Challenges and Opportunities for Implementation of Interventions to Prevent and Control CVD in Low-Resource Settings

A Report From CESCAS in Argentina

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In Argentina, cardiovascular diseases cause an estimated 100,000 deaths and more than 250,000 coronary heart disease and stroke events annually, at a cost of more than $1 billion international dollars. Despite progress in the implementation of several programs to combat noncommunicable diseases in Argentina over the past few years, most health resources are still dedicated to infectious diseases and maternal and child health. The Institute for Clinical Effectiveness and Health Policy, an independent academic institution affiliated with the University of Buenos Aires medical school, runs the South American Centre of Excellence in Cardiovascular Health (CESCAS), a center devoted to epidemiology, implementation, and policy research. At the CESCAS, there are 3 ongoing randomized clinical trials focused on implementation science: 1) a mobile health intervention, for preventing the progression of prehypertension in low-income, urban settings in Argentina, Guatemala, and Peru; 2) a comprehensive approach to preventing and controlling hypertension in low-resource settings in Argentina; and 3) an educational approach to improving physicians' effectiveness in the detection, treatment, and control of hypercholesterolemia and high cardiovascular disease risk in low-resource settings in Argentina. All of these trials involve the design and implementation of complex interventions for changing the behaviors of providers and patients. The rationale of each of the 3 studies, the design of the interventions, and the evaluation of processes and outcomes are described in this article, together with the barriers and enabling factors associated with implementation-research studies. There is a strong need in Argentina and all of Latin America for building the health-research capacity and infrastructure necessary for undertaking implementation studies that will translate evidence from research findings into improvements in health policy and practice with regard to cardiovascular diseases and their risk factors.

CARDIOVASCULAR DISEASE BURDEN IN ARGENTINA

Coronary heart disease (CHD) and stroke are the leading causes of death worldwide (12.9 million, or 1 in 4 deaths, in 2010) [1]. Eighty percent of these deaths occur in low- and middle-income countries (LMICs), almost half in people younger than 70 years of age, compared with 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 men and women) compared with increases of 28% in women and 50% in men in developed countries during the same period [3]. The INTERHEART (Effect of Potentially Modifiable Risk Factors Associated With Myocardial Infarction in 52 Countries) study [4] from Latin America showed that the majority of cardiovascular risk in the Southern Cone could be explained by tobacco use, abnormal lipids, abdominal obesity, and high blood pressure (BP). In Argentina, CVDs are estimated to cause about 100,000 deaths and more than 250,000 events each year, at a cost of more than $1 billion international dollars [5]. Recent estimates indicate that more than 600,000 disability-adjusted life-years (DALYs) and almost 400,000 years of potential life lost are due to CHD and stroke, with modifiable risk factors explaining 75% of fatal and nonfatal acute CHD and stroke events (82% of acute CHD events and 62% of strokes) and 71% of DALYs lost [6]. These estimates are alarming given that the prevalence of all major CVD risk factors in Argentina (hypertension, diabetes, obesity, physical inactivity, and poor nutrition) increased between 2005 and 2009 according to the National Cardiovascular Risk Factors Surveys. The prevalence of diabetes rose by 14.1%, from 8.4% to 9.6%; obesity rose by 23.3%, from 14.5% to 18.0%; and low physical activity rose by 19%, from 46.2% to 55% [7]. There has been important progress in the implementation of several programs to combat noncommunicable disease (NCD) in Argentina at both the national and subnational levels; however, most health resources are still dedicated to infectious diseases and maternal and pediatric health. Looking forward, NCD prevention and control are promising. Argentina recently

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established strong policies against tobacco and unhealthy diets as well as increased support for universal health coverage of some of the most prevalent NCDs that are moving up the national health agenda, including CVD, cancer, chronic obstructive pulmonary disease, diabetes, and mental health.

