Tobacco control campaign in Uruguay: Impact on smoking cessation during pregnancy and birth weight

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We analyzed a nationwide registry of all pregnancies in Uruguay during 2007–2013 to assess the impact of three types of tobacco control policies: (1) provider-level interventions aimed at the treatment of nicotine dependence, (2) national-level increases in cigarette taxes, and (3) national-level non-price regulation of cigarette packaging and marketing. We estimated models of smoking cessation during pregnancy at the individual, provider and national levels. The rate of smoking cessation during pregnancy increased from 15.4% in 2007 to 42.7% in 2013. National-level non-price policies had the largest estimated impact on cessation. The price response of the tobacco industry attenuated the effects of tax increases. While provider-level interventions had a significant effect, they were adopted by relatively few health centers. Quitting during pregnancy increased birth weight by an estimated 188 g. Tobacco control measures had no effect on the birth weight of newborns of non-smoking women.

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1. Introduction

The tobacco epidemic continues to represent a serious public health threat throughout the world. By one recent estimate, the worldwide annual mortality burden has already reached 5 million deaths from direct tobacco smoking and another 600,000 deaths attributable to the effects of environmental smoke (World Health Organization, 2012). Within the next 20 years, annual deaths from tobacco are projected to continue to rise to 8 million, of which more than 80% will occur in low- and middle-income countries (Mathers et al., 2008).

Beginning in 2005, Uruguay instituted a series of aggressive anti-smoking measures that placed this small South American country of 3.3 million inhabitants in the forefront of tobacco control policy worldwide. By 2012, the Uruguayan government had prohibited smoking in enclosed public spaces and workspaces, banned nearly all advertising and promotion of tobacco products, mandated that pictograms with warnings cover 80% of the front and back of each pack, banned misleading marketing terms such as “light” and “mild,” and outlawed multiple versions of the same brand such as Silver or Blue. Tobacco taxes were increased, and all healthcare providers were required to offer treatment for nicotine dependence.

In a previous report, two of us (JH and PT) found that Uruguay’s comprehensive nationwide antismoking campaign was associated with a substantial, unprecedented decrease in tobacco use (Abascal et al., 2012). During 2005–2011, per capita cigarette consumption decreased by 4.3% per year, while the 30-day prevalence of cigarette use among students aged 13–17 years and the overall population prevalence of current tobacco use declined at annual rates of 8.0% and 3.3%, respectively. The observed declines in each of these three indicators of tobacco use were significantly larger than those seen in neighboring Argentina, a culturally similar country that had not conducted a comprehensive antismoking campaign and served as a control.

While our previous study contributed to the evaluation of the overall impact of Uruguay’s tobacco control campaign, it did...
not address the quantitative contributions of individual campaign components. Pursuing that objective here, we classify the interventions implemented in Uruguay during 2007–2013 into three categories: (1) provider-level interventions aimed at the treatment of nicotine dependence, (2) national-level increases in cigarette taxes, and (3) national-level non-price regulation of cigarette packaging and marketing. We study the effects of these individual campaign components on a critical target population – pregnant women.

Studying the population of pregnant women is important not only for the well-recognized adverse health consequences of smoking during pregnancy (Permutt and Hebel, 1989; da Veiga and Wilder, 2008; McCowan et al., 2009), but also for the narrow nine-month window during which pregnant women have heightened susceptibility to health-related interventions. We take advantage of a continuous nationwide registry of all live pregnancies from 2007 to 2013 to study the effects of the campaign on two main outcomes: the probability that a pregnant smoker will quit smoking by her third trimester and her infant’s birth weight.

To identify the effect of the provider-level interventions, we use a difference-in-differences (DID) approach, exploiting the fact that these policies were implemented at different health centers at different times. To assess the effect of taxes, we rely upon a series of discrete tax increases during our study period. Finally, to assess the effects of non-price regulation of packaging and marketing, we take advantage of the fact that these measures went into effect at different times. As an additional control, we compare the effect of these interventions on the birth weight of children whose mothers smoked during pregnancy with the corresponding effect, if any, on the offspring of mothers who did not smoke.

Our study contributes to an extensive literature evaluating the impact of such tobacco control policies as tax increases, control of environmental tobacco smoke, cigarette pack warnings, restrictions on cigarette marketing, regulation of tobacco constituents, mass media anti-smoking campaigns, and the treatment of addiction (Saffer and Chaloupka, 2000; Wakefield and Chaloupka, 2000; Powell et al., 2005; Blecher, 2008; Carpenter and Cook, 2008; DeCicca et al., 2008; Anger et al., 2011; Hammond, 2011; Hoek et al., 2011; Chaloupka et al., 2012; Emery et al., 2012; Mons et al., 2013). Our work is distinguishable in that we exploit an extensive micro database to evaluate the relative impacts of multiple types of interventions in the context of a nationwide tobacco control campaign conducted in a developing country.

We find persuasive evidence on the impact of each of the three policy categories analyzed – provider-level interventions, taxes, and non-price policies – on the likelihood of quitting smoking during pregnancy and on birth weight. In terms of the relative contributions of each of these policies to the observed increase in quit rates, the regulation of marketing and packaging had the strongest effect, accounting for 71% of the total observed variation in quit rates during 2007–2013. While interventions to treat nicotine dependence had a strong effect at the level of the individual provider, relatively few prenatal care centers adopted these interventions during the study period, thus contributing little to the overall increase in the quit rate. Tax increases, on the other hand, explained an estimated 25% of the variation in quit rates during 2007–2013. While real taxes increased 122% during that time, the tobacco-industry passed on only a fraction of the tax increases to consumers, so that real cigarette price increased by only 17%. Finally, we find that smoking cessation was associated with a significant increase in birth weight. By contrast, the tobacco control policies under study had no effect on the birth weight of offspring of mothers who did not smoke.

