



# Exposure to maternal depressive symptoms in childhood and suicide-related thoughts and attempts in Canadian youth: test of effect-modifying factors

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## Abstract

**Purpose** To (1) determine the association between exposure to maternal depressive symptoms in childhood and offspring suicide-related thoughts (SRT) and attempts (SA) in youth and young adults and (2) identify effect measure modifiers (offspring sex, family structure, maternal perceived social support, and social cohesion) of the association in 1.

**Method** A cohort was constructed by linking all cycles from the National Longitudinal Survey of Children and Youth, a Canadian nationally representative survey, from 1994 to 2009 in 16,903 subjects 0 to 25 years. Exposure to maternal-reported depressive symptoms was measured when offspring were between 0 and 10 years. Offspring self-reported incident and recurrent SRT and SA were measured between 11 and 25 years. Time-to-event models under a counting process framework were used to estimate adjusted hazard ratios (HR) and relative rates (RR) and 95% confidence intervals (CI). Effect measure modifiers were examined across adjusted stratum-specific estimates.

**Results** In offspring exposed to maternal depressive symptoms, the adjusted rates of incident SRT and SA (HR: 1.67, 95% CI 1.37, 2.08; HR: 1.93, 95% CI 1.43, 2.50) and of recurrent SRT and SA (RR: 1.61, 95% CI 1.33, 1.96; RR: 1.87, 95% CI 1.40, 2.36) were significantly elevated compared to non-exposed offspring. The stratum-specific rates of incident and recurrent SRT and SA were significantly elevated in females but not in males.

**Conclusions** Girls exposed to maternal depressive symptoms in childhood are a target group for childhood suicide preventive strategies. Family-based preventions, and strategies to identify and effectively treat maternal depressive episodes could be beneficial for suicide prevention in offspring.

**Keywords** Suicide · Suicide attempts · Adolescence · Maternal depression · Social support

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## Introduction

Suicide is the second leading cause of death among 15 to 34 years olds, globally [1]. Suicide-related thoughts (SRT) and behaviours are among the strongest predictors of suicide [2]. Suicide accounts for a high proportion of deaths compared to other causes [1], with lifetime prevalence estimates between 12 and 20 years of SRT and suicide attempts (SA) of approximately 10 and 30%, respectively [3]. Despite the high burden of suicide among youth, we lack strong evidence about the nature, timing, and impact of specific exposures on the onset and persistence of SRT and SA. This stems in part from poor measurement of childhood exposures and little investigation of effect measure modifiers, which are helpful for guiding preventive interventions [4].

Some studies have linked maternal psychopathology to offspring SRT and SA [4, 5] and an earlier age of onset

[6–8], but the nature of this relationship is not well-understood. The association may in part be due to shared genetic susceptibility, or it may be that exposure to maternal illness when children are neurodevelopmentally and emotionally sensitive increases risk through neuroendocrine programming involving the hypothalamic pituitary adrenal axis [9]. While genetics indeed play an important role in creating susceptibility for SA, they likely act in concert with environmental exposures surrounding family upbringing, stressful life events, and other social factors [10].

A recent systematic review [4] indicated that the investigations of the association between parental mood disorder and offspring SRT and SA have yielded mixed findings with most studies meeting high risk of bias (mostly related to the measurement of the exposure). Furthermore, this review reported that approximately 70% of studies did not verify if the exposure to parental psychopathology occurred in childhood [4]. The few prospective studies confirming childhood exposure to parental mood disorder support an elevated risk of SRT and SA compared to adolescent offspring of well mothers [11–13], even of mothers with sub-clinical depressive symptoms [13].

An important, yet missed focus of research to date on how parental mood disorder impacts mental health outcomes in offspring is the question: for whom and why? Not all children of parents with major mood disorders develop psychopathology, and there has been little investigation into effect measure modifying influences of variables that might buffer this association [4]. There is evidence that the risk of hospital presentation of suicide-related behaviour among offspring exposed to parental psychopathology is higher among those coming from non-intact families compared to intact families [14]. Low offspring perceived social support increases risk for adolescent SRT and SA [15, 16] and the relative contribution of perceived social support from parents has been found to be more strongly related to SRT and SA compared to support from peers [16]. Furthermore, there is evidence that the protective effect of parental secure attachment on adolescent SA risk is enhanced among families reporting high social cohesion within their neighborhood [17]. However, it is unclear how parental perceived social support or cohesiveness might buffer the risk of SRT and SA in their children among parents who are depressed. Furthermore, in light of higher rates of SRT and SA in females compared to males [18], and possible differences in the effects of maternal depression in boys and girls through different gender-specific socializations by parents [19], sex may also act as an effect measure modifier of this association. Examining effect measure modifiers of the association between parental depression and offspring SRT and SA risk could be beneficial for preventive strategies involving the identification of target groups and improving knowledge for parents with major mood disorders to reduce perceived

burden and anxiety about imposed risk on children. This line of research is important, because informing parents with a major mood disorder that the risk of mental health problems is elevated in their children is associated with increases in anxiety and distress [20].