NCD RESEARCH IN ARGENTINA

Insufficient research funding and infrastructure are 2 of the greatest obstacles of performing and publishing research in Latin America. For example, Argentina dedicates only 0.65% of the gross domestic product to research, having approximately 3 researchers per 1,000 economically active adults [8], and only 6% of its biomedical research funds applied to clinical and public health research [9]. Performance of health research in Latin America has been poor; from 2001 through 2010, Latin American nations contributed just over 3% of the overall publications worldwide, of which almost 80% came from only 3 countries: Argentina, Brazil, and Mexico. Most of the research papers were related to basic research; just 22% were publications regarding clinical investigation or public health. Of these, <10% (1,338 papers) were focused on CVD. Not surprisingly, only 8 were randomized clinical trials conducted only in Latin American countries and not as a part of multinational studies sponsored by the industry [10]. More concerning is the fact that upper-middle income countries (UMICs) are increasingly being considered ineligible for several funding opportunities from the donors and research agencies of developed countries. If this tendency were to spread among funding agencies, the role of research institutions in UMICs will strongly decrease. Because Argentina is a UMIC according to the World Bank classification [11], there may be a further reduction in funding for public health and clinical research in that country.

A CENTER OF EXCELLENCE IN SOUTH AMERICA FOR PROMOTING HIGH-QUALITY RESEARCH ON NCDS

The Institute for Clinical Effectiveness and Health Policy, an independent academic institution affiliated with the University of Buenos Aires medical school, runs the South American Centre of Excellence in Cardiovascular Health (CESCAS) (Buenos Aires, Argentina), created in 2009 through a competitive award from the National Heart, Lung and Blood Institute (NHLBI) in partnership with the School of Public Health and Tropical Medicine, Tulane University (New Orleans, LA, USA). The CESCAS staff is composed of physicians, epidemiologists, nutritionists, nurses, health economists, social scientists, and statisticians, as well as trainees at the postdoctoral, doctoral, and master's degree levels. The center is devoted to epidemiology, implementation, and policy research training in cardiovascular health and to technical cooperation with national, regional, and international bodies. The center also advocates for the translation of evidence into policy and practice by promoting a policy dialogue between researchers, policymakers, the media, nongovernment organizations, and the general public to combat CVD at a regional level. Since June 2009, CESCAS has undertaken different observational, implementation, and policy research studies.

POST-TRANSLATIONAL RESEARCH STUDIES CONDUCTED AT CESCAS

Implementation science is about providing methods of translating research findings from interventions into health care policy and practice to help to bridge the gap between what is known and what is actually done. It seeks to understand the behavior of health care providers, patients, health care organizations, and policymakers in a particular context, as key variables to promote the adoption, implementation, and uptake of evidence-based interventions. Unlike interventions tested in most randomized clinical trials, which are generally simpler, more straightforward, and targeted directly at patients as units of analysis, those tested in the implementation-research field are more complex because they usually act on patients indirectly, through the behavioral changes of providers, organizations, or at even higher levels such as health services and systems. These complex interventions usually contain multiple interacting components with several dimensions of complexity, including the number of elements in the intervention package itself, such as the different behaviors required by those delivering or receiving the intervention, the number of groups or organizational levels targeted by the intervention, the number and variability of outcomes, and the degree of flexibility or tailoring of the intervention permitted. All of these components imply that a lack of effect may reflect implementation failure rather than true ineffectiveness [12]. Moreover, evaluation may be compromised by problems with acceptability, compliance, delivery of the intervention, recruitment and retention, and smaller-than-expected effect sizes that could have been prevented if a feasibility or pilot study were planned ex ante [13]. For these reasons, it is crucial that in the evaluation of the results of these trials, both outcome measures and process measures are planned in order to explore the way in which the interventions have been actually implemented. This approach can disentangle the different components of the planned intervention and provide valuable insight into why an intervention worked, failed, or yielded unexpected results and how it could be optimized if successful. Process evaluations nested within these trials can be used for assessing fidelity and quality of implementation, clarifying causal mechanisms, and identifying contextual factors associated with variation in outcomes [14]. Notwithstanding, the evaluation of the process is not a substitute for the evaluation of the outcomes; however, it can be extremely helpful, particularly in negative studies in which a complex intervention can be like a "black box."

