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► To cite this version:

Massimiliano Orri, Nicholas Chadi, Marilyn N Ahun, Jean R Séguin, Richard E Tremblay, et al.. Suicidal ideation and attempt in adolescents exposed to maternal smoking across pregnancy and childhood: A 20-year prospective cohort study. *Journal of Affective Disorders*, 2021, 286, pp.10-18. <10.1016/j.jad.2021.02.047>. <hal-03169229v2>

HAL Id: hal-03169229

<https://hal.science/hal-03169229v2>

Submitted on 29 Nov 2021

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Title: Suicidal ideation and attempt in adolescents exposed to maternal smoking across pregnancy and childhood: a 20-year prospective cohort study

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Accepted version

Citation: Orri M, Chadi N, Ahun MN, Seguin JR, Tremblay RE, Boivin M, Turecki G, Geoffroy MC, Côté SM. Suicidal ideation and attempt in adolescents exposed to maternal smoking across pregnancy and childhood: A 20-year prospective cohort study. *J Affect Disord.* 2021 Feb 23;286:10-18. doi: 10.1016/j.jad.2021.02.047.

Introduction

Youth suicidal thoughts and behavior are an important public health concern (Hawton & O'Connor, 2012). Both population and clinical studies suggest that prior suicide attempt and serious suicidal ideation are predictive of later suicide death (Hawton & Harriss, 2007; Hawton & O'Connor, 2012), and increase the risk of negative educational, social, and mental health outcomes in adulthood (Borschmann et al., 2017; Goldman-Mellor et al., 2014). Prevention of suicidal ideation and attempt in youth is therefore crucial to minimize serious long-term consequences. Suicide results from the influence of multiple biological, social, and environmental factors over the lifespan that shape individual vulnerability to suicide (Turecki & Brent, 2016). Studies supporting a developmental model of suicide risk (Séguin et al., 2014; Turecki et al., 2012) show that such vulnerability may arise during pregnancy and early childhood via exposure to adversities that can impact children's neurodevelopment (Mittendorfer-Rutz & Wasserman, 2008; Orri, Gunnell, et al., 2019; Orri, Russell, et al., 2020).

Exposure to maternal smoking during pregnancy is widely recognized as a potential risk factor for adverse childhood neurodevelopmental outcomes (Wehby et al., 2011) and has been associated with risk of important childhood and adult mental health problems, including conduct disorder, attention deficit hyperactivity disorder, and bipolar disorder (Gaysina et al., 2013; Huijbregts et al., 2007; Sourander et al., 2019; Talati et al., 2013). However, causality for these associations has not been clearly demonstrated (Obel et al., 2016; Quinn et al., 2017). Importantly, evidence of the association between exposure to maternal smoking and suicide risk are scant. As smoking is arguably one of the most important modifiable risk behaviors in mothers, understanding whether exposure to maternal smoking increases offspring's suicide risk is necessary for early identification of individuals at risk.

To our knowledge, only four studies have investigated the association between exposure to maternal smoking and suicide outcomes (Alaräsänen et al., 2012; Cnattingius et al., 2011; Ekblad et al., 2010; Geoffroy et al., 2014). These studies investigated in-utero exposure to smoking and found inconsistent evidence for an association with suicide mortality (Alaräsänen et al., 2012; Cnattingius et al., 2011; Ekblad et al., 2010; Geoffroy et al., 2014) and suicide attempt (Alaräsänen et al., 2012). Furthermore, focus on in-utero exposure to

smoking did not allow for testing the possibility that the increased risk occurred via postnatal exposure to maternal smoking. Indeed, as the brain continues to develop during childhood and adolescence (Casey et al., 2008), postnatal exposure to smoking (i.e., secondhand smoking) may have negative effects on neurodevelopment (Goriounova & Mansvelder, 2012; Hamer et al., 2011; Padrón et al., 2016; Tiesler et al., 2011). Additionally, observing parents who smoke may reinforce smoking behaviors in the offspring through behavioral modeling effects (Vuolo & Staff, 2013), which in turn can increase the risk of negative mental health outcomes, including suicide attempt (Orri, Séguin, et al., 2020). Currently, we lack information on whether exposure to smoking during the postnatal period is associated with increased suicide risk in the offspring. This is relevant as previous studies suggest that patterns of maternal smoking around pregnancy and early childhood are highly heterogeneous, with some mothers consistently smoking across pregnancy and the postnatal period, others quitting during pregnancy and relapsing after childbirth, and some mothers quitting smoking only after pregnancy (De Genna et al., 2017; Mumford et al., 2014; Munafò et al., 2008). These patterns may be associated with different etiological mechanisms that are necessary to elucidate how vulnerability to suicide emerges.

The aim of this study was to investigate the association of patterns of exposure to prenatal and postnatal maternal smoking with suicidal ideation and suicide attempt in adolescence.

Methods

Participants

This study is based on the Québec Longitudinal Study of Child Development (QLSCD), a representative birth cohort from Québec, Canada (M Orri, Boivin, et al., 2020). The sample includes 2120 children born in 1997/98 and selected from the birth registry using a random procedure based on living areas and birth rates. Families were included if pregnancy lasted 24 to 42 weeks and if the mother could speak French or English. The present study is based on 1623 participants (77% of the initial sample; 778 [47.9%] males and 845 [52.1%] females; **Table 1**) for which data on the study outcomes were available. Inverse-probability weighting was used to reduce bias due to differential attrition associated with male sex, socioeconomic difficulties, and childhood

physical aggression (all more likely among nonincluded participants). The QLSCD study is conducted in collaboration with the Institut de la Statistique du Québec (ISQ), who collected the data. The ISQ Ethics Committee and the Research Ethics Board of the Sainte-Justine Research Center approved each phase of the study, and informed consent was obtained.