The objectives of this study were to examine the association between childhood exposure to maternal depressive symptoms and offspring self-reported SRT and SA in Canadian youth and young adults, and to identify possible effect measure modifiers of this association including family structure, maternal-reported social support and cohesion, and offspring sex that have potential implications for prevention strategies targeting exposures occurring prior to SRT and SA onset.

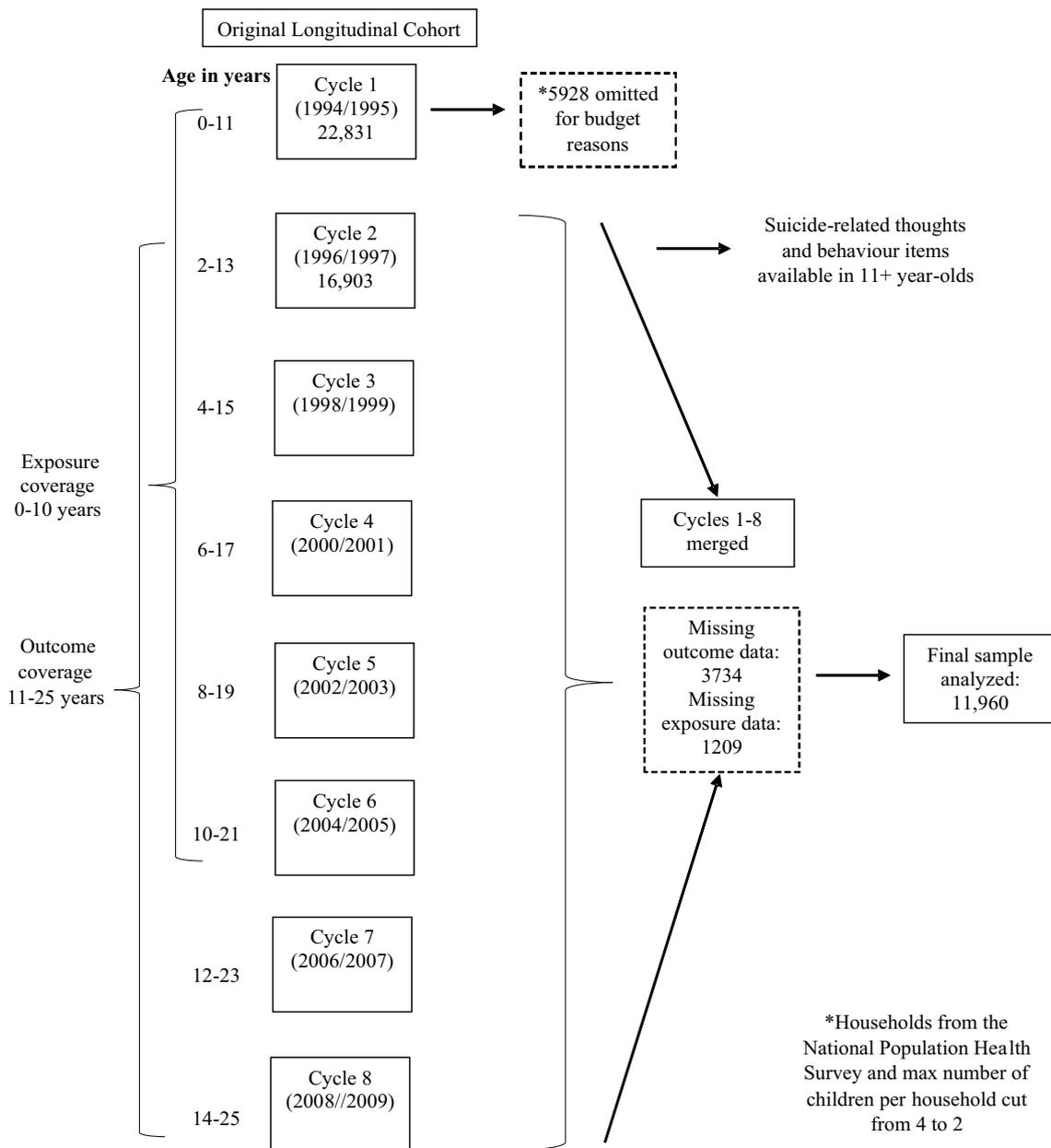
## Methods

### Data source

The National Longitudinal Survey of Children and Youth (NLSCY) is a nationally representative cohort panel survey conducted by Statistics Canada for which Canadian children (herein referred to as offspring) and the person most knowledgeable (PMK) of each participating household were followed from 1994 to 2009. The survey included a maximum of 8 cycles of data collection spaced every 2 years. Children were between 0 and 11 years of age at cycle 1 and were followed into young adulthood, up to age 25. The NLSCY sampling frame was based on Statistics Canada Labor Force Surveys, which cover approximately 97% of the Canadian population and exclude residents of Yukon, Nunavut, Northwest Territories and Indian reserves, full-time members of the Canadian Armed Forces, and inmates of institutions [21]. All NLSCY cycles were linked using unique personal identifiers.

### Study population

This study used the original longitudinal cohort from the NLSCY, which was comprised of 22,831 children initially sampled in 1994/1995. Twenty-six percent of the original longitudinal sample ( $n = 5928$ ) were omitted after cycle 1 due to Statistics Canada budget cuts and to reduce subject burden (Fig. 1). These excluded individuals were randomly selected to reduce potential selection biases, and the remaining sample accurately reflected the survey population [21]. The study population used in this study, therefore, included 16,903 offspring between the ages of 11 to 25 years of age (Fig. 1). This study was approved by the Research Ethics Board at the University of Toronto (#00032787).



**Fig. 1** Flow diagram of sample selection from the National Longitudinal Survey of Children and Youth, 1994 to 2009

**Procedure**

The NLSCY includes both PMK reported and offspring reported measures. Offspring age appropriate for the child and youth questionnaires (11 to 17 years, starting in cycle 2) completed self-reported measures in schools. When offspring reached 18 years of age, the youth survey was completed by computer-assisted telephone interviews to accommodate the aging cohort and capture those no longer in school. PMKs were the biological mother in 90% of cases and are herein referred to as mothers [21]. Mothers were

interviewed either in person or by telephone using computer-assisted interviewing by Statistics Canada trained personnel at every cycle. The mother completed informed consent for their child offspring in the study, and offspring completed informed consent when they became of age to complete the computer-assisted interviewing [21].