Currently, there are 3 ongoing implementation-research randomized controlled trials (RCTs) ongoing at the South American Center of Excellence for Cardiovascular Health. All of these studies involve the design and implementation of complex interventions for changing the behaviors of

providers and patients. The rationale of each of the 3 studies, the design of the interventions, and the evaluation of processes and outcomes are described briefly.

A MOBILE HEALTH INTERVENTION FOR PREVENTING THE PROGRESSION OF PREHYPERTENSION IN LOW-INCOME, URBAN SETTINGS IN ARGENTINA, GUATEMALA, AND PERU

Prehypertensive patients are at a high risk for progressing to hypertension and CVD. Early interventions that promote the adoption of healthier life-styles in these subjects could reduce BP, decrease the rate of progression of elevated BP to hypertensive levels, and even prevent hypertension [15,16]. However, primary health care services in most Latin American countries, particularly in low-income settings, lack the infrastructure and resources to implement effective health-promotion interventions. On the other hand, health promotion is shifting toward new delivery modes (e.g., the Internet and cell phones) to reach a larger part of the population. However, evidence regarding the effectiveness of these interventions for life-style modification is unclear. Reported overall effects have been small and variable, and reach has been limited to highly educated female patients in high-income countries [17]. *Mobile health* (mHealth) refers to the use of mobile-telecommunication and multimedia technologies for health care delivery [18,19]. This technology is emerging as a tool useful for addressing several health care system constraints, such as limited health care workforce and financial resources, high burden of disease combined with high population growth, and the challenge of extending health care to hard-to-reach and vulnerable populations living in low-resource settings [20]. Mobile-phone strategies, using either voice or short message system (SMS) messages, have been reported to improve patient–provider communication, encourage behavioral changes, and assist in chronic-disease management [21–24].

Our study was an individual RCT, sponsored by the NHLBI and conducted in collaboration with the Institute of Nutrition of Central America and Panama in Guatemala and the Center of Excellence in Chronic Diseases from the Universidad Peruana Cayetano Heredia in Peru. This study aimed at promoting life-style changes (improvements in diet quality and physical activity) in 660 prehypertensive subjects in low-income, urban settings in Argentina, Guatemala, and Peru, through an mHealth intervention along 1 year of follow-up. This study ended in 2014, and the main process and outcomes results are being evaluated. In short, the intervention, led by nutritionists who completed a 3-day training session, had 3 components. First, semistructured counseling interviews were conducted using mobile phones to promote life-style modification, according to the motivational interviewing technique [23]. The participants in the intervention arm received counseling on 1 of 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. Information regarding readiness to change was based on the Transtheoretical Model [25] and was collected during monthly calls to the participants. Second, after the counselor's call, participants received a weekly text message via an SMS that was tailored to the state of change regarding a particular target behavior of the subject, identified by the counselor. Both the content and wording of SMSs had been previously validated in each of the countries (results of the validation process are not yet published). Third was the use of a Web-based application to deliver the interventions. This setup allowed for the following functions: 1) participants' baseline information for the nutritionist who made the calls, 2) an agenda for scheduling monthly calls, 3) a database for collecting information on the treated behavior and the stage of change, 4) a customized SMS desktop where messages were generated and tailored to each patient's stage of change and target behaviors, and 5) progress reports (Figure 1). The rationale of the trial was informed by a systematic review previously performed by our group to identify what was already known about mHealth intervention on chronic-disease outcomes in developing countries and the methods that have been used for evaluating its effectiveness [24], as well as focus groups conducted in each country, with participants with similar characteristics and attributes as the eligible patients (results of the qualitative research are not yet published). The design of the intervention was supported by an appropriate theory [25] that provided a good theoretical understanding that was necessary for knowing how the intervention causes change, so that weak links in the causal chain can be identified and strengthened [13]. In addition, a feasibility study was performed in 45 prehypertensive patients, before the initiation of study enrollment, to test the different components of the intervention program [26].

