

Comparing Strategies for Lipid Lowering in Argentina: An Analysis from the CVD Policy Model–Argentina

Jonatan Konfino, MSc¹, Alicia Fernandez, MD^{1,2}, Joanne Penko, MPH², Antoinette Mason, MS³, Eugenio Martinez, MS⁴, Pamela Coxson, PhD², David Heller, MD⁵, Andrew Moran, MPH^{6,7}, Kirsten Bibbins-Domingo, PhD², Eliseo J. Pérez-Stable, MD^{8,9}, and Raul Mejía, PhD^{1,2,3,4,5,6,7,8,9,10}

¹Centro de Estudios de Estado y Sociedad (CEDES), Buenos Aires, Argentina; ²Division of General Internal Medicine, Department of Medicine, University of California San Francisco, San Francisco, CA, USA; ³University of California San Diego School of Medicine, La Jolla, CA, USA; ⁴Instituto de Investigaciones Económicas, Facultad de Cs. Económicas, Universidad Nacional de Salta, Salta, Argentina; ⁵Arnold Institute for Global Health, Icahn School of Medicine at Mount Sinai, New York, NY, USA; ⁶Division of General Internal Medicine, Columbia University Medical Center, New York, NY, USA; ⁷New York College of Physicians and Surgeons, Columbia University, New York, NY, USA; ⁸Division of General Internal Medicine, Department of Medicine, Medical Effectiveness Research Center for Diverse Populations, University of California San Francisco, San Francisco, CA, USA; ⁹Office of the Director, National Institute of Minority Health and Health Disparities, National Institutes of Health, Bethesda, MD, USA; ¹⁰Hospital de Clinicas, University of Buenos Aires, Buenos Aires, Argentina.

INTRODUCTION: In Argentina, the national guidelines for lipid control emphasize the use of relatively inexpensive low- or moderate-potency statins by patients at high risk (>20 %) of a cardiovascular event. The objective of this study was to compare the impact and costs of the current national CVD prevention guidelines with regard to morbidity and mortality in Argentina with the impact and costs of three strategies that incorporate high-potency statins.

METHODS: We used the CVD Policy Model–Argentina to model the proposed interventions. This model is a national-scale, state-transition (Markov) computer simulation model of the CVD incidence, prevalence, mortality, and costs in adults 35–84 years of age. We modeled three scenarios: scenario 1 lowers the risk threshold for treatment to >10 % according the Framingham Risk Score (FRS); scenario 2 intensifies statin potency under current treatment thresholds; and scenario 3 combines both scenarios by lowering the treatment threshold to ≥ 10 % FRS and intensifying statin potency.

RESULTS: Scenario 1 would translate into 1400 fewer MIs and 500 fewer CHD deaths every year, a 3 % and 2 % reduction, respectively. Scenario 2 would lead to 2000 fewer MIs and 1000 fewer CHD deaths every year. Scenario 3 would result in the greatest reduction in MIs and CHD deaths, with 3400 fewer MIs and 1400 fewer CHD deaths every year, which translates to a 7 % and 6 % reduction, respectively. All scenarios were cost-effective if the cost of a high-potency statin pill was under US\$0.25.

CONCLUSION: Incorporating those individuals with greater than 10 % cardiovascular risk and the use of high-potency statins into Argentina's national lipid guidelines could result in fewer CHD deaths and events at a reasonable cost.

KEY WORDS: cardiovascular disease; Argentina; statin; coronary heart disease; hydroxy-3-methylglutaryl-coenzyme A reductase inhibitor; prevention.

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INTRODUCTION

Cardiovascular disease (CVD) is the leading cause of death in Argentina, and is responsible for 34 % of total deaths.¹ Recent data indicate that the prevalence of hyperlipidemia, hypertension, and diabetes, already among the highest in Latin America, is increasing.² The search for efficient and cost-effective strategies to improve primary and secondary prevention of cardiovascular disease is a national priority. Although lipid control represents one of the most effective strategies for reducing CVD risk, in Argentina (as in much of the rest of the world), cholesterol medications are underused, and only about 34 % of those with a diagnosis of hypercholesterolemia² and 15 % of individuals requiring secondary prevention³ report using a medication to reduce low-density lipoprotein cholesterol (LDL-C). By contrast, although in the United States only 19 % of the population aged 30–79 are on statins, this percentage increases to 58 % among people with coronary artery disease.⁴

Statins are efficacious for primary and secondary prevention, and their use is a key recommendation of international CVD prevention guidelines.^{5, 6} More recent international guidelines emphasize the use of high-potency statins^{7, 8} and suggest lowering treatment thresholds for primary prevention for patients whose overall risk profile conveys moderate cardiac risk. The 2013 American College of Cardiology/American Heart Association (ACC/AHA) guideline on the treatment of blood cholesterol recommends high-potency statins for individuals with a clinical history of CVD or with LDL-C ≥ 190 mg/dL; moderate-potency statins for diabetics

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aged 40–75; and moderate- to high-potency statin therapy for primary prevention in those aged 40–75 with CVD risk of 7.5 % or higher.⁹