Maternal smoking patterns

When the participants were 5 months, 1½, 2½, 3½, 5, 7, 10, and 12 years of age, their mothers reported the number of cigarettes they smoked per day. At the first data collection, mothers retrospectively reported the daily number of cigarettes smoked before and during pregnancy.

Adolescent suicidal ideation and suicide attempt

At ages 13, 15, 17, and 20 years participants were asked: “in the past 12 months, did you ever seriously think of attempting suicide” and, if yes, “how many times did you attempt suicide” (Côté et al., 2017). At age 20 years, they were additionally asked if they “ever went to the emergency department for a suicide attempt”, and if they “have ever been hospitalized for a suicide attempt”. We defined two outcomes: serious suicidal ideation, coded yes if participants reported any serious suicidal ideation at any time point but never reported suicide attempt; suicide attempt, coded yes if participants reported suicide attempt at any time point.

Maternal and family background characteristics

A range of potential characteristics related to the mother’s probability of smoking (parent-reported at child age 5 months) were selected based on the literature (Crume, 2019). *Sociodemographic characteristics*: maternal and paternal age; socioeconomic status, an aggregate of 5 items (parental educational level, occupation, and income; (Willms & Shields, 1996); non-intact family (yes/no), indicating whether the family was mono-parental/blended vs with both biological parents; presence of older siblings (yes/no); parents’ Canadian origin (vs other, e.g., French, Caribbean). *Maternal mental health and substance use*: alcohol, recreational drug, and prescribed and nonprescribed medications use in pregnancy (all yes/no); depressive symptoms, assessed using the Centre for Epidemiological Study Depression Scale (CES-D) short form (Poulin et al., 2005); youth antisocial behavior, assessed with binary questions on 5 different conduct problems based on the DSM-IV criteria for conduct disorder and antisocial personality disorder (range 0-5, higher scores indicating more antisocial behaviors;

(Zoccolillo, 2000). *Paternal mental health and smoking*: current tobacco smoking (yes/no); depressive symptoms, assessed with the CES-D; youth antisocial behavior, assessed as previously reported for mothers. *Breastfeeding*: a binary variable assessing whether the mother had or was currently breastfeeding the child.

Analysis

First, we analyzed the repeated measures of maternal smoking using group-based trajectory modeling (GBTM), an approach based on mixture models that aims to identify homogeneous groups of individuals based on similarities in the longitudinal pattern they follow on a given behavior over time. Second, we selected background characteristics showing differential distribution across patterns of maternal smoking, as expressed by a standardized mean difference (SMD) ≤ 0.1 . These variables were then used in a multinomial regression model to estimate a propensity score (Austin, 2011), which represents the probability that each mother follows a given pattern of smoking behavior based on all of her background characteristics. The inverse of the propensity score was used to generate inverse-probability weights (IPW; (Austin, 2011)). Third, we estimated associations of maternal smoking patterns with suicidal ideation and attempt using logistic regression. We estimated (i) an unadjusted model and (ii) a model adjusted for child sex and using propensity score IPW. For the patterns for which we found evidence of an association, we calculated the proportion of the effect attributable to exposure to this pattern in the population (population attributable fraction) as $p \times (1 - OR/OR)$, in which OR is the adjusted odds ratio for a given pattern, and p is the proportion of children exposed to a given pattern. (Rockhill et al., 1998) Fourth, to further test whether maternal smoking heaviness at any specific time point was related to suicide outcomes, we estimated the association between the number of cigarettes/day smoked at each time point and suicide outcomes using logistic regression. Both unadjusted and propensity score-adjusted models were estimated. This analysis informs on whether there were any potentially sensitive periods of exposure to maternal smoking (e.g., pregnancy) driving the observed associations, as opposed to the patterns of use over time. Fifth, we conducted two sensitivity analyses. In the first one, we estimated our model additionally adjusting for variables whose distribution across maternal smoking patterns were unbalanced despite the IPW. In the second one, we calculated the E-value (VanderWeele & Ding, 2017), defined as the minimum strength of association – on the risk ratio (RR) scale – that an unmeasured confounder would need to have with both the exposure and the

outcome to fully explain away a specific exposure–outcome association. Therefore, this sensitivity analysis informs on whether it is plausible to consider that a potential unmeasured factor may explain any significant associations we may find.

Results

By age 20 years, 147 out of 1623 (9.1%) youth reported suicidal ideation and 134/1623 (8.3%) reported suicide attempt. Both suicidal ideation and attempt were more prevalent in girls (respectively 93/845, 11%, and 91/845, 10.8%) than boys (respectively 54/778, 6.9%, and 43/778, 5.5%). The corresponding girls/boys risk ratio was 1.59 (1.15-2.19) for suicidal ideation and 1.95 (1.37-2.76) for suicide attempt. These prevalence rates and sex ratios were in line with those reported in previous population-based studies for the same age group (Nock et al., 2013; Orri, Scardena, et al., 2020; Orri, Russell, et al., 2020).