We included the following indicators as a part of the process evaluation: reach (the proportion of the intended target population that received the intervention), dose (components implemented), and attrition (the percentage of participants who dropped out of the intervention). The intervention package included an introductory call and monthly mobile-phone counseling calls and weekly SMSs during the year of intervention.

A COMPREHENSIVE APPROACH TO HYPERTENSION PREVENTION AND CONTROL IN LOW-RESOURCE SETTINGS IN ARGENTINA

Hypertension is a global public-health challenge because of its high prevalence and concomitant increase in the risk for CVD [27]. Approximately 80% of the attributable burden of hypertension is in LMICs [28]. According to recent estimates from CESCAS I, a large-scale, population-based cohort study that our center is conducting in 4 cities of the Southern Cone [29], the prevalence of hypertension in adult population aged 35 to 74 years is 43.3%. Overall, 62.2% of hypertensive patients are aware of their diagnosis, 47.7% are undergoing drug treatment, and only 21.5%

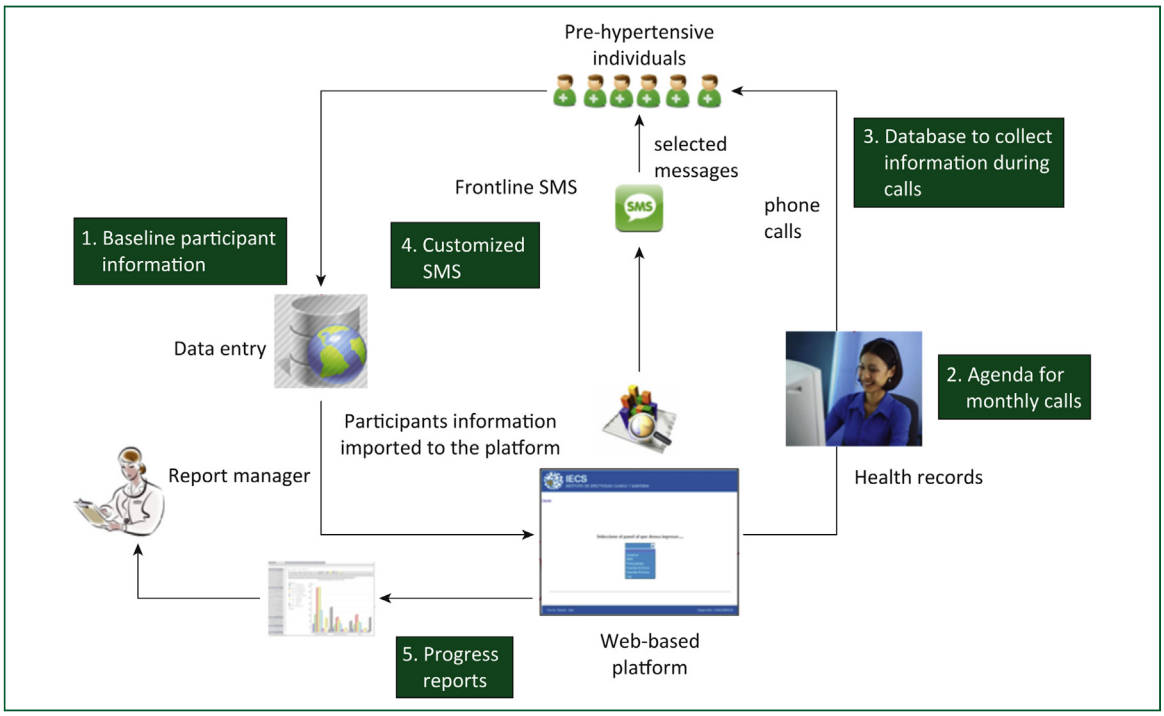

FIGURE 1. Functions of the Web-based platform to provide mHealth interventions. The Web-based platform allowed for the following functions: 1) baseline participant's information for the nutritionist who made the calls, 2) an agenda for scheduling monthly calls, 3) a database to collect information of the treated behavior and the stage of change, 4) a customized short message system (SMS) desktop where messages were generated and tailored to the patient's stage of change and target behaviors, and 5) progress reports.

achieve BP control [30]. The hypertension-control rate is even lower in underserved populations in Argentina. For example, even though antihypertensive drugs are delivered free of charge by public primary care clinics to uninsured populations, only 57% of uninsured hypertensive patients are actually treated. In those treated, almost 75% of patients receive medication for <4 months per year, and only 11.8% receive it for more than 9 months per year [31]. Barriers to hypertension control have been identified at the health care system, health care provider, and patient levels. Lack of access to health care, medication costs, and poor