In Argentina, the guidelines released by the Ministry of Health in 2009 recommend simvastatin for primary prevention in patients with diabetes or with 20 % or greater chance of having a myocardial infarction in the next 10 years, according to the Pan-American Heart Organization Cardiovascular Risk Calculator for Latin America, region B.¹⁰ In Argentina, however, the cost-effectiveness of using high- versus moderate-potency statins for secondary prevention and for high-risk primary prevention is unknown. As many Argentines fall into a moderate-risk category, with a 10–19 % chance of developing a cardiac event over 10 years, the cost-effectiveness of a broadened approach to primary prevention would also need to be established. This lack of data can impede decision-making, particularly among policymakers responsible for government health and medication programs, who must consider whether limited resources should be directed toward higher-cost medications versus other priorities such as expanding the reach of current guidelines.

In order to help address these urgent policy questions, we used a well-established computer simulation model to determine the impact on morbidity and mortality in Argentina of a) using high-potency statins to treat individuals with diabetes or 20 % or greater chance of experiencing a CVD event over the next 10 years; b) using simvastatin or other moderate-potency statins to treat people with 10 % or greater chance of a CVD event over the next 10 years; and to determine c) the cost-effectiveness of each approach from the perspective of the national government, which both administers a large national medication program for low-income people and bears the cost of hospitalization for their CVD events.

METHODS

Cardiovascular Disease Policy Model—Argentina

The CVD Policy Model is a national-scale, state-transition (Markov) computer simulation model of the coronary heart disease and stroke incidence, prevalence, mortality, and costs in adults 35–84 years of age, originally developed for the United States and used for over 25 years to forecast CVD trends and simulate the impact of CVD interventions in the US.^{11, 12} The model was adapted for the population of Argentina using Argentina-specific demographic and epidemiologic inputs wherever possible, and calibrating to reproduce CVD events and deaths observed in the Argentine population. The CVD Policy Model—Argentina has been used previously to evaluate population-wide policies aimed at tobacco control¹³ and dietary salt restriction^{14, 15} (see Supplementary Online Appendix 1 for details).

The model is composed of three sub-models: the demographic–epidemiological sub-model, the bridge sub-model,

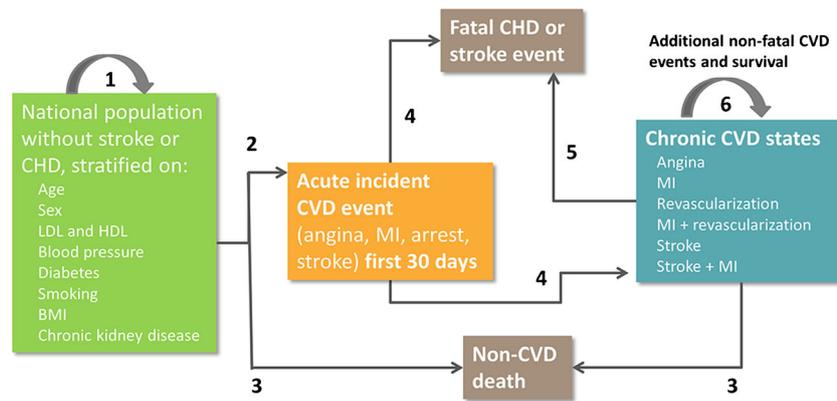
and the disease history sub-model. The demographic–epidemiological sub-model predicts coronary heart disease (CHD) and stroke incidence and non-CVD mortality in the population without CVD stratified by age, sex, and six modifiable risk factors: smoking status (active smoker or secondhand smoke-exposed or no exposure), systolic blood pressure (SBP), high-density lipoprotein cholesterol (HDL-C), LDL-C, use of medication to lower cholesterol (statins, other drugs, or no use), and presence or absence of diabetes mellitus. The incidence of CHD, stroke, and non-CVD death is determined by beta coefficients estimated from Framingham Heart Study Original Cohort (exams 13–28) and Offspring Cohort (exams 1–7) data using the counting process extension of the Cox proportional hazards model, which allows for time-dependent covariates.^{16–20} For the fraction of the population developing CVD, the bridge sub-model characterizes the initial CVD event and related events over the next 30 days. The disease history sub-model then predicts the rate of subsequent CVD events and deaths, stratified by age, sex, and CVD event history (Fig. 1). The model is written in Fortran 95 and compiled using the Lahey Fortran 95 compiler v7.2 (Lahey Computer Systems, Incline Village, NV). Table 1 summarizes the data sources for the CVD Policy Model—Argentina.

A more detailed explanation of the CVD Policy Model and its translation to the Argentine population can be found in supplementary Online Appendix 1.

