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Title: Perinatal adversity profiles and suicide attempt in adolescence and young adulthood: Longitudinal analyses from two 20-year birth cohort studies

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Abstract

Background. We aimed to identify groups of children presenting distinct perinatal adversity profiles and test the association between profiles and later risk of suicide attempt.

Methods. Data were from the Québec Longitudinal Study of Child Development (QLSCD, N=1623), and the Avon Longitudinal Study of Parents and Children (ALSPAC, N=5734). Exposures to 32 perinatal adversities (eg, fetal, obstetric, psychosocial, and parental psychopathology) were modeled using latent class analysis, and associations with self-reported suicide attempt by age 20 were investigated with logistic regression. We investigated to what extent childhood emotional and behavioral problems, victimization, and cognition explained the associations.

Results. In both cohorts, we identified 5 profiles: *No perinatal risk*, *Poor fetal growth*, *Socioeconomic adversity*, *Delivery complications*, *Parental mental health problems* (ALSPAC only). Compared to children with *No perinatal risk*, children in the *Poor fetal growth* (pooled estimate QLSCD-ALSPAC, OR=1.89, 95%CI=1.04-3.44), *Socioeconomic adversity* (pooled-OR=1.42, 95%CI=1.08-1.85), and *Parental mental health problems* (OR=1.74, 95%CI=1.27-2.40), but not *Delivery complications*, profiles were more likely to attempt suicide. The proportion of this effect mediated by the putative mediators was larger for the *Socioeconomic adversity* profile compared to the others.

Conclusions. Perinatal adversities associated with suicide attempt cluster in distinct profiles. Suicide prevention may begin early in life and requires a multidisciplinary approach targeting a constellation of factors from different domains (psychiatric, obstetric, socioeconomic), rather than a single factor, to effectively reduce suicide vulnerability. The way these factors cluster together also determined the pathways leading to suicide attempt, which can guide decision-making on personalized suicide prevention strategies.

Keywords: suicide attempt, perinatal adversity, latent class analysis, ALSPAC, QLSCD

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Introduction

Suicide attempt in adolescence and young adulthood is an important public health problem, with rates ranging from 3.1% to 8.8% in community samples of youth aged 15-25 years (Cha et al., 2018; Nock et al., 2008, 2013; Orri et al., 2020). Suicide attempt is associated with important health and social consequences, such as increased risk of suicide mortality (second leading cause of death in 15-24 year-olds), poor mental and physical health, and negative social outcomes (Bostwick, Pabbati, Geske, & McKean, 2016; Goldman-Mellor et al., 2014; Hawton & O'Connor, 2012; Reinherz, Tanner, Berger, Beardslee, & Fitzmaurice, 2006). Early identification of individuals at risk for suicidal behavior is critical in order to implement timely preventive interventions.

Despite risk factors such as exposure to violence (Geoffroy et al., 2018, 2016; Geoffroy, Orri, Girard, Perret, & Turecki, 2020), drug abuse (Gobbi et al., 2019), and psychopathology (Arsenault-Lapierre, Kim, & Turecki, 2004; Orri, Galera, et al., 2018; Orri, Perret, Turecki, & Geoffroy, 2018; Orri et al., 2020; Turecki, 2005) being important proximal predictors of adolescent suicidal behaviors, past studies including a recent meta-analysis suggested that exposure to adversities during the perinatal period may also substantially contribute to increased susceptibility to suicidal behavior later in life (Geoffroy, Gunnell, & Power, 2014; O'Donnell & Meaney, 2016; Orri et al., 2019; Turecki & Brent, 2016). For example, evidence showed that perinatal factors such as poor fetal growth (e.g., low birth weight), adverse socioeconomic environment (e.g., low socioeconomic status), family characteristics (e.g., nonintact family), and exposure to alcohol/drugs during pregnancy are associated with suicide risk in both adolescence and adulthood (Cnattingius, Svensson, Granath, & Iliadou, 2011; D'Onofrio et al., 2013, 2014; Geoffroy et al., 2014; Mittendorfer-Rutz, Rasmussen, & Wasserman, 2004; Orri et al., 2019). Documenting the association between such perinatal factors and suicide attempt may help with the early identification of children more at risk of suicide later in life (Aizer & Currie, 2014; Gunnell, 2015).

Current knowledge of associations between perinatal factors and suicide-related outcomes has several gaps. First, previous studies showing associations between perinatal adversity and suicide risk have focused on one or few factors (Orri et al., 2019), and a comprehensive study assessing a range of fetal, psychosocial, obstetric, and parental health factors is lacking. Second, previous studies have not considered the co-occurrence of such perinatal factors within the same individual. For example, low birth weight is more common in infants from impoverished backgrounds, mothers who smoked during pregnancy, suffer from depression (Grote et al., 2010) and have low education (Aizer & Currie, 2014; Parker, Schoendorf, & Kiely, 1994). By relying on statistical models such as multiple regression, previous studies documented independent associations of a limited range of perinatal factors with

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suicidal behavior (e.g., the effect of birth weight on suicidal behavior as if all mothers have equal levels of depression, education, smoking (D'Onofrio et al., 2013, 2014; Mittendorfer-Rutz et al., 2004)), but did not capture the co-occurrence of multiple risk factors among the same individual (e.g., accounting for the fact that mothers having low birth weight children are also more likely to experience depression, low education, and to smoke). Third, perinatal factors are also associated with later emotional (e.g., depression (Gale & Martyn, 2004)), behavioral (e.g., hyperactivity-impulsivity (Class, Rickert, Larsson, Lichtenstein, & D'Onofrio, 2014; Lim et al., 2018), and conduct problems (Mathewson et al., 2017)), interpersonal (e.g., peer victimization), and cognitive problems (Flensborg-Madsen & Mortensen, 2017). As these problems are also independent risk factors for suicidal behaviors (Geoffroy et al., 2016; Richard-Devantoy et al., 2019; Turecki & Brent, 2016), the association between perinatal adversity and suicidal behavior reported in previous studies is likely to be explained, at least partially, by such factors (Orri et al., 2019). Therefore, studies are needed to clarify whether the association of perinatal factors with suicidal behavior is mediated by more proximal childhood factors.