insurance coverage are major health system—level barriers [32]. Provider-level barriers include a lack of adherence to guidelines, willingness to accept elevated BP, and failure to prioritize BP control among multiple chronic medical issues. Patient-level barriers to BP control are primarily related to therapy adherence and include low perceived risks of high BP, low health literacy, lack of motivation, out-of-pocket medication costs, and adverse side effects [33—36].

In addition, low-income countries as well as poor settings in middle-income countries are facing a health workforce crisis [37]. Community health workers (CHWs)—also known as lay health workers, nonphysician health workers, health educators, patient navigators, and promoters—can compensate for this shortage through task-shifting and importantly can also provide direct links between health services and communities [38]. CHWs can increase the capacity of an already overburdened health care system by using health care resources more effectively and by increasing the quality of care [39]. The inclusion of CHWs in the primary care team is an example of an organizational change to address system-level barriers by simplifying the physician's tasks and transferring some responsibility for patient care to another team member (task-shifting). Team-change strategies have resulted in median reductions in systolic BP of 9.7 mm Hg and in diastolic BP of 4.2 mm Hg according to a meta-analysis [32]. In addition, CHWs may help to remove barriers to BP control and medication adherence due to cultural, educational, and language differences between community members and the health care system [40]. A systematic review of RCTs using CHW to implement BP control programs found significant improvement in 7 of 8 studies, primarily in poor, urban, minority communities [41]. Task-shifting from physicians to other health team members was an important ingredient in a large-scale hypertension program in an integrated health care delivery system in the United States that was able to almost double hypertension-control rates in 8 years by reducing

appointment times, providing increased scheduling flexibility, and decreasing health care costs [42]. Moreover, these interventions have been shown to be also effective in LMICs [43].