Four patterns of maternal smoking were identified (**Figure 1**): *no smoking* (n=1079; 66.5%), included mothers who did not smoke at all time points; *decreasing smoking* (n=151; 9.3%), included mothers who smoked before pregnancy, progressively decreased during pregnancy, and quit in the postnatal period; those mothers smoked on average ~11 cigarettes/day before pregnancy and 4 cigarettes/day while pregnant; *increasing smoking* (n=93; 5.5%), included mothers who reported low smoking before pregnancy (average ~4 cigarettes/day) and pregnancy (average ~1 cigarette/day) but progressively reported smoking increasing numbers of cigarettes during the postnatal period; *persistent smoking* (n=300; 18.5%), included mothers who persistently smoked before and during pregnancy (on average ~17 and ~11 cigarettes/day, respectively), as well as during the postnatal period. Of note, all mothers who smoked before pregnancy decreased the number of cigarettes smoked per day while pregnant, although to different extents.

We found differences between mothers showing these different patterns of smoking in terms of background characteristics (**Table 1**). For example, compared to non-smoking mothers, mothers who smoked (all patterns) were younger, had lower socioeconomic status, and were more likely to have nonintact families, higher depressive symptoms, antisocial behaviors, and to use recreational drugs during pregnancy. They were also more likely to have partners who smoked and reported high depressive symptoms. Differences were larger

for mothers showing a persistent smoking pattern than for those showing increasing and decreasing patterns, compared to the no smoking group. Propensity score IPW successfully balanced most of these background differences (**Figure 2**).

In unadjusted models, we found that children of mothers showing increasing (OR, 2.06; CI, 1.13-3.74) and persistent (OR, 2.92; CI, 1.99-4.30) smoking patterns were more likely to report suicide attempt in adolescence (**Table 2**). However, in propensity score IPW models, there was no association between the increasing smoking pattern and suicide attempt (OR, 0.95; CI, 0.39-1.09), suggesting that background differences between mothers with increasing smoking and no smoking patterns fully accounted for this association. Accounting for background characteristics also explained a portion (9%) of the association between persistent smoking and suicide attempt, but evidence for an association was still observed over and beyond these characteristics (OR, 2.30; CI, 1.04-4.99). The corresponding population attributable fraction for this association was 37%. No association was found between any maternal smoking patterns and suicidal ideation (**Table 2**).

Logistic regression analyses testing whether exposure to smoking during any specific period was driving the observed association are shown in **Figure 3**. In unadjusted models, we found significant associations between maternal smoking heaviness and suicide attempt at all time points except at children's ages 10 and 12. However, none of the associations were significant after propensity score adjustment for previously selected background variables. For example, the odds of reporting suicide attempt increased by 26% for each standard deviation (SD) increase in the number of cigarettes/day smoked during pregnancy (1 SD was 5.6 cigarettes/day; OR, 1.26; CI, 1.09-1.45), but this was fully explained by background confounding factors (OR, 0.97; CI, 0.76-1.24 after propensity score adjustment). This analysis suggests that the observed association between mothers' persistent smoking pattern and suicide attempt was not attributable to heavy exposure during a sensitive period (e.g., pregnancy), but rather to the cumulative exposure over time.

Sensitivity analyses were conducted to test the robustness of our main findings. After IPW, the following variables remained slightly unbalanced across groups (i.e., in at least one of the 4 comparisons, **Figure 2**), according to the $SMD \leq 0.1$ threshold: socioeconomic status, paternal smoking, maternal alcohol use,

presence of siblings, and non-intact family. When the propensity score IPW model was additionally adjusted for these variables in sensitivity analyses, we still found evidence for an association between exposure to a persistent maternal smoking pattern and suicide attempt (OR, 2.65; CI, 1.25-6.04). Moreover, sensitivity analyses with the E-value suggested that if an unmeasured confounding factor was associated with both maternal persistent smoking and adolescent suicide attempt at $RR=4.03$ then there would no longer be a statistically significant association between persistent smoking pattern and suicide attempt. However, confounding factors with weaker associations than $RR=4.03$ would not explain the association.

Discussion

Using data from a large population-based birth cohort, we identified a group of children exposed to a pattern of persistent maternal smoking from before pregnancy to the entire childhood period. These children were more than twice as likely as non-exposed children to attempt suicide in adolescence. Maternal smoking behavior is a marker for a wide range of adversities and genetic predispositions. However, the risk of suicide attempt for children of mothers with persistent smoking remained higher than those of non-exposed children after accounting for a range of background maternal and family characteristics which reflect both environmental adversities and (in part) genetic vulnerabilities. It is worth noting that it is the pattern of use that may be key, as we did not find any evidence indicating that exposure to smoking in any particular period (including pregnancy) was driving the observed association. We also found that children exposed to maternal smoking only during the postnatal period (i.e., increasing pattern) were more likely than never exposed children to attempt suicide in adolescence, but this was entirely attributable to background family, maternal, and paternal characteristics. The likelihood of reporting suicidal ideation only (i.e., no attempt) was similar across patterns of maternal smoking.