This study aimed to 1) identify clusters of children presenting distinct risk profiles of perinatal adversity (including fetal, obstetric, psychosocial, parental mental health problems and substance use); 2) test the association between identified perinatal adversity profiles and suicide attempt by early adulthood; 3) determine if perinatal adversity profiles are independently associated with suicide attempt, or whether the association is explained by childhood emotional, behavioral, interpersonal, and cognitive problems that are a consequence of perinatal adversity. We utilized data from 2 independent birth cohorts to provide replication of our findings.

Methods

Participants and data

Data were from the Québec Longitudinal Study of Child Development (QLSCD) in Québec, Canada, and the Avon Longitudinal Study of Parents and Children (ALSPAC) in the UK. QLSCD (which is conducted by the Institut de la statistique du Québec, ISQ) is an ongoing birth cohort initially including 2120 singletons born in 1997/98 to mothers living in the Canadian Province of Québec (http://www.jesuisjeserai.stat.gouv.qc.ca/default_an.htm). Participants were selected from birth registers following a random procedure based on living areas and birth rates. The target population represents 94.5% of the Québec population of singleton births, including all ranges of socioeconomic status. Families were included if pregnancy lasted 24-42 weeks and if the mother could speak French or English. The QLSCD protocol was approved by the ISQ and the St-Justine Hospital Research Centre ethics committees, and

informed consent was obtained at each assessment. ALSPAC is an ongoing birth cohort: pregnant women resident in Avon, UK, with expected dates of delivery 1st April 1991 to 31st December 1992 were invited to participate. The cohort initially included 14,062 live births and 13,988 children who were alive at 1 year of age. More were added in a later data collection, for a total of 15,589 live births (14,901 children alive at one year of age)(Boyd et al., 2013; Fraser et al., 2013; Northstone et al., 2019). Ethical approval for the study was obtained from the ALSPAC Law and Ethics committee and local research ethics committees, and informed consent was obtained from participating families. Informed consent for the use of data collected via questionnaires and clinics was obtained from participants following the recommendations of the ALSPAC Ethics and Law Committee at the time. Please note that the study website contains details of all the data that is available through a fully searchable data dictionary and variable search tool (http://www.bristol.ac.uk/alspac/researchers/our-data/). One of each twin pair was excluded at random for the current analysis, and it should be noted that only a subsample of ALSPAC (n=8369) had data from obstetric records extracted due to funding restrictions (detail available from authors on request).

All participants were followed-up until early adulthood (i.e., 20 years for QLSCD and 21 years for ALSPAC) with repeated assessments from parents/teachers/self-reports and linkage with hospital records.

We included 1623 participants from QLSCD (845, 52.1% females; representing 77% of the original sample) and 5765 participants from ALSPAC (3356, 58.2% females; representing 41% of the original sample) with information on suicide attempt. Included participants differed from non-included on some characteristics, such as being more likely to be female, and having parents with higher socioeconomic status (see **Table S1**). To reduce the influence of differential attrition on our analyses, we used inverse probability weighting, in which weights represent the probability of inclusion in the sample estimated from characteristics independently predicting missingness. Missing data on prenatal and perinatal variables (**Table S1**) were handled using Full Information Maximum Likelihood.

Suicide attempt by early adulthood

Suicide attempt (i.e., self-harm with intent to die) was assessed via self-report questions at 13, 15, 17 and 20 years in QLSCD and at 16 and 21 years in ALSPAC. In QLSCD, adolescents endorsing serious thought of attempting suicide were asked: "in the past 12 months: how many times did you attempt suicide?" (0 vs ≥1). At age 20, lifetime suicide attempt was also assessed through the questions: "Did you ever go to the emergency department for a suicide attempt", and "Have you ever been hospitalized for a suicide attempt". In ALSPAC, adolescents reporting self-harm, i.e., positive answer to the question: "Have you ever hurt yourself on purpose in any way (e.g., by taking an overdose

of pills or by cutting yourself)?" were asked: "On any of the occasions when you have hurt yourself on purpose, have you ever seriously wanted to kill yourself?", and "wanted to die" to assess intentionality. In both cohorts, if a participant endorsed any of the suicide attempt questions or manifested intent to die at any time point, they were coded as positive for our outcome.

Perinatal adversity

We assessed 32 perinatal adversity factors, including adversities related to fetal growth, socioeconomic status, exposure to substances during pregnancy, and exposure to parental mental health problems. These variables are detailed in **Table 1**.