Our study, a cluster RCT, was designed to test an intervention strategy of hypertension prevention and control in Argentina, driven by CHWs' providing education and counseling to patients, liaison with physicians at the primary care clinic, training of physicians on hypertension management, and mHealth support tools in 18 primary health care centers of the Argentine public network, enrolling 2,000 uninsured hypertensive patients and their families. This study, sponsored by NHLBI under the umbrella of the Global Alliance of Chronic Disease, was implemented in collaboration with the School of Public Health and Tropical Medicine of Tulane University, and the Argentine Ministry of Health [44]. Briefly, we are comparing the effectiveness and cost-effectiveness of a comprehensive intervention program to those of usual care, to decrease systolic and diastolic BP in uncontrolled hypertensive patients and their families and to improve hypertension control in hypertensive patients over an 18-month period. Our strategy integrates patient evidence—based interventions shown to be effective in overcoming the barriers of hypertension control, as shown in Table 1. There are several components of the intervention. First is task-shifting within the primary care team (from physicians and nurses at the primary care clinic to CHWs at patients' homes). Trained CHWs who completed an initial 2-day workshop, reinforced by weekly phone calls by a field supervisor and on-site periodic refreshments, visit participants' homes monthly for the first 6 months of the intervention and every other month thereafter. CHWs educate and counsel participants and their families about medication adherence, at-home BP monitoring, and life-style—modification strategies. All study participants are given a pill box and an at-home BP monitor. CHWs also deliver antihypertensive medications to patients' homes in special cases as needed and help patients to schedule appointments with primary care doctors at the clinic when necessary. During follow-up home visits, CHWs provide tailored counseling to address barriers to hypertension self-management and effective behavioral change of targeted life-styles (i.e., improving diet quality, training patients to read food labels, and increasing physical activity). Second is physician education through workshops and distance-learning modules to reinforce clinical practice guidelines on hypertension prevention and control as well as management of patients' adherence to prescribed medication. Third, an individualized SMS was sent out weekly to participants to promote life-style changes and as reminders to reinforce medication adherence. Messages are based on hypertension status and perceived barriers to behavioral change, identified during CHW motivational-counseling sessions, and consist of motivational statements and behavioral-change techniques to reinforce in-person educational interventions.

In addition to the outcomes measures, such as the lowering of systolic and diastolic BP, some process measurements are being taken, including the number of CHW services provided (i.e., home visits), the percentage of CHW follow-up visits kept, the number of SMSs sent to each participant, patients' use of at-home BP monitors, patients' weight control and use of pill boxes, as well as improvements in targeted life-style habits, such as smoking, diet quality, and physical activity. These data collected in the field will be analyzed to evaluate whether the desired interventions are adopted by participants and the extent to which they are translated into better outcomes.

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

Hypercholesterolemia, a major cause of disease burden in both the developed and developing world, causes an estimated 2.6 million deaths each year (4.5% of all deaths), one-third of cases of ischemic heart disease, and 29.7 million DALYs [45]. In 2008, the global prevalence of elevated total cholesterol among adults was 39% (37% in men and 40% in women) [46]. In Argentina, the National Risk Factor Surveys conducted by the Ministry of Health indicated that between 2005 and 2009, the self-reported prevalence of hypercholesterolemia rose from 27.9% to 29.1%. Of these, only 54.8% received some treatment, 56.3% of whom were on lipid-lowering drugs (the rate of those receiving treatment was <20% among uninsured subjects, including subjects with more than 3 risk factors) [47]. The CESCAS I study (Detection and Follow-Up of Cardiovascular Disease and Risk Factors in the Southern Cone of Latin America) [29] recently reported baseline results—that the prevalences of hypercholesterolemia in Argentina were 23.1% in men and 25.6% in women, and according to the Framingham CHD risk measure, the prevalence of nonoptimal low-density lipoprotein cholesterol concentration was 28.0%. On the other hand, the percentage of subjects with hypercholesterolemia who were aware of their condition was 37.3%, and the percentage of those who were undergoing pharmacological treatment was dismally low: only 11.1%. Furthermore, only 1 in 4 subjects with a self-reported diagnosis of CHD was taking a statin, and most of those with CHD who were on treatment with a statin had a suboptimal low-density lipoprotein cholesterol concentration (personal communication, Rubinstein et al., 2013). These findings are especially relevant because hypercholesterolemia accounts for 25% of the burden of CHD in Argentina, as we showed recently in another study [48]. The Argentine Ministry of Health provides free ambulatory drugs to vulnerable people without health insurance who attend public primary care clinics. Until this year, statins had not yet been included in the list of drugs delivered by the program.

