BMJ Open

Educational intervention to improve effectiveness in treatment and control of patients with high cardiovascular risk in low-resource settings in Argentina: study protocol of a cluster randomised controlled trial

Pablo Gulayin,[1] Vilma Irazola,[1] Alfredo Lozada,[2] Martin Chaparro,[1] Marilina Santero,[1] Laura Gutierrez,[1] Rosana Poggio,[1] Andrea Beratarrechea,[1] Adolfo Rubinstein[1]

To cite: Gulayin P, Irazola V, Lozada A, *et al*. Educational intervention to improve effectiveness in treatment and control of patients with high cardiovascular risk in low-resource settings in Argentina: study protocol of a cluster randomised controlled trial. *BMJ Open* 2017;**7**: e014420. doi:10.1136/bmjopen-2016-014420

► Prepublication history for this paper is available online. To view these files please visit the journal online (http://dx.doi.org/10.1136/bmjopen-2016-014420).

Received 3 October 2016
Revised 3 January 2017
Accepted 4 January 2017

[1]Institute for Clinical Effectiveness and Health Policy (IECS), Buenos Aires, Argentina
[2]Lipid Clinic at Austral University, Pilar, Argentina

Correspondence to
Professor Adolfo Rubinstein; arubinstein@iecs.org.ar

ABSTRACT

Introduction: Hypercholesterolaemia is estimated to cause 2.6 million deaths annually and one-third of the cases of ischaemic heart disease. In Argentina, the prevalence of hypercholesterolaemia increased between 2005 and 2013 from 27.9% to 29.8%. Only one out of four subjects with a self-reported diagnosis of coronary heart disease is taking statins. Since 2014, statins (simvastatin 20 mg) are part of the package of drugs provided free-of-charge for patients according to cardiovascular disease (CVD) risk stratification. The goal of this study is to test whether a complex intervention targeting physicians and pharmacist assistants improves treatment and control of hypercholesterolaemia among patients with moderate-to-high cardiovascular risk in Argentina.

Methods and analysis: This is a cluster trial of 350 patients from 10 public primary care centres in Argentina to be randomised to either the intervention or usual care. The study is designed to have 90% statistical power to detect a 0.7 mmol/L reduction in low-density lipoproteins cholesterol from baseline to 12 months. The physician education programme consists of a 2-day initial intensive training and certification workshop followed by educational outreach visits (EOVs) conducted at 3, 6 and 9 months from the outset of the study. An on-site training to pharmacist assistants during the first EOV is performed at each intervention clinic. In addition, two intervention support tools are used: an app installed in physician's smartphones to serve as a decision aid to improve prescription of statins according to patient's CVD risk and a web-based platform tailored to send individualised SMS messages to patients.

Ethics and dissemination: Ethical approval was obtained from an independent ethics committee. Results of this study will be presented to the Ministry of Health of Argentina for potential dissemination and scale-up of the intervention programme to the entire national public primary care network in Argentina.

Trial registration number: NCT02380911.

Strengths and limitations of this study

- There is scarce information about the effectiveness of educational interventions targeted to primary care physicians to improve primary prevention of cardiovascular diseases in low- and middle-income countries (LMIC), particularly in low-resource settings.
- Cluster randomised clinical trials are an adequate and powerful tool to evaluate educational interventions to change clinical practice.
- This implementation research study is highly integrated into the health services provided by the public health system in Argentina, which allows for potential scalability of findings.
- As most of complex interventions based on multiple components, the whole is more than the sum of the parts for what it is difficult to disentangle the individual effect of each single component. However, measurement of process measures can help understand the change triggered by the intervention or the lack thereof.
- If effective, this intervention should be replicated at a larger scale and with longer follow-up to assess sustainability.

HYPERCHOLESTEROLAEMIA: A MAJOR GLOBAL PUBLIC HEALTH CHALLENGE

Hypercholesterolaemia, a condition that accounts for a significant disease burden in the developed and developing world, is estimated to cause 2.6 million deaths annually

