Impacts of Canada's minimum age for tobacco sales (MATS) laws on youth smoking behaviour, 2000–2014

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► Additional material is published online only. To view please visit the journal online (http://dx.doi.org/10.1136/tobaccocontrol-2017-053869).

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Received 1 June 2017
Revised 18 November 2017
Accepted 27 November 2017
Published Online First 13 January 2018

To cite: Callaghan RC, Sanches M, Gatley J, *et al*. *Tob Control* 2018;**27**:e105–e111.

ABSTRACT

Background Recently, the US Institute of Medicine has proposed that raising the minimum age for tobacco purchasing/sales to 21 years would likely lead to reductions in smoking behavior among young people. Surprisingly few studies, however, have assessed the potential impacts of minimum-age tobacco restrictions on youth smoking.

Objective To estimate the impacts of Canadian minimum age for tobacco sales (MATS) laws on youth smoking behaviour.

Design A regression-discontinuity design, using seven merged cycles of the Canadian Community Health Survey, 2000–2014.

Participants Survey respondents aged 14–22 years (n=98 320).

Exposure Current Canadian MATS laws are 18 years in Alberta, Saskatchewan, Manitoba, Quebec, the Yukon and Northwest Territories, and 19 years of age in the rest of the country.

Main outcomes Current, occasional and daily smoking status; smoking frequency and intensity; and average monthly cigarette consumption.

Results In comparison to age groups slightly younger than the MATS, those just older had significant and abrupt increases immediately after the MATS in the prevalence of current smokers (absolute increase: 2.71%; 95% CI 0.70% to 4.80%; P=0.009) and daily smokers (absolute increase: 2.43%; 95% CI 0.74% to 4.12%; P=0.005). Average past-month cigarette consumption within age groups increased immediately following the MATS by 18% (95% CI 3% to 39%; P=0.02). There was no evidence of significant increases in smoking intensity for daily or occasional smokers after release from MATS restrictions.

Conclusion The study provides relevant evidence supporting the effectiveness of Canadian MATS laws for limiting smoking among tobacco-restricted youth.

INTRODUCTION

In 2015, an expert scientific panel of the USA's Institute of Medicine (IOM) concluded that raising the minimum legal purchasing/sales age for tobacco products from 18 to 19 years to 21 years of age would have a significant positive impact on public health and save lives.[1] According to the IOM modelling study, higher tobacco minimum-age policies not only would significantly reduce tobacco-use initiation among teenagers and young adults, but also substantially decrease the subsequent smoking-caused mortality burden among the cohort of US children and adolescents born between 2000 and 2019 by an estimated 249 000 fewer premature deaths, including 45 000 fewer deaths from lung cancer, and 4.2 million fewer years of life lost.[1] In 2016, both Hawaii and California implemented statewide legislation to raise the minimum tobacco purchasing/sales age to 21 years.[2 3]

Recently, in Canada, the setting for the present study, Health Canada,[4] provincial tobacco control leaders[5] and research organisations,[6] as well as provincial lawmakers[7] also have proposed raising the minimum age for tobacco sales (MATS) from the currently legislated age of 18 or 19 years to 21 years as a key policy option for reducing the country's tobacco-smoking epidemic.[8] Smoking is currently responsible for 37 000 Canadian deaths each year[9] and $18.7 billion (in year 2013) in annual health and economic costs.[10] In 2014, approximately 18% of the Canadian general population reported that they were current smokers,[11] and a large majority (80%) of Canadian smokers 'support' or 'strongly support' raising the legal age for purchasing cigarettes/tobacco to at least 21 years.[5]