Modeling Assumptions and Simulated Interventions

We modeled four statin interventions, including one simulation representing wider implementation of current Argentine statin use guidelines and three scenarios reflecting variations to national guidelines, with input assumptions as detailed in Table 2. For our main simulations, we assumed 50 % compliance among those who qualify for a statin under the given scenario but are not currently taking a statin. The four simulated interventions were as follows:

- (1) **Current guidelines.** For those without a history of cardiovascular disease, we treated 50 % of those not on a statin who had either greater than 20 % cardiovascular risk based on the Framingham Risk Score (FRS) or a history of diabetes. For those with a history of CVD, we assumed that 15 % were already on a statin, based on responses to a national survey³, and treated 50 % of the remaining CVD population. In alignment with current national guidelines, those newly treated were assumed to be on a moderate-dose statin (such as simvastatin 40 mg), with a corresponding decrease in mean LDL-C of 40 %.^{29, 30}
- (2) **Scenario 1 – expansion of primary prevention target population.** For scenario 1, we treated the population described for the current guidelines scenario and expanded the primary prevention population to include 50 % of treatment-naïve individuals with an FRS score



*The CVD Policy Model is a state-transition simulation model of CVD in adults. State transitions are numbered in the diagram: Transition 1 = remain in CVD-free state; Transition 2 = incident CVD; Transition 3 = non-CVD death; Transition 4 and 5 = survival or case fatality; Transition 6 = survival with or without repeat CVD event in chronic CVD patients. LDL = low density lipoprotein cholesterol; HDL = high density lipoprotein cholesterol; BMI = body mass index; MI = myocardial infarction.

Fig. 1 Cardiovascular disease (CVD) policy model structure.

of 10–20 %, assuming treatment with a moderate-dose statin.

- (3) **Scenario 2 – use of high-potency statins with current guideline’s target population.** For scenario 2, we treated the same population as described for the current guideline scenario, but simulated the effects of a high-potency statin (such as atorvastatin 40–80 mg, or rosuvastatin 20–40 mg), with an assumed decrease in LDL-C of 55 %.^{29, 30} Those already taking a statin were assumed to experience the incremental benefit of moving from a moderate-dose to a high-potency statin.
- (4) **Scenario 3 – expansion of primary prevention and use of high-potency statin with high-risk population.** Scenario 3 involved a combination of interventions in scenarios 1 and 2, with those qualifying under current

national guidelines treated with a high-potency statin and those with no history of CVD but an FRS score of 10–20 % treated with a moderate-dose statin.

We conducted 10-year simulations for the adult population of Argentina aged 35–84 years, a relevant time frame for near-term decision-making by the Argentine government. Results from scenarios 1, 2, and 3 were compared to those from the current guidelines simulation to describe the impact of alterations to national guidelines on myocardial infarctions, CHD deaths, and cost-effectiveness outcomes. All four scenarios were compared to a baseline simulation assuming current levels of statin use as observed in national surveys to determine the numbers needed to treat under each scenario to prevent one MI or CHD death over 10 years.

Table 1 Data Sources for the Cardiovascular Disease (CVD) Policy Model–Argentina

Data	Source
Population of Argentina and incoming 35-year-old persons, 2010–2050	Argentina National Statistics and Census Institute ²¹
Prevalence	
Risk factor (means and distributions)	2009 National Risk Factors Survey, Ministry of Health ²² Cardiovascular Risk Factor Multiple Evaluation in Latin America (CARMELA) Study ²³
Incidence	
Acute myocardial infarction (MI)	Population-based MI registry in a Buenos Aires district ²⁴
Stroke	National Hospital Discharge Registry ²⁵
MI and stroke prevalence 2010	Population-based risk factor telephone survey in Buenos Aires, Ministry of Health ¹⁰
Mortality	
Coronary heart disease*	Statistics and Information Department, Ministry of Health ²⁵
Stroke [‡]	Statistics and Information Department, Ministry of Health ²⁵
One-day and 28-day CHD case fatality	
CHD	Argentine national hospital survey ²⁶ Ministry of Health admissions database ²⁵ Argentine National Registry (RENACER) ²⁷ Iquique Stroke Study (PISCIS) ²⁸
Stroke	
Stroke 28-day case fatality	

*International Classification of Diseases, 10th revision (ICD-10) codes I21, I22 for myocardial infarction; ICD-10 codes I20, I23–I25 for angina and other CHD; ICD-10 codes I461, I469, I472, I490, I460, I500, I501, I509, I514, I515, I516, I519, I709 for poorly defined cardiovascular disease events and death

‡ICD-10 codes I60–I69 for stroke deaths

Table 2 Input Parameters and Assumptions for CVD Policy Model Simulations

Parameter	Base case value	Range for sensitivity analyses	Reference
Treatment-associated reduction in LDL-C, %			29, 30
Moderate-potency	40	36–44	
High-potency	54.77	50.77–58.77	
Annual cost of statin treatment (US\$/person treated)			31
Moderate-potency	43.80	21.90–65.70	
High-potency	91.25	45.63–136.88*	
Treatment compliance/adherence	50 %	25 %–75 % [†]	Assumed
Costs associated with medication management			32, 33
Physician visit at treatment initiation	12.90	6.45–19.35	
Liver panel at treatment initiation	9.16	4.58–13.74	
Annual lipid panel during treatment	12.60	6.30–18.90	
Costs and QALY decrements from adverse events			
Myopathy			
Annual risk of episode	0.0001		29
Annual QALY penalty per episode	0.00996	0.00498–0.0149	34
Annual cost, &/episode [‡]	33.51	16.76–50.27	32, 33
Stroke			
Annual risk of episode	0.0001		29
Annual QALY penalty per episode	0.3120	0.156–0.468	34
Annual cost, &/episode [‡]	1083.69	541.85–1625.54	32, 33
Diabetes			
Annual risk of episode	0.00098	0.00029–0.001667	35
Annual QALY penalty per episode [§]	0.0762	0.0381–0.114	34
Annual cost, &/episode [‡]	4451.1	2225.55–6676.65	32, 33
Annual discount rate	3 %	0–5 % [†]	Assumed