(4.5% of all deaths) and one-third of the cases of ischaemic heart disease.[1] Globally, mean total cholesterol levels changed little between 1980 and 2008, falling by <0.1 mmol/L per decade for men and women. In 2008, the global prevalence of elevated total cholesterol among adults was 39% (37% for males and 40% for females).[2] Observational studies show that there is a continuous positive relationship between coronary heart disease (CHD) and blood cholesterol concentrations.[3] The Cholesterol Treatment Trialists' (CTT) Collaboration reported a meta-analysis[4] of individual data from 90 000 individuals in 14 randomised trials of statin therapy versus control. Statin regimens resulted in a mean difference of about 1.0 mmol/L in low-density lipoprotein cholesterol (LDL-C) and a proportional reduction of 20% in major vascular events (defined as coronary death, non-fatal myocardial infarction, coronary revascularisation or stroke). A recent meta-analysis showed that trials comparing less intensive versus more intensive statin regimens produced further reductions in major vascular events.[5–8]

Although higher serum lipids level seems to be an almost inevitable consequence of economic development, urbanisation, westernisation and nutritional transition, these determinants can be offset through healthier diets and pharmacological interventions. Consequently, statins and other lipid-lowering drugs are increasingly used in high-income countries.[9 10] In low-income and middle-income countries, however, coverage of screening and treatment is still very low.[11–16]

In Argentina, the National Risk Factor Surveys conducted by the Ministry of Health indicate that between 2005 and 2013[17] self-reported prevalence of hypercholesterolaemia rose from 27.9% to 29.8%. Of these, 54.8% received some treatment, and only 56.3% of patients treated were prescribed with lipid-lowering drugs (the rate of those receiving treatment was <20% among uninsured subjects, including subjects with >3 risk factors).[18] Recent baseline results from the CESCAS I Study—a population-based prospective cohort study for the detection and follow-up of cardiovascular disease (CVD) and risk factors in 7600 adults from four cities in Argentina, Chile and Uruguay[19 20] found that the prevalence of hypercholesterolaemia in Argentina was 23.1% in men, and 25.6% in women. According to the Framingham heart study risk equation, the prevalence of non-optimal LDL-C was 28.0%. On the other hand, the percentage of subjects with hypercholesterolaemia who were aware of their condition was 37.3% (95% CI 32.8 to 41.9), and the percentage of aware patients under pharmacological treatment was dismally low: only 11.1%. Furthermore, only one in every four subjects with a self-reported diagnosis of CHD is taking statins, and most of those with CHD who are on statins have suboptimal LDL-C levels (Rubinstein *et al*. Personal communication. Data not yet published). This is especially relevant because hypercholesterolaemia accounts for 25% of the burden of CHD in Argentina, as shown in another study.[21]

Use of evidence-based clinical practice guidelines (CPG) to improve effectiveness and quality of treatment for patients with dyslipidaemia

As CHD is highly prevalent and lipid-lowering drugs, particularly statins, are among the most frequently prescribed drugs, lipid treatment guidelines have important implications for the health of the population and for the use of healthcare resources.[22] The International Atherosclerotic Society (IAS) has recently issued a CPG for the management of suboptimal LDL-C. It recommends statins as first-line therapy, choosing the type of statin based on availability and costs and adjusting the dose according to patient's CVD risk.[23] More recently, the 2013 American College of Cardiology and the American Heart Association (ACC/AHA) panels updated their blood cholesterol guidelines. They recommend the prescription of high-intensity statin therapy (lowering LDL–C ≥50%) or moderate-intensity therapy (lowering LDL–C by ~ 30% to <50%), based on the presence of prior CVD, LDL-C levels, type 2 diabetes, age and the estimated 10-year risk of CVD according to the risk estimates of pooled cohort equation.[5] Owing to a lack of evidence from randomised controlled trials (RCTs) regarding the efficacy of titrating statins to reduce CVD, guidelines no longer recommend this treatment to meet specific LDL-C or non-high-density lipoprotein cholesterol (HDL-C) goals.[5] However, the publication of a CPG does not ensure its application in clinical practice and, therefore, it is necessary to design effective implementation plans specially tailored to the organisational context targeted by the CPG.

Interventions to improve CPG implementation

Despite the availability of evidence-based practice guidelines, multiple barriers hinder the appropriate management of hypercholesterolaemia in primary care settings. These barriers include organisational hurdles 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,[24] multiple competing demands on physicians' time and lack of reimbursement for preventive counselling.[25] In addition to this, there are other barriers related to (1) the healthcare system (eg, lack of access, cost of medications and poor insurance coverage); (2) healthcare providers (eg, lack of adherence to guidelines, willingness to accept elevated high cholesterol and failure to prioritise this issue among multiple chronic medical issues) and (3) patients (eg, reluctance to take medication).[24]

