Modelling the impact of plain packaging of tobacco products on cardiovascular disease in Argentina

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ABSTRACT

Introduction Tobacco packaging design is conceived to be attractive. Plain packaging of tobacco products reduces this attractiveness by standardising their shape, size, font and colours.

Methods To evaluate the effect of applying plain packaging to tobacco products on cardiovascular events and mortality in Argentina, we used the Cardiovascular Disease Policy Model–Argentina, a local adaptation of a well-established computer simulation model that projects cardiovascular and mortality events for the population 35–94 years old using local demographic and consumption data, during the period 2015–2024. After a literature review, we estimated that the implementation of plain packaging of tobacco products would result in an absolute decrease in tobacco prevalence of 0.55% (base-case scenario) and performed a sensitivity analysis assuming a higher and lower decrease of 1.01% and 0.095%, respectively.

Results Over the 2015–2024 period, the decrease in smoking prevalence associated with plain packaging (0.55%) is projected to avert 1880 myocardial infarctions (MI), 820 strokes and 4320 total deaths in Argentina. The higher estimate of smoking prevalence reduction (1.01%) would translate into 3450 fewer MIs, 1490 fewer strokes and 7920 fewer deaths, while the lower estimate of smoking prevalence reduction (0.095%) would result in 330 fewer MIs, 140 fewer strokes and 750 fewer deaths.

Conclusions The implementation of plain packaging of tobacco products could reduce cardiovascular events in Argentina, even in the absence of other tobacco control measures. Actual health benefits are likely higher than those presented here, since plain packaging may be most impactful by preventing young people from initiating smoking.

INTRODUCTION

Argentina has one of the world's highest rates of cardiovascular disease, driven in part by high rates of tobacco use. About 22% of Argentine adults smoke, as do an estimated 20% of adolescents. Current estimates are that tobacco consumption is responsible for 13% of total deaths (CVD and non-CVD) annually.[1 2]

In 2011, the Congress approved a National Tobacco Control Law imposing advertising and marketing restrictions on tobacco products. Although the law banned the promotion of tobacco products, it did not address the design of tobacco product packaging itself.[3] Tobacco packaging currently is one of the main strategies tobacco companies use to promote their products, it is designed to be attractive and to appeal mainly to youth.[4] Plain packaging of tobacco products reduces this attractiveness by standardising the shape, size, font and colours of tobacco packages and specifies that the manufacturer includes no other information than the brand, the quantity and the contact information. Plain packaging also eliminates misleading information by addressing package design techniques that may suggest that some products are less harmful than others and increase the noticeability and effectiveness of health warnings.[4–6] Plain packaging laws are relatively straightforward to implement (though not to pass) and have been approved in several countries, such as Australia, France, the UK, Canada, New Zealand, Norway, Ireland, Uruguay and Saudi Arabia.[7]

We used a well-established computer simulation model of cardiovascular disease adapted to represent Argentine adults, the Cardiovascular Disease Policy Model (CVDPM)-Argentina, to provide local policymakers projections for the impact of plain packaging policies on cardiovascular events and mortality over 10 years in Argentine adults 35–94 years of age.

METHODS

CVDPM-Argentina

We used the CVDPM-Argentina (CVDPM-Arg), a dynamic population, state-transition (Markov) computer simulation model that estimates the prevalence and incidence of cardiovascular disease by using demographic, epidemiological, vital statistic and hospital data measured in Argentine adults of 35 to 94 years of age.[8 9] The adult population is divided by the model into those without and with pre-existing cardiovascular disease. In annual cycles, the population without pre-existing CVD is stratified into clusters by age, gender and the following CVD risk factors: systolic blood pressure, low-density lipoprotein cholesterol, high-density lipoprotein cholesterol, smoking status, type II diabetes status and body mass index; their probability of experiencing incident coronary heart disease (CHD), incident stroke or death from noncardiovascular causes is estimated by risk functions from the 1971–2001 Framingham Original and Offspring Cohort studies.[10–13] Smoking cessation in those without prior CVD has a direct effect on the probability of transitioning to incident CHD, stroke or non-CVD death as well as an indirect effect on these outcomes through changes in other CVD risk factors.[14 15] The population with prior CVD has annual baseline rates of recurrent cardiovascular events or deaths from cardiovascular or noncardiovascular causes, with transition rates dependent on age, sex and prior CVD status. Each annual cycle, new 35-year olds enter the simulated