**Measures**

The exposure in this study was exposure to maternal-reported depressive symptoms in childhood. This measure

was drawn from cycles 1 to 6 when offspring were between 0 and 10 years of age as this was hypothesized as a biologically plausible exposure period, encompassing childhood sensitive periods [9]. The NLSCY included the 12-item short form of the Center for Epidemiologic Studies Depression Scale (CES-D) [22], designed to assess the frequency and severity of past-week depressive symptoms. A score of nine has been established as a clinical cutoff on this shortened CES-D version that is indicative of a diagnosis of depression [23]. A measure of exposure was derived from the repeated maternal-reported measures, constructed by dividing total scores at each cycle by number of cycles participated in, and then dichotomizing these average scores to  $\geq 9$  and  $< 9$  (Supplementary Table 1). The exposure was coded in this way to ensure mothers' different numbers of cycle participation were accounted for. This was necessary to correct for a greater chance of exposure among offspring whose mothers had more cycles of response.

The outcomes in this study were incident and recurrent SRT and SA from 11 to 25 years of age measured between cycles 2 to 8. SRT and SA were measured by asking offspring: "During the past 12 months, did you seriously consider attempting suicide?" and "During the past 12 months, how many times did you attempt suicide?" [21]. Outcomes were coded as time-to-event variables reflecting time to incident (first event) and subsequent recurrent events corresponding to age at each cycle. Both incident and recurrent events were examined to determine the association between the exposure and the development and persistence of events over adolescence and young adulthood.

Potential effect measure modifiers were identified a priori, including: maternal-reported social cohesiveness and social support, family structure, and offspring sex. These effect measure modifiers were examined given their potential to inform upstream suicide prevention strategies. Therefore, we specifically chose variables that were measured in the offspring's childhood, before the onset of SRT and SA as these variables have stronger implications for prevention compared to factors occurring during adolescence, in parallel with SRT and SA. All of these variables were coded as time-fixed, dichotomous variables with some variables deriving from repeated measures reflecting an average over the offspring's first decade of life. Detailed information on all these variables can be found in Supp. Table 1. Maternal-reported social cohesiveness at cycle 1 was measured by a revised version of the Simcha-Fagan Neighborhood Questionnaire [24], designed to assess perceived social cohesion within the mother's neighborhood. Maternal-reported social support at cycle 1 was measured by a shortened 6-item version of Weiss's Social Provisions Model [25]. Only cycle 1 measures of social support and cohesion were used (reflecting a time period when offspring were between 0 and 10 years of age) as these measures were dropped at cycle 2 and