The interventions that have been effective in dealing with barriers related to clinical practice include multifaceted educational outreach visits (EOVs),[26 27] audits and feedback.[27 28] EOVs have the potential to change health professional practice, particularly physicians' prescribing patterns. The term EOV or 'academic detailing' is used to describe a personal visit by a trained person to health professionals in their own settings. A recent systematic review on interventions to improve adherence to

cardiovascular disease clinical guidelines showed a global positive impact in intervention group compared with usual care.[27] The key principles of this approach include surveys of practitioners to determine barriers for appropriate practice and the subsequent development of an intervention tailored to address those barriers using simple messages; contacting practitioners with low compliance and delivering the intervention through respectable persons. Interventions often include feedback on existing practices.[29] EOVs alone or combined with other interventions have been effective in improving practice in the majority of circumstances: studies with dichotomous health professional outcomes (eg, proportion of patients treated in accordance with the guideline) showed a 5.6% improvement, while studies with continuous outcomes (eg, mean number of prescriptions) showed at least 20% improvement.[26] A recent Cochrane review indicates that patient re-enforcement and reminders seem to be the most promising interventions to increase adherence to lipid-lowering drugs. Other interventions associated with increased adherence were simplification of the drug regimen and patient information and education.[30]

Most of the interventions targeted to change provider's behaviours are usually defined as 'complex interventions'. Complex interventions are described as interventions that contain several interacting components or ingredients and also other characteristics such as a number and difficulty of behaviours required by those delivering or receiving the intervention, distinct groups or organisational levels targeted by the intervention, a number and variability of outcomes and a bigger latitude in the flexibility or tailoring of the intervention that is permitted.[31] In order to avoid that these complex interventions become 'black boxes', it is critical that process measures, in addition to outcomes, be planned to be assessed along with the study.[32]

Throughout the implementation of this study, we will consider the conceptual framework for evaluation of implementation fidelity proposed by Carrol *et al*.[32] The modified framework is presented in figure 1. Usually there is no linear relationship between intervention and outcomes, but there are a number of effect modifiers that affect these relationships, such as participants' response, components, strategies to facilitate the intervention, intervention quality, recruitment and last but not least, context. These factors influence the implementation fidelity of the study in terms of adherence of participants (health managers, providers, patients, users, etc) to achieve desired outcomes.

Challenges and opportunities for the implementation of interventions to prevent and control CVD in low-resource settings in Argentina

The prevalence of CVD and risk factors in Argentina is high. However, awareness, treatment and control, particularly for hypercholesterolaemia, are very low. The Remediar programme is a programme of the National Ministry of Health that provides free ambulatory drugs at the point of care to vulnerable people without health insurance who attend public primary care centres (PCCs) in Argentina.[33] The programme uses the WHO package for the assessment and management of cardiovascular risk in low-resource settings.[34]

To date, Remediar has provided drugs for the treatment of different cardiovascular risk factors such as antihypertensive and antidiabetic drugs and low-dose aspirin. Recently, in mid-2014, statins (simvastatin 20mg) became part of the package of drugs delivered free-of-charge for patients with high cholesterol and/or CVD risk, according to CVD risk stratification.

Although the inclusion of statins is crucial to reduce CVD in vulnerable uninsured subjects with high cholesterol and moderate-to-high risk CVD, a study that analysed prescriptions for patients with hypertension at the point of care in Argentine public clinics reported that only 57% of patients with hypertension covered by Remediar were treated. Of those treated, almost 75% received medication for <4 months/year, and only 12% for ≥9 months/year.[35] Thus, a comprehensive intervention aimed at changing practitioners' practices and improving patients' adherence to drugs is key to reduce CVD.

Study objectives

The overarching goal of this study is to test whether a multifaceted educational intervention targeted to physicians and pharmacist assistants at primary care clinics located in low-income settings improves treatment and control of hypercholesterolaemia among mostly uninsured patients with moderate-to-high cardiovascular risk in Argentina. The intervention will focus on the public primary care system through healthcare provider education, audit and feedback on the implementation of a CPG to improve management of statins and global CVD risk in these patients. The specific aims of this cluster randomised trial are:

1. to test whether a multifaceted educational intervention programme lowers LDL-C levels and CVD risk in patients with moderate-to-high cardiovascular risk;
2. to test whether this intervention programme improves physician compliance with clinical practice guidelines;
3. to test whether this intervention programme improves patient care management and adherence to medication;
4. to estimate the cost-effectiveness of this comprehensive intervention programme as compared with usual standard of care.