population, measured from census projections,[16 17] and those who die or reach 95 years of age exit the simulated population. A more detailed explanation of model development and update are found in online supplemental appendix as well as in a previous publication.[8]

Input parameters and data sources

We conducted a search of published articles up to June 2020 on MEDLINE, EMBASE, LILACS and the Cochrane Library; the websites of major tobacco control organisations and reports published by countries who have already applied plain packaging policies. We found that there are few estimates of the effect of plain packaging of tobacco products in real-world scenarios.

A Cochrane review found that applying plain packaging would reduce tobacco smoking prevalence by 0.5%. This absolute estimate was driven by a study involving 700 000 participants who were followed 1 year after standardised packaging was implemented in Australia in 2012.[18] Using the same data set and a slightly different methodological approach, the Australian Department of Health reported similar findings of 0.55% (95% CI 0.095 to 1.01) decrease in smoking prevalence over the post-implementation period.[19]

Our base-case analysis compares an intervention scenario, assuming an absolute reduction in smoking prevalence of 0.55% applied to each age stratum and sex stratum of smokers in the first year of our simulation that remains at this lower level throughout the 10-year intervention, to a status-quo scenario that assumes no change in smoking prevalence.[19] We assumed that smoking cessation reduces the incidence of CHD and stroke, their related recurrence and mortality, along with death from causes other than CHD or stroke both in the population without CVD and as well as in the population with previous CVD. We evaluated the difference in outcomes between the intervention and status-quo simulations over a 10-year period from 2015 to 2024. A more detailed description of the inputs used for the simulations is found in online supplemental appendix.

Sensitivity analysis

We used one-way sensitivity analyses to evaluate the sensitivity of our results to the assumed change in smoking prevalence, running separate simulations using the lower and upper bounds of the decrease in smoking prevalence observed in source data (an absolute change of 0.095% and 1.01%, respectively).[19] We used Monte Carlo simulations to simultaneously vary inputs for the change in smoking prevalence and the effects of cessation on outcomes to generate 95% uncertainty intervals (UIs) around our base-case scenario results. There were 1000 random draws from a standard normal distribution, scaled to the mean and CI, and then analysed to generate 95% UIs for each outcome.

RESULTS

A 0.55% decline in smoking prevalence associated with plain packaging would translate into 102 000 fewer smokers (17 600 and 187 200 for our low and high estimate of decline, respectively).

Model simulations project that this decline would avert 1880 myocardial infarctions (MI), 820 strokes and 4320 total deaths (CVD and non-CVD) in Argentina over 10 years in the base-case scenario. The higher estimate of smoking prevalence reduction (1.01%) would translate into 3450 fewer MIs, 1490 fewer strokes and 7920 fewer deaths, while the lower estimate of smoking prevalence reduction (0.095%) would result in 330 fewer MIs, 140 fewer strokes and 750 fewer deaths in the same period (table 1).

DISCUSSION

Our study found that the implementation of plain packaging of tobacco products in Argentina would lead to a slight but significant reduction in cardiovascular morbidity and mortality, even in the absence of other tobacco control measures. Even though a 0.55% absolute decrease in smoking prevalence may seem small, it correlates with the reductions estimated for other isolated tobacco control policies such as smoke-free policies, health warnings, advertising restrictions and affordability reduction, with percentages of smoking prevalence decline ranging from 0.3% to 2.2%.[20]

It is worth noting that actual health benefits are likely higher than those presented here, since plain packaging may be most impactful by preventing young people from initiating smoking[21–23]—an effect that would only be visible later in their life course. Our model population includes only 35–94-year olds and the vast majority of those assumed to quit smoking in our simulation are under the age of 65, when there is a lower baseline risk of developing CVD or dying from CVD or other causes in a 10-year simulation.