**Table 1** Standardized mean differences between proportions of sample characteristics in offspring exposed and non-exposed to maternal depressive symptoms in childhood, weighted<sup>h</sup> to reflect the Canadian general population

	Exposed	Non-exposed	
	%	%	SMD <sup>g</sup>
Offspring sex			
Male	49.16	49.65	
Female	50.84	50.35	0.01
Missing	0.00	0.00	
Offspring participation in religious activities <sup>a</sup>			
0—not at all	20.44	20.57	0.00
1—at least once	20.53	22.45	0.05
2—at least once a month	11.63	13.04	0.04
3—at least 3 or 4 times a year	12.06	13.13	0.03
4—at least once a year	8.21	8.06	0.01
Missing <sup>f</sup>	27.13	22.74	
Socio-economic status (baseline) <sup>b</sup>			
1—Lowest	19.02	7.08	0.36
2	23.24	13.98	0.24
3	27.41	28.59	0.03
4	20.61	24.40	0.09
5—Highest	8.78	25.23	0.45
Missing	0.94	0.73	
Maternal binge drinking (0 to 10 years) <sup>c</sup>			
No	93.20	95.93	
Yes	6.62	4.01	0.12
Missing	0.18	0.06	
Spouse binge drinking (0 to 10 years) <sup>c</sup>			
No	88.45	89.67	
Yes	10.74	9.63	0.04
Missing	0.80	0.70	
Family intact (0 to 10 years) <sup>d</sup>			
No	35.89	12.29	
Yes	64.11	87.71	0.57
Missing	0.00	0.00	
Maternal-reported social support (baseline)			
High	13.22	26.38	
Low	85.46	72.75	0.32
Missing	1.31	0.87	
Maternal-reported social cohesion (baseline)			
High	7.62	11.21	
Low	82.74	81.10	0.04
Missing	9.65	7.69	
Offspring stressful life event (4 to 10 years) <sup>e</sup>			
No	17.89	31.30	
Yes	82.11	68.69	0.32
Missing	0.00	0.01	

SMD standardized mean differences

<sup>a</sup>Presented as offspring participation in religious activities at first available cycle (cycle 2). In multivariable models, this variable reflects a time varying measure from offspring age 11 to 21 years

<sup>b</sup>Socio-economic status corresponding categories are presented in

**Table 1** (continued)

## Supplementary Table 1

<sup>c</sup>Represents proportion of maternal and spouse binge drinking occasions over ten when offspring were between 0 and 10 years

<sup>d</sup>Family intact: married or common law for entire first 10 years of offspring's life; Not intact, at least 1 report of divorced, widowed, separated or single never married

<sup>e</sup>Yes reflects any maternal report of child offspring experiencing a stressful life event from 4 to 10 years of age

<sup>f</sup>The offspring participation in religious activities was only measured in 11 to 19 years. 92% of the missing values for this variable reflects valid skips of offspring over 19 years of age

<sup>g</sup>Absolute values of 0.2=small, 0.5=medium, and 0.8=large effect sizes

<sup>h</sup>Inverse probability weights were used to produce estimates that accurately reflect the characteristics of the Canadian population in 1994/1995 (the baseline of the longitudinal cohort from the NLSCY), excluding full-time members of the Canadian Armed Forces, inmates of institutions, and those residing (during the time of the survey) in Yukon, Nunavut, Northwest Territories and Indian reserves

changed during subsequent cycles [26]. Family structure was derived from the marital status variable that was repeated each cycle. A non-intact family was coded as presence of divorce, separation, or single parent, while an intact family was coded as offspring living with parents who were married or common law when offspring were between the ages of 0 and 10 years. Offspring sex was measured by asking mothers if their children in the study were male or female.

Confounders were also identified a priori from the literature and then were tested as potential confounders by estimating their association with the exposure and outcome. Confounders accounted for in multivariable models included: offspring sex, offspring participation in religious activities (time varying from 11 to 21 years of age), offspring stressful life events (4 to 10 years of age), maternal and spouse binge drinking (when offspring were between 0 and 10 years), and socio-economic status (SES).

## Statistical analysis

Differences in baseline descriptive characteristics between exposed and non-exposed offspring were estimated using standardized mean differences (SMD), which can be interpreted as small (0.20), medium (0.50), and large (0.80) effect sizes [27], that are invariant to large sample sizes [28].

Unadjusted rates of incident SRT and SA between exposed and non-exposed were estimated, and the mean cumulative number of recurrent SRT and SA was estimated using the mean cumulative function approach, where calculations were conducted as a function of age. Hazards and rates of incident and recurrent SRT and SA among youth were modeled, and hazard ratios and relative rates (HR, RR) and their corresponding 95% confidence intervals (CI) were

estimated for offspring exposed to maternal depressive symptoms (vs. not).