Mediators

In both cohorts, we used teacher ratings of emotional and behavioral problems, self-reports of peer victimization, and standardized assessments of cognitive skills. Emotional (i.e., anxiety/depressive symptoms) and behavioral (i.e., conduct and hyperactive-impulsive) problems were assessed with the Social Behavior Questionnaire (Murray, Eisner, & Ribeaud, 2017) in QLSCD at ages 6, 7, 8, 10, and 12, and with the Strengths and Difficulties Questionnaire (Goodman, 1997) in ALSPAC at ages 7/8, and 10/11. Peer victimization was assessed with a modified version of the Self-report victimization scale (Ladd & Kochenderfer-Ladd, 2002) in QLSCD at ages 6, 7, 8, 10, and 12, and with a modified version of the Bullying and Friendship Interview Schedule (Wolke, Woods, Bloomfield, & Karstadt, 2000) in ALSPAC at ages 8 and 10. Cognitive skills (i.e., verbal intelligence) were measured using the Peabody Picture Vocabulary Test (Dunn, Thériault-Whalen, & Dunn, 1993) in QLSCD at age 4, 7, and 10, and with the Wechsler Preschool & Primary Scale of Intelligence and the Wechsler Intelligence Scale for Children (Wechsler, 1949) in ALSPAC at ages 4 and 8, respectively. Each measure was averaged across the available data points. We provided details on each measure in **Table S2**.

Statistical analysis

Analyses were conducted in QLSCD, and subsequently replicated in ASLPAC. Models were estimated using Mplus version 7.3 and 8 (Muthén & Muthén, 1998-2017) with Maximum Likelihood and robust (Huber-White) standard errors.

Descriptive statistics and associations. Prevalence of each perinatal adversity was estimated for each cohort. Then, we described the association between each perinatal adversity and suicide attempt from sex-adjusted binary logistic regression. This was estimated in both cohorts separately, then estimates were pooled using inverse-variance weighted meta-analysis.

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Identifying perinatal adversity profiles. We used Latent Class Analysis to identify homogeneous groups of children having distinct patterns of exposure to the 32 perinatal adversity factors (Lanza & Rhoades, 2013; Orri et al., 2017). Latent Class Analysis models with 1 to 6 latent classes were sequentially fitted, and the optimal number of classes was chosen considering established fit indices (Bayesian Information Criterion, Vuong-Lo-Mendel-Rubin Likelihood Ratio Test), the proportion of participants in each class, and the interpretability of the model. Entropy, indicating the accuracy with which models classify individuals into their most likely class (range 0–1, higher values indicating better classification accuracy) was also considered. After the selection of the best model in each sample, individuals were assigned to a latent class according to their highest posterior probability.

Association of perinatal adversity profiles with suicide attempt. We used binary logistic regression (adjusted for sex) to estimate the association between the identified perinatal adversity profiles and later suicide attempt (total effect). No sex-by-profile interaction was found.

Mediation analysis. We conducted mediation analysis in Mplus using the product of coefficients method for the perinatal profiles showing evidence of total association with suicide attempt. We calculated the indirect (i.e., association between perinatal adversity profiles and suicide attempt through mediators) and direct effects (i.e., association between perinatal adversity profiles and suicide attempt independent from -not explained by- the mediators). Additionally, we calculated the proportion of the association that was mediated using the ratio between indirect and total effects. Models with all mediators entered simultaneously and models with each individual mediator were estimated.

Estimating pooled effect sizes. For all models, associations were estimated for each cohort, then the estimates were pooled using inverse-variance weighted meta-analysis.

Results

Prevalence of suicide attempt

The prevalence of suicide attempt was similar in both QLSCD (134 of 1623, 8.3%) and ALSPAC (484 of 5765, 8.4%). In both cohorts, girls were more likely to report suicide attempt than boys (QLSCD: girls, n=91 of 845, 10.8%; boys, n=43 of 778, 5.5%; $P<0.001$; ALSPAC: girls, n=383 of 3356, 11.4%; boys, n=101 of 2406, 4.2%; $P<0.001$).

Prevalence of perinatal adversities and association with suicide attempt

Most perinatal adversities were similarly prevalent in the two cohorts, with several exceptions (e.g., short birth length, long hospitalization; see **Table 2**). Associations of each perinatal adversity with suicide attempt are reported in **Table**

2. Evidence of association with suicide attempt was found for low birth weight (OR, 1.52; 95%CI,1.05-2.20), low socioeconomic status (OR, 1.64; 95%CI, 1.29-2.08), nonintact family (OR, 1.93; 95%CI, 1.51-2.47), low maternal age (OR, 1.87; 95%CI, 1.16-3.02), exposure to smoking during pregnancy (OR, 1.94; 95%CI, 1.62-2.32), maternal depression (OR, 1.64; 95%CI, 1.27-2.12) and anxiety (OR, 1.64; 95%CI, 1.27-2.12), and paternal antisocial behavior (OR, 1.93; 95%CI, 1.32-2.84) when estimates from both cohorts were pooled.

Perinatal adversity profiles

We identified the following perinatal profiles (**Figure 1**): *Poor fetal growth* (n=75, 4.6% in QLSCD; n=298, 5.2% in ALSPAC), including children with the highest probabilities of showing fetal growth adversity, but also showing high probability of other adversity such as birth/delivery adversity, psychosocial adversity and to be exposed to maternal smoking in pregnancy, and having mothers showing depression; *Socioeconomic adversity* (n=351, 21.6% in QLSCD; n=946, 16.5% in ALSPAC), including children with the highest probabilities of being born in a socioeconomically disadvantaged milieu, exposures to smoking, drugs, alcohol, and medications during pregnancy, and, in QLSCD only, parents with antisocial behaviors and high depressive symptoms; *Delivery complications* (n=397, 24.5% in QLSCD; n=591, 16.6% in ALSPAC), including children born with caesarean section and having longer neonatal hospitalization; *Parental mental health problems* (n=448, 7.8% in ALSPAC only), including children with parents having high rates of anxiety and depressive symptoms. The remaining children were part of the *No perinatal risk* profile (n=801, 49.5% in QLSCD; n=3091, 53.9% in ALSPAC), including children with average probability of all perinatal adversity factors. Difference in the prevalence of the 32 perinatal adversities in each profile compared to the reference profile (i.e., *No perinatal risk*) is reported in **Figure 2**. The proportion of girls and boys within the identified profiles was similar in QLSCD (*P*=0.877) but varied in ALSPAC (*P*<0.001) with a somewhat higher proportion of boys in the *delivery complications* profile than other profiles (47% vs ≤42% for other profiles).