Previous studies on the association between maternal smoking and offspring suicide risk were limited to exposure during pregnancy (Alaräisänen et al., 2012; Cnattingius et al., 2011; Ekblad et al., 2010; Geoffroy et al., 2014). As such, they could not account for the fact that many mothers quit or significantly reduce smoking during pregnancy but relapse within the first months after childbirth (Colman & Joyce, 2003; Tong et al., 2009). These studies, including one using a robust sibling-comparison design (Cnattingius et al., 2011), suggest that

confounding factors account for the association between intrauterine smoking exposure and suicide attempt, consistent with what we observed in this sample (**Figure 3**). In our study, by taking into account maternal smoking in the postnatal period, we were able to distinguish between mothers who diminish their tobacco consumption during pregnancy and quit afterward (i.e., decreasing pattern) from those who consistently smoked a high number (>10) of cigarettes/day from pregnancy to child age 12 years (i.e., persistent pattern). While no increased suicide attempt risk was found for offspring of mothers who decreased smoking across pregnancy and postnatally, the offspring of persistent smoking mothers were at higher risk of attempting suicide in adolescence. It is worth noting that although mothers showing a persistent pattern of smoking reported significantly heavier smoking during pregnancy than those showing a decreasing pattern, heaviness of smoking during pregnancy was not associated with suicide attempt. This suggests that the increased risk of suicide attempt cannot be uniquely linked to the heavy exposure to intrauterine smoking of children of persistent smoking mothers; rather, it may be linked to persistent heavy exposure to smoking during a longer period of time (across pregnancy and childhood). Future studies in larger samples able to identify groups exposed to a persistent but moderate quantity of smoking may shed light on the role of smoking heaviness and allow for the testing of dose-response associations.

Multiple mechanisms may account for the association between persistent maternal smoking exposure and offspring suicide attempt. First, at the biological level, exposure to maternal smoking has negative effects on development. These may result from exposure during fetal development (Faber et al., 2017; Knopik, 2009; Quelhas et al., 2018) as well as during childhood. Indeed, children's brains continue developing well into adolescence (Casey et al., 2008; Gogtay et al., 2004), and exposure to secondhand smoking has been previously linked to mental health problems in childhood and adolescence (Bandiera et al., 2011; Hamer et al., 2011; Padrón et al., 2014, 2016; Tiesler et al., 2011). Although exposure during either pregnancy alone or childhood alone is unlikely to explain our results, vulnerability to suicide attempt may increase in cases of cumulative exposure to maternal smoking from in-utero to the entire childhood period. Second, psychosocial mechanisms may also be at play. Specifically, children observing parents smoking may also be prone to engage in smoking behaviors because of modeling effects (Vuolo & Staff, 2013). Offspring smoking, in turn, may be associated

with higher risk of suicide attempt, as well as with the use of alcohol and cannabis – both potential risk factors for suicide attempt (Orri, Séguin, et al., 2020). Future studies testing such hypotheses may be useful to identify targets for interventions. Third, this association may be due to confounding factors. Specifically, genetic confounding influences could not be controlled for in this study. Therefore, future genetically informed designs are necessary to test this hypothesis (Pingault et al., 2018). Finally, previous studies point to the key role of impulsive-aggression (and related behaviors, such as irritability and hyperactivity) in both the etiology of suicide attempt (Galera et al., 2020; Orri, Galera, et al., 2018; Orri, Perret, et al., 2018; Orri, Galera, et al., 2019) and the intergenerational transmission of suicide risk (McGirr et al., 2009; McGirr & Turecki, 2007; Orri, Geoffroy, et al., 2019), especially among youth (McGirr et al., 2008). Impulsive-aggression is highly heritable (Orri, Geoffroy, et al., 2019) and genetically associated with smoking (Liu et al., 2019), thus it is likely to be an important mechanism explaining our results.

An important feature of this study is the use of a robust design (propensity score IPW) to account for background characteristics that make mothers likely to exhibit a given pattern of smoking, including socioeconomic adversity, partner’s smoking, as well as emotional, behavioral, and substance use problems. These characteristics have been linked to offspring suicide attempt in the literature (Batty et al., 2018), and may thus act as potential confounding factors. When randomized trials are unfeasible, quasi-experimental designs such as propensity score IPW can strengthen causal inference while maximizing ecological validity (Austin, 2011). Accounting for these factors fully explained the observed increased risk of suicide attempt of children exposed to a pattern of increasing maternal smoking in late childhood, suggesting that this association was more likely due to factors such as adverse socioeconomic circumstances, family characteristics, and parental psychopathology, rather than exposure to smoking. This is in line with previous studies showing no association between maternal postnatal smoking and children’s behavioral outcomes (Fergusson et al., 1993). In contrast, we found that such background characteristics did not fully explain the higher suicide attempt risk of children exposed to a pattern of persistent maternal smoking. This is important, as our adjustment accounts for important confounding factors which are known to play a role in the association between maternal smoking and child adjustment over and beyond genetic factors (D’Onofrio et al., 2003).

Finally, an interesting finding from this study is that persistent maternal smoking was associated with suicide attempt, but not with suicidal ideation. Although suicidal phenomena are part of a continuum from passive suicidal ideation to suicide death (Orri, Scardena, et al., 2020; Posner et al., 2007), previous studies have shown that specific factors may distinguish people who have suicidal thoughts from those who act on such thoughts (Mars et al., 2018; O'Connor & Kirtley, 2018) Our findings inform this line of research.