Herein, a counting process framework was employed, with age in year at interview as the time scale (11 to 25 years). Owing to the NLSCY response structure, discontinuous risk intervals (e.g., gaps in respondent time) were present. These gaps in time were present both by design, because the NLSCY assessments were spaced every 2 years, while the outcome measure of SRT and SA reflects a 1-year look back window, and by participant drop-out and re-entry into the survey at a later time. A counting process framework was used to account for both these types of discontinuous risk intervals, which uses a time variable with a start and stop time; representing the specific time periods each offspring was observed as at risk. A survival model [29] was used to estimate the risk of incident outcome, while risk of recurrent outcome was estimated using an Anderson-Gill recurrent event model [30]. Recurrent event models were adjusted for potential within-subject correlation and dependency of events over time using a robust sandwich estimator and adjusting for prior events, respectively.

All models are adjusted for sex (also tested as an effect measure modifier), offspring age in years at baseline, offspring participation in religious activities (time varying), offspring stressful life event, SES, and maternal and paternal binge drinking. Interaction and effect measure modification was tested by adding interaction terms to models and using adjusted stratum-specific effect estimates that reflect the adjusted effect of the exposure on the outcome within each level of the effect measure modifier.

To account for the NLSCY's complex, survey design, the longitudinal weights, and bootstrap weights provided by Statistics Canada were used to calculate point estimates and variances to produce unbiased estimates of the Canadian population and account for post-stratification and non-response, respectively [21]. Survival model assumptions were verified graphically. All analyses were performed using SAS software (version 9.4).

## Results

### Characteristics of the sample

The final study sample comprised 11,960 offspring after excluding 3734 (22%) and 1209 (7%) offspring with missing outcome or exposure measurements, respectively (Fig. 1). 75.4% of offspring had complete follow-up data, or no more than 2 instances of cycle non-response, where they missed a cycle and re-entered the survey at a subsequent cycle. Cycle non-response was associated with baseline age (Supplementary Table 2), which was adjusted for in multivariable models.

14.4% of offspring were exposed to maternal depressive symptoms between 0 and 10 years of age. There was a higher proportion of exposed compared to non-exposed offspring coming from families with lower SES (SMD = 0.36; Table 1). Furthermore, there was a higher proportion of exposed offspring reporting significant stressful life events from 4 to 10 years of age (SMD = 0.32), coming from non-intact families (SMD = 0.57), and coming from families whose mothers reported low social support (SMD = 0.32) compared to non-exposed offspring.

### Hazard of SRT and SA

The unadjusted proportion of exposed offspring reporting at least 1 instance of SRT was 20.6% compared to 13.0% of non-exposed offspring from 11 to 25 years of age. Furthermore, among exposed offspring, 13.2% reported at least 1 instance of SA, while 6.3% of non-exposed offspring reported SA from 11 to 25 years of age. The mean cumulative number of SRT recurrences was higher in the exposed compared to non-exposed at all ages (Supplementary Fig. 1). By age 17 years, the cumulative number of SRT recurrences per 100 persons was 75 in exposed, and 49 in non-exposed, while the cumulative number of SA recurrences was 36 in exposed and 19 in non-exposed (Supplementary Fig. 1).

At any given age between 11 and 25 years, the incident hazard rates of SRT and SA in exposed offspring were significantly elevated by 1.7 times (95% CI 1.51, 2.14) and 2.2 times (95% CI 1.81, 2.86), respectively, compared to non-exposed offspring. After adjustment for confounders, these hazard rates remained significantly elevated among exposed compared to non-exposed offspring (SRT adjusted HR: 1.67

95% CI 1.37, 2.08) and (SA adjusted HR: 1.93 95% CI 1.43, 2.50), (Table 2). The pattern of findings was similar in models predicting recurrent SRT and SA (Table 2).

### Interaction and effect measure modification

There was no significant evidence of interaction between any of the potential effect measure modifiers predicting either incident or recurrent SRT and SA (all  $p > 0.05$ ). Among males, the stratum-specific adjusted hazard of SRT and SA was not significantly different in exposed vs. non-exposed, while among females, the stratum-specific adjusted hazards of incident SRT and SA were significantly elevated (HR: 1.67 95% CI 1.44, 2.19) and (HR: 1.93 95% CI 1.43, 2.50), respectively (Fig. 2). The stratum-specific adjusted hazards of incident SA were not statistically significant among offspring, whose mothers reported high social cohesion or support, or coming from intact families, while the hazards were statistically significantly elevated among offspring whose mothers reported low social cohesion, social support, or coming from non-intact families (Fig. 2). The pattern of interaction and effect measure modification findings for recurrent SRT and SA was similar to the incident SRT and SA findings (Supplementary Table 4).