The rationale for raising the MATS laws is based on a number of important findings. Almost all smokers begin smoking in adolescence or early adulthood,[12] and it is expected that the primary impact of higher MATS laws would be both to delay and prevent smoking initiation among youth, resulting in short-term and long-term decreases in smoking prevalence in the general population.[1] The adolescent brain is uniquely vulnerable to the rewarding effects of nicotine[13]—a sensitivity that diminishes with age.[14 15] Youth smoking experimentation (even at low levels) can more quickly lead to nicotine dependence, resulting in increased likelihood of long-term persistence,[16] more severe nicotine dependence[17] and increased difficulties in smoking cessation.[12 18–21] As a result, even delaying the age of youth tobacco experimentation or initiation not only can reduce the risk of transition to regular daily tobacco use, but also can increase the likelihood of successful quitting, if young people do become regular smokers.[12 18–21] In addition, most adolescent smokers primarily acquire cigarettes and other tobacco products from social sources (especially friends and classmates just older than the minimum tobacco sales age, but still in their social network), and it is expected that raising the MATS laws will reduce tobacco availability for older high school students—the age group with the highest

propensity to initiate smoking behaviour[22]—because they will be less likely to have legal-aged sources within their social network. This reduced availability will likely result in decreased patterns of smoking experimentation and subsequent escalation to daily smoking.[23–25]

Surprisingly few studies[26–31] actually have evaluated how changes in minimum-age laws might affect population-level patterns of tobacco use among young people, and the results are mixed. Two[26 27] studies indicated that the implementation of higher minimum-age laws was associated with significant reductions in youth smoking behaviour in tobacco-restricted age groups, ranging from relative decreases of 30%–45% in smoking prevalence. A regression-discontinuity (RD) study using US natality records from Pennsylvania (1992–2002) also showed that release from minimum-age tobacco restrictions was associated with significant and immediate increases in maternal smoking prevalence and poorer infant health outcomes (ie, premature births and lower infant birth weights).[29] Two other studies presented null results from their primary analyses,[28 30] but confident interpretation of these null findings appears to be undermined by research design limitations, such as: lack of statistical power to detect a meaningful public health effect[30]; absence of baseline assessments prior to law implementation;[28] and a lack of accounting for the effects of other tobacco control policies implemented at the same time as minimum-age laws.[28] Also, a recent pre-post study[31] showed no evidence of changes in smoking prevalence among those aged 15 and 16 years associated with the raising of minimum age of tobacco sales laws in some European countries to 18 years during the period from 2007 to 2009.

Building on this initial work, the current study relies on an innovative quasi-experimental research design—a RD approach. This approach does not require a change in MATS laws to provide credible estimates of the possible effects of current Canadian MATS laws on population-level smoking patterns among young people. It was expected that in comparison to youth slightly younger than the MATS those individuals just older would have significant and immediate increases in the prevalence and intensity of smoking behaviour immediately following release from MATS restrictions. This primary hypothesis drew support from prior work showing that tobacco minimum-age laws have an impact on youth smoking,[26 27 29] as well as from a large body of RD studies demonstrating that release from minimum legal drinking age (MLDA) laws is associated with significant and abrupt increases in alcohol consumption and alcohol-related harms among young people.[32–42]

METHODS

Data access

Study team members (RCC, MS, JG) gained approval from Statistics Canada to access the required restricted-use data files at secure Regional Data Centre locations (Toronto, Victoria), and they agreed to abide by the Statistics Canada Regional Data Centre security and confidentiality requirements.

Data sources

The project relied on smoking-related data from seven merged cycles of the Canadian Community Health Survey (CCHS)—a national, cross-sectional population survey of individuals at least 12 years of age: 2000/2001 (cycle 1.1); 2003 (cycle 2.1); 2005 (cycle 3.1); 2007/2008 (cycle 4.1); 2009/2010 (cycle 5.1); 2011/2012 and 2013/2014. Collecting information related to health status, healthcare utilisation and health determinants for the Canadian population, the Statistics Canada-run CCHS survey employs a probability-based, stratified multistage sampling design, with Computer-Assisted Telephone Interviewing and Computer-Assisted Person Interviewing methods for the administration of the survey questionnaire. National response rates varied across the survey cycles used in the current study: 84.7% (2000/2001 cycle); 80.7% (2003 cycle); 78.9% (2005 cycle); 77.6% (2007/2008 cycle); 71.5% (2009/2010 cycle); 67.0% (2011/2012 cycle) and 65.6% (2013/2014 cycle).[43–49]

MATS laws

MATS laws are currently 18 years of age in Alberta, Saskatchewan, Manitoba, Quebec, the Yukon and Northwest Territories, and 19 years of age in the rest of the country. The current MATS of 18/19 years did not change across the CCHS survey waves (2000–2014), except in Nunavut, where the MATS law was raised from 18 to 19 years on 1 February 2004.[50] As a result, Nunavut was considered a MATS-18-year territory before 1 February 2004 and a MATS-19-year territory from 1 February 2004 onwards.