2. Background and data

2.1. Nationwide anti-smoking policies

In 2005, one year after the legislature had ratified the Framework Convention on Tobacco Control, Uruguay’s newly elected administration launched a National Program for Tobacco Control that formed the basis for a succession of progressively more stringent tobacco control policies (Abascal et al., 2012). In March 2006, all enclosed public spaces and all public and private workplaces were declared 100% smoke-free. In June 2008, the scope of tobacco-free spaces was extended to taxis, buses, airplanes and other public transport.

These curbs on environmental tobacco smoke were paralleled by a series of advertising restrictions on tobacco products. In May 2005 the government banned cigarette advertising on television during children’s viewing hours (before 9:30 pm) and prohibited advertising, promotion or sponsorship by tobacco companies of all sporting events. These restrictions were subsequently codified in March 2008, when comprehensive tobacco control legislation (Law 18.256) prohibited all advertising and promotion of tobacco products except at point of sale. In October 2008, logos, trademarks and other tobacco-related symbols were banned on non-tobacco products. In May 2014, all advertising was prohibited, even at the point of sale.

In addition, the Uruguayan government promulgated warning requirements on cigarette packages and imposed restrictions on manufacturers’ branding practices. A May 2005 ministerial decree banned all references to “light,” “ultra light,” “mild,” “low tar” and other descriptors that might misleadingly imply reduced harm. The decree also mandated a series of rotating warnings with images covering 50% of the front and back of each cigarette pack. The deadline for compliance with the first round of these rotating warnings was April 2006. Subsequent rounds had respective deadlines of December 2007, February 2009, February 2010, January 2012, and April 2013. A “single presentation rule,” issued as a ministerial decree along with the third round of warnings, barred the marketing of multiple versions of the same brand, such as Silver or Blue. Finally, a 2009 decree mandated that the size of the warnings be increased to 80% of the front and back of each pack. This requirement was implemented with the fourth round of warnings and became effective by February 2010.1

Fig. 1 shows a timeline summarizing the major nationwide non-price regulatory measures from 2005 to 2013. The blue text describes each of the six rounds of package warnings, while the boldface red text describes regulatory measures other than the mandated warnings. The black lines point to the compliance deadlines for each regulatory measure.2

Fig. 2 further describes the six rounds of rotating package warnings. In each round, we show only one of several mandated images. The relative sizes of the images in the figure correspond to their relative sizes on each pack, with the last three rounds reflecting the required increase from 50% to 80% of the front and back surfaces.

2.2. Smoking cessation programs directed at healthcare providers

In 2008, the comprehensive tobacco control law mandated that every primary care provider, whether public or private, incorporate

1 This “80% rule” was promulgated 3 months before the issuance of the fourth round of images. However, we have no evidence of significant compliance with the 80% rule before the deadline for compliance with the fourth round of images.

2 With the exception of the comprehensive tobacco control law, all measures provided for a 180-day compliance period. By specifying the end of the compliance period as the effective date of each measure, we assumed that tobacco manufacturers waited until each deadline to comply.
the diagnosis and treatment of tobacco dependence into its menu of basic services. Pursuant to this legislation, in 2009 the Ministry of Public Health and the National Resource Fund ("Fondo Nacional de Recursos" or FNR), the governmental agency responsible for financing resource-intensive medical technologies, established national guidelines for primary care providers on the diagnosis and treatment of nicotine dependence. Through a set of agreements ("convenios") with the FNR, healthcare institutions were eligible to receive training and free nicotine patches and bupro- pion in return for setting up a smoking cessation program with little or no patient copayments (Esteves et al., 2011). Health centers that had no agreements with the FNR were required to provide smoking cessation services in accordance with the guidelines, but they were permitted to charge nontrivial copayments to patients. In what follows, we refer to these agreements between health centers and the FNR as “provider-level agreements.”

Among all sites providing prenatal care to pregnant women, the proportion with FNR agreements increased from 7 to 12% during 2005–2013. Concurrently, the proportion of all pregnant women receiving prenatal care at sites with FNR agreements increased from 13% in 2005 to 36% in 2007, but then declined to 31% by 2013.

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**Fig. 1.** Timeline of nationwide non-price tobacco control measures. The blue text refers to the deadlines for each of the six rounds of rotating package warnings, while the boldface red text refers to other tobacco control measures.

**Fig. 2.** Timeline of six rounds of rotating package warnings. Each round displays only one of several mandated images. The relative sizes of the images correspond to their relative sizes on each pack, with the last three rounds reflecting the required increase from 50% to 80% of the front and back surfaces.
2.3. Cigarette tax increases

In addition to the foregoing policy interventions, the Uruguayan government increased its indirect taxes on tobacco products. Imposed solely at the national level, these taxes consist of an excise tax (“impuesto específico interno” or IMESI) and a value added tax (“impuesto al valor agregado” or IVA). The IMESI, which was first applied to cigarettes in 1993, underwent a series of discrete increases in June 2002, May 2003, July 2007, June 2009, and February 2010. The IVA, by contrast, was first applied to cigarettes in July 2007 and since then has constituted 22% of the pre-tax price including the IMESI or, equivalently, 18% of the retail price. Fig. 3 shows the estimated real price and real tax on a pack of cigarettes during 2001–2013. Only 45% of the abrupt increase in cigarette taxes in July 2007 was passed on to consumers in the form of higher retail prices. The construction of the real price and tax series is described in our working paper (Harris et al., 2014).