### Sensitivity analyses

Primary associations were estimated in a subset of the sample excluding offspring with any instance of cycle non-response. The primary associations remained similar, and statistically significant among this subset with effect estimates attenuating slightly (Supplementary Table 3). Primary

**Table 2** Hazard ratios, relative rates, and 95% confidence intervals of suicide-related thoughts and attempts in 11 to 25 year olds among those exposed and non-exposed to maternal depressive symptoms in childhood, weighted<sup>c</sup> to reflect the Canadian general population

	Unadjusted			Adjusted <sup>a</sup>			
	Hazard ratio	95%CI <sup>b</sup>		Hazard ratio	95% CI <sup>b</sup>		#observations (unweighted)
SRT incident	1.74	1.51	2.14	1.67	1.37	2.08	17,973
SA incident	2.24	1.81	2.86	1.93	1.43	2.50	22,693
	Relative rate	95%CI <sup>b</sup>		Relative rate	95%CI <sup>b</sup>		#observations (unweighted)
SRT recurrent	1.67	1.28	2.00	1.61	1.33	1.96	18,478
SA recurrent	2.00	1.45	2.54	1.87	1.40	2.36	22,945

CI confident intervals, SA suicide attempt, SRT suicide-related thoughts

<sup>a</sup>Adjusted for sex, socio-economic status, offspring participation in religious activities (time varying), maternal and spouse binge drinking (0 to 10 years), child stressful life event (4 to 10 years), and offspring age at cycle 1

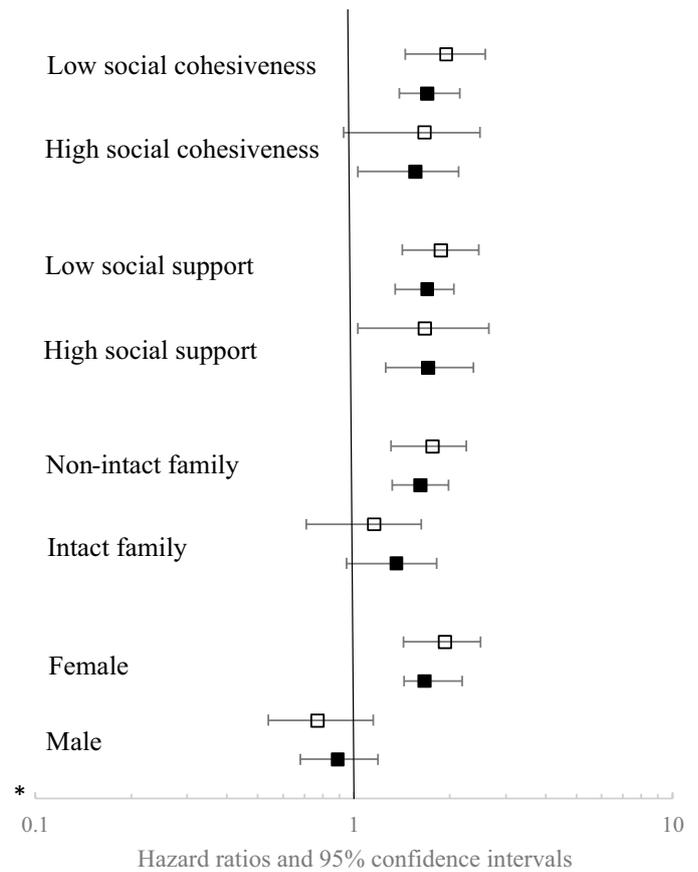
<sup>b</sup>Estimated using Statistics Canada Bootstrap weights

<sup>c</sup>Inverse probability weights were used to produce estimates that accurately reflect the characteristics of the Canadian population in 1994/1995 (the baseline of the longitudinal cohort from the NLSCY), excluding full-time members of the Canadian Armed Forces, inmates of institutions, and those residing (during the time of the survey) in Yukon, Nunavut, Northwest Territories and Indian reserves

**Fig. 2** Stratum-specific adjusted<sup>a</sup> hazard ratios and 95% confidence intervals of suicide-related thoughts and attempts in 11 to 25-year-old offspring exposed vs. non-exposed to maternal depressive symptoms in childhood, weighted<sup>b</sup> to reflect the Canadian general population. <sup>a</sup>Adjusted for sex (not in models testing effect measure modification of sex), socio-economic status, offspring participation in religious activities (time varying), maternal and spouse binge drinking (0 to 10 years), child stressful life event (4 to 10 years), and offspring age at cycle 1. <sup>b</sup>Inverse probability weights were used to produce estimates that accurately reflect the characteristics of the Canadian population in 1994/1995 (the baseline of the longitudinal cohort from the NLSCY), excluding full-time members of the Canadian Armed Forces, inmates of institutions, and those residing (during the time of the survey) in Yukon, Nunavut, Northwest Territories and Indian reserves