* Sensitivity to this assumption tested both with probabilistic sensitivity analyses using the range listed and with deterministic analyses that evaluate the cost per pill values: \$0.15, \$0.20, \$0.25 (main assumption), \$0.30, \$0.35

[†] Sensitivity to this assumption tested with deterministic sensitivity analyses that evaluate the low and high end of the range

[‡] Cost for each episode of myopathy from one physician visit and three creatinine kinase blood tests

[§] QALY decrements associated with neuropathy and infections of the extremities

Cost-Effectiveness Estimates

Health care costs were estimated from the perspective of the health care system, and treatment costs assumed the direct cost of statin pills, medication management costs including laboratory tests and physician visits, and costs associated with adverse events including myopathy, diabetes, and stroke (Table 2). Indirect costs such as work loss or family assistance were not included in the analysis. Health care costs were obtained from Ministry of Health publications,³⁶ the National Institute of Statistics and Census,³⁷ reviews from non-governmental organizations,^{32, 33, 38, 39} and published papers in peer-reviewed journals.^{40–42} The estimated cost per person per year of statin treatment was based on the direct cost of medications that the government currently pays for moderate-potency statins. Costs for moderate-potency statins were US\$0.12 per day.⁴³ To estimate the cost of high-potency statins from the government's perspective, we applied a price ratio of high- to moderate-potency statins based on the average over-the-counter price difference between atorvastatin 40 mg pill (high) and simvastatin 40 mg pill (moderate), which yielded a ratio of 2.08 for high- to moderate-potency costs.³¹ Based on this adjustment, we estimated that a high-potency statin would cost US\$0.25 per day.

Model inputs for QALYs associated with cardiovascular disease outcomes were derived from the Global Burden of Disease study.³⁴ In each of our statin intervention simulations, we included quality-of-life decrements associated with adverse events, but excluded QALYs for the burden

of taking a pill every day (Table 2), with our base case analyses assuming the same rate of toxicity for moderate- and high-potency statins. In our base case simulations, we used an annual discount rate of 3 %, ⁴⁴ with costs and QALYs discounted at the same rate. All monetary values are expressed in current US dollars at December 2013 conversion rates.

Sensitivity Analyses

We used both probabilistic and deterministic analyses to evaluate the sensitivity of our findings to our input assumptions. Monte Carlo simulations were used to generate 95 % confidence interval (95 % CI) around our primary outcomes measures for each intervention scenario. In addition to inputs relating to statin effectiveness, costs, and QALYs described in Table 2, we also varied beta values defining the relationship between LDL-C and incident CHD. There were 1000 random draws from a standard normal distribution, scaled to the mean and confidence interval for each varied parameter. The Monte Carlo program was written in Python and results analyzed using Microsoft Excel 2010. We used deterministic approaches to evaluate the sensitivity of our results to assumptions about the degree of statin compliance (range evaluated: 25–75 %), the discount rate (range evaluated: 0–5 %), and the rate of toxicity in moderate- vs. high-potency statins (sensitivity analysis assumed twofold greater toxicity for high-potency statins).

Table 3 Projected Average Annual Myocardial Infarctions, Coronary Heart Disease Deaths and Quality-Adjusted Life Years, and Changes in these Outcomes Relative to Expanding Statin Use Under Current Guidelines, Estimated Using the CVD Policy Model—Argentina

Simulation scenario*	Average annual number treated [§]	Total MIs (95 % UI)	% Change in MI [†]	Total CHD deaths (95 % UI)	% Change in CHD deaths [†]	Total QALYs	Change in QALYs (95 % UI) [‡]
Current guidelines (comparator)	3,700,900	47,300 (46,100–48,500)		23,000 (22,500–23,400)		15,633,000 (15,632,000–15,634,000)	
Scenario 1: lower primary prevention treatment threshold [‡]	4,900,800	45,900 (44,600–47,170)	–3.03 %	22,500 (21,900–23,000)	–2.13 %	15,635,000 (15,634,000–15,637,000)	2500 (1500–3500)
Scenario 2: use high-potency statin for high-risk patients	3,700,900	45,300 (43,900–46,700)	–4.24 %	22,000 (21,300–22,600)	–4.35 %	15,636,000 (15,634,000–15,638,000)	3300 (2300–4300)
Scenario 3: use high-potency statins for those at risk under current guidelines [‡] ; use moderate-potency with those 10–20 % FRS	5,000,900	44,000 (42,400–45,500)	–7.11 %	21,500 (20,800–22,200)	–6.30 %	15,638,500 (15,636,000–15,641,000)	5600 (4200–7000)