In Uruguay, an estimated 99% of tobacco users smoke manufactured cigarettes, hand-rolled cigarettes, or both (Abascal et al., 2012). Manufactured cigarettes, in particular, make up more than 85% of taxable cigarette consumption (Dirección General Impositiva, 2012). During 2004–2012, by one estimate, contraband cigarette sales constituted approximately 12% of total cigarette consumption on average (Curti, 2013). With the possible exception of less densely populated provinces (“departamentos”) along Uruguay’s borders with Brazil and Argentina, where contraband tobacco use appears more prevalent, there has been little effective geographical variation in retail price.

2.4. Perinatal information system (SIP)

Our source of micro data on the smoking practices of pregnant women was the Perinatal Information System (“Sistema Informático Perinatal” or SIP), a mandatory nationwide electronic registry operating in all prenatal care clinics in Uruguay since 1990. Developed and overseen by the Latin American Center for Perinatology (“Centro Latinoamericano de Perinatología” or CLAP) of the Pan American Health Organization, the database contained information at the level of the individual pregnancy on maternal characteristics, self-reported smoking behavior, current and past obstetric history, the timing of prenatal care, the sites of prenatal care and delivery, and birth outcomes including birth weight (CLAP, 2001). In 2012, the SIP covered an estimated 94% of all live births in Uruguay.

Our analyses relied upon the following individual-level maternal characteristics, derived from the SIP registry: the timing of the first prenatal visit (first-trimester prenatal care); the mother’s age (<16, 17–19, 20–34, 35–39, and 40+ years), marital status (single, married, cohabiting, other), and educational attainment (primary, secondary, university); the number of prior deliveries (0, 1, 2, 3, 4+); number of prior abortions; a history of diabetes or hypertension; whether any complications of pregnancy were observed, in particular, the presence of preeclampsia or eclampsia; the mother’s body mass index based on her self-reported height and weight prior to the pregnancy (underweight, normal weight, overweight, obese); the mother’s use of alcohol or illicit drugs; the sites of prenatal care; and the newborn’s sex and birth weight.1

Prior to 2007, each individual record in the SIP database contained the pregnant woman’s smoking status only at the time of initiation of prenatal care. It did not show changes in smoking, if any, during the course of her pregnancy. Under a new data entry system beginning in 2007, the prenatal record noted the woman’s smoking status separately in each trimester of her pregnancy. For example, if a woman initiated prenatal care in her second trimester, the healthcare provider recorded her smoking status in the first trimester, based on her recall, as well as in the current trimester. Her smoking status would subsequently be recorded in a follow-up prenatal visit during her third trimester. The perinatal data derived from this new system, which we refer to as the “new SIP,” were the focus of our analysis.

Fig. 3. Real price and real taxes per pack of cigarettes, 2001–2013. The vertical lines show the timing of non-price nationwide policy measures, as described in Fig. 1. (A) Smoking prohibited in all enclosed public spaces and all public and private workplaces. (B) 1st round of package warnings. (C) 2nd round of package warnings. (D) Comprehensive tobacco control legislation. (E) 3rd round of package warnings; brands restricted to a single presentation. (F) 4th round of package warnings; warnings must cover 80% of front and back. (G) 5th round of package warnings. (H) 6th round of package warnings.

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1 To avoid loss of observations, we included dummy variables equal to 1 when some maternal characteristics were missing. For further details on maternal and pregnancy characteristics, including descriptive statistics, see our working paper (Harris et al., 2014).
3. Principal endpoints: smoking cessation and birth weight

To assess the impact of Uruguay’s tobacco control campaign, we focused our attention primarily on pregnant women who smoked cigarettes at any time from the first prenatal visit onward. Within this target group of pregnant smokers, our principal endpoint was smoking cessation by the third trimester. Our analysis of this endpoint was confined to the interval from 2007 to 2013, when data on smoking habits during each trimester were available through the new SIP system. Fig. 4 shows the progressive increase in the annual mean quit rate among pregnant smokers from 15.4% in 2007 to 42.7% in 2013. Our main research objective was to determine what proportion of this substantial rise in quit rates could be attributed to Uruguay’s multi-component campaign.

Why did we not focus on the prevalence of smoking at the onset of pregnancy? Unfortunately, within the limitations of Uruguay’s SIP system, this alternative endpoint was subject to a critical source of potential measurement bias. Starting in July 2008, the Uruguayan Ministry of Health established a new system of financial incentives for providers to increase the completeness of data reporting on SIP records. As Fig. 5 shows, the prevalence of smoking at the first prenatal visit remained stable at about 25% from 2000 to 2005. Thereafter, with the onset of the tobacco control campaign, the prevalence had declined toward 15% by the early months of 2009. In April 2009, however, nine months after the institution of the new system of financial incentives, the prevalence abruptly increased. At the same time, as shown in Fig. 5, the proportion of records with missing data declined dramatically from about 20% in 2009 to 1−2% by 2013.