Sample size

The sample (n=98 320; 48 991 females) consisted of respondents aged 14–22 years across the seven merged CCHS survey cycles (2000–2014). The sample sizes for each age-in-months age bin comprised approximately 750–1150 individuals, with a mean size of approximately 1000 young people.

Data collection and data processing: CCHS

All smoking-related questions and response categories required for our hypotheses were constructed in the same manner across survey waves. We followed the Statistics Canada guidelines for merging the CCHS waves by following the 'pooled approach' method[51]—a method which combines the survey cycles at the micro-data level and rescales the original sampling weights by a constant factor $j=1/k$ (with k being the number of survey cycles being combined). The pooled approach accounts for the sampling design (stratification, clustering and weights) since it still allows for the use of the Statistics Canada CCHS bootstrap weights to estimate the variability. Also, an attractive advantage of the pooled approach is the increase in statistical power associated with increased sample size from combined survey waves.[51]

Respondents' age

For each of the respondents, we calculated age in months, based on the respondent's date of birth information in the restricted CCHS files, with respondents' age-in-months centred (as 0 months) at the provincial/territorial legislated minimum age (18 or 19 years).

Primary outcomes

The current study focused on the following primary outcomes: current-smoker status; occasional smoking status; daily smoking status; smoking frequency (smoking days in the past month) and intensity (number of cigarettes smoked on smoking days) among occasional smokers; smoking intensity among daily smokers; and average past-month cigarette consumption per person (which included both smokers and non-smokers).

Definition of smoking status outcomes

The current study used three categories of smokers. Daily smokers reported smoking daily at the survey interview. Occasional smokers were defined as individuals who indicated

smoking one or more cigarettes on at least one day in the last month, but who did not identify themselves as daily smokers at the survey interview. Current-smokers were defined as daily smokers or occasional smokers.

Analytic plan

Regression-discontinuity

We employed an RD design[52]—a quasi-experimental approach which can provide credible estimates of the causal effect of an intervention on a specified outcome.[53] Our RD design took advantage of the sharp discontinuity in the legality of tobacco sales for young people appearing at the MATS: our approach assigned individuals younger than the MATS to the 'tobacco-restricted' group and young adults no longer subject to the MATS to the 'tobacco-accessible' group. The primary, intuitive idea of the RD approach is that individuals slightly older than the MATS and those slightly younger than the MATS will be similar on observed (and unobserved) characteristics—except for the influence of the removal of the MATS laws in the tobacco-accessible group. The RD design assumes that all observed and unobserved variables (which might influence the smoking outcomes) are smoothly distributed across the age cut-off,[54] and the effects of the MATS can be inferred if the regression line shows a discontinuity at the MATS.[55] In other words, since the observed and unobserved determinants of the tobacco-use outcomes (other than the legal granting of access to tobacco products) are likely to be distributed smoothly across the MATS threshold, any abrupt increases in smoking patterns immediately following the MATS can reasonably be attributed to legal availability of tobacco products.

Application of RD models to the aggregated CCHS cycles

The CCHS uses a stratified multistage sampling design to select survey respondents, and the computation of correct variances and statistical tests in such design requires the use of specific statistical methods and software. The approach recommended by Statistics Canada is the bootstrap, for which bootstrap weights are appended to each survey cycle. The SAS program 'bootvar' is made available for analyses using these weights.[56] All our analyses were conducted at the Statistics Canada Regional Data Centre of Toronto, using the program 'bootvar' and SAS System V.9.4.[56]