STUDY DESIGN AND METHODS

Overview of study design

The proposed study tests whether a multifaceted educational programme targeted at primary care physicians and pharmacy assistant improves processes and

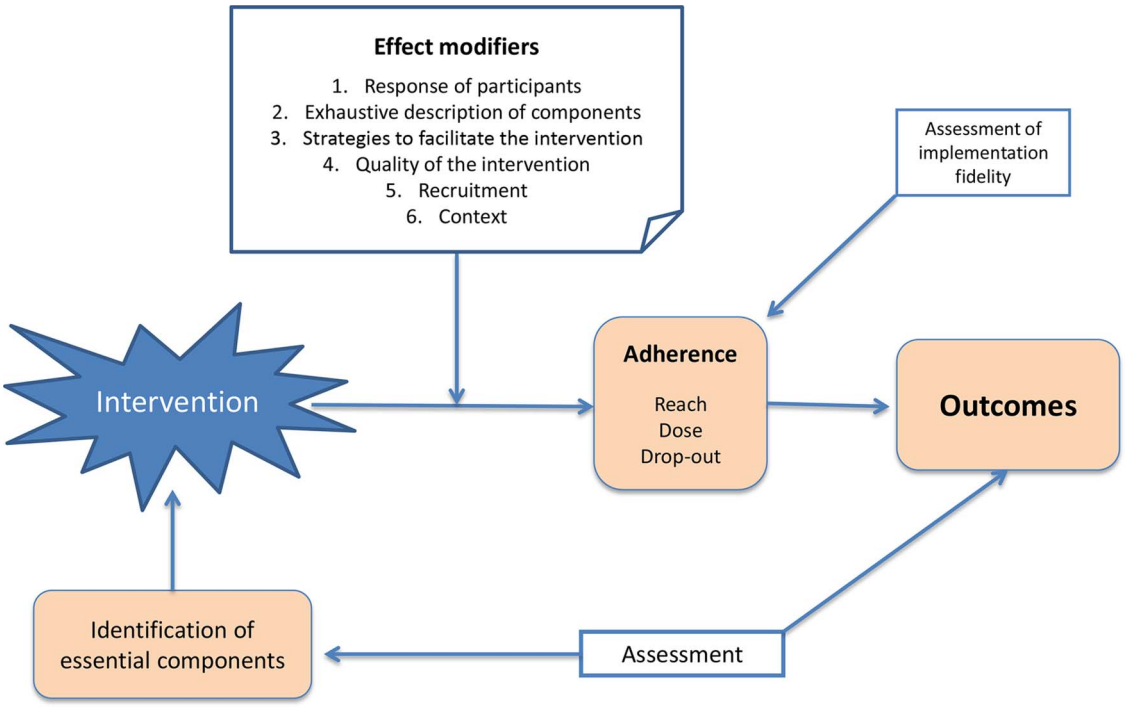

Figure 1 Conceptual framework for implementation fidelity. Adapted from Carrol C. Implementation Science, 2007.[32]

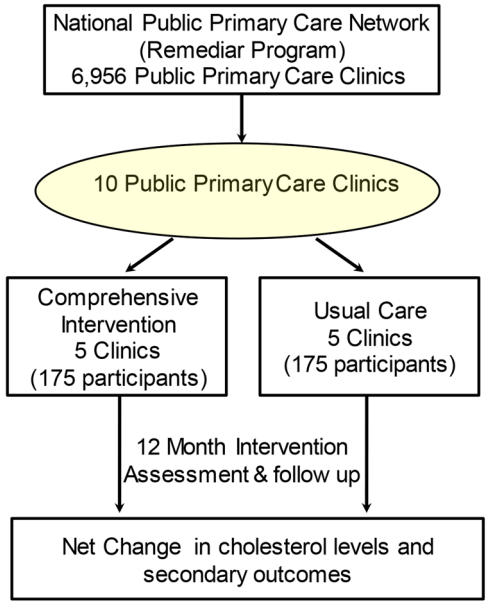

Figure 2 Study design.

outcomes of care in mostly uninsured patients with hypercholesterolaemia and moderate-to-high cardiovascular risk, in low-resource settings. This cluster RCT is conducted in 10 public PCCs in Argentina: five clinics were randomised to receive the intervention programme and five were randomised to receive usual care (figure 2). It is important to highlight that all clinics, irrespective of their assignment, will provide statins as prescribed. The intervention consists in an educational programme focused on the implementation of a CPG to improve management of statins in patients with moderate-to-high CVD risk. The programme includes innovative tools as mobile phone (mHealth) applications to provide decision aids to physicians and a web-based platform to send tailored SMS messages to patients. The study will recruit 35 patients in each clinic for a total of 350 study participants. Eligible patients will have 12 months of follow-up after randomisation.