The best explanation for the abrupt break in prevalence is that women with missing data on smoking at the onset of pregnancy were more likely to be smokers. Moreover, as the Ministry of Health imposed increasingly strict goals for data completeness, the effect of including these previously unreported smokers in the prevalence calculation is likely to have grown ever larger. While we did have some data on the Ministry’s data-completeness goals, we concluded that the task of correcting for this missing data bias and at the same time identifying the effects of post-2009 tobacco control measures would prove intractable.

On the other hand, we did not detect any comparable break in the monthly time series of smoking cessation rates. We thus considered the quitting to be a more reliable and sensitive endpoint than smoking prevalence. Still, to the extent that the new system of data-completeness goals recorded an increasing number of hardcore smokers, our estimates in Fig. 5 of quit rate during 2009–2013 would be biased downward. We stress that our principal endpoint represents the rate of cessation conditional upon smoking on or after the first prenatal visit.

Smoking cessation during pregnancy is known to reduce its adverse health effects. Accordingly, as an additional endpoint, we studied the impact of Uruguay’s tobacco control campaign on birth weight. As shown in Fig. 6, the difference in birth weight between non-smokers and continuing smokers was on the order of 210g, while the corresponding difference between non-smokers and quitters was only about 25g. Although the smaller number of quitters in the SIP database during 2007–2008 decreased the precision of the mean birth weight estimates, Fig. 6 still shows a background increase in birth weight for all three groups. The analysis of birth weight also helped us address the concern that the SIP registry contained self-reported data on smoking habits. If women had falsely reported having quit smoking with increasing frequency as the campaign progressed, we would have expected to see a growing reduction in the apparent favorable effects of cessation on birth weight.

3.1. Impact on quitting during pregnancy

3.1.1. Individual-level analysis

We first investigate the effect of the provider-level agreements and national-level tobacco control policies on the quit rate during pregnancy. To that end, we begin with a linear probability model based upon observations at the level of the individual pregnant woman:

\[ y_{sit} = \beta_0 + \beta_1 x_{is} + \beta_2 z_{it} + \epsilon_{sit} \]  

(1)

where the subscript \( i \) indexes each woman, the subscript \( s \) refers to the health center where she received prenatal care, and the subscript \( t \) refers to the calendar date corresponding to the midpoint of her third trimester. The data \( y_{sit} \) are binary variables representing smoking cessation, where \( y_{sit} = 1 \) if the woman quit and \( y_{sit} = 0 \) if she continued to smoke through her third trimester. The vector of exogenous variables \( s_{it} \) represents individual-level maternal characteristics, while \( x_{is} \) represents the presence or absence of a provider-level agreement at health center \( s \) on calendar date \( t \), and the vector \( z_{it} \) represents those national-level policy variables including cigarettes taxes that were in effect at calendar date \( t \). The parameters \( \beta_1 \) represent health center-specific fixed effects. We assume that the unobserved error terms \( \epsilon_{sit} \) are uncorrelated with the observed explanatory variables and have zero means.

Since the presence or absence of a provider-level agreement \( x_{is} \) varied by health center and calendar date, the impact of these programs was identifiable via a DID model. With respect to the national-level policies \( z_{it} \), however, we needed to be careful about what policy impacts could and could not be identified from the data. Successive increases in cigarette taxes during the 2007–2013 observation period, beginning with the inclusion of tobacco in the value-added tax on July 1, 2007 (Fig. 3), permitted us to identify the impact of this policy. On the other hand, we could not identify the impacts of the two non-price policies that went into effect before the start of our observation period: the prohibition of smoking in public places and enclosed workspaces (March 1, 2006) and the requirement that all packs contain rotating images with warnings covering 50% of the front and back of each pack (April 18, 2006). Moreover, the effective dates of the second, third and fourth rounds of warnings were either close to or coincident with other policy measures, and thus their impacts could not be separately identified without additional strong assumptions concerning their effects over time (Fig. 1).

That left us with five non-price, national-level policies: the comprehensive tobacco legislation banning nearly all advertising (in effect from March 6, 2008 onward); the single presentation rule (in effect from February 14, 2009 onward); the increase in the warning size from 50% to 80% of the front and back of each pack (in effect from February 28, 2010 onward); the fifth round of warnings (in effect from January 7, 2012 through April 7, 2013); and the sixth round of warnings (in effect from April 8, 2013 onward).

Column (A) of Table 1 shows our results. We estimated the parameters of Eq. (1) by ordinary least squares (OLS) with Huber-White robust standard errors implemented at the individual level. The presence of an agreement between the woman’s health center and the FNR increased the probability of quitting by an estimated 4.8 percentage points (\( p = 0.024 \)). The coefficient of the log tax per pack was 0.079 (\( p = 0.031 \)). At the sample mean value of the dependent variable equal to 0.377, the estimated elasticity of the smoking cessation with respect to cigarette taxes was

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4 For the individual-level model of Eq. (1), we assigned a woman to calendar date \( t \) based on the midpoint of her prenatal care visits during her third trimester of pregnancy. If she had no prenatal visits, we assigned her a date \( t \) equal to 30 days prior to delivery.
0.079/0.377 = 0.21. All five of the non-price nationwide policies had significant effects, with the comprehensive tobacco control law assuming the dominant role. All five non-price policies combined increased the probability of quitting by an estimated 26.9 percentage points ($p < 0.001$).