We acknowledge the following limitations. First, the causal role of the reported associations cannot be inferred from our findings due to our observational design. Propensity score is a quasi-experimental approach increasing our ability to control for measured confounding effects, but it cannot account for unmeasured ones. However, our sensitivity analysis based on the E-value suggests that only potential unmeasured confounding factors strongly associated with both maternal smoking and offspring suicide attempt (RR of approximately 4) can account for the reported association over and beyond those factors already considered in the propensity score. Although it seems unlikely that such a strong potential *environmental* confounding factor was unmeasured in our study, we cannot exclude the presence of strong unmeasured *genetic* confounding factors. However, (i) no genetic score available to date shows such a large association with suicide attempt (Lim et al., 2020), and (ii) environmental measures (e.g., parental depression or education), are also genetically influenced, therefore partially accounting for genetic risk (Kendler & Baker, 2007). Second, because of non-random attrition, caution should be used in generalizing our results to the original Québec population. However, we limited this bias by using sample weights for attrition. Third, smoking was self-reported by mothers, thus the measure may be influenced by desirability bias yielding conservative estimates. Smoking before and during pregnancy was retrospectively reported at child age 5 months, which may add measurement errors due to memory bias. Fourth, we used information of maternal smoking during pregnancy considering pregnancy as a whole. However, given that an important number of mothers quit smoking at the early stage of pregnancy, a finer grained analysis of smoking during each trimester would have been a useful additional information.

Conclusions

This study identified a group of mothers who persistently smoked from pregnancy to child age 12 years and showed that their offspring were at higher risk of attempting suicide in adolescence, compared to offspring of

nonsmoking mothers. Importantly, this risk remained after accounting for maternal, paternal, and family characteristics that putatively influence maternal likelihood to smoke. Identifying mothers with persistent smoking behaviors may inform research on suicide risk in the offspring, thus opening a window for early identification of vulnerable children and adolescents. Future studies are needed to identify the mechanisms (biological and environmental) underlying this association and to test the extent to which confounding genetic factors may explain this association.

Declaration of Competing Interest

The authors declare no conflict of interest.

Acknowledgements

We are extremely grateful to all families who participated in the QLSCD, as well as all the professionals involved in the cohort project. Dr Orri holds a NARSAD Young Investigator Award. Dr Turecki holds a Canada Research Chair (Tier 1), a NARSAD Distinguished Investigator Award, and is supported by grants from the Canadian Institute of Health Research (CIHR) (FDN148374 and EGM141899). Drs Geoffroy and Turecki are supported by the Fonds de recherche du Qu'ébec—Sant'é (FRQS) through the Quebec Network on Suicide, Mood Disorders and Related Disorders. Dr Geoffroy receives funding from the American Foundation for Suicide Prevention and holds a Canada Research Chair (Tier 2). Dr Boivin holds a Canada Research Chair (Tier 1). Dr S'eguín is supported by grants from the CIHR (PJT-148551) and a CIHR Canadian Center on Substance Use and Addiction Catalyst Grant and by the Fond Monique Gaumond pour la recherche sur les maladies affectives. Dr Tremblay is funded by the Social Sciences and Humanities Research Council of Canada (SSHRC). Ms. Ahun is funded by a Vanier Canada Graduate Scholarship from SSHRC. This project has received funding from the European Union's Horizon 2020 research and innovation programme under the Marie Skłodowska-Curie grant agreement No 793396.

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Table 1. Background characteristics for the whole sample and by maternal smoking patterns

	Whole sample N=1623	By maternal smoking pattern				<i>P</i> -value
		No (n=1079; 66.5%)	Decreasing (n=151; 9.3%)	Increasing (n=93; 5.5%)	Persistent (n=300; 18.5%)	
Maternal age	29.39 (5.16)	30.24 (4.82)	27.27 (5.20)	28.29 (5.08)	27.77 (5.61)	<0.001
Paternal age	32.26 (5.49)	32.70 (5.23)	31.10 (5.49)	31.31 (5.85)	31.34 (6.29)	<0.001
Canadian parents, n (%)	1020 (63.3)	645 (61.2)	77 (65.3)	101 (62.7)	206 (71.0)	0.021
Intact family, n (%)	1317 (81.4)	930 (88.2)	78 (66.1)	123 (76.4)	187 (64.5)	<0.001
Socioeconomic Status	0.06 (1.00)	0.32 (0.97)	-0.42 (0.87)	-0.10 (0.88)	-0.64 (0.82)	<0.001
Maternal depression	1.37 (1.32)	1.23 (1.26)	1.70 (1.56)	1.37 (1.22)	1.73 (1.41)	<0.001
Paternal depression	0.99 (0.94)	0.96 (0.91)	1.17 (0.96)	1.07 (1.00)	1.17 (1.06)	0.002
Maternal antisocial behavior	0.82 (0.93)	0.64 (0.81)	1.00 (1.12)	1.14 (0.94)	1.23 (1.06)	<0.001
Paternal antisocial behavior	0.66 (0.93)	0.56 (0.85)	0.77 (0.93)	0.95 (1.08)	0.96 (1.04)	<0.001
Alcohol use, n (%)	622 (38.5)	401 (38.0)	46 (39.0)	68 (42.2)	108 (37.2)	0.744
Recreational drugs, n (%)	22 (1.4)	<5 (<0.5)	<5 (4.2)	<5 (3.1)	17 (5.9)	<0.001
Prescribed medication, n (%)	671 (41.6)	440 (41.7)	52 (44.1)	61 (37.9)	123 (42.4)	0.730
Nonprescribed medication, n (%)	625 (38.8)	433 (41.1)	38 (32.2)	54 (33.5)	102 (35.2)	0.047
Siblings, n (%)	947 (58.4)	601 (57.0)	71 (60.2)	77 (47.8)	198 (68.3)	<0.001
Breastfeeding, n (%)	1190 (73.3)	829 (78.7)	85 (72.0)	118 (73.3)	158 (54.5)	<0.001
Paternal smoking, n (%)	475 (31.5)	207 (19.6)	59 (50.0)	84 (52.2)	192 (66.2)	<0.001
Siblings, n (%)	947 (58.4)	601 (57.0)	71 (60.2)	77 (47.8)	198 (68.3)	<0.001
Breastfeeding, n (%)	1190 (73.3)	829 (78.7)	85 (72.0)	118 (73.3)	158 (54.5)	<0.001
Paternal smoking, n (%)	475 (31.5)	207 (19.6)	59 (50.0)	84 (52.2)	192 (66.2)	<0.001