Association of perinatal adversity profiles with suicide attempt

Prevalence of suicide attempt by profile, in QLSCD and ALSPAC respectively, was 14.9% (11 of 74) and 11.1% (33 of 298) in the *Poor fetal growth* profile, 10.5% (37 of 351) and 10.2% (96 of 946) in the *Socioeconomic adversity* profile, 7.6% (30 of 397) and 6.5% (62 of 951) in the *Delivery complications* profile, 12.5% (56 of 448) in the *Parental mental health problems* profile, and 7.0% (56 of 801) and 7.7% (237 of 3091) in the *No perinatal risk* profile (**Figure S1**).

Sex-adjusted logistic regression showed that children in the *Poor fetal growth* profile were more likely to attempt suicide by early adulthood than children in the *Low perinatal adversity* profile, with pooled OR across

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QLSCD and ALSPAC of 1.89; 95%CI, 1.04-3.44 (cohort specific ORs were QLSCD: 2.84; 95%CI, 1.32-6.10, ALSPAC: 1.51; 95%CI, 1.02-2.23). Children in the *Socioeconomic adversity* (pooled OR, 1.42; 95%CI, 1.08-1.85; QLSCD: OR, 1.76; 95%CI, 1.10-2.81; ALSPAC: OR, 1.30; 95%CI, 1.01-1.67) and in the *Parental mental health problems* (ALSPAC only: OR, 1.74; 95%CI, 1.27-2.40) profiles also had increased risk of suicide attempt by early adulthood, compared with children in the *No perinatal risk* profile. Finally, children in the *Delivery complications* profile did not show increased risk of later suicide attempt (pooled: OR, 0.92, 0.71-1.86; QLSCD: 1.06, 0.64-1.75; ALSPAC: 0.87, 0.65-1.18) compared with children in the *No perinatal risk* profile.

Direct and indirect association between perinatal adversity profiles and suicide attempt

Mediation analysis investigated the proportion of increased risk of attempting suicide for children in the *Poor fetal growth*, *Socioeconomic adversity,* and *Parental mental health problems* profiles that were explained by our putative mediators. For the *Poor fetal growth* profile, we found that the putative mediators explained 15.0% of the association (13.7% in QLSCD and 19.6% in ALSPAC), with a pooled OR for the indirect effect of 1.10 (95%CI, 1.04-1.16; see **Table 3** for cohort-specific and mediator-specific direct and indirect effects). Similar results were observed for the *Parental mental health problems* profiles, with mediators explaining 13.6% of the association (indirect effect OR, 1.08; 95%CI, 1.03-1.13). However, for the *Socioeconomic adversity* profile, the investigated mediators explained a larger portion of association (39.9% in pooled analysis, 37.1% in each cohort), with an OR for the indirect effect of 1.15; 95%CI, 1.03-1.28. Results were consistent for each mediator analyzed singularly, with hyperactivity/impulsivity appearing as the key mediator in all analyses.

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Discussion

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To our knowledge, this is the first study identifying distinct profiles of exposure to a range of perinatal adversities and elucidating pathways leading to suicide attempt by early adulthood. Using 2 large independent population samples, we identified 5 profiles of perinatal adversity, which were similar in the 2 samples in terms of nature of adversity, population prevalence, and association with suicide attempt. The similarity of findings in the 2 cohorts, coming from 2 different continents, gives confidence that findings were not sample specific. However, despite the aforementioned similarity, we also found some differences, most of which related to delivery complications rates. For example, prevalence of long hospitalization was higher in ALSPAC compared to QLSCD for each profile (especially in the *Delivery complication* and *Socioeconomic adversity* profiles). This may be related to differences in the healthcare system and medical protocols, as well as to measurement differences and the differential extraction of obstetric data

for a selected subsample of mothers in ALSPAC. A profile clustering children exposed to parental mental health problems was identified only in ALSPAC. In this cohort, the larger sample size (Nylund, Asparouhov, & Muthén, 2007), the presence of parental anxiety measures (not assessed in QLSCD), and the assessment of maternal depression closer in time with childbirth compared to QLSCD (postnatal depression prevalence declines sharply over time)(Vliegen, Casalin, & Luyten, 2014) may explain why this profile was not identified in QLSCD.

Our profiles were mainly characterized by high rates of a specific group of perinatal adversities (e.g., fetal growth adversities for children in the *Poor fetal growth* profile). However, some profiles also presented higher rates of adversities pertaining to other adversity groups, compared with the *No perinatal risk* profile. For example, children in the *Poor fetal growth* profile also had higher rates of long hospitalization and birth induction (although lower than for children in the *Delivery complications* profile), low parental education and SES (although lower than for children in the *Socioeconomic adversity* profile), and maternal smoking in pregnancy (similar to children in the *Socioeconomic adversity* profile). This finding indicates that perinatal adversities tend to cluster not only within each group (e.g., several fetal adversities cluster together) but also across groups (e.g., fetal and psychosocial adversities cluster together), as previous studies suggested (Aizer & Currie, 2014; Grote et al., 2010; Parker et al., 1994).