We used the results of our individual-level analysis to compute the relative contributions of each of the three categories of tobacco control policy to the overall change in smoking cessation rates observed during the 2007–2013 study period. To that end, we first computed the predicted values $\hat{y}_{ist}$ derived from Eq. (1) and then calculated the corresponding sum $\hat{Y} = \sum_{i,s,t} \hat{y}_{ist}$ over all observations. We then recomputed the predicted values $\hat{y}_{ist}$ and corresponding sums $\hat{Y}$, successively setting all values of the provider-level agreement variable $x_{ist}$ equal to 0, then all values of the log real tax rate equal to the initial level in January 2007, and then all indicators of non-price policies $z_{it}$ equal to 0. Based on this decomposition procedure, we estimated the following attributable proportions: provider-level agreements, 4.3%; tax increases, 25.2%; and regulations of packaging and marketing, 70.5%.

### 3.2. Health center level analysis

It is arguable that an individual-level analysis of Eq. (1) overstates the precision of estimated policy impacts. The central thrust of this criticism is that the agreements for smoking cessation services were made with health centers rather than with individual patients. Moreover, the tax increases and non-price policies were carried out at the national rather than the individual level. To address these concerns, we performed a series of aggregate analyses at both the health center level and national level. Following
We first-order health the D. C. Fst (Fig. 192 A. others, for sentencing Amemiya, Log Single 80% Tobacco Sixth * Significant OLS estimation on individual maternal-level observations, based on Eq. (1). White-Huber robust standard errors. Coefficients of individual maternal characteristics and health center fixed effects not shown.

B. OLS estimation on observations grouped by health center and calendar quarter, based on Eq. (3). Standard errors adjusted for clustering at level of health center. Observations weighted by inverse of standard errors of fixed effects derived from Eq. (2).

C. FGLS estimation on observations grouped by health center and calendar quarter, based on Eq. (3). Standard errors adjusted for clustering at level of health center. Uniform first-order serial correlation estimated to equal 0.0210. Observations weighted by inverse of standard errors of fixed effects derived from Eq. (2).

D. FGLS estimation on observations grouped by health center and calendar quarter, based on Eq. (3). Standard errors adjusted for clustering at level of health center. Uniform first-order serial correlation estimated to equal 0.0237. Observations weighted by inverse of standard errors of fixed effects derived from Eq. (2).

E. OLS estimation on observations grouped by calendar quarter, based upon Eq. (4). Newey-West standard errors adjusted for heteroskedasticity and serial correlation. Observations weighted by inverse of standard errors of fixed effects derived from Eq. (2).

(Amemiya, 1978; Hansen, 2007; Imbens and Woolridge, 2014) and others, we specified the following two-stage model.

\[
y_{ist} = \gamma_{i} \beta_{0} + F_{ist} + u_{ist} \tag{2}
\]

\[
F_{ist} = \gamma_{ist} \beta_{1} + \gamma_{ist} \beta_{2} + G_{i} + \nu_{ist} \tag{3}
\]

Here, the subscript \( s = 1, \ldots, S \) continues to index health centers, while the subscript \( t = 1, \ldots, T \) now indexes calendar quarters. The subscript \( i = 1, \ldots, N_{i} \) now indexes women who received prenatal care at health center \( s \) and whose third trimester occurred in calendar quarter \( t \).

In the first stage (Eq. (2)), the data \( y_{ist} \) are binary variables representing smoking cessation and the exogenous variables \( \gamma_{i} \) represent individual-level maternal characteristics, while \( F_{ist} \) are fixed effects for each of the \( ST \) combinations of health center and calendar quarter. In the second stage (Eq. (3)), the data \( \gamma_{ist} \) represent the presence or absence of a provider-level agreement at health center \( s \) during calendar quarter \( t \), while the data \( \gamma_{ist} \) denote the national-level policies in effect in calendar quarter \( t \). The parameters \( G_{i} \) are S health center-specific fixed effects. We assumed that the unobserved error terms \( u_{ist} \) and \( \nu_{ist} \) were uncorrelated with the observed explanatory variables and with each other, and had zero means.

To estimate the model parameters, we first ran OLS on Eq. (2), thus obtaining estimates \( \hat{F}_{ist} \) of the parameters \( F_{ist} \). In effect, these OLS estimates represented the predicted quit rate in each health center \( s \) and calendar quarter \( t \) of a pregnant smoker in the reference category of maternal characteristics. We then estimated the parameters of the DID model (3), where the dependent

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\* A woman in the reference category was married, aged 20–34 years, had less than a high school education, did not seek prenatal care in her first trimester, had no prior abortions or deliveries, a pre-pregnancy body mass index 18.5–24.9 kg/m\(^2\), no history of diabetes, hypertension, eclampsia or pre-eclampsia, and gave birth to...
variable \( F_{st} \) was replaced by its estimated value \( \hat{F}_{st} \). We weighted the observations by the inverse of the standard errors of the estimates \( \hat{F}_{st} \).

Within the context of this aggregate model, researchers have expressed concerns that traditional OLS estimation of DID models ignores serial correlation of errors and thus overstates the precision of the coefficient estimates (Bertrand et al., 2004; Cameron et al., 2008). In our context, serial correlation would arise when health centers were subject to common unobserved shocks that persisted for more than a calendar quarter. To address these concerns, we estimated the parameters of Eq. (3) by feasible generalized least squares (FGLS) under varying specifications of the covariance matrix \( V = \{v_{t}\}_{t=1}^{T} \).