TABLE 1. Strategies to overcome barriers to hypertension control

Barrier	General approach	Specific strategy to overcome the barrier
Systems level		
Insufficient time	Task shifting	Simplify the physician's task; assign some responsibility for life-style changes to CHW
Lack of time for physician counseling	Task shifting	Shift some responsibility for life-style changes to CHW
Lack of continuity of care	Team change	CHWs liaise physician appointments
Discontinuation of prescribed free medications	Policy change	CHW facilitates delivery of prescribed drugs to patient's home
Poor access of patients to PHC clinic	Home visits by CHWs	Improve family-based approach and liaison with the PHC clinic
Provider level		
Lack of adherence to treatment guidelines, "clinical inertia"	Physician education	Interactive, case-based workshops delivered by opinion leaders following adult learning theory
Uncertainty of whether office BP represents usual BP	At-home BP monitoring	Provide at-home BP-monitoring records to physician at clinical visit
Patient level		
Passive attitude and misperceptions about high BP	Improve self-efficacy	Provide automated at-home BP monitor and BP log to involve patients in self-monitoring and control
Poor adherence to medications	Family-support, patient education, at-home BP monitoring	SMS reminders to reinforce adherence to medications; family members help to remind each other; provide pill box and review medications; self-monitoring provides immediate feedback
Hypertension knowledge/risk perception	Patient education	Information on importance of maintaining BP control; life-style change counseling tailored to patient's risk factors
Poor memory	Reminding, family support, patient education	SMS reminders to mobile phone or e-mail; family members help to remind each other; provide pill box and review medications
Low health literacy	Patient education	Transmit consistent, clear messages on life-style changes; recruit CHW from local community to ensure that health information is culturally and linguistically appropriate
Poor motivation	Reminding, family support, patient education, at-home BP monitoring	Use motivational interviewing to tailor intervention; tailor text/e-mail reminders to reinforce behavior change; family support for life-style changes; self-monitoring provides immediate feedback to reinforce life-style changes
Medication costs	Policy change, physician education, patient education	Leverage clinical network to improve access; train physicians to adhere to clinical practice guidelines; healthier life-styles may decrease need for medication
Adverse effects	Physician education, patient education	Discuss any medication adverse events with provider

BP, blood pressure; CHW, community health worker; PHC clinic, primary health care clinic; SMS, short message system.

Despite the availability of evidence-based practice guidelines, several barriers hinder the appropriate management of hypercholesterolemia in the primary care setting. These can be organizational barriers within primary care clinics, confusing and conflicting guidelines from external sources, errors and omissions by primary care doctors, communication problems at the interface between secondary and primary care [49], multiple competing demands on physicians' time, and a lack of reimbursement for preventive counseling [34]. Among the interventions that have been effective in dealing with barriers related to clinical practice are multifaceted educational outreach visits (EOVs) [50] and audit and feedback [51]. EOVs have the potential to change health professional practice, particularly the prescribing patterns of physicians. The term *educational outreach visit (EOV)*, or *academic detailing*, is used for describing an in-person visit by a health care professional to a physician's workplace. The intervention often includes feedback on existing practices. A recent Cochrane review indicated that patient re-enforcement and reminders seem to be the interventions most promising for increasing adherence to lipid-lowering drugs [52]. This study, a cluster RCT recently funded by a competitive independent grant from Pfizer and the International Atherosclerotic Society, will test an educational intervention to improve physicians' effectiveness in the detection, treatment, and control of hypercholesterolemia and high CVD risk in 350 patients from 10 primary care clinics in

low-resource settings in Argentina. This trial is timely because statins (simvastatin), as mentioned earlier, are now being incorporated into the package of drugs delivered free of charge to patients with high cholesterol concentrations, according to CVD risk stratification.