MI myocardial infarction, CHD coronary heart disease, QALY quality-adjusted life years

* Current guidelines: treat anyone with a history of cardiovascular disease (CVD), diabetes, or >20 % cardiovascular risk based on the Framingham Risk Score (FRS) with a moderate potency statin. Scenario 1: expand current guidelines to include those with >10 % risk based on FRS. Scenario 2: treat those qualifying under current guidelines with a high potency instead of moderate-potency statin. Scenario 3: combination of scenarios 1 and 2. All scenarios assume 50 % compliance among those who qualify for but are not taking a statin

[†] Changes in % MIs, % CHD deaths, and QALYs shown for simulations 1, 2, and 3 result from a comparison to the “current guidelines” simulation, which models the expansion of treatment with moderate-dose statins to 50 % of those who qualify under current national guidelines but who are not currently treated with statins

[‡] 50 % of untreated gain the effect of going from no statin to a high-potency statin; those already on statins gain the additional LDL lowering by moving from moderate to high potency

[§] Includes those currently taking statins

Model Calibration

The CVD-Policy Model—Argentina is based on assumptions originally derived from the Framingham population. Although the beta coefficients have a similar effect in different populations,⁴⁵ we compared the predicted number of CHD deaths derived from the CVD Policy Model—Argentina to the actual CHD deaths captured in Argentina’s vital statistics for the years 1997–2009. We used the total CHD deaths in ages 35–84 years, which included definite CHD deaths (*International Statistical Classification of Diseases and Related Health Problems, 10th revision* [ICD-10] codes I20–I25) plus a percentage of poorly defined deaths (named “garbage” codes) that could be attributed to CHD (ICD-10 codes I461, I469, I472, I490, I460, I500, I501, I509, I514, I515, I516, I519, I709).⁴⁶ We found a difference of less than 5 % between the total CHD deaths mentioned in the national statistics in the last year available (24,246 for 2009) and the first estimation of total CHD deaths from the CVD Policy Model (25,640 for 2010).¹ Regarding stroke deaths, the difference observed was less than 10 %.

RESULTS

Projected Impact of Change in Lipid Control Guidelines

Estimates from the CVD Policy Model suggest that if half of those who qualified for statins under current guidelines were

treated, approximately 3.7 million people would be treated. The three proposed scenarios predict a significant reduction in MIs and CHD deaths, compared with treating more people under current guidelines (Table 2). Scenario 1 (expand primary prevention with moderate statins) lowers the risk threshold to >10 % FRS and would translate into 1400 fewer MIs (95 % UI: 900–2000) and 500 fewer CHD deaths (95 % UI: 200–800) every year, a 3 % and 2 % reduction, respectively.

Scenario 2 (high-potency statins for high-risk patients) intensifies statin potency under current guidelines; this intensification would lead to 2000 fewer MIs (95 % UI: 1400–2700) and 1000 fewer CHD deaths (95 % UI: 700–1300) every year. Scenario 3 (lower primary treatment threshold plus high-potency statin for high-risk patients) combines scenarios 1 and 2, and would result in the greatest reduction in MIs and CHD deaths, with 3400 fewer MIs (95 % UI: 2500–4200) and 1400 fewer CHD deaths (95 % UI: 1100–1800) every year, which translates to reductions of 7 % and 6 %, respectively.

The combined impact on morbidity and mortality using QALYs is also illustrated in Table 3. Compared to treating more people under current guidelines, an additional 2500 (95 % UI: 1500–3400), 3300 (95 % UI: 2300–4300), and 5600 (95 % UI: 4200–7000) QALYs could be gained if scenarios 1, 2, and 3 were implemented, respectively.

We also examined the number needed to treat (NNT) to avoid an MI or CHD death in the next decade (Fig. 2). Compared to baseline, an additional 39 (95 % UI: 32–47) individuals who qualify for statins under current guidelines