Columns (B) and (C) in Table 1 show our regression estimates of the parameters \( \beta_{1} \) and \( \beta_{2} \) of Eq. (3) under two different assumptions concerning the covariance matrix. In column (B), we assumed clustering of errors within each health center. In column (C), we assumed first-order temporally correlated errors with a uniform correlation coefficient among health centers. We found quite similar results when we estimated Eq. (3) under the assumption that the coefficient of serial correlation varied by health center (not shown in Table 1). In comparison with the maternal-level estimates (column A), we observed larger coefficients for two policies: the log real cigarette tax and the comprehensive tobacco control law. However, their corresponding standard errors were also increased, so that we could not reject the hypothesis that their impacts equalled those estimated at the individual-level data. Finally, in both columns (B) and (C), the combined effect of the five non-price policies was indistinguishable from the effect estimated from individual-level data.

3.3. National level analysis

It is arguable that the 2-stage model of Eqs. (2) and (3) still overstates the precision of the estimated impacts of cigarette taxes and non-price regulations of cigarette packaging and marketing, as these policies were carried out at the national level. To address this criticism, we extended our two-stage model of Eqs. (2) and (3) to three stages. In particular, we continued to specify the first-stage model of Eq. (2), but replaced Eq. (3) with the following two equations:

\[
F_{st} = x_{st}^\prime y_{1} + H_{s} + J_{t} + \xi_{st} \tag{4}
\]

\[
J_{t} = \tilde{z}_{t}^\prime y_{2} + \eta_{t} \tag{5}
\]

As before, we assumed that the unobserved error terms in (2), (4) and (5) were uncorrelated with their respective explanatory variables.

The second-stage Eq. (4) differs from (3) in that \( F_{st} \) now depends on the presence or absence of a provider-level agreement \( x_{st} \) at health center \( s \) during calendar quarter \( t \) as well as health center fixed effects \( H_{s} \), calendar quarter fixed effects \( J_{t} \), and an unobserved random error \( \xi_{st} \) with mean zero. To estimate the policy impact parameters \( y_{1} \) in (4), we replaced the fixed effects \( F_{st} \) with their estimates \( \hat{F}_{st} \) from Eq. (2). As in the two-stage model, Eq. (4) was estimated by feasible GLS under various assumptions concerning the covariance matrix of the errors, where the observations were weighted by the inverse of the standard errors of the estimates \( \hat{F}_{st} \).

In third-stage Eq. (5), the calendar quarter fixed effects \( J_{t} \) in turn depend on national level policies as well as an unobserved random error \( \eta_{t} \) with mean zero. To estimate the policy impact parameters \( y_{2} \) in (5), we replaced the fixed effects \( J_{t} \) with their estimates \( \hat{J}_{t} \) from the second stage Eq. (4). We then estimated the linear model (5) by OLS with Newey–West standard errors with a maximum lag of 4 calendar quarters to take account of possible heteroskedasticity and serial correlation of the error terms (Newey and West, 1987). Similarly, we weighted the observations by the inverse of the standard errors of the estimates \( \hat{J}_{t} \).

Fig. 7 motivates the logic underlying the third stage of our analysis. The vertical axis measures the estimated fixed effects \( \hat{J}_{t} \), which represent calendar quarter-specific quit rates adjusted for individual maternal characteristics, health center fixed effects, and the presence or absence of a provider-level agreement. The horizontal axis measures the corresponding calendar quarter \( t \). Highlighted are the dates on which the value added tax was imposed on tobacco, comprehensive tobacco legislation was passed, only brands with a single presentation were permitted, images with warnings were mandated to cover 80% of the front and back of each pack, and the fifth and sixth rounds of images went into effect.

Columns (D) and (E) show the results of our three-stage procedure. Column (D) shows the estimate of \( y_{1} \) in Eq. (4) in the case of FGLS with serially correlated errors. As in the previous models, the presence of provider-level agreement increased the probability of smoking cessation by 5.6 percentage points (\( p = 0.027 \)). Column (E) shows the estimates of the policy impact parameters \( y_{2} \) in Eq. (5). The estimated policy impacts are comparable to those derived from the 2-stage model (columns B and C). The point estimate of the impact of cigarette taxes is larger and statistically significant (\( p < 0.045 \)), implying an estimated elasticity of quitting equal to 0.36. Still, we could not reject the hypothesis that the estimated tax impact equalled that estimated from maternal-level data. Finally, the estimated effects of the five non-price policies combined was indistinguishable from the estimates based on the individual-level and two-stage models.

4. Impact on birth weight

We relied upon maternal-level data to assess the effect of quitting smoking during pregnancy and birth weight. Following (Permutt and Hebel, 1989), we adopted a simultaneous equation framework in which Uruguay’s anti-smoking policies served as instruments for the endogenous variable of smoking cessation. In addition, we took advantage of the birth-weight endpoint to strengthen our identification of the causal effect of Uruguay’s tobacco control campaign. Employing the population of non-smoking pregnant women as a control group, we performed a falsification test to determine whether the same policy instruments had any effect on the birth weight of infants delivered by non-smokers.