Given that the statistical software aimed at fitting non-parametric RD models currently does not accommodate the CCHS bootstrap weights, the current study used a parametric regression approach. Following best-practice guidelines for RD analyses,[55] we made the functional form more flexible by using a quadratic term and by allowing the function to differ on both sides of the cut-off by adding interactions in the model. For the RD models, we controlled for the CCHS survey cycles, Canadian Regions (Atlantic, Quebec, Ontario, Prairies and BC+Territories) and MATS regions (MATS-18 and MATS-19 provinces/territories). For the binary outcomes (ie, current-smoker and daily-smoker outcomes), we used logistic regression with binomial distribution and log-odds link. In the logistic regression procedures, we transformed the δ coefficient from log-odds to a proportion value and calculated its CI using the bootstrap method in the Statistics Canada 'bootvar' software. Ordinary least-squares regression was used for the smoking intensity (ie, number of cigarettes) outcome. Each RD model worked on a 96-month span of data—48 months before and after the provincial/territorial MATS.

RD models were used to assess the possibility of significant and immediate increases immediately following the MATS laws in self-reported prevalence of (1) current-smokers, (2) daily smokers and (3) occasional smokers. Second, among daily smokers, RD models estimated whether the average number of cigarettes smoked per day increased immediately after release from MATS laws. In addition, among occasional smokers, RD analyses assessed potential changes in the number of smoking days in the past month and average number of cigarettes smoked on smoking days in the past month. Additional RD models estimated potential post-MATS increases in average monthly cigarette consumption per person (which included both smokers and non-smokers).

RESULTS

Given that MATS-by-gender interaction terms in all of the primary RD models were not statistically significant (P>0.05), the primary RD results were based on combined male and female samples. Online supplemental table 1 provides a description of key respondent and smoking status variables across CCHS survey cycles (2000–2014).

Patterns of smoking prevalence

Table 1 shows our main numerical RD results, generated by parametric regression quadratic models. In comparison to individuals slightly younger than the MATS, those just older than the MATS had significant and abrupt increases immediately following the MATS in the prevalence of current-smokers (estimated absolute increase in prevalence: 2.71%; 95% CI 0.70% to 4.80%; P=0.009; estimated relative increase in prevalence: 17.00%; 95% CI 3.10% to 30.90%) (see figure 1); and daily smokers (estimated absolute increase in prevalence: 2.43%; 95% CI 0.74% to 4.12%; P=0.005; estimated relative increase in prevalence: 24.59%; 95% CI 5.47% to 43.70%) (see figure 2). There was no evidence of significant increases in the prevalence of occasional smokers across the MATS (estimated absolute increase in prevalence: 0.56%; 95% CI −0.56% to 1.68%; P=0.32); estimated relative increase in prevalence: 9.58%; 95% CI −10.63% to 29.80%).

Patterns of smoking frequency and intensity

Among occasional smokers, there was no evidence of changes across the MATS in the average number of days smoking in the past 30 days (estimated absolute change: increase of 0.113 smoking days in the past month; 95% CI −1.44 to 1.67; P=0.89; estimated relative change: 1% increase in the average number of days smoking in the past 30 days; 95% CI −19% to 21%) or usual number of cigarettes smoked on smoking days (estimated absolute change in average number of cigarettes smoked on smoking days in the past month: −0.09; 95% CI −0.62 to 0.45; P=0.75; estimated relative change: −3.0%; 95% CI −23% to 17%). Among daily smokers, there was no evidence of change across the MATS in average number of cigarettes smoked per day in the past month (estimated absolute change in average number of cigarettes smoked per day in the past month: −0.196; 95% CI −1.19 to 0.80; P=0.70; estimated relative change: −2%; 95% CI −10% to 7%).

Patterns of average monthly cigarette consumption

In comparison to age groups slightly younger than the MATS, those just older had sharply higher average past-month cigarette consumption: absolute average increase of 8.45 cigarettes (95% CI 1.22 to 15.67; P=0.02) smoked per month per person

Table 1 Regression-discontinuity (RD) results estimating smoking outcomes occurring immediately after the minimum age of tobacco sales in Canada, 2000–2014