Rationale for using a cluster RCT design

Cluster trials are an adequate design for evaluating educational outreach and related interventions. Randomisation by primary care clinic (PCC) is preferable because it avoids the potential contamination that could occur if randomisation were to be done at individual level (eg, the cholesterol treatments for patients in one clinic are more similar to each other than to patients from another clinic) and also because the effect of the intervention can be assessed in the natural practice environment.[36]

Study population

Ten PCCs from the provinces of Chubut in the Patagonia (four clinics), Corrientes in the north-east (four clinics) and La Rioja in the north-west (two clinics) were included in this trial. Box 1 presents the eligibility criteria for PCCs and patients. Study participants meeting eligibility criteria were recruited from participating PCCs to test the intervention in 'real-world' clinical settings. Selected PCC staff (physicians, nurses and pharmacist assistants) worked closely with the study

Box 1 Eligibility criteria for study clinics and participants

Eligibility criteria for study clinics (PCCs)

- The clinic is affiliated with the Remediar programme.
- The clinic is located in a poor urban area according to 2010 census data.
- The clinic has ≥800 outpatient adult visits each month (to ensure recruitment of enough participants).
- Physician visits and statins are available free-of-charge to patients at the point of care.
- The minimum distance between PCCs is 10 km (different catchment area) and they do not share health professionals (to minimise intervention bias).
- Good performance of the PCCs (and their pharmacy) according to the reports of Remediar programme.

Eligibility criteria for study participants

Inclusion criteria

Patients aged ≥40 years and <75 years who received primary care at participating PCCs with at least one of the following criteria:

- Arteriosclerotic cardiovascular disease (ASCVD): defined as acute coronary syndrome; history of myocardial infarction, stable or unstable angina, coronary revascularisation, stroke or transient ischaemic attack presumed to be of atherosclerotic origin or revascularisation.
- High CVD risk according to the WHO charts adapted by the National MoH (estimated 10-year CVD risk ≥ 20%).[37]
- Low-density lipoprotein cholesterol (LDL-C) level ≥190 mg/dL.
- Type 2 diabetes.

Exclusion criteria

- Statin treatment.
- Pregnant women.
- Bed-bound patients.
- Patients who cannot give informed consent.
- History of end-stage chronic kidney disease treated with dialysis, HIV/AIDS, alcohol or drug abuse or active tuberculosis.

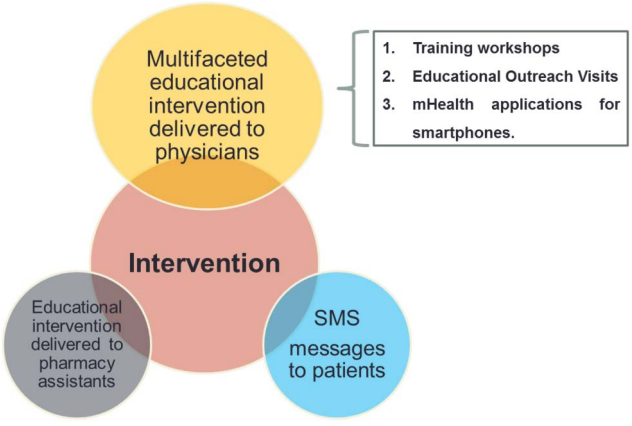

Figure 3 Intervention components.

team in order to optimise the referral of eligible patients to study nurses.

Randomisation

The 10 selected PCCs fulfilling the inclusion criteria were randomised to either the intervention or the control group: five PCCs to the intervention and five to the control group. Randomisation was stratified by province (Corrientes, Chubut and La Rioja), and it was conducted at the data management centre at the Institute for Clinical Effectiveness and Health Policy (IECS).