We found increased risk of suicide attempt for children who had poor fetal growth. This finding is in line with a previous meta-analysis (Orri et al., 2019) showing higher risk of suicide, suicide attempt, and suicidal ideation among children with low birth weight. However, while this meta-analysis did not find associations for other factors such as prematurity, premature children were overrepresented in our *Poor fetal growth* profile. This finding, which originates from the utilization of a person-centered approach (i.e., LCA) as opposed to a variable-centered approach (i.e., regression), indicates that a given factor may not be a risk factor in the population as a whole, but can be so for a specific subgroup of children presenting with a cluster of adversities (e.g., low birth weight, prematurity, as well as socioeconomic adversities and exposure to smoking in pregnancy). This is especially evident for delivery complication adversities: caesarean section, which have similar prevalence in the *Poor fetal growth* and *Delivery complications* profiles, may be a marker of suicide risk only for children presenting with all associated adversities characterizing the *Poor fetal growth* profile. This finding calls for a multidisciplinary approach in the assessment of perinatal risk factors, in which information from multiple domains (obstetric, psychopathology, early fetal growth, socioeconomic) needs to be considered jointly to estimate the individual risk of later suicide attempt.

In line with previous studies showing negative effects of deprived socioeconomic environments on mental health and suicide risk (Orri et al., 2019; Poulton et al., 2002), we found that children in the *Socioeconomic adversity*

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profile were at higher risk of suicide attempt. Individual socioeconomic adversities were also those who showed the most consistent associations across the 2 cohorts at the population level (i.e., not considering profiles). It is worth noting that maternal and paternal socioeconomic adversity were similarly overrepresented in this profile, in line with evidence on assortative mating (Nordsletten et al., 2016).

This study also provides insights into mechanisms leading to increased suicide risk for children in the *Poor fetal growth, Socioeconomic adversity* and *Parental mental health problems* profiles, suggesting that different pathways are involved for children in different profiles. On the one hand, the increased suicide attempt risk of children exposed to psychosocial adversities was largely explained by childhood emotional, behavioral, interpersonal problems and lower cognitive skills. Prevention of these problems across childhood may be helpful in order to reduce suicide attempt in youth. On the other hand, those symptoms explained a small proportion of the increased suicide attempt risk of children exposed to fetal growth adversities and parental mental health problems. This suggests that, to improve suicide prevention for those children, it is critical to identify other mechanisms implicated in the pathways to suicide attempt. Biological understanding of the consequences of fetal growth problems on the brain (Walhovd et al., 2012) and the role of pre-existing vulnerability to psychopathology (Nivard et al., 2017) is still poor, and research pointing in this direction may substantially contribute to better understand suicidal risk in those children.

Strengths and limitations

This study is based on large population-based cohorts with over 20 years of follow-up, allowing adequately powered analyses to study rare outcomes and exposures. Main findings have been replicated across the 2 independent samples, strengthening confidence in our conclusions. However, the following limitations should be noted. First, because of attrition, analyses were conducted on a subset of the initial representative samples. Although we used inverse probability weighting to account for the probability of missing at follow-up, caution should be used in generalizing our findings because unmeasured factors can still affect differential attrition. Second, both samples come from high-income western countries, therefore it is unknown if results will generalize to other populations. Third, despite the overall similarity in the measures of our perinatal factors across QLSCD and ALSPAC, important differences for some factors were present (e.g., maternal depression). Fourth, although we did not find any sex-interaction, our analyses might have not been powered enough to detect such differential associations for boys and girls. Fifth, although we investigated a wide range of perinatal factors, they are not an exhaustive list of all potential perinatal influences on suicide attempt. For example, inclusion of factors such as maternal nutrition, stressful life events, and exposure to specific drugs during pregnancy, exposure to traumatic events and violence (unmeasured in our study)

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may have helped us refining our latent classes. In the same way, it is important to acknowledge that other mediators that those investigated in this study may explain the observed associations, and future study should identify other potential pathways.

Conclusions and implication of the findings

Most research on the early risk factors for suicide focuses on the independent role of one (or few) factors. By using a comprehensive approach, this study showed that perinatal risk factors for suicide cluster in distinct profiles, which have specific associations with suicide attempt, as well as specific mediation pathways explaining these associations. This suggests that early-life suicide prevention requires health care professionals to adopt a multidisciplinary approach targeting a constellation of factors from different domains (psychological, obstetric, socioeconomic) to effectively reduce later vulnerability to suicide. Furthermore, the way these factors cluster together also determined the pathways leading to suicide attempt. Therefore, while potential interventions focusing on reducing the risk of childhood behavioral, emotional, interpersonal, and cognitive problems may substantially reduce suicide attempt risk for children exposed to socioeconomic adversity, targeting such factors may be less effective for children exposed to poor fetal growth and parental mental health problems. This information may help targeting suicide prevention interventions.

Ethical standards: The authors assert that all procedures contributing to this work comply with the ethical standards of the relevant national and institutional committees on human experimentation and with the Helsinki Declaration of 1975, as revised in 2008.