□ Suicide attempts  
 ■ Suicide-related thoughts

\*x-axis is on the log10 scale



associations were also estimated in a subset of the sample, excluding offspring, whose PMK was not the biological mother (~8%). This sensitivity analysis showed negligible differences in primary associations and the proportion of exposed and non-exposed with and without the outcome was almost identical to that reported in the entire study sample. Finally, we estimated the exposure using a count method, estimating the proportion of mothers reporting scores over the CES-D cutoff by offspring age to determine the degree of possible misclassification of the exposure due to the averaging of scores across cycles. The proportion of offspring exposed to maternal depressive symptoms from 0 to 10 years of age using a count method was quite stable, and very similar to the proportion exposed calculated by averaging total scores to account for different numbers of cycle participation used in primary analyses (Supplementary Fig. 2).

**Discussion**

This study reports on prospective associations between childhood exposure to maternal depressive symptoms and offspring SRT and SA in adolescence and young adulthood, using nationally representative data from the NLSCY with up to 25 years of follow-up in some offspring. Exposure

to maternal depressive symptoms in childhood was associated with an almost doubled hazard of SA between 11 and 25 years of age and a 70% increased hazard of SRT. This exposure was also associated with the persistence of these thoughts and behaviors between 11 and 25 years of age, suggesting that this exposure might produce enduring effects on offspring’s vulnerability towards SRT and SA. These associations remained statistically significant after adjustments for offspring stressful life event(s), maternal and spouse binge drinking behaviour, offspring religious activity involvement, offspring sex, and household SES.

Few studies have specifically tested the association between exposure to maternal depression in childhood and offspring adolescent SRT and SA risk. Most existing studies have not verified if the exposure to maternal illness occurred in the offspring’s childhood, measuring the exposure retrospectively, and using lifetime measures of DSM diagnoses [4]. Findings from prospective studies that confirmed the exposure occurred in childhood agree with the primary findings of this study. Specifically, a study from the Avon Longitudinal Study of Parents and Children reported an elevated risk of SRT and SA at age 16 among offspring exposed to maternal depression from birth to 11 years of age [13] and importantly reported that these associations were not accounted for by maternal suicide attempt. Furthermore,

high-risk studies of offspring of mothers with mood disorder confirmed by clinicians using gold standard interviews have reported these offspring to be at an elevated risk for SRT and SA in adolescence relative to offspring of mothers with no major mood disorder [11, 12].

Exposure to maternal depression in childhood might increase risk of suicide-related outcomes through vulnerability incurred by exposure during sensitive neurodevelopmental windows [e.g., rapid hypothalamic pituitary adrenal (HPA) axis development] in childhood [9, 31]. Specifically, lack of expected experiences necessary for normal brain development during these critical periods (e.g., consistent parental care), and family stress may interfere with emotional and behavioral maturation, and manifest as a vulnerable phenotype possibly reflecting psychological deficits and/or psychiatric symptoms [9]. In support of this, 1 longitudinal study reported that psychiatric disorders at age 15 years significantly mediated the association between maternal depression from 0 to 11 years of age and offspring SRT and SA at age 16 [32].

We also found that primary associations were modified by offspring sex, such that these associations were only found among females and not males. Consistent with these findings, Tsypes et al [33] reported an elevated risk of SRT in females exposed to maternal major depression but not in males. In contrast, Hammerton et al. [13] did not find any sex differences in the association between maternal depression in childhood and adolescent SRT. Others have reported on associations between maternal depression and other offspring outcomes (e.g., depression, externalizing symptoms) by sex with mixed findings [34–36]. Plausible explanations for an association between maternal depression and SRT and SA in females, but not in males could be linked to neurodevelopmental differences during exposure to maternal depression, where females are more vulnerable to these effects in comparison with males. Furthermore, gender-specific responses to child behaviour by parents might also explain these sex differences. It has been suggested that female offspring of depressed mothers are at a greater risk for SRT and emotional problems than boys, as they are more sensitive to the stressors associated with maternal depression such as relationship strain. Alternatively, boys may be impacted by maternal depression, but under-report SRT and SA [19].