	Absolute effect†				Relative jump‡		
Smoking outcomes	Effect (%)	Lower CI (%)	Upper CI (%)	P value	Jump (%)	Lower CI (%)	Upper CI (%)
Current-smokers: prevalence	2.70**	0.70	4.80	0.009	17.00	3.10	30.90
Daily smokers: prevalence	2.43**	0.74	4.12	0.005	24.59	5.47	43.70
Daily smokers: number of cigarettes smoked per day	−0.196	−1.187	0.796	0.70	−2	−10	7
Occasional smokers: prevalence	0.56	−0.56	1.68	0.32	9.58	−10.63	29.80
Occasional smokers: number of cigarettes smoked on smoking day	−0.087	−0.623	0.448	0.75	−3	−23	17
Occasional smokers: number of smoking days, past month	0.113	−1.439	1.665	0.89	1	−19	21
Average number of cigarettes smoked past month, per person (smokers and non-smokers)	8.45*	1.22	15.67	0.02	18	3	39

*P value<0.05.
**P value<0.01.
†The estimated absolute effect in the smoking outcome appearing immediately after the MATS. Positive values reflect increases.
‡The relative effect ('jump') in the smoking outcome appearing immediately after the MATS, calculated by dividing the RD model absolute effect by the RD model intercept (the estimated point where the pre-MATS regression line meets the MATS). Positive values reflect increases.
MATS, minimum age for tobacco sales; RD, regression-discontinuity.

immediately after the MATS; relative increase of 18% (95% CI 3% to 39%) in past-month cigarette consumption per person (see figure 3).

DISCUSSION

Study results demonstrated that Canadian MATS laws were associated with a significant impact on smoking behaviour among young people. In comparison to persons slightly younger than the MATS, age groups just older had sharply higher prevalence of current smoking and daily smoking, as well as higher rates of past-month cigarette consumption. However, there was no evidence that occasional or daily smokers had significant increases in smoking intensity immediately after release from MATS restrictions. Given these findings, it seems reasonable to argue that raising Canada's MATS laws would likely attenuate young people's initiation to current-smoker or daily-smoker status and total cigarette volume consumption in newly restricted age groups.

Release from MATS restrictions was also found to be associated with significant and immediate increases in the prevalence of current-smokers and daily smokers, but with no evidence of changes in smoking intensity (ie, number of cigarettes smoked per smoking day) for both daily and occasional smokers. This pattern suggests that MATS laws might have effects on youth smoking prevalence, but not on smoking intensity. Of the six prior studies assessing the impacts of MATS laws on youth smoking behaviour,[26–31] three reported that tobacco minimum-age laws had an impact on smoking prevalence.[26 27 29] Only two of the six studies assessed how such restrictions might influence smoking intensity,[29 30] and one of these found that release from MATS laws was associated with significant and immediate increases in smoking intensity among young mothers.[29] Given the paucity of research in this area, the rationale for our disparate findings is unclear. Nonetheless, at the population level, release from MATS restrictions and the corresponding increases in commercial availability of tobacco products may facilitate the conversion of youth non-smokers/experimenters to daily or occasional smokers. Whereas for daily or occasional smokers, the new legal availability of tobacco products may not affect the usual number of cigarettes smoked on smoking days as these smokers already may have an established smoking intensity pattern and tobacco supply network. Future research in this area should aim to collect information related to both smoking prevalence and intensity in order to inform the possibility of specific impacts of MATS laws on various aspects of youth smoking behaviour.