INTERVENTION PROGRAMME

The physician education programme consists of a 2-day initial intensive training and certification workshop at IECS. The sessions topics included global cardiovascular risk assessment and management; diagnosis, treatment and monitoring of patients with dyslipidaemia, the chronic care model components and management of adherence issues in patients with chronic diseases. The training was followed by EOVs conducted on quarterly basis (at 3, 6 and 9 months from the outset of the study), tailored to the needs of clinics' individual practitioners to identify the barriers to appropriate prescribing (eg, adequate statin dosage according to CPGs, side effects of statins, barriers to chronic treatment adherence and so on). EOVs include CPG practical exercises, prescription-related audits and feedback using selected charts from patients with high CVD risk and recommendations to improve practice administration/procedures (eg, support for systematic identification, particularly for complex patients with low adherence). Finally, an mHealth application installed in physicians' smartphones used to facilitate evidence-based and guideline-driven decision aids to improve patient management. The application was developed using SANA framework (http://sana.mit.edu), a highly customisable, open-source, android-based mHealth information system.

Usual care at clinics consists of mostly unscheduled appointments with a primary care physician on patient's demand. All clinics in the network provide ambulatory drugs free-of-charge at the point of care and most of the physicians, irrespective of the assignment, have received previous training in global cardiovascular risk management by trainers of the Ministry of Health. In addition, all clinics were provided with educational flyers and written material to be displayed at the PCCs, including charts with the CPG on the use of statins.

In summary, physicians of PCCs randomised to the intervention group receive a 3-component intervention: training workshop, EOV's and an mHealth application uploaded to their smartphones (figure 3).

In addition to the two main educational components aimed at primary care physicians, two intervention support tools are used:

1. A web-based platform tailored to send individualised SMS messages to encourage patients to adopt healthy lifestyles, prompts and reminders to engage in regular visits to their primary care doctors as well as to improving adherence to statins and other medication in participating intervention clinics.
2. On-site training to pharmacist assistants during the first EOV at each intervention clinic. This training

was focused on counselling to improve medication adherence among patients initiating statin therapy, enforced at each patient visit to the clinic to refill drug prescriptions. Additionally, pharmacist assistants received educational flyers to be displayed at the pharmacy.

Treatment algorithm

The algorithm for the use of statins in the treatment of high cholesterol according to CVD risk was adapted from the new ACC/AHA Guideline on the Treatment of Blood Cholesterol to reduce Atherosclerotic Cardiovascular Risk in Adults[5] and the WHO CVD risk charts.[37] Physicians prescribe statins in moderate-to-high intensity (simvastatin 40 mg) or low-intensity (simvastatin 20 mg) doses according to the CPG (figure 4).

STUDY OUTCOMES

In table 1 is shown which primary and secondary outcomes will be measured at the end of the trial following the specific aims mentioned before.

DATA COLLECTION

All questionnaires and measurements are performed by trained nurses who do not participate in the study intervention. After identifying each potentially eligible participant, a research physician/nurse explains the goals and scope of the study, and invites her/him to participate and sign a written consent form. The study has been approved by an independent Internal Review Board (IRB) at Hospital Italiano of Buenos Aires. A research nurse administers a questionnaire and records physical and biochemical measurements at baseline and at 6 and 12 months during follow-up (table 2).

Study forms and questionnaires include sociodemographics, history of CVD and risk factors, health behaviour (eg, smoking, diet and physical activity) and health services usage patterns and costs. Adherence to chronic medications are assessed with the Morisky-Green questionnaire.[38]

The average value of two blood pressure measurements is obtained at each visit using an automatic device (OMRON HEM-7200).[39] At the clinic visit, anthropometric measurements are taken on individuals in light clothing (barefoot) using a standard protocol. *Body weight* is measured to the nearest 0.1 kg on a dedicated scale; *body height* is measured to the nearest 0.1 cm with a free-standing stadiometer; *body mass index* (weight in kilograms divided by the square of height in metres) is calculated as an index for overall obesity and *waist circumference* is measured (at the smallest circumference between the ribs and iliac crest) in centimetres to the nearest 0.1 cm. We use the Gulick II tape measure (Gays