From a qualitative standpoint, our findings also raise questions about possible protective effects of residing with intact families in childhood and maternal perceived high social cohesion and support against SRT and SA among exposed offspring. Findings were less conclusive pertaining to the social support and cohesion variables; however, these measures were discontinued at cycle 2, and changed in subsequent cycles in the NLSCY; thus, their measurement was restricted to the baseline measure. It was not possible to produce an average measure of these constructs over the

first decade of life. This may have contributed to the overlapping 95% CIs and smaller differences in point estimates. That is, these types of social influences might operate in a cumulative way over time, and if measured at 1 point in time, might not be sensitive enough to detect true differences. Being exposed to family break-up in childhood and lack of social resources might contribute to a greater severity of illness in mothers and/or greater vulnerability in offspring and requires further study.

### Strengths and limitations

This study took advantage of a comprehensive, nationally representative survey with up to 25 years of follow-up in some offspring starting from the first year of life. The application of a survival model under a counting process framework to estimate rates for incident and recurrent SRT and SA accounting for discontinuous risk intervals from survey design and participant cycle non-response was unique. However, the following limitations should be considered.

Measures were based on self-report, which could lead to misreporting; however, offspring were ensured confidentiality and anonymity when completing measures. Furthermore, using a self-reported outcome, we were able to determine how maternal depressive symptoms is associated with SRT (an outcome not systematically collected in health administrative data) and SA, irrespective of hospitalization.

The main exposure in this study varied in offspring by age of entry and number of participation cycles, meaning that the number of measurements available by age varied. While accounted for, exposure misclassification may still be possible, where older non-exposed offspring at cycle 1 could have been exposed at earlier ages. However, this misclassification would likely be non-differential, and the proportion of exposed offspring between 0 and 10 years of age was relatively stable. Furthermore, the numbers were too low to restrict the sample to those who were 0 at cycle 1, i.e., a birth cohort; therefore, the influence of timing of exposure or a cumulative effect could not be explored.

25% of offspring had 2 or more cycles of non-response. Although, several offspring respondents with cycle non-response dropped out and then re-entered the survey. Our analytic approach uniquely accommodated these scenarios by accounting for these discontinuous risk intervals in the estimation of the effect estimates. Furthermore, our sensitivity analysis indicated that primary associations were not appreciably different among those with compared to without cycle non-response indicating that the bias incurred through these missing data was minimal.

There is no measure of family or parental history for suicide-related behaviour in the NLSCY; therefore, we were unable to examine their roles. Maternal SA is indeed linked to offspring SA [4]; however, there is evidence of independent

pathways from maternal depression to offspring SRT and SA risk [37]. The NLSCY also did not include detailed information on the nature of maternal depressive symptoms in terms of treatment. There is some evidence that reduction of acute maternal depressive episodes improves, in parallel, offspring depressive symptoms [38], suggesting that effective treatment of depression in mothers could reduce risk in offspring, although the long-term impact is less clear. There is also no specific measure of childhood abuse in the NLSCY. This is an established risk factor for suicide-related behaviour and depending on the timing may be associated with maternal depression. However, the stressful life event variable encompassed a summary variable that included a question about abuse [21], although numbers were too low to isolate this item. Finally, most variables were maternal reported, and there is limited paternal information available from the NLSCY. The lack of available paternal information is a limitation of many national surveys and more effort should be focused on collecting information in fathers.

## Implications

There is an established link between exposure to maternal depression in childhood and psychiatric disorders in offspring [39], and findings from this study confirm an association with onset and persistence of SRT and SA in female youth. This information is helpful for guiding preventive efforts in terms of identifying high-risk groups and for clinician monitoring of high-risk children; however, without understanding of the context of this association, we lack necessary information to inform such prevention strategies. Suicide intervention studies have been dominated by studies of populations of youth identified via treatment settings or already in crisis and tend to exclude those not going to the hospital [40]. However, the implementation and evaluation of family-based interventions that support high-risk families before children get to a crisis stage in the field of suicide prevention is growing [41–43], and there is a need to further inform and develop these prevention strategies. Furthermore, interventions involving improving social support networks for vulnerable mothers exist and have shown to be effective in increasing health-promoting behaviours [44]. More research is needed to identify which forms of social support are most effective in reducing maternal depression, and might have most impact on suicide prevention in offspring, as some forms of social networking have been shown to produce negative effects on maternal mental health [44].

## Conclusions

Exposure to maternal depressive symptoms before age 11 in girls significantly elevates the risk of the development and persistence of thinking about suicide and reporting attempts

before 25 years of age. These individuals reflect a target group for early preventive strategies and clinician monitoring. A shift in research focus to identifying protective factors and how these differ by sex and gender in predicting SRT and SA risk among offspring of depressed mothers could be useful in informing future effective preventions. Ultimately, these strategies should support families and their high-risk children before the onset of offspring suicide-related behaviour, halting progression towards suicide.

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## Compliance with ethical standards

**Conflict of interest** All authors declare that they have no conflicts of interest relating to this manuscript.

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