Variables are described with a mean and standard deviation if not otherwise specified. All variables were assessed when the child was 5 months of age (first data collection point). Alcohol, recreational drugs, prescribed medications, and nonprescribed medications refer to maternal consumption during pregnancy. *P*-values are based on t-tests or chi-square (Fisher's exact test if $n < 5$)

Data were compiled from the final master file of the Québec Longitudinal Study of Child Development (1998–2018), ©Gouvernement du Québec, Institut de la statistique du Québec

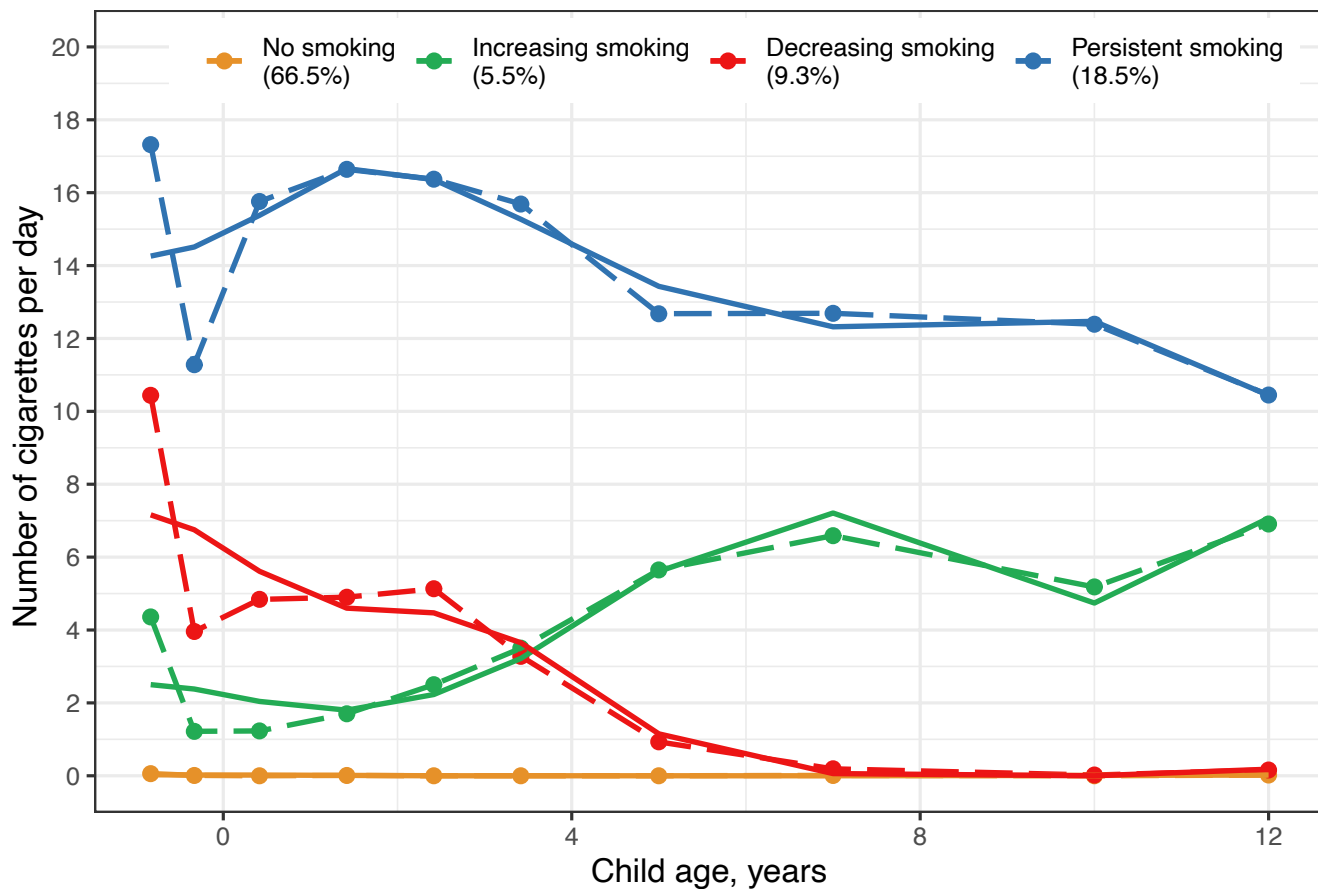
Table 2. Association of maternal smoking patterns with adolescent suicidal ideation and suicide attempt