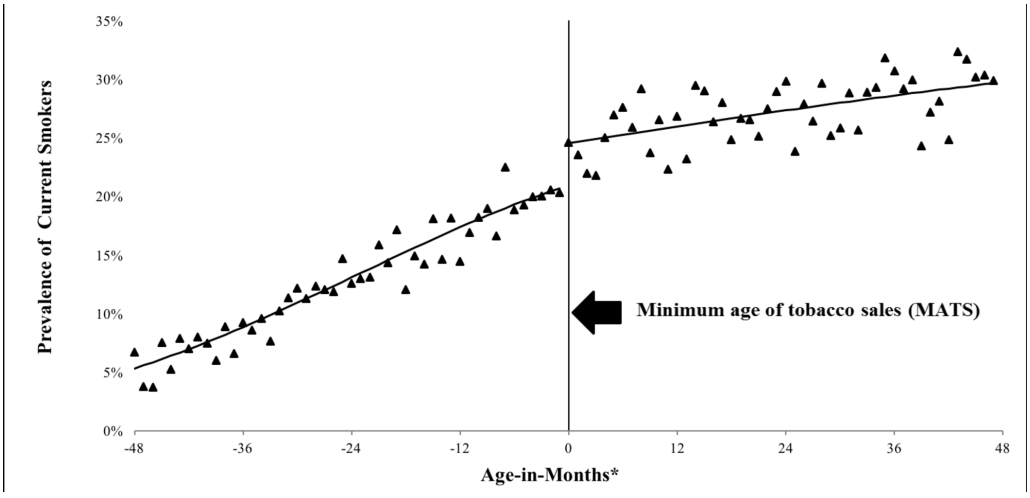

Figure 1 Prevalence of current smokers by respondents' age in months across minimum age of tobacco sales, Canada (2000-2014). *0 represents the legislated minimum age for tobacco sales (MATS) at the provincial/territorial level. Each triangle represents one age-in-months' group.

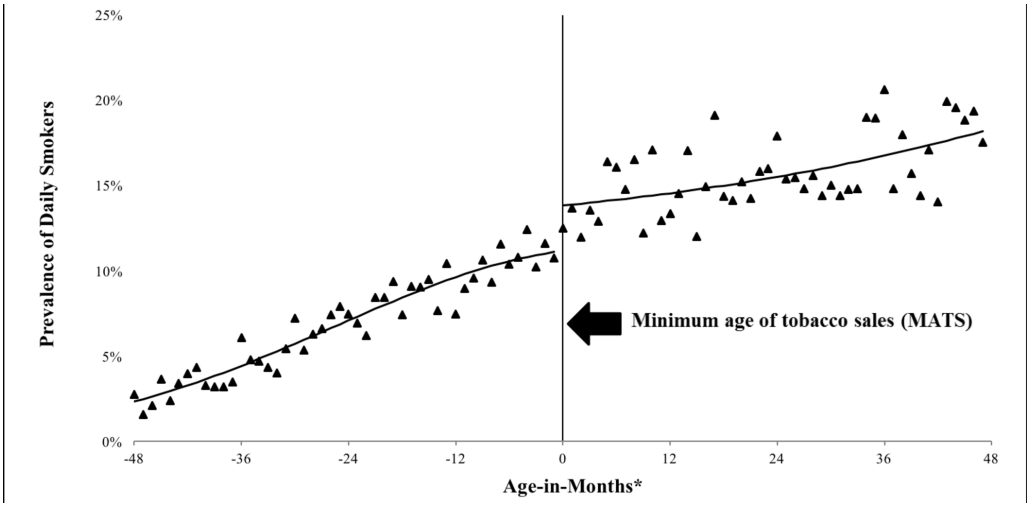

Figure 2 Prevalence of daily smokers by respondents' age in months across minimum age of tobacco sales, Canada (2000–2014). *0 represents the legislated minimum age for tobacco sales (MATS) at the provincial/territorial level. Each triangle represents one age-in-months' group.

Proposals to raise MATS laws will likely galvanise political, scientific and popular debate—and legal challenge from the tobacco industry. Systematic reviews on the topic have focused primarily on retailer compliance and underaged tobacco purchasing behaviour vis-à-vis MATS laws, and these studies have reached different conclusions about the effectiveness of youth access laws to reduce youth smoking.[57 58] The inconsistent findings in the literature, however, appear to vary systematically as a function of the differing qualities of minimum-age enforcement strategies and retailer compliance specific to each study jurisdiction, with strong and active minimum-age enforcement and consequent interruption of commercial tobacco sales to youth being significantly associated with reduced youth smoking.[57] Canada has achieved high levels of retailer compliance regarding MATS legislation,[59] and the current results demonstrate that MATS laws in such a national youth tobacco control context appear to dampen smoking behaviour in tobacco-restricted age groups compared with their counterparts newly released from MATS law restrictions. As a result, the findings from the current study indicate that minimum-age restrictions in the Canadian setting can play an important role in influencing youth smoking behaviour at the population level.