We need to acknowledge some limitations. First, as in any modelling study, our results are only as good as the inputs we used. In the case of the CVDPM-Arg, due to a lack of better information, we had to assume local or provincial data as representative of the national level for some inputs. Also, the coefficients used to estimate the relative risk of developing cardiovascular disease in this local version of the CVDPM were taken from

Table 1 Cumulative estimates of CVD events and mortality prevented for the period 2015–2024 after plain packaging of tobacco products implementation in Argentina

			Sensitivity analysis	
	Total number of events in the population	Prevented events in the base-case scenario	Low estimate of smoking prevalence decline	High estimate of smoking prevalence decline
		N, 95% UI (%)	N (%)	N (%)
Myocardial Infarction	491 700	1880, 330–3698 (0.38)	330 (0.07)	3450 (0.70)
Stroke	728 800	820, 125–1780 (0.11)	140 (0.02)	1490 (0.20)
CHD deaths	411 600	730, 128–1447 (0.18)	130 (0.03)	1350 (0.33)
Stroke deaths	228 500	210, 33–470 (0.09)	40 (0.02)	390 (0.17)
Total deaths	3 309 200	4320, 784–8192 (0.13)	750 (0.02)	7920 (0.24)

Total deaths: cardiovascular +non-cardiovascular deaths.
Smoking prevalence decline: base-case scenario: 0.55%; low estimate: 0.095%; high estimate: 1.01%.
CHD, coronary heart disease; CVD, cardiovascular disease; UI, uncertainty intervals.

the Framingham study[24]; nevertheless, there is evidence that the associations between risk factors and events are the same in different populations.[25–27] Another limitation is that the CVDPM assumes that the incidence and distribution of risk factors remain stable, which may not be true over time, especially when considering that smoking prevalence decreases would affect other CVD risk factors. Finally, the short time that has elapsed since this policy has been effectively implemented in other countries implies that there is limited evidence on the immediate effect of plain packaging policies and also its long-term effects. It is possible that plain packaging could result in further reduction in smoking prevalence. Moreover, it is unclear whether Argentina would be more, or less, sensitive to the impact of plain packaging on consumption.

Currently, Uruguay is the only Latin American country that has implemented plain packaging policies, in 2019.[28] Unlike Uruguay, Argentina does not have a plain packaging of tobacco products' law, and general efforts to ratify the WHO Framework Convention on Tobacco Control (signed in 2003) have been obstructed by tobacco industry manoeuvres.[29 30] Our results indicate that the implementation of plain packaging of tobacco products would be a low-cost public policy with important benefits for public health in Argentina, both directly in terms of CVD events avoided and indirectly as a reinforcement of ongoing tobacco control measures. Policymakers should considerer implementation of plain packaging in national efforts for tobacco control.

What this paper adds

- Tobacco packaging colours, shape and overall design are conceived to be attractive.
- Plain packaging of tobacco products reduces this attractiveness by standardising their shape, size, font and colours, with inclusion from the manufacturer of no other information than the brand, the quantity and the contact information
- There are few estimates of the effect of plain packaging of tobacco products in real-world scenarios.
- The objective of this study was to evaluate the effect of applying plain packaging to tobacco products on cardiovascular events and mortality in Argentina over the 2015–2024 period
- A 0.55% decrease in smoking prevalence associated with plain packaging is projected to avert 1880 myocardial infarctions, 820 strokes and 4320 total deaths.
- The implementation of plain packaging of tobacco products could reduce cardiovascular events in Argentina, even in the absence of other tobacco control measures.
- It is worth noting that actual health benefits are likely higher than those presented here, since plain packaging may be most impactful by preventing young people from initiating smoking