	n (%)		OR (95% CI)	
	Yes	No	Unadjusted	Fully adjusted (IPW)
Suicide attempt				
Non-smoking	69 (6.4)	987 (93.6)	1 [reference]	1 [reference]
Decreasing smoking	14 (8.7)	147 (91.3)	1.40 (0.80-2.46)	0.74 (0.30-1.60)
Increasing smoking	13 (11.0)	105 (89.0)	2.06 (1.13-3.74)	0.95 (0.39-2.09)
Persistent smoking	40 (13.8)	260 (86.2)	2.92 (1.99-4.30)	2.30 (1.04-4.99)
Suicidal ideation				
Non-smoking	99 (9.4)	955 (90.6)	1 [reference]	1 [reference]
Decreasing smoking	9 (5.6)	152 (94.4)	0.64 (0.35-1.17)	0.46 (0.18-1.05)
Increasing smoking	14 (11.9)	104 (88.1)	1.03 (0.56-1.90)	0.78 (0.37-1.57)
Persistent smoking	25 (8.6)	265 (91.4)	0.83 (0.53-1.31)	0.72 (0.36-1.60)

Odds Ratio (OR) estimated using binary logistic regression. Confidence intervals were calculated using bias-corrected bootstrap (10000 resampling). To take into account the uncertainty due to the probabilistic nature of the GBTM used to identify patterns of maternal smoking, these patterns were indexed in the logistic regression model by using the posterior probability of group membership.(Bolck et al., 2004)

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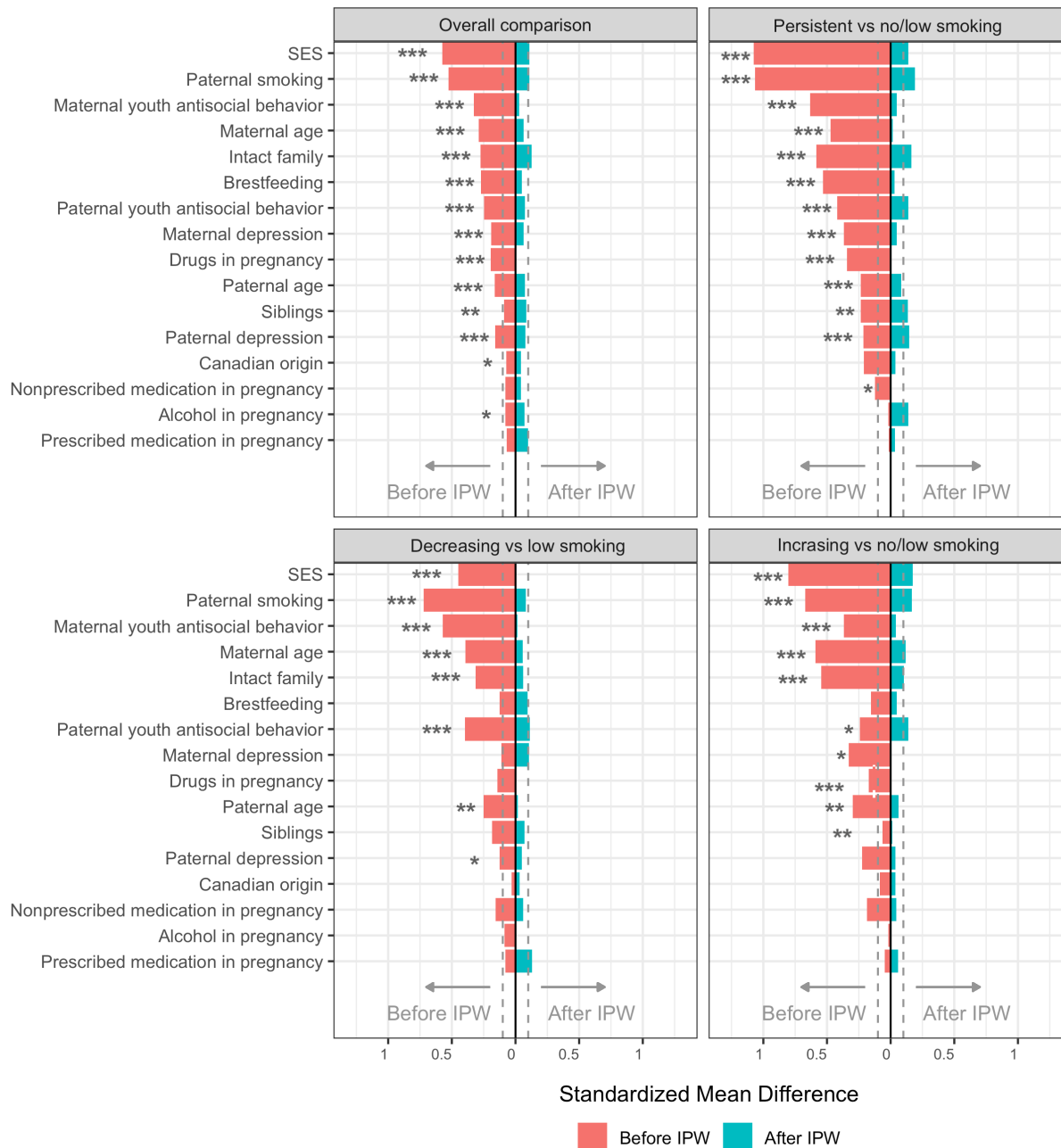
Figure 1. Maternal smoking patterns