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Table 1. Description of the perinatal adversity measures in QLSCD and ALSPAC

	QLSCD	ALSPAC
Fetal growth adversities		
Short birth length	<47 vs ≥47 cm [a]	<47 vs ≥47 cm
Low birth weight	<2500 vs ≥2500 grams [a]	<2500 vs ≥2500 grams
Short head circumference	<10th percentile (32 cm) vs ≥10th percentile [a]	<10th percentile (33 cm) vs ≥10th percentile
Growth restriction	Intrauterine growth retardation suspected during pregnancy before onset of labor [a]	Intrauterine growth retardation suspected during pregnancy before onset of labor [a]
Prematurity	<37 vs ≥37 weeks of gestational age [a]	<37 vs ≥37 weeks of gestational age
Pregnancy complications		
Mother hemorrhage	Hemorrhage during childbirth (ICD-9 code 641) [a]	Hemorrhage prior to delivery [b]
Mother hypertension	Hypertension complicating pregnancy (ICD-9 code 642) [b]	Gestational hypertension without pre-existing hypertension [b]
Mother diabetes	Diabetes mellitus complicating pregnancy childbirth (ICD-9 code 648.0) [b]	Diabetes noted during pregnancy before onset of labor [b]
Birth/delivery adversities		
Long hospitalization	Baby discharged from hospital >3 days after birth [a]	Baby discharged from hospital >3 days after birth [a]
Transfer hospital	Transfer to a specialized hospital [a]	Yes to the question: "Was your baby admitted to a special care baby unit or neonatal intensive care unit or other hospital ward?" [b]
Low APGAR	APGAR score 5 minutes <7 [a]	APGAR score 5 minutes <7 [a]
Birth induction	Induced delivery [a]	Induced delivery [a]
Delivery acceleration	Labor augmented [a]	Labor augmented [a]
Caesarean section	Method of delivery as Caesarean [a]	Method of delivery as Caesarean [a]
Child hypoxia/asphyxia	ICD-9 code 766 [a]	Not available
Socioeconomic adversities		
Low maternal education	Did not obtain high school diploma at child age 5 months [b]	Did not obtain GCSE at 32 w. gestation [b, d]
Low paternal education	Did not obtain high school diploma at child age 5 months [c]	Did not obtain GCSE at 32 w. gestation [b, d]
Low socioeconomic status	<25th percentile - measured using a standardized aggregate index of five items relating to parental education, parental occupation, and annual gross income (Willms & Shields, 1996)	<25th percentile- derived from housing tenure, employment, education and social class (maternal and paternal) during pregnancy
Nonintact family	Biological father not living with study child and mother at child age 5 months [b]	Father or partner not living with study child and mother within one year of birth [b]
Low maternal age	<20 years old at childbirth [b]	<20 years old at childbirth [b]
Advanced paternal age	>35 years old at childbirth [c]	>35 years old at childbirth [c]
High birth order	4th or later born reported at child age 5 months [b]	4th or later born reported at 32 weeks of gestation [b]
Exposures during pregnancy		
Maternal smoking	Smoked tobacco during any trimester of pregnancy [b]	Smoked tobacco during any trimester of pregnancy [b]
Maternal alcohol use	>1 glass per week alcohol during any trimester of pregnancy at child age 5 months [b]	>1 glass per week alcohol use in 1st trimester and/or last 2 months of pregnancy [b]
Maternal drug use	Use of any illicit drug during pregnancy at child age 5 months [b]	Use of any of amphetamines, barbiturates, crack, cocaine, heroin, methadone, ecstasy, or other drug during pregnancy [b]
Maternal medication use	Use of any medication (prescribed and over-the-counter) during any trimester of pregnancy [b]	Use of any medication for any of nausea, heartburn, vomiting, anxiety, infection, migraine, difficulty with sleep, pain, allergies, skin conditions, bleeding, depression, piles, constipation, cough or other reason during pregnancy [b]
Parental mental health problems		
Maternal depression	CESD short (13-items) version >2.67 [b]	EPDS ≥13 [b]
Paternal depression	CESD short version >2.67 [c]	EPDS ≥13 at child age 8 months (partner-reported)
Maternal anxiety	Not available	CCEI ≥8 [b]
Paternal anxiety	Not available	CCEI ≥8 [c]
Maternal antisocial behavior	≥2 out of 5 conduct problems based on the DSM-IV criteria for conduct and antisocial personality disorders [b]	Not available
Paternal antisocial behavior	≥2 out of 5 conduct problems based on the DSM-IV criteria for conduct and antisocial personality disorders [c]	Not available

[a] From medical records; [b] Mother-reported; [c] Father/partner-reported; [d] collected at 32 weeks of gestation
Mother and father reports have been collected when the children were 5 months of age in QLSCD and 8 months of age in ALSPAC (where not otherwise specified).
APGAR: Appearance, Pulse, Grimace, Activity, and Respiration; CCEI: Crown Crisp Experiential Index; CESD: Centre for Epidemiological Study Depression Scale; DSM: Diagnostic and Statistical Manual of Mental Disorders; EPDS: Edinburgh Postnatal Depression Scale; GCSE: General Certificate of Secondary Education - age 16; ICD: International Classification of Diseases.