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SUPPLEMENTAL MATERIAL

Modeling the Impact of Plain Packaging of Tobacco Products on Cardiovascular Disease in Argentina

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Contents

Overview of Model Structure

This study uses the Cardiovascular Disease (CVD) Policy Model – Argentina to simulate the impact of a decrease in smoking prevalence from national tobacco plain packaging policies on cardiovascular events and deaths in Argentine adults aged 35-94 years over a 10-year timescale. The CVD Policy Model is a dynamic population, state-transition (Markov) model of cardiovascular disease (CVD) originally developed to represent adults 35-94 years of age in the United States [1-5] and adapted to the Argentine population using input estimates and calibration target data sourced from the Argentina census, health surveys, and hospitalization databases (discussed in detail starting on page 7) [6-15].

The structure and transitions in the CVD Policy Model are shown in Supplemental Figure S1. The Model separates the population into those without CVD and those with existing CVD, including coronary heart disease (myocardial infarction (MI), arrest, or angina) and stroke (ischemic and hemorrhagic). In annual cycles, new 35-year-olds enter the model population, those who die or reach 95 years of age exit the population, and those remaining alive transition among cells defined by age, sex, risk factors, and prior CVD history.

The population without pre-existing CVD is stratified into clusters defined by age, gender and levels of cardiovascular risk factors including smoking status, body mass index, diabetes status, systolic blood pressure, low-density lipoprotein cholesterol, and high-density lipoprotein cholesterol. Those with existing CVD are stratified into groups according to age, sex, and prior cardiovascular event history. In annual cycles, the non-CVD population experiences probabilities of incident coronary heart disease, stroke, or death from non-cardiovascular causes with baseline risk determined for each cluster based on age, sex, and the combinations of cardiovascular risk factors. Following incident events, the model characterizes the event type and its sequelae for the first 30 days, after which survivors move into the CVD state aligned with initial and subsequent events and procedures occurring during the acute phase. In the population with existing CVD, the annual baseline risks (i.e., in the absence of a risk factor

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interventions) of additional CVD events and deaths from coronary heart disease, stroke, and non-cardiovascular causes are a function of age sex, and prior cardiovascular event history.