Patterns of maternal smoking (cigarettes per day) estimated using group-based trajectory modeling. Dotted lines represent observed values, solid lines represent estimated values. The first dot of each trajectory refers to smoking before pregnancy, while the second dot of each trajectory refers to smoking during pregnancy. Model estimation was based on a Zero-Inflated Poisson model to accommodate the distribution of our variables, and parameters were estimated using Maximum Likelihood (which handles missing data in smoking variables). As recommended, (Nagin, 2005) models with different numbers of groups were subsequently fitted and compared using both fit statistics (e.g., Bayesian Information Criterion), quality of the classification (e.g., within-group posterior probability of class membership), and interpretability of the model to choose the optimal number of groups.

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Figure 2. Covariate-balance before and after propensity score inverse-probability weighting

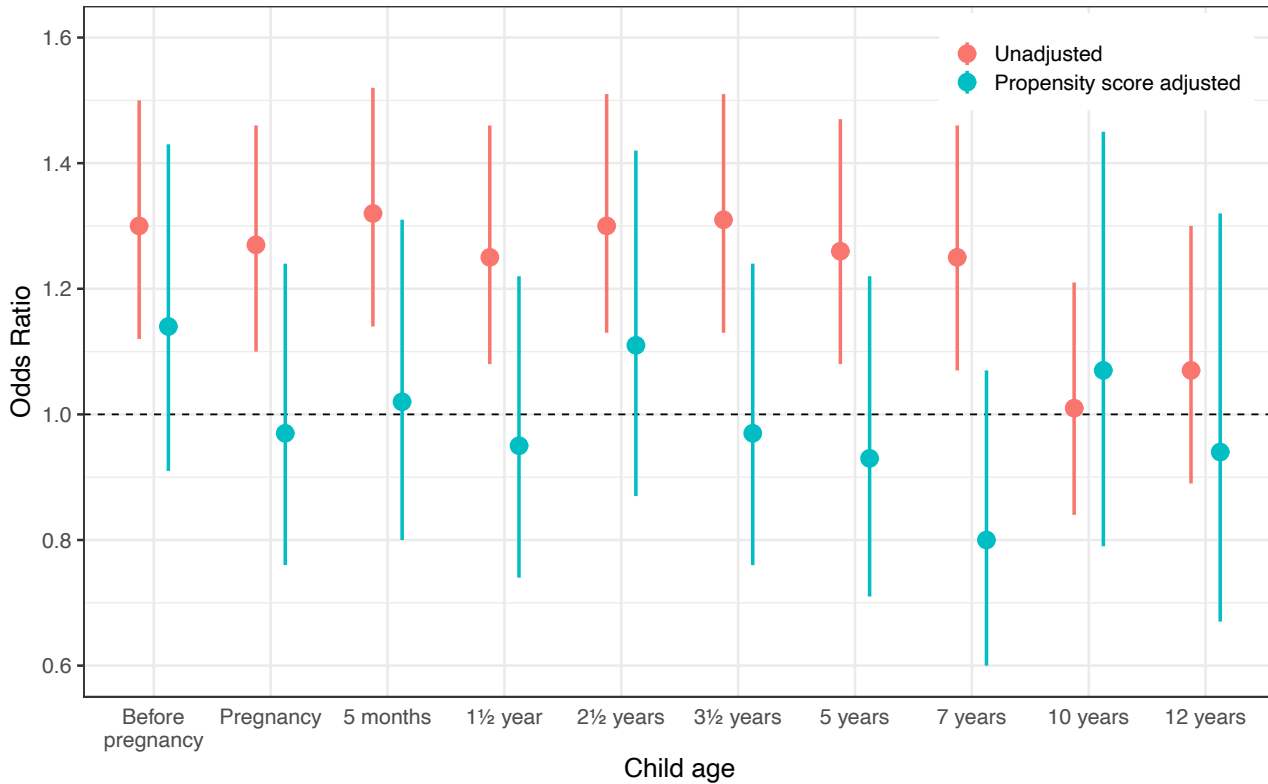


The figure shows, for each background variable (y-axis), the standardized mean differences units (SMD; x-axis) across the patterns of maternal smoking before applying propensity score weighting (red bars) and after applying propensity score weighting (blue bars). Propensity score was estimated using multinomial logistic regression, and the resulting weights were normalized and truncated at the 99th percentile (Austin, 2011).

*** $P < 0.001$; ** $P < 0.01$; * $P < 0.05$

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Figure 3. Associations between maternal smoking heaviness (cigarettes per day) at each time point and adolescent suicide attempt



The figure reports the increase in odds of suicide attempt for each SD-increase in maternal smoking heaviness at each time point, in unadjusted and propensity score-adjusted logistic regression models. N for the analyses is 1623, as multiple imputation was used to enhance comparability of the analyses across time points. Generalized propensity score was estimated using linear regression.

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