Table 2. Distribution of perinatal adversities in QLSCD and ALSPAC, and association with suicide attempt

Early-life adversity	QLSCD[a], N=1623				ALSPAC, N=5734				Combined[b], N=7357
	n (%) in the sample	n (%) by suicide attempt Yes 134 (8.3%)	No 1489 (91.7%)	OR (95% CI)	n (%) in the sample	n (%) by suicide attempt Yes 484 (8.4%)	No 5250 (91.6%)	OR (95% CI)	OR (95% CI)
Fetal growth adversities									
Short birth length	130 (8.7)	13 (10.4)	117 (8.5)	1.28 (0.72-2.13)	158 (4.3)	12 (4.1)	146 (4.3)	0.84 (0.45-1.56)	1.06 (0.71-1.59)
Low birth weight	51 (3.1)	<5 (3.7)	≥46 (≥3.0)	1.31 (0.50-2.87)	227 (4.0)	28 (5.9)	199 (3.8)	**1.57 (1.04-2.37)**	**1.52 (1.05-2.20)**
Short head circumference	133 (8.2)	17 (12.7)	116 (7.8)	**1.87 (1.10-3.04)**	349 (7.7)	37 (9.9)	312 (7.5)	1.17 (0.81-1.69)	1.43 (0.91-2.26)
Growth restriction	129 (8)	13 (9.7)	116 (7.8)	1.44 (0.79-2.45)	98 (2.8)	9 (2.8)	89 (2.8)	1.02 (0.51-2.04)	1.26 (0.81-1.95)
Prematurity	78 (4.8)	9 (6.7)	69 (4.6)	1.30 (0.59-2.51)	261 (4.6)	21 (4.3)	240 (4.6)	0.97 (0.61-1.53)	1.05 (0.72-1.55)
Pregnancy complications									
Mother hemorrhage	47 (2.9)	<5 (<3.7)	≥42 (≥2.8)	0.29 (0.04-1.06)	25 (0.8)	<5 (<1.6)	≥24 (≥0.8)	0.37 (0.05-2.77)	0.32 (0.09-1.11)
Mother hypertension	62 (3.8)	5 (3.7)	57 (3.8)	1.15 (0.46-2.44)	806 (14.4)	54 (11.5)	752 (14.7)	0.78 (0.58-1.05)	0.82 (0.62-1.08)
Mother diabetes	5 (0.3)	<5 (<3.7)	≤5 (≤0.3)	NA	32 (0.9)	5 (1.6)	27 (0.8)	1.93 (0.73-5.09)	1.93 (0.73-5.09)
Birth/delivery adversities									
Long hospitalization	130 (8.2)	9 (6.9)	121 (8.3)	0.93 (0.44-1.76)	1477 (44.3)	122 (40.7)	1355 (44.7)	0.88 (0.69-1.12)	0.89 (0.71-1.12)
Transfer hospital	24 (1.9)	<5 (<3.7)	≥19 (≥1.3)	0.36 (0.01-2.02)	319 (5.8)	30 (6.5)	289 (5.7)	1.24 (0.84-1.84)	1.15 (0.63-2.09)
low APGAR	25 (1.6)	<5 (<3.7)	≥19 (≥1.3)	1.65 (0.38-4.88)	28 (0.8)	<5 (<1.6)	≥24 (≥0.8)	1.91 (0.68-5.37)	1.80 (0.81-3.96)
Birth induction	495 (31.3)	43 (32.6)	452 (31.2)	1.04 (0.73-1.48)	656 (19.1)	56 (18.1)	600 (19.2)	0.99 (0.73-1.34)	1.01 (0.80-1.27)
Delivery acceleration	756 (51.9)	60 (52.2)	696 (51.9)	0.94 (0.66-1.34)	1982 (63.9)	177 (62.3)	1805 (64.0)	0.94 (0.73-1.22)	0.94 (0.77-1.16)
Caesarean section	242 (15)	17 (12.8)	225 (15.2)	0.82 (0.49-1.31)	581 (10.4)	51 (10.9)	530 (10.3)	1.07 (0.79-1.46)	0.99 (0.76-1.29)
Child hypoxia/asphyxia	154 (9.5)	13 (9.7)	141 (9.5)	1.13 (0.62-1.91)					
Socioeconomic adversities									
Low maternal education	273 (16.8)	26 (19.5)	247 (16.6)	1.42 (0.89-2.19)	1129 (20.3)	101 (21.6)	1028 (20.2)	1.04 (0.83-1.31)	1.14 (0.86-1.51)
Low paternal education	251 (16.8)	28 (23.9)	223 (16.2)	**1.81 (1.15-2.76)**	1341 (24.7)	128 (28.4)	1213 (24.4)	1.17 (0.94-1.45)	1.39 (0.91-2.11)
Low socioeconomic status	370 (23)	41 (31.1)	329 (22.3)	**1.76 (1.18-2.57)**	513 (14.1)	59 (20.2)	454 (13.6)	**1.56 (1.16-2.11)**	**1.64 (1.29-2.08)**
Nonintact family	300 (18.6)	34 (25.4)	266 (17.9)	**1.69 (1.13-2.48)**	343 (6.2)	53 (11.4)	290 (5.7)	**2.10 (1.54-2.87)**	**1.93 (1.51-2.47)**
Low maternal age	39 (2.4)	5 (3.7)	34 (2.3)	1.96 (0.59-5.01)	105 (1.8)	16 (3.3)	89 (1.7)	**1.85 (1.08-3.18)**	**1.87 (1.16-3.02)**
Advanced paternal age	444 (29.5)	23 (19.7)	421 (30.3)	0.57 (0.37-0.86)	804 (20.1)	84 (24.6)	720 (19.7)	**1.39 (1.07-1.81)**	0.91 (0.38-2.15)
High birth order	71 (4.4)	8 (6.0)	63 (4.2)	1.33 (0.59-2.65)	513 (9.2)	39 (8.3)	474 (9.3)	0.86 (0.61-1.21)	0.94 (0.66-1.34)
Exposures during pregnancy									
Maternal smoking	393 (24.3)	44 (33.8)	349 (23.5)	**1.86 (1.29-2.64)**	1050 (18.4)	143 (29.7)	907 (17.4)	**1.97 (1.60-2.43)**	**1.94 (1.62-2.32)**
Maternal alcohol use	622 (38.5)	46 (35.4)	576 (38.8)	0.85 (0.61-1.19)	1677 (29.6)	141 (29.6)	1536 (29.6)	1.04 (0.84-1.27)	0.98 (0.82-1.17)
Maternal drug use	22 (1.4)	<5 (<3.7)	≥19 (≥1.3)	2.59 (0.74-7.01)	284 (5.0)	28 (5.8)	256 (4.9)	1.19 (0.79-1.79)	1.48 (0.75-2.91)
Maternal medication use	1026 (63.6)	79 (60.8)	947 (63.9)	0.88 (0.63-1.24)	3711 (66.1)	328 (69.6)	3383 (65.8)	1.22 (0.99-1.49)	1.07 (0.79-1.45)
Parental mental health problems									
Maternal depression	222 (13.7)	24 (18.2)	198 (13.3)	1.47 (0.94-2.25)	403 (7.6)	52 (11.7)	351 (7.2)	**1.74 (1.27-2.37)**	**1.64 (1.27-2.12)**
Paternal depression	80 (5.7)	7 (6.4)	73 (5.7)	1.02 (0.44-2.04)	99 (2.6)	11 (3.4)	88 (2.5)	1.23 (0.65-2.33)	1.14 (0.70-1.85)
Maternal anxiety	NA	NA	NA	NA	1346 (25.2)	139 (31.2)	1207 (24.7)	**1.39 (1.12-1.72)**	**1.39 (1.12-1.72)**
Paternal anxiety	NA	NA	NA	NA	166 (4.3)	16 (4.9)	150 (4.2)	1.10 (0.64-1.89)	1.10 (0.64-1.89)
Maternal antisocial behavior	315 (20.2)	27 (21.3)	288 (20.1)	1.27 (0.83-1.88)	NA	NA	NA	NA	1.27 (0.85-1.91)
Paternal antisocial behavior	326 (23.4)	35 (32.1)	291 (22.7)	**1.94 (1.31-2.84)**	NA	NA	NA	NA	**1.93 (1.32-2.84)**