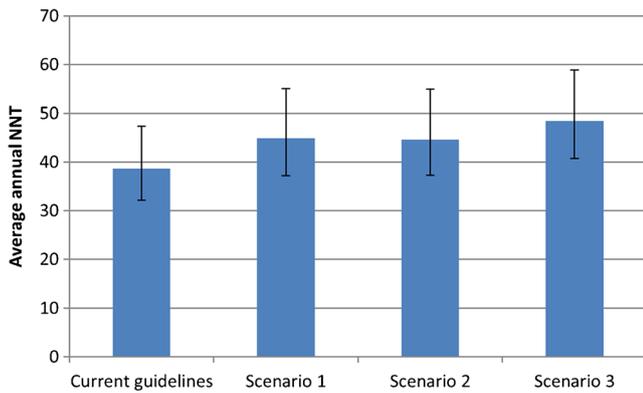


Fig. 2 Projected numbers needed to treat (NNT) annually, in addition to those currently treated, to avoid one coronary heart disease death or myocardial infarction over 10 years. Current guidelines: treat anyone with a history of cardiovascular disease (CVD), diabetes, or >20 % cardiovascular risk based on the Framingham Risk Score (FRS) with a moderate-potency statin. Scenario 1: expand current guidelines to include those with >10 % risk based on FRS. Scenario 2: treat those qualifying under current guidelines with a high-potency instead of moderate-potency statin. Scenario 3: combination of scenarios 1 and 2. To estimate the numbers needed to treat, each scenario (including “current guidelines”) was compared to a simulation assuming no change in statin treatment from status quo. Numbers treated include only treatment-naïve individuals (i.e., those not on statins under status quo conditions) for the current guidelines simulation and for scenario 1; in scenarios 2 and 3, the total treated include those on statins at baseline who are assumed to move from a moderate- to high-potency statin. Error bars represent 95 % uncertainty intervals from Monte Carlo simulation results.

but are not receiving them would need to be treated each year with a moderate-dose statin to avoid one MI or CHD death over 10 years. The corresponding NNT over 10 years to avoid a CHD death or MI for scenarios 1, 2, and 3 was 45 (95 % UI: 37–55), 45 (95 % UI: 37–55), and 48 (95 % UI: 41–59), respectively.

Cost and Cost-Effectiveness Analysis

We estimated that achieving 50 % compliance with current statin use guidelines would cost approximately US\$108 million every year in medication costs. Scenario 1 would cost an additional US\$66 million per year but would save US\$17 million annually in terms of total health care costs. Scenarios 2 and 3 would cost US\$15 million and US\$21 million more, respectively, than increasing the number treated under current guidelines, but would save US\$11 million and US\$28 million in annual health care costs, respectively (Table 4).

The incremental cost-effectiveness ratio (ICER; additional cost/QALY gained) is projected to be 19,900 for scenario 1 (95 % UI: cost saving, 66,800), 42,200 for scenario 2 (95 % UI: cost saving, 93,400), and 33,100 for scenario 3 (95 % UI: 2300–67,500), with each scenario compared to increasing to 50 % compliance with current guidelines. With a gross domestic product (GDP) per capita in Argentina (2009–2013) of approximately US\$14,760,⁴⁷ all three scenarios would be considered cost-effective, as ICERs less than 1 times the per capita

GDP are typically considered very good values and ICERs 1–3 times the per capita GDP are acceptable values under the WHO guidelines on cost-effectiveness.^{48–50}

Sensitivity Analyses

Table 5 shows results from scenarios 2 and 3 using different values for the cost of high-potency statins. Both scenarios were cost-effective at a cost per pill of US\$0.25 or lower.

Although changes in the compliance rate (25 and 75 %) modified the magnitude of events avoided, the three scenarios remained effective in terms of reducing myocardial infarctions and CHD deaths. The three scenarios remained cost-effective under a broad range of assumptions. Results were moderately sensitive to changes in compliance rate. Only scenario 2, when assuming 75 % of compliance, did not remain cost-effective (ICER 48,100). Results were somewhat sensitive to the level of toxicity assumed for high-potency statins; scenario 2 was not cost-effective (ICER 51,600) when high-potency statins were assumed to have twofold increased toxicity compared to moderate-dose statins. Results were not sensitive to varying discount rates.

Willingness-to-pay acceptability curves for scenarios 2 and 3 are presented in Fig. 3.

DISCUSSION

In this study, we modeled the potential health impact, cost, and cost-effectiveness of changing the national guidelines for lipid control for cardiovascular disease prevention in Argentina. We found that the three strategies examined—lowering primary prevention treatment thresholds, using high-potency statins for high-risk patients, and doing both simultaneously—would not only avoid thousands of cardiac events and deaths every year, but would also be cost-effective under international criteria.^{48–50}

These results are similar to published data from other countries, which found that 56⁵¹ to 104 people⁵² needed to be treated with a statin for 5 years to avoid a major CVD event. A separate study found that high-potency statins in national guidelines could be cost-effective only if the cost of the pills were sufficiently low.⁴¹ Our study extends these observations to an Argentine context.

Our study adopts a government perspective on cost tradeoffs between medications and hospitalizations. As in many countries in Latin America, Argentina’s government plays a large role in ensuring health care. In early 2014, Argentina included simvastatin in the national medication program REMEDIAR, which over the past 10 years has provided “essential drugs” at no cost to 16 million people receiving health care within the national network of primary care centers.^{53, 54} In general, in Argentina, access to essential medications such as lipid-lowering drugs has been considered a social good that

Table 4 Projected Average Annual Costs and Cost-Effectiveness for Simulation Scenarios Compared to Current Guidelines, Estimated using the CVD Policy Model–Argentina (in US\$)