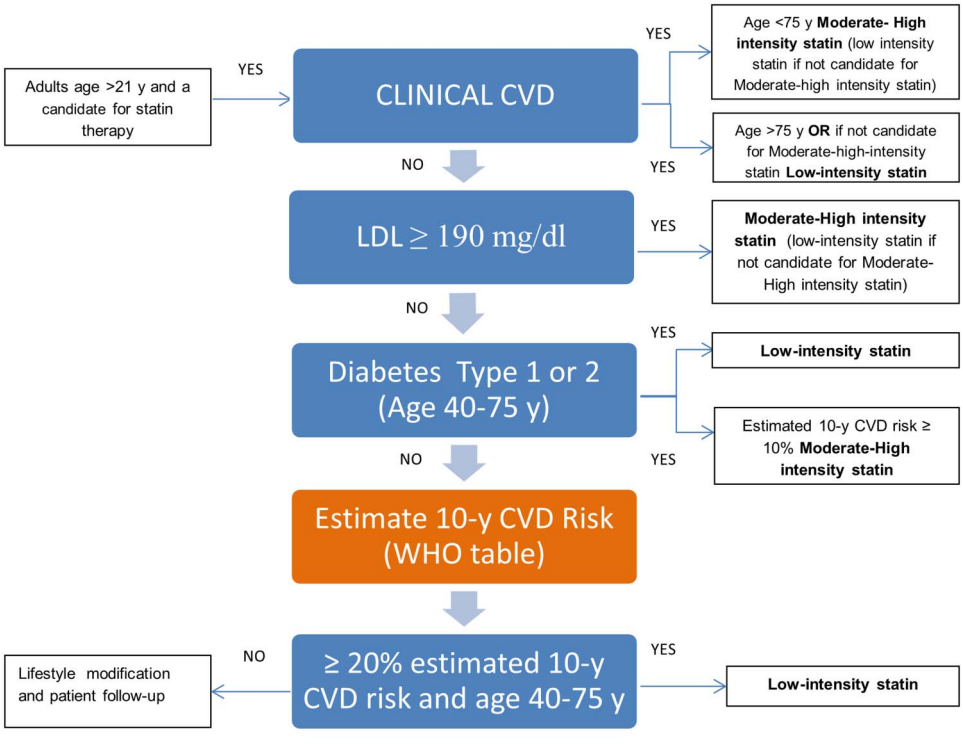

Figure 4 Treatment algorithm.

Table 1 Study outcomes

Specific aim 1	▶ Net change in LDL-C levels from baseline to month 12 in the intervention group vs the control group.	Primary outcome
Specific aim 1	▶ Proportion of patients with moderate and high CVD risk who have reduced their LDL-C by 30% and 50%, respectively.	Secondary outcomes
Specific aim 2	▶ Proportion of patients with high CVD risk who are on statins and are receiving an appropriate dose according to the CPG.	
Specific aim 3	▶ Net change in 10-year-CVD Framingham Risk Score before and after program implementation.	
	▶ Annual number of follow-up visits to the PCC for high CVD risk patients' level of treatment adherence evaluated through questionnaire among treated patients.	
Specific aim 4	▶ Incremental cost-effectiveness ratio (ICER) as cost per mg/dL of change in LDL-C, per treated case, per case receiving an appropriate dose according to the CPG and per QALY using the Argentina EuroQol EQ-5D.	

CPG, clinical practice guidelines; CVD, cardiovascular disease; LDL-C, low-density lipoprotein cholesterol; PCC; primary care centres.

Table 2 Data collection schedule

Measures	Baseline visits	6-month follow-up visit	12-month termination visit
Informed consent	X		
Medical history and questionnaires	X	X	X
Physical measurements	X	X	X
Delivery of statins	X	X	X
Biochemical measurements*	X	X	X
Statins adherence questionnaire		X	X
Assessment of outcomes		X	X

*Total cholesterol, estimated low-density lipoprotein cholesterol, high-density lipoprotein cholesterol, triglycerides and glucose.

Mills, WI) with a no-stretch, retractable tape and tensioning device to minimise measurement error. Each PCC, irrespective of the assignment, was provided with a point-of-care testing device, Cholestech LDX and LDX Capillary Plungers (Alere Cholestech LDX Analyser) to measure total cholesterol (TC), estimated LDL-C, HDL-C, triglycerides (TG) and glucose. Point-of-care testing with this device has been validated in several studies.[40–43] A fasting capillary blood sample is obtained by finger stick at baseline and during follow-up visits using a Cholestech LDX analyser.

Follow-up visits are scheduled at 6 and 12 months (final visit) after the baseline visit. Blood pressure, anthropometric measures, biochemical measures and updated information on the use of medications, cigarette smoking, alcohol drinking, diet, physical activity and costs of treatment are also obtained.