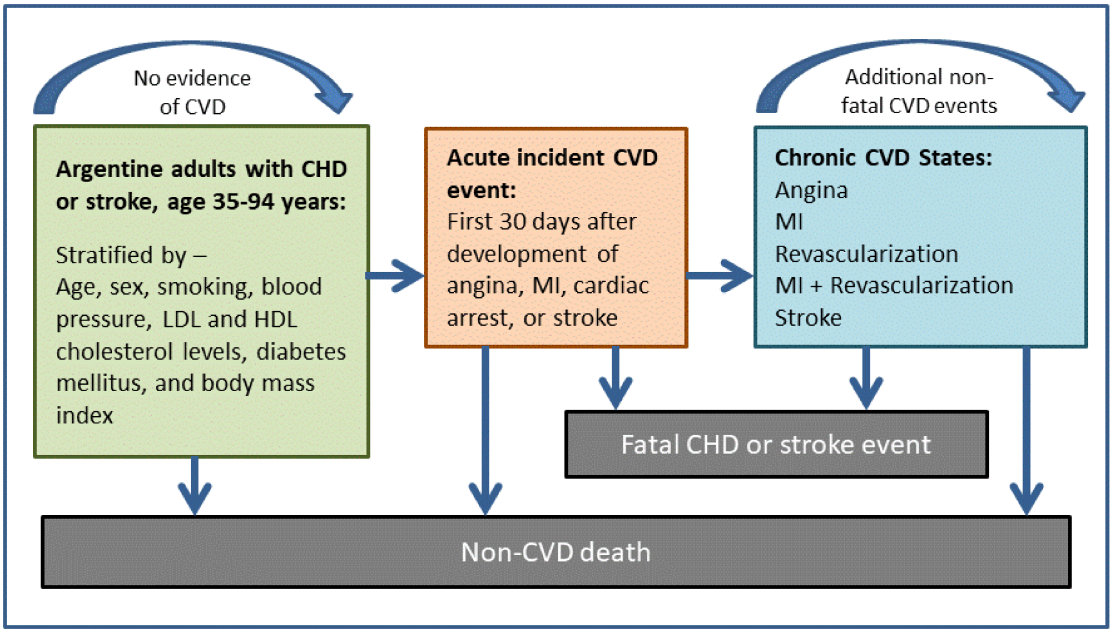

Figure S1. Schematic of the Cardiovascular Disease Policy Model. Abbreviations: CHD, coronary heart disease; CVD, cardiovascular disease; HDL, high-density lipoprotein; LDL, low-density lipoprotein; MI, myocardial infarction.

The CVD Policy Model is programmed in Lahey Fortran 95. Monte Carlo simulations are programmed in Python. Outcomes were analyzed using Python and Excel 2016 (Microsoft); statistical analyses were performed using SAS version 9.4 (SAS Institute Inc) and R version 3.4 (R Foundation for Statistical Computing). Additional technical details on core model inputs, transition probabilities, and model calibration are on page 7.

Key Input Parameters and Model Simulations for the Current Analysis

A summary of key study-specific input parameters is shown in Supplemental Table S1. The base case analysis compares an intervention scenario simulating the effect of a national policy of plain packaging for tobacco products to a status quo scenario that quantifies cardiovascular events, cause-specific deaths, and death from all causes in the absence of a plain packaging policies. Simulations include all adults in Argentina who are 35-94 years of age from in 2015 and follows them through 2024, until they die, or until they reach 95 years of age, whichever comes first [11 12]. New 35-year-olds enter the simulated population each annual cycle, quantified from Argentine census projections [11 12].

In the status quo scenario, the population experiences changes in smoking prevalence over time reflecting demographic shifts expected as the population ages. In the intervention scenario, we assumed that a national tobacco plain packaging policy would reduce the population prevalence of smoking by 0.0055 (95% CI: 0.00095, 0.0101) [16], as observed in Australia following passage of the Tobacco Plain Packaging Act in November 2011 and implementation of the policy throughout 2012 [17]. We assumed smoking prevalence goes down in the first simulation year and stays at the lower level throughout the 10-year simulation. We operationalized the intervention by converting the absolute reduction in smoking prevalence into a relative reduction that represents the percent of current smokers who are expected to not smoke in the presence of plain packaging policies. The relative reduction was calculated by first determining the total number of adults expected to quit smoking (i.e., total number of adults 35-94 years of age in Argentina multiplied by 0.0055) and then dividing by the total number of current smokers aged 35-94 years, estimated from the 2013 National Risk Factor Survey (Supplemental Table S1) [11-13]. This resulted in a relative reduction of 0.0254 (range: 0.0044, 0.0467), which in the simulated intervention is applied to clusters of current smokers stratified by age decile, sex, and prior CVD status and other CVD risk factors. As a result, the count of current smokers assumed to not smoke under plain packaging policies is concentrated at younger ages and in those without prior cardiovascular disease.