We estimated the following equation on our sample of smoking pregnant women:

\[
w_{ist} = \delta_{1}y_{ist} + c_{i}^\prime \delta_{0} + K_{s} + \zeta_{ist} \tag{6}
\]

where the variable \( w_{ist} \) denotes the birth weight of the infant delivered by mother \( i \) in health center \( s \) and the calendar date \( t \) refers to the midpoint of her third trimester of pregnancy. In Eq. (6), birth weight depends on smoking cessation (\( y_{ist} \)), individual maternal characterics (\( c_{i} \)), a health center fixed effect (\( K_{s} \)), as well as a random error term (\( \zeta_{ist} \)) with zero mean.

If the random error \( \zeta_{ist} \) is correlated with \( y_{ist} \), then the coefficient \( \delta_{1} \) will be biased when Eq. (6) is estimated by OLS. There is, in fact, good reason to believe that this is the case. For example, a woman with a propensity to engage in risky behaviors will tend not to quit smoking and deliver a low-weight baby. In that case, failure to account for the unobserved heterogeneity will overestimate the parameter \( \delta_{1} \). Alternatively, a woman who runs into complications during her pregnancy will be under pressure to quit smoking and

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a singleton female. For further details on maternal and pregnancy characteristics, including descriptive statistics, see our working paper (Harris et al., 2014).
tend to deliver a low-weight baby. In that case, the parameter $\delta_1$ will be underestimated.

To address the potential endogeneity of the quit variable $y_{ist}$, we therefore estimated Eq. (6) by two-stage least squares (2SLS), where the first stage is defined by Eq. (1) and the instruments for smoking cessation are the policy variables $x_{it}$ and $z_t$. As shown in Table 2, estimation of Eq. (6) by OLS, with clustering of standard errors by health center, gave an estimate of $\hat{\delta}_1 = 123.2$ g ($p < 0.001$). By contrast, estimation of (6) by 2SLS, similarly with standard errors clustered by health center, gave an estimate of $\hat{\delta}_1 = 187.9$ g ($p = 0.028$). While 2SLS increased the estimated standard error of $\hat{\delta}_1$, all tests rejected the hypotheses of weak instruments or over-identification. Although the 95% confidence intervals of the two estimates of $\hat{\delta}_1$ overlapped substantially, the results still suggest that the OLS estimate may be biased downward.

For our falsification test, we used the parameters estimated from the first-stage Eq. (1) to predict the values of $y_{ist}$ for those women who did not report smoking during pregnancy. We then estimated the model of Eq. (6) on all women in this comparison group, replacing $y_{ist}$ with its predicted value. If the tobacco control policies captured in the variables $x_{it}$ and $z_t$ in fact improved birth weight by increasing the rate of quitting, then the estimate of $\hat{\delta}_1$ in (6) should be indistinguishable from zero in the comparison group of non-smoking pregnant women. On the other hand, if these policies are simply correlated with other unobserved factors that improved birth weight, then the estimate of $\hat{\delta}_1$ in (6) should be significantly positive for non-smokers as well. In fact, as shown in Table 2, the estimate of $\hat{\delta}_1$ was indistinguishable from zero among non-smokers ($-27.8$ g, $p = 0.527$).

### Table 2

<table>
<thead>
<tr>
<th>Population</th>
<th>OLS</th>
<th>2SLS</th>
<th>Falsification test</th>
</tr>
</thead>
<tbody>
<tr>
<td>Smokers</td>
<td>123.2$^{**}$ (10.8)</td>
<td>187.9$^{**}$ (85.5)</td>
<td></td>
</tr>
<tr>
<td>Non-smokers</td>
<td>$-27.8$ (43.8)</td>
<td></td>
<td>126,504</td>
</tr>
</tbody>
</table>

$^{**}$ Significant at $p < 0.001$.

$^a$ All estimates correspond to the parameter $\delta_1$ in Eq. (6).

$^b$ All standard errors adjusted for clustering by health center.

5. Discussion and conclusions

To assess the impact of Uruguay’s nationwide tobacco control campaign, we analyzed a comprehensive nationwide registry of pregnancies ending in a live birth during 2007–2013. We focused sharply on smoking cessation among those women who reported smoking at any time during pregnancy, as well as the consequences of smoking cessation for birth weight. We observed a striking increase in the proportion of pregnant smokers who had quit by their third trimester, from 15.4% in 2007 to 42.7% in 2013.

We employed a difference-in-differences approach to evaluate the effects of provider-level agreements on quit rates during pregnancy. We found that smoking cessation programs established under agreements between health centers and the National Resource Fund increased quit rates by between 4.8 and 5.6 percentage points. Unfortunately, no more than one-third of pregnant smokers received care at health centers with contractual agreements during the period of analysis, and by 2013, the proportion of women exposed to such treatments had declined. As a result, these provider-level agreements contributed little to the overall increase in smoking cessation observed during 2007–2013.

Although real taxes per pack increased by 122% during our study period (Fig. 3), tax increases alone explained only about 20% of the overall rise in smoking cessation during pregnancy. In addition, our estimates of the tax elasticity of quitting, ranging from 0.21 to 0.36, were lower than those reported in the U.S. (Ringel and Evans, 2001; Colman et al., 2003). The principal explanation for this limited influence is that manufacturers moderated their retail prices in response to the application of the value added tax to cigarettes in July 2007 and other non-price regulatory policies enacted during 2007–2009 (Fig. 3) (Harris et al., 2014). As a result, the real retail price of cigarettes increased by only 17% during 2007–2013. Endogenous responses of the tobacco industry to state and nationwide tax increases have been previously documented in the U.S. (Harris, 1987; Harris et al., 1996; Chaloupka et al., 2010; Miura, 2010).