Simulation scenario	Cost of intervention† (95 % UI)	Change in cost of intervention‡ (95 % UI)	Total health care costs§ (95 % UI)	Change in total health care costs ‡ (95 % UI)	ICER‡ (95 % UI)
Current guidelines (assumed to reach 50 % currently untreated) (comparator)	107,878,000 (53,594,000 to 160,225,000)		79,414,310,000 (79,152,317,000 to 79,607,511,000)		
Scenario 1: expand current guidelines to include 50 % of FRS 10–20 %	173,939,000 (89,441,000 to 253,980,000)	66,061,000 (–31,558,000 to 162,110,000)	79,397,070,800 (79,134,772,000 to 79,591,351,000)	–17,239,000 (–13,128,000 to –21,729,000)	19,900 (cost saving, 66,800)
Scenario 2: use high-potency statins for those at risk under current guidelines*	256,399,000 (116,972,000 to 379,007,000)	148,522,000 (5,866,000 to 281,032,000)	79,403,200,000 (79,142,744,000 to 79,594,989,000)	–11,110,000 (–8,223,000– –14,655,000)	42,200 (cost saving, 93,400)
Scenario 3: use high-potency statins for those at risk under current guidelines*; use moderate-potency with those 10–20 % FRS	322,087,800 (165,585,100 to 492,008,500)	214,210,300 (37,991,000 to 396,783,000)	79,386,273,000 (79,122,326,000 to 79,580,634,000)	–28,036,800 (–22,291,000 to –34,120,000)	33,100 (2300 to 67,500)

ICER incremental cost-effectiveness ratio (additional cost per quality-adjusted life years gained)

*50 % of untreated gain the effect of going from no statin to a high-potency statin; those already on statins gain the additional LDL lowering by moving from moderate to high potency

†Includes cost of medication, chronic disease management related to statin delivery and assessment, and cost associated with adverse events (diabetes, stroke, and myopathy)

‡Changes in costs and ICERs are computed for each scenario relative to a simulation assuming current guidelines are expanded to reach 50 % of the untreated population

§Includes costs associated with coronary heart disease, stroke, and background health care costs

should be made readily available to all.⁵⁵ As the government also bears the costs of CVD hospitalization for approximately 40 % of the population, cost-effectiveness studies such as this one are highly relevant for government policymakers.

Argentina has used evidence-based strategies in the past to inform national policy. For example, other modeling studies using the CVD Policy Model–Argentina on tobacco control¹³ and salt consumption^{14, 15} suggested policies that were subsequently implemented. Other Latin American countries including Chile and Brazil also have national CVD prevention guidelines^{56, 57} that focus on lipids; modeling exercises like

this one, which are commonly used, for example, in countries of the United Kingdom,⁵⁸ can be instrumental in the development of evidence-based guidelines that incorporate resource impact.

Given the limited resources available, only those interventions that can lead to large reductions in the CVD burden at relatively low cost are likely to be sustainable.⁵⁹ The scenarios modeled in this study highlight the importance of lipid-lowering drugs and guidelines for cardiovascular disease prevention in Argentina. Two of our scenarios extend drug treatment to large numbers of the

Table 5 Projected Cost and Cost-Effectiveness Outcomes Assuming Varying Costs of High-Potency Statins, Estimated Using the CVD Policy Model–Argentina (in US\$)

Scenario	Price per pill (high-potency)	Annual cost of intervention	Change relative to current guidelines	Annual total health care cost	Change relative to current guidelines*	ICER†
Scenario 2	0.35	370,749,000	262,872,000	79,403,200,000	–11,109,000	77,300
Scenario 3		436,154,000	328,276,000	79,386,273,000	–28,037,000	53,400
Scenario 2	0.3	313,582,000	205,705,000	79,403,200,000	–11,109,500	59,800
Scenario 3		379,129,000	271,251,000	79,386,273,000	–28,037,000	43,300
Scenario 2	0.25	256,399,000	148,522,000	79,403,200,000	–11,109,000	42,200
Scenario 3		322,088,000	214,210,000	79,386,273,000	–28,037,000	33,100
Scenario 2	0.2	199,233,000	91,355,000	79,403,200,000	–11,109,000	24,700
Scenario 3		265,063,000	157,186,000	79,386,273,000	–28,037,000	23,000
Scenario 2	0.15	142,066,000	34,188,000	79,403,200,000	–11,109,000	7100
Scenario 3		208,039,000	100,161,000	79,386,273,000	–28,037,000	12,800

*Differences between each scenario and the base case of current guidelines are shown in parentheses

†ICER = incremental cost-effectiveness ratio (additional cost per quality-adjusted life years gained). ICERs are relative to the base case of current guidelines