Smoking cessation in the intervention scenario (compared to continuing to smoke under status quo conditions) is assumed to directly impact the risk of cardiovascular events and deaths from CVD and non-CVD causes, with the same magnitude applied to those with and without existing cardiovascular disease (Supplemental Table S1). In those without prior CVD, smoking cessation is also assumed to have indirect effects through changes in other CVD risk factors, mediated through body mass index [18 19]. Smoking is assumed to more than double the risk of myocardial infarctions, arrests, and coronary heart disease deaths compared to not smoking (Supplemental Table S1), as estimated from longitudinal cohorts associated with the National Heart, Lung, and Blood Institute in the United States [20]. Smokers compared to non-smokers are at increased risk of stroke events (fatal and non-fatal) as well as deaths from non-cardiovascular causes, with risk computed as a function of cigarettes smoked per day (Supplemental Table S1); increased risk per-cigarette-per-day effects were calculated separately for stroke and non-CVD deaths in Cox proportional hazards analysis of Framingham Original and Offspring cohort data[21 22]. The model assigns a given cell of smokers the age- and sex-specific value of mean cigarettes per day measured for Argentine adults in the 2013 National Risk Factor Survey to compute the increased risk from smoking (Supplemental Table S1)[13].

Additional Technical Details on the CVD Policy Model - Argentina

Core model inputs

Originally developed in 2009 [8-10 23], the CVD Policy Model – Argentina was recently updated, as detailed in a previous publication[7]. Updated model inputs were as follows (also in Supplemental Table S2):

- The National Census conducted in 2010 was used to update the model to reflect the 2010 Argentine population and to estimate 35 years-olds entering the modeled population each year from 2011 to 2100[11 12].
- The 2013 National Risk Factor Survey, a national representative survey of Argentine population 18 years and older living in private homes in urban areas of 5,000 and more inhabitants, was used to update age and sex-specific means and distributions for BMI, smoking and diabetes[13].
- The "Study for the detection and follow up of cardiovascular disease risk factors in the southern cone of Latin America", coordinated through the Centro de Excelencia en Salud Cardiovascular para América del Sur (CESCAS I study), an on-going observational prospective cohort designed to study cardiovascular disease prevalence and risk factors in Southern Latin America, provided information on age and sex specific means and prevalence for LDL-c, HDL-c and SBP[14]. These variables were not measured in the 2013 National Risk Factor Survey.
- The Program for the epidemiological evaluation of stroke in Tandil (PrEViSTA) study, which reports local information on First-Ever Stroke and Transient Ischemic Attack Incidence, was used to update age- and sex-stratified stroke incidence rates[15].

Cardiovascular risk factors and risk functions

After separating the Argentine population into those with and without prior CVD, the CVD Policy Model further stratifies the non-CVD population into cells defined by age, sex and levels of the following cardiovascular risk factors estimated from the 2013 National Risk Factor Survey and the CESCAS I study:

- **Smoking status**: no current smoking, passive smoke exposure, active smoking
- **Systolic blood pressure (SBP):** <130; 130-139.9; ≥ 140 mmHg
- **Low-density lipoprotein cholesterol (LDL-c):** < 100; 100-129.9; ≥130 mg/dl
- **High-density lipoprotein cholesterol (HDL-c):** <40; 40-59.9; ≥ 60 mg/dl
- **Type II Diabetes status:** yes or no
- **Body mass index:** <25; 25-29.9; ≥ 30 kg/m^2

The non-CVD population is distributed into 58,320 cells (60 ages * 2 sex groups* 3^5 (five risk factors with three levels) * 2 (one risk factor with 2 levels)), one representing each possible combination of risk factor levels. The model assigns each cell the age-, sex-specific mean values for all risk factor levels represented by the given cell.

Each annual cycle, a proportion of the CVD-free population experiences an incident CVD event. The remaining population, remaining free of CVD, transitions among cells at rates that preserve age-specific risk factor trends over time. Incident events occurring in the CVD-free population are characterized as coronary heart disease (stable and unstable angina, hospitalized myocardial infarction (MI), or arrests occurring outside or inside the hospital), stroke (hospitalized ischemic or hemorrhagic stroke), or death from a cause other than cardiovascular disease. Annual rates of incident events are defined by risk functions that include age- and sex-specific beta coefficients, which determine the relationship between CVD risk factors and incident events; and alpha coefficients, which are generated by fitting to annual incidence rates for coronary heart disease, stroke, and non-CVD death. The risk for each outcome is then calculated for every cell using alpha and beta coefficients, along with mean values for each CVD risk factor level represented by the cell, using the following equation:

$$r = e^{(\alpha + \sum_{k=1}^{6} \beta_k m_k)} / (1 + e^{(\alpha + \sum_{k=1}^{6} \beta_k m_k)})$$

where *r* represents risk, with separate risks for coronary heart disease, stroke, and non-CVD death; α represents age- and sex-specific intercepts for each risk function determined by the model when fitting to incidence rates in the base year; β represents the effect on risk for one-unit changes in a given CVD risk factor; *m* represents mean values for a given risk factor; and k represents a counter over all six CVD risk factors that have an effect on coronary heart disease, stroke, and/or non-CVD death risk (i.e., smoking, SBP, LDL-C, HDL-C, diabetes, and BMI).

Risk function beta coefficients were estimated for incident coronary heart disease, stroke, and non-cardiovascular disease death, separately, using competing risk Cox proportional hazards analysis of data collected during Framingham Heart Study examinations 13-28 and Framingham Offspring Study examinations 1-7 [21 22]. The Model incorporates indirect effects of changes in BMI on modeled outcomes through changes in SBP, LDL-c, and HDL-c, with coefficients sourced through literature review [18 19], and through changes in diabetes incidence as calculated from Framingham data [21 22].

Incident event characterization

Those who experience an incident coronary heart disease or stroke event in a given year are transitioned into the "bridge" portion of the model, a 30-day period with heightened probability of procedures, recurrent events, and cause-specific death. The risk of new onset coronary heart disease is assumed to be independent of the incidence of stroke in the same year. Those with incident coronary heart disease are first portioned into event type (myocardial infarction, arrest, or angina). Risk factors are assumed to affect each category in proportion to overall coronary heart disease incidence, except for tobacco smokers who are assumed to have a higher relative risk for infarction and arrest [20 24] and a proportionately lower coefficient for angina. Environmental tobacco exposure is assumed to carry a relative risk of 1.26 for myocardial infarction and cardiac arrest compared with non-exposed non-smokers [25].

Transition probabilities and model calibration

The population with prior CVD has annual baseline rates of recurrent CVD events or CVD deaths that are dependent on CVD event history, age and sex and are determined from natural history studies [26], and hospitalization databases and are adjusted during calibration to national targets. Initial event rates were assumed from the prior version of the CVD Policy Model –Argentina and were adjusted iteratively until the model predictions came within <1% of observed health statistic data for CVD events and deaths in Argentina in 2010 (Supplemental Table S3).

CVD, non-CVD, and total deaths (by age and gender) in 2010 were estimated from Argentina's National Vital Statistics [27]. The actual total number of deaths attributable to coronary heart disease was estimated as a compound of both definite coronary heart disease deaths (codes I20-I25 of the International Classification of Diseases, 10th Revision [28]) in health records plus a percentage of poorly defined deaths (named 'garbage' codes, already defined) that could be attributed to coronary heart disease deaths[8 29]. Garbage codes are codes assigned to deaths that were supposedly misclassified, a percentage of which belong actually to coronary heart disease deaths[8 29]. The total number of deaths obtained was later corrected by a factor determined for countries with low quality of registry (such as Argentina) in the Global Burden of Disease initiative[30]. A similar method was then used to compare predicted and reported stroke deaths (codes I60-I69).

Due to the absence of national data on the total number of myocardial infarction, arrest, or stroke events occurring annually in each age and gender group, we used data from local studies including the Sindromes Coronarios Agudos en Argentina study [31], a multicenter registry of coronary heart disease events in Argentina, and the PrEViSTA Study [4], in conjunction with US event rates [4], in order to infer annual targets used to calibrate the Argentina model.