To the contrary, most of the observed increase in quit rates was attributable to non-price regulation of the marketing and packaging of cigarettes. While the combined effect of all five non-price policies
was indistinguishable across the models that we tested (Table 1), it was nonetheless difficult to identify with precision the quantitative impacts of the individual component policies. We could not distinguish immediate versus long-run effects of policies, nor could we identify synergies between policies. Our analysis at best identified the average impacts of the tobacco control measures over time, conditional upon a specific temporal sequence of policy interventions. Thus, the increase in the size of warnings from 50 to 80% of the front and back of each pack of cigarettes, in effect since February 28, 2010, was associated with a 3 percentage point increase in the cessation rate (Table 1). However, this estimated impact was in the context of the coincident fourth round of warnings, as well as a ban on smoking in public places and private workspaces (March 1, 2006), the comprehensive tobacco control law (March 6, 2008), the single presentation rule (February 14, 2009) and other policies in effect at the same time (Figs. 1 and 2).

While we had micro data on smoking cessation at the individual level, the tobacco control policies that we evaluated were carried out at either the health center level or the national level. Accordingly, if there were significant inter-correlation of quitting behavior among women who attended the same health center or who were pregnant in the same calendar quarter, then the effective number of observations could be far less than the approximate 31,000 shown in column A of Table 1. However, our estimates on data aggregated at the health center level (columns B and C) and at the national level (columns D and E) generally confirmed our individual-level results.

Some economists have suggested that the impact of smoking cessation during pregnancy on birth weight, as estimated from cross-sectional databases, may be exaggerated by the presence of unobserved heterogeneity (Lien and Evans, 2005; Abrevaya, 2006; Abrevaya and Dahl, 2008; Walker et al., 2009; Juarez and Merlo, 2013). That is, a woman who tends to engage in risky behaviors will continue to smoke during pregnancy and have lower weight babies. However, the presence of unobserved heterogeneity can also result in an underestimate of the impact of smoking cessation. Thus, a woman who encounters complications in the third trimester, such as intrauterine growth retardation, will quit smoking and have a lower weight baby. Our OLS estimate of the effect of quitting on birth weight was 123 g (95% CI, 102–145). When we used Uruguay's tobacco control policies as instruments for quitting smoking, our 2SLS estimate was 188 g (95% CI, 20–356). While our 2SLS estimate reinforces the conclusions that smoking cessation during pregnancy, even in the third trimester, has a significant positive effect on birth weight, the confidence interval surrounding that estimate was too wide to draw definitive conclusions about the direction of bias, if any, in the OLS estimate. Our results confirm that even delayed cessation of smoking can reduce the adverse effects of smoking during pregnancy (Lieberman et al., 1994; Kaatikainen et al., 2007; Batech et al., 2013; Van and Groothuis, 2013).

As we have already noted, Uruguay’s tobacco control campaign was associated with declines in per capita cigarette consumption, adult smoking prevalence and adolescent cigarette use that were significantly greater than those observed in Argentina, a country with a common international border, language and culture that served as a control (Abascal et al., 2012). Unfortunately, we were unable to locate reliable nationwide data from Argentina on the smoking practices of pregnant women during 2007–2013, and thus could not construct a comparable external control group for this study. Still, our falsification test took advantage of an internal control group, namely, pregnant Uruguayan women who did not smoke during pregnancy. We found, in particular, that the tobacco control policies implemented in Uruguay during 2007–2013 had no effect on the birth weight of mothers in this non-smoking control group.

Our data on smoking from the SIP registry were self-reported. It is conceivable that Uruguay's tobacco control campaign increased the social pressure on a pregnant woman to deny smoking when queried by her obstetrician. While we cannot completely rule out misreporting bias, we note that if women had falsely reported having quit smoking with increasing frequency as the campaign progressed, we would have expected to see a growing reduction in the apparent favorable effect of quitting on birth weight. That is not what we observed in Fig. 6. Moreover, if the apparent increase in smoking cessation during 2007–2013 were solely the result of increasing misreporting, then we would have observed no relation between quitting and birth weight. That is not what we observed in Table 2. In the context of smoking during pregnancy, a number of authors have found a strong correlation between self-reported cigarette consumption and objectively measured levels of nicotine metabolites (Castellanos et al., 2000; Althabe et al., 2008; Himes et al., 2013).

During 2005–2009, the prevalence of smoking during pregnancy declined from approximately 25% to 15% (Fig. 5). Unfortunately, missing data biases seriously complicated the interpretation of prevalence trends thereafter. Moreover, there is evidence that some women who quit during pregnancy later resumed smoking and then quit once again during the next pregnancy (Harris et al., 2014). Still, if the trend observed during 2005–2009 is an accurate indicator of an overall decline in prevalence, then our results on smoking cessation may substantially understate the overall impact of Uruguay's tobacco campaign.

Our results have important implications for future research and for the future design of tobacco control policies. Our findings suggest that enhanced targeting of healthcare providers in the implementation of tobacco cessation programs, as well as increased recruitment of patients, could have a high payoff. At the same time, our findings strongly suggest that non-price policies, in particular regulation of marketing and packaging, can have an important impact in reducing tobacco use.

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Conflicts of interest

We have no conflicts of interest to declare.

Authors' contributions

All three coauthors contributed to the conceptualization and design of this study, the analysis of the data, and the writing of this report.

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