The current study has a number of limitations. Our RD approach assumes that potentially confounding variables are smoothly distributed across the MATS cut-off and that any 'jump' in smoking behaviour appearing immediately after the MATS can be inferred to be a direct result of release from MATS restrictions. A number of potential threats to this assumption may bias the estimation of the 'jumps' in smoking behaviour seen immediately after the MATS. First, MATS laws occur at an age in late adolescence when many youth experience life transitions, such as leaving home, graduating from high school, changing social networks or attending college or university. These life transition experiences may affect smoking behaviour. However, it is unlikely that these factors would unduly influence the RD estimates in our study because the RD design relies on smoking behaviour trends across individuals' age in months; that is, a finely grained age variable. In other words, young people close in age to the MATS would likely be experiencing the same life transitions, especially given that these major changes

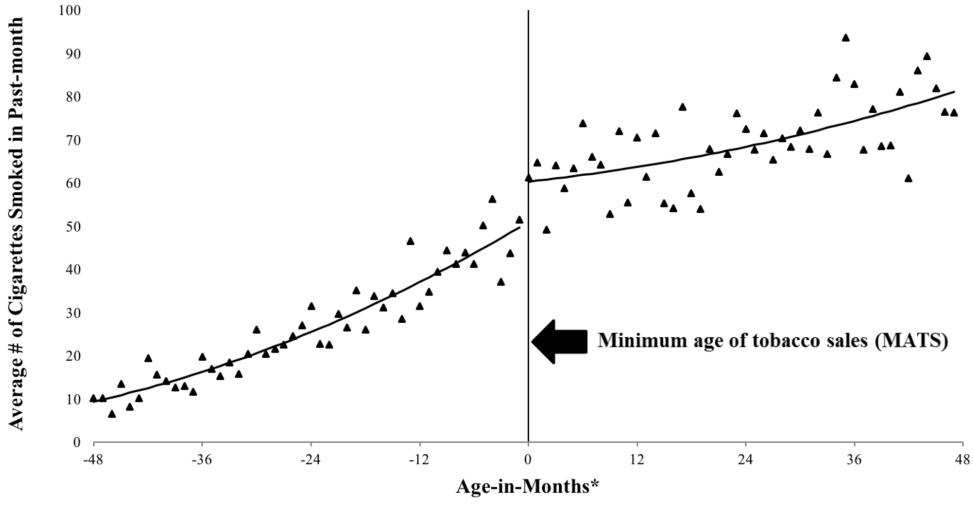

Figure 3 Average number of past-month cigarettes smoked per person across respondents' age-in-months, Canada (2000–2014). *0 represents the legislated minimum age for tobacco sales (MATS) at the provincial/territorial level. Each triangle represents one age-in-months' group. Each age-in-months' group includes smokers and non-smokers. Non-smokers were assigned a value of '0' for cigarettes smoked in the past month.

do not occur at exactly the age of 18 or 19 years, but rather their occurrence likely is smoothly distributed across ages near the MATS. Second, the age of majority in Canada corresponds to the minimum age of tobacco sales in all Canadian provinces/territories (except Ontario and Prince Edward Island) and, as a result, the age of majority and the concomitant potential effects of 'adult' smoking norms may have influenced the observed increases in smoking prevalence appearing immediately after the MATS in our study. Third, the current MATS is the same age as the current MLDA in every province and territory, except Saskatchewan (where the drinking age is 19 years and the MATS is 18 years). As a result, it is not possible to untangle the potential smoking-related effects of concomitant release from the MATS and MLDA laws. Prior research employing RD analyses on national health survey data from the USA, however, has found that while release from US drinking age restrictions at age 21 years was associated with significant and immediate increases in patterns of alcohol consumption,[60] there was no evidence of corresponding changes across the US MLDA-21-year threshold for a range of tobacco-use variables, such as prevalence of any smoking in the last 30 days, number of days smoking in the last 30 days, number of cigarettes smoked on smoking days in the past 30 days or average number of cigarettes smoked by the respondent per day in the last month.