Supplemental Tables

Supplemental Table S1. Key input parameters for current analysis			
Input Parameter	**Men**	**Women**	**Source***
Argentina population in 2015			
35 – 44 years of age	2,910,500	2,971,300	2010 National Census, Argentina National Statistics and Census Institute [11 12]
45-54 years	2,143,000	2,283,000	
55-64 years	1,770,300	1,968,800	
65-74 years	1,168,800	1,454,900	
75-84 years	541,400	862,100	
85-94 years	137,100	321,000	
Prevalence of active smoking (%)			
35- 44 years	25.5	18.5	National Risk Factor Survey (2013) [13]
45-54 years	28.8	22.6	
55-64 years	30.0	19.1	
65-74 years	18.3	14.6	
75-84 years	12.8	4.4	
85-94 years	0.8	1.0	
Mean daily exposure among active smokers (cigarettes/day)			
35 – 44 years	16.9	12.4	National Risk Factor Survey (2013) [13]
45-54 years	14.5	14.6	
55-64 years	19.1	13.6	
65-74 years	14.2	14.6	
75-84 years	13.0	11.1	
85-94 years	7.6	10.3	
Intervention effects			
Absolute reduction in smoking prevalence from tobacco plain packaging policy* (95% confidence bounds)	0.0055 (0.00095, 0.0101)		Post-Implementation Review: Tobacco Plain Packaging. Appendix A: Study of the Impact of the Tobacco Plain Packaging Measure on Smoking Prevalence in Australia [16]
Relative risk of myocardial infarction, arrest or coronary heart disease death in smokers compared to non-smokers[a, b]	2.6		Analysis of NHLBI cohort data [20]
Relative risk of stroke events and deaths per 20 cigarettes/day [a, b] ǂ	1.56		Analysis of Framingham Heart Study exams 13-28 and Offspring Cohort exams 1-7[21 22]
Relative risk of death from non-cardiovascular causes per 20 cigarettes/day [a, ǂ]	1.70		

* absolute reduction in smoking prevalence was converted into relative percent reduction in smokers for model simulations

[a] the same estimates of effects of smoking cessation on events and deaths are applied to those without and with prior cardiovascular disease

[b] average effect

ǂ the model assigns each smoker the mean number of cigarettes smoked per day reported for their age and gender stratum in the 2013 National Risk Factor Survey [13], and that those who quit smoking reduce their exposure by the specified mean cigarettes per day

Supplemental Table S2: Local data sources for CVD policy model-Argentina update and calibration

Information	Source
2010 Argentina's Population and Projections	2010 National Census, Argentina National Statistics and Census Institute [11 12]
CVD Risk Factors (mean values and prevalences)	National Risk Factors Survey 2013 [13] and CESCAS I study [14 32]
MI Prevalence	National Risk Factors Survey 2013 [13]
Stroke Incidence	PREVISTA Study [15]
CVD and Non-CVD mortality	Argentina National Statistics and Census Institute [27]
Total number of MIs in 2010	SCAR study (Síndromes Coronarios Agudos en Argentina) [31]
Total number of Strokes in 2010	PREVISTA Study [15]

CVD: cardiovascular Disease; MI: myocardial infarction.

Supplemental Table S3: comparison of overall outcomes between model predictions and actual statistics in Argentina, 2010

	Real statistics (n)	**Model Predictions (n)**	**Difference (%)**
Total number of Mis	41219	41265	**0.11**
Total number of arrests	10122	10132	**0.10**
Total number of Strokes	58658	58584	**-0.13**
MI Deaths	5354	5359	**0.09**
Arrest Deaths	10122	10132	**0.10**
Stroke Deaths	18241	18253	**0.07**
Non-CVD Deaths	231396	230391	**-0.43**
Total deaths	281710	280707	**-0.36**

CVDPM-Arg: Cardiovascular Disease Policy Model – Argentina; MI: myocardial infarction; CVD: cardiovascular disease

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