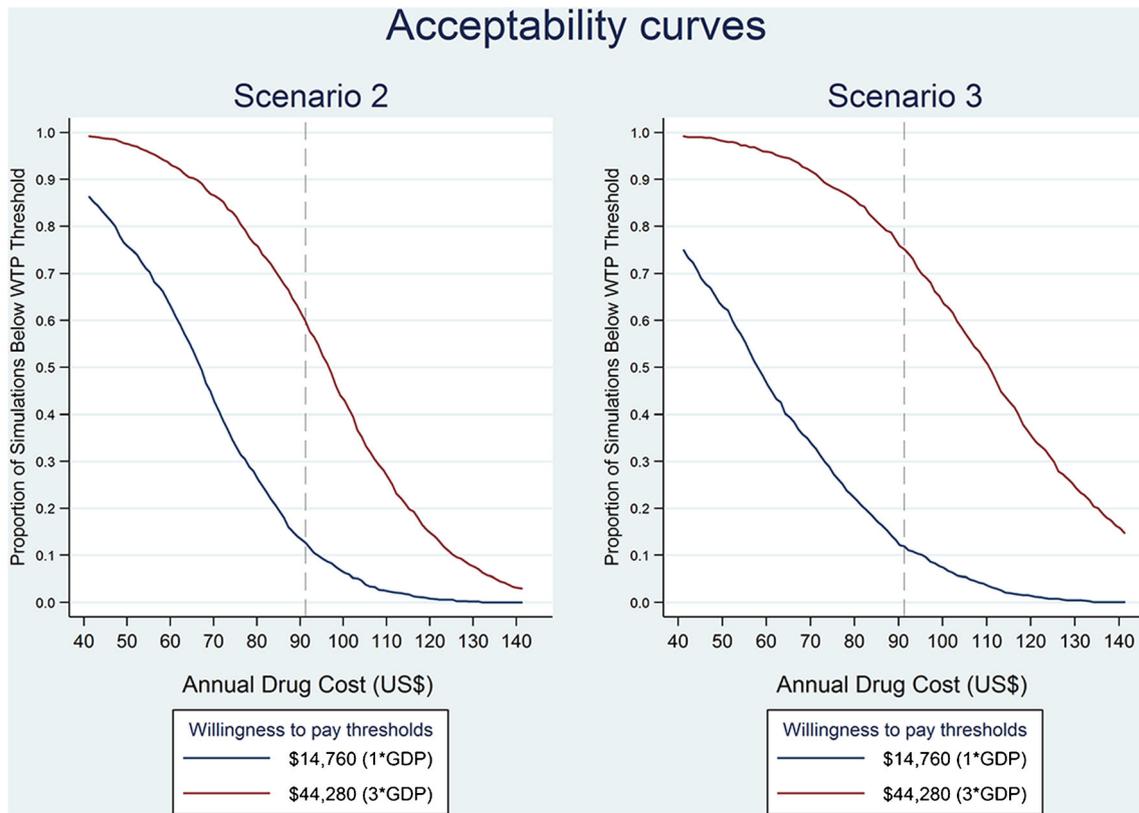


Fig. 3 Willingness-to-pay acceptability curves.

population. This raises the potential for “over-medicalization” and for the tacit acceptance of unhealthy elements of the Argentine diet. We made no attempt to consider other alternatives, such as government-funded social marketing campaigns that could contribute to sustained cholesterol lowering, as we have no data on their effectiveness from an Argentine perspective. Much more research on the effective promotion of broad changes in diet is needed in Argentina and in Latin America as a whole.

Some other limitations of our study should be considered. We assumed that everyone who was currently on statin therapy in Argentina was treated with a moderate-potency statin, as is currently suggested by national guidelines. As there are no national data available on which statins patients are actually using, we were unable to test this assumption. Second, as noted, we considered the health care costs from the government’s perspective; these results might not be generalizable to the private health sector, which has different health care costs. Finally, all modeling studies are limited by the integrity of their inputs. We used the best available data from Argentina to adapt the US CVD Policy Model for Argentina. Although there is debate on how relevant the Framingham Risk Score is to non-US populations,⁶⁰ because of a lack of Argentine data, we used the Framingham data to determine the association between CVD risk factors and CVD outcomes. Prior studies adapting Framingham to other international contexts have

suggested that the associations between risk factors and CVD events (beta) appear to be similar across populations, although actual event rates (alpha) may differ among populations.⁶¹ Event rates for the CVD Policy Model–Argentina were calibrated with the best available epidemiological data from Argentina, comparing the predictions of the CVD Policy Model with local vital statistics; differences in event rate are less than 5%. Previously published papers have used the CVD Policy Model to accurately predict outcomes in the Argentine population, which increases our confidence in the model’s accuracy.^{13–15, 62}

Despite these limitations, we believe that this study contributes to the ongoing debate in Argentina by projecting the health benefits of three possible strategies for lipid control in cardiovascular disease prevention. To our knowledge, this study is the first to analyze the impact of current national guidelines for cardiovascular disease prevention in Latin America or to model alternatives to current guidelines based on lowering the primary prevention threshold or treating high-risk patients with high-potency statins, as is currently recommended in many other international guidelines. Incorporating modeling strategies in the development of national guidelines could help provide a better understanding of cost-effective interventions in the region. This type of approach may also be useful in the future for modeling additive interventions in this population, such as control of hypertension and use of low-dose aspirin. The data provided here should be key inputs

for policymakers who seek to improve cardiovascular disease prevention in Argentina.

Corresponding Author: Jonatan Konfino, MSc; Centro de Estudios de Estado y Sociedad (CEDES), Buenos Aires, Argentina (e-mail: jkonfino@gmail.com).

Compliance with Ethical Standards:

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