseline and 3 months. 2) Depressive symptoms at baseline and 3 months (PHQ-9). 3) Social functioning at baseline, and 3 months (WHO-DAS 2.0). 4) Quality of life at baseline and 3 months (EQ-5D). 5) Adherence to

							medication for diabetes and hypertension at baseline, and 3 months (Morisky Medication. Adherence Scale-MMAS-4) 6) Level of activity at baseline and 3 months (Behavioral Activation for Depression Scale BADS). 7) Cost-

							effectiveness and process evaluation outcomes.

SBP, (systolic blood pressure), DBP (diastolic blood pressure), ICT (Information and Communication Technology System), PCCs (Primary Care Clinics), CHWs (community health workers), mCDSS (A clinical decision support systems in a mobile apps), PHCP (Primary Health Care Providers)