In addition, our RD approach has a number of potential shortcomings as a tool for modelling the impacts of MATS laws on youth smoking behaviour. First, the effects of MATS laws may be complex, and possible MATS impacts may differ in age groups proximal and distal to the designated tobacco minimum age. The RD approach used in the current study focused only on estimating the impacts of MATS laws on smoking outcomes in groups near to the tobacco minimum age, and our approach cannot address possible MATS effects on individuals much younger than the MATS. Second, the RD design does not provide specific estimates of potential smoking behaviour reductions associated with raising the Canadian MATS to the proposed 21-year cut-off, nor do the study findings identify 21 years as the 'best' tobacco minimum age. Third, the study team used the RD strategy to assess expected discontinuous jumps in smoking behaviour appearing immediately after the MATS. While the scant literature in this area does not appear consistently to support the likelihood of lagged MATS effects on youth smoking behaviour, future research in this area may want to explore this possibility.

Despite these potential limitations, study results provide important population-based evidence that release from MATS laws is associated with significant and immediate increases in young people's smoking behaviour, including initiation into current-smoker or daily smoker status, as well as in age-group-level cigarette consumption. Given that MATS laws appear to limit smoking behaviour among age-restricted youth, it is reasonable to argue that raising Canada's MATS laws to 21 years would likely decrease smoking behaviour in newly restricted age groups.

What this paper adds

- Recently, the US Institute of Medicine has proposed that raising the minimum age for tobacco products to 21 years would likely be an effective policy option for reducing patterns of smoking behavior among young people.
- Surprisingly few studies, however, have assessed the potential impacts of minimum-age tobacco restrictions on youth smoking, and the findings are mixed.
- The field lacks evidence from large-scale quasi-experimental studies assessing the impacts of minimum-age tobacco laws on national youth smoking behaviour.
- Using a quasi-experimental regression-discontinuity approach, the current study found that on ageing out of Canadian minimum age for tobacco sales (MATS) restrictions, young people experienced sharp increases in national prevalence of current-smokers and daily smokers.
- Results demonstrated no evidence of post-MATS increases in smoking intensity among occasional or daily smokers.
- Given that MATS laws appear to limit smoking prevalence among age-restricted youth, the study provides relevant evidence that raising MATS laws to 21 years would likely be associated with decreases in smoking behaviour in newly restricted age groups.

Contributors RCC and MS had full access to all the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis. RCC oversaw all aspects of the study design and scientific requirements for its completion. In particular, RCC contributed to the conception and design of the work, as well as the acquisition, analysis and interpretation of the data. He prepared the initial manuscript and provided oversight for the final revision. MS contributed expertise in the design of the study and conducted the statistical analyses. He helped to prepare and revise the manuscript and provided critically important insight into the interpretation of the findings. JG made substantial contributions to the original design of the study, especially in the acquisition of the data and drafting the initial draft of the guiding research plan. JKC provided substantial contributions to the interpretation of the data and the revision of the final manuscript. MOC and RS made substantial contributions to the interpretation of the findings, and both made important contributions to the final version of the manuscript. SB made substantial contributions to the design of the project, as well as to the revision of the final manuscript. CB provided substantial contributions to the interpretation of the data and the preparation and revision of important content in the final version of the manuscript. All authors take responsibility for the contents of the paper.

Funding The Canadian Institutes of Health Research (CIHR) provided an operating grant to the lead author (RCC) to support the conduct of this research study. CIHR had no role in the following aspects of the study: design and conduct of the study; collection, management, analysis, and interpretation of the data; preparation, review, or approval of the manuscript; and decision to submit the manuscript for publication. The analyses presented in this paper were conducted at the Regional Data Centre (RDC) at the University of Toronto, with vetting of the analytic results occurring at the Regional Data Centre at the University of Victoria. Both of these RDCs are part of the Canadian Research Data Centre Network (CRDCN). The services and activities provided by the University of Toronto and the University of Victoria are made possible by the financial or in-kind support of the Social Sciences and Humanities Research Council of Canada (SSHRC), the CIHR, the Canadian Foundation for Innovation (CFI), Statistics Canada and the University of Toronto/University of Victoria. This work was supported by the Institute of Human Development, Child and Youth Health (grant number 383501).

Disclaimer The views expressed in this paper do not necessarily represent the CRDCN's or that of its partners'.

Competing interests None declared.

Provenance and peer review Not commissioned; externally peer reviewed.

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