STATISTICAL ANALYSIS

Sample size

The study is designed to have 90% statistical power to detect a 0.7 mmol/L (27 mg/dL) reduction in LDL-C level at a significance level of 0.05 using a 2-tailed test, assuming an intracluster correlation coefficient (ICC) of 0.06.[44 45] Power calculations account for cluster design effect by using the formula developed by Donner and Klar,[46 47] which was implemented in the Power Analysis and Sample Size (PASS 2008) software (NCSS, Kaysville, UT). An 85% follow-up rate is assumed. Considering 10 clusters, the estimated sample size for each cluster (PCC) is 35, accounting for 175 in each group, based on these assumptions. This sample size ensures adequate power for testing our secondary outcomes as well.

Analytical planning

The difference in LDL-C levels from baseline to month 12 will be compared between intervention and control arm. The primary research hypothesis is that this difference will be greater in the intervention arm compared with the control arm, showing a greater reduction in LDL-C level in the intervention arm. We will use mixed-effects regression analysis with participants and clinics included as random effects, group, time and group-by-time interaction as fixed effects.

Intention-to-treat analyses will be conducted. In order to assess comparability between arms, we will compare the baseline characteristics of patients (demographics, clinical variables, lifestyle factors, anthropometrics measures and laboratory measurements) in the intervention group versus the control group using one-way ANOVA or χ^2 tests. In addition to this, we will perform subgroup analyses on primary and secondary outcomes according to diabetes status and level of CVD risk.

An economic evaluation component based on patient-level trial data will be supplemented by a model-based component to extrapolate long-term costs and effects. The trial-based primary economic evaluation will use patient-level data collected from the proposed study. We

will document all resources involved in conducting this comprehensive intervention programme, as well as all patient-level costs, in 2017 Argentine Pesos adjusted by Argentina's Consumer Price Index and then converted into international dollars. The primary incremental cost-effectiveness ratio (ICER) measure will be cost per mg/dL of change in LDL-C. Secondary measures will be cost per treated case, per case receiving an appropriate dose according to the CPG, and per quality-adjusted life-year (QALY) using the Argentina EuroQol EQ-5D.[48]

Dissemination

The dissemination plan is designed to translate, communicate and implement the research findings to inform health policy, health practice and public opinion. We will publish the study findings in international and national peer-review journals and make presentations at national and international professional meetings. The results of this implementation research study will be presented to the Ministry of Health of Argentina for dissemination and scaling-up.

Conclusions and policy implications

Hypercholesterolaemia imposes a heavy burden (with clinical and economic consequences) on Argentina's already overburdened healthcare system. This trial is designed with an implementation focus and has several distinctive aspects: there is a high prevalence of undiagnosed and uncontrolled population with dyslipidaemia and high CVD risk in Argentina as well as in most developing countries.[13 14 16] To the best of our knowledge, this is the first trial in Latin America that tests an educational intervention to reduce CVD risk targeting primary care physicians.[27] This study is very timely because statins were recently (2014) added to the national list of ambulatory drugs provided free-of-charge at Argentine public primary care clinics, and because there is no CPG in place in public PCCs aimed specifically at addressing the management of dyslipidaemia and statins by health providers. Promoting the adequate use of CPG leads to the reduction of inappropriate variability in clinical practice.[49 50] In addition, this study is innovative since it will use a mobile health application as a decision aid to support physician decision-making and a web-based platform to send tailored SMS messages to patients to promote behaviour change with respect to improving adherence to medications, clinical visits and lifestyles and behaviours.

As the study intervention targets mostly uninsured populations living in low-income settings, if successful, it can have an immediate impact in the real world through the dissemination and scale-up of the intervention programme to the entire national public primary care network in Argentina, thereby reducing health disparities in CVD risk management and control.

In summary, this study will generate urgently needed data on effective, practical and sustainable intervention programmes aimed at preventing and controlling CVD risk, which can be directly used in other primary care settings and healthcare systems in LMICs.

Contributors AR, VI and PG conceptualised and designed the manuscript, and revised and approved its final version. AR is the principal investigator of this trial and VI coinvestigator. AL, AB, RP and PG participated in the intervention implementation. LG collaborated in the design of statistical analyses. MC, MS and PG are involved in the field implementation and coordination of the trial. All the authors have revised and approved the final version.

Funding International Atherosclerotic Society—Pfizer grant (ID # 11526941).

Competing interests None declared.

Ethics approval Ethical approval was obtained from an independent ethics committee (Comité de Ética de Protocolos de Investigación—Hospital Italiano de Buenos Aires, Argentina). The study protocol and the informed consent were reviewed and approved by this board.

Provenance and peer review Not commissioned; externally peer reviewed.

Data sharing statement The study is ongoing and no data from this study has been published previously. Please contact the authors for any question or needed information.

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