In summary, we will compare the effectiveness and cost-effectiveness of a multifaceted educational intervention program to those of usual care to lower cholesterol levels and CVD risk in patients at moderate to high cardiovascular risk and to determine whether this intervention program improves physicians' compliance with clinical practice guidelines as well as patient-care management and adherence over 1 year of follow-up. There are several components of the intervention. First is the development of an educational program for physicians. This program will start with an intensive 2-day workshop, followed by distance-learning modules, to train doctors on global cardiovascular risk assessment and management; epidemiology, diagnosis, treatment and monitoring of patients with dyslipidemia; and management of adherence issues in patients with chronic diseases. This initial training will be reinforced through quarterly EOVs to the primary care clinics of the intervention arm, where respected clinician—educators (academic detailers) will provide physicians with an on-site retraining program on evidence-based practice guidelines, as well as auditing and feedback through a review of medical charts and prescribing patterns. The second component is the development of an application for physicians' smart phones to provide evidence-based and guideline-driven decision aids for improving patient management. Third is the design and implementation of a Web-based platform to send tailored SMSs for life-style modification, and prompts and reminders for clinic appointments to improve treatment adherence by patients participating in the intervention clinics.

BARRIERS TO, AND ENABLERS OF, IMPLEMENTATION RESEARCH STUDIES IN ARGENTINA

Implementing evidence-based health interventions in low-resource settings is a challenge in LMICs [53], particularly when these intervention strategies are tested within a research framework. The main identified barriers to implementation research studies in poor settings include, but are not limited to, the complexity of interventions, with multiple components acting on providers and patients but also on 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; a complex social, cultural, and political context; and a community usually not engaged in or ready for the adoption of the health intervention.

However, to sort out these "bottlenecks," we have also identified some enablers that in our experience can be the key for success in implementation research studies, particularly in poor settings. First and foremost, the engagement of local authorities, community nongovernment organizations, local media, and other stakeholders is key for obtaining buy-in from the local community. In this regard, continuous involvement of health authorities, participation in community activities, visibility in local media before the beginning of recruitment, and fieldwork for the delivery of the intervention facilitate the ownership of and commitment to the study by both the health providers and the participants. Other factors that have proved to be enablers of success are: 1) building local capacity to enhance the perceived skills and motivation of the health personnel participating in the research study as an avenue to facilitate scaling-up (*scaling-up* has been defined as "the ambition or process of expanding the coverage of health interventions" [54]); 2) training and periodic retraining of the study personnel, necessary not only for avoiding departures from the protocol, which might be a risk in these studies, but also for introducing rigorous methods of assessment derived from clinical research in order to create an evaluative environment; 3) close monitoring of the field work, both on-site and through telephone and e-mail follow-up, is important for auditing and feedback and, perhaps more important, for supporting the local research team in dealing with the many hurdles that usually arise during implementation studies of complex interventions; 4) 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; and 5) design of a data-management workflow that allows for efficient and timely data and quality-control measures.

SUMMARY AND POLICY IMPLICATIONS

Crucial challenges of the successful implementation of postclinical translational research studies include the dissemination of results and scaling up. Interventions that are more likely scaled-up are those that are simple and technically sound, with also a widespread consensus about their value. An important aspect of implementation research is therefore to simplify delivery. Also, 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 [55]. In this regard, our ongoing studies engaged the National Ministry of Health from the outset on different aspects of the design and the delivery of the intervention. This involvement will probably facilitate the uptake, ownership, dissemination, and scaling up of the intervention strategy across public primary care clinics countrywide if these studies show positive results.

Despite the increasing burden of CVD in Argentina, which over the past few decades has been ranked as the main cause of mortality and morbidity, national health programs and policies are still mostly focused on interventions aimed at tackling communicable diseases or perinatal or childhood conditions. Therefore, there is a strong need in Argentina and the rest of Latin America for building the health research capacity and infrastructure necessary for undertaking

implementation studies to translate evidence from research findings into improvements in health policy and practice, in turn to address CVD and its risk factors. This need is even more urgent in poor populations, who are disproportionally affected by the epidemic of CVD and hence need effective, cost-effective, acceptable, and feasible interventions for helping to bridge the equity gap and counter CVD, particularly in low-resource settings in developing countries.

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