Odds Ratios (OR) are adjusted for sex and estimated using inverse probability weighing to account for attrition

Number below 5 and associated proportion have been rounded at <5 (data reporting rule to ensure confidentiality). This may contain zero.
NA, Not Available

Table 3. Direct and indirect effect of perinatal adversity profiles on suicide attempt in QLSCD, ALSPAC, and pooled estimates

Early-life adversity profile and mediator	QLSCD[a]			ALSPAC			Combined[b]		
	Direct effect OR (95%CI)	Indirect effect OR (95%CI)	% mediated	Direct effect OR (95%CI)	Indirect effect OR (95%CI)	% mediated	Direct effect OR (95%CI)	Indirect effect OR (95%CI)	% mediated
Poor fetal growth									
Emotional problems	2.64 (1.26-5.53)	1.08 (0.99-1.17)	7.1	1.45 (0.98-2.14)	1.04 (1.00-1.07)	9.1	1.79 (1.03-3.14)	1.04 (1.01-1.08)	6.5
Behavioral problems	2.65 (1.24-5.67)	1.07 (0.99-1.15)	6.0	1.46 (0.99-2.15)	1.03 (1.00-1.06)	3.0	1.79 (1.03-3.12)	1.03 (1.01-1.06)	5.3
Hyperactivity-impulsivity	2.55 (1.19-5.47)	1.11 (1.01-1.22)	10.0	1.43 (0.97-2.12)	1.05 (1.01-1.09)	12.0	1.74 (1.02-2.96)	1.06 (1.02-1.11)	9.2
Peer victimization	2.76 (1.29-5.88)	1.03 (0.98-1.10)	3.2	1.46 (0.99-2.15)	1.03 (0.99-1.06)	6.6	1.84 (1.01-3.36)	1.03 (1.00-1.06)	4.5
Cognitive skills	2.70 (1.28-5.67)	1.04 (0.97-1.12)	4.1	1.47 (1.00-2.17)	1.02 (0.98-1.06)	4.8	1.83 (1.04-3.23)	1.02 (0.99-1.06)	3.9
All mediators	2.46 (1.17-5.18)	1.15 (1.02-1.31)	13.7	1.39 (0.9- 2.06)	1.08 (1.02-1.15)	19.6	1.69 (0.99 2.88)	1.10 (1.04-1.16)	15.0
Socioeconomic adversity									
Emotional problems	1.58 (0.98-2.54)	1.13 (1.04-1.22)	20.5	1.27 (0.99-1.64)	1.03 (1.01-1.05)	10.2	1.33 (1.07-1.67)	1.07 (0.98-1.16)	17.9
Behavioral problems	1.58 (0.98-2.54)	1.13 (1.03-1.23)	20.7	1.26 (0.98-1.63)	1.04 (1.01-1.07)	4.0	1.33 (1.06-1.66)	1.07 (0.99-1.16)	19.5
Hyperactivity-impulsivity	1.57 (0.99-2.50)	1.13 (1.04-1.22)	20.8	1.23 (0.96-1.59)	1.07 (1.03-1.11)	23.4	1.30 (1.04-1.63)	1.08 (1.03-1.14)	22.3
Peer victimization	1.62 (1.01-2.58)	1.10 (1.03-1.18)	16.6	1.24 (0.97-1.60)	1.05 (1.02-1.08)	18.0	1.32 (1.06-1.65)	1.06 (1.02-1.11)	17.4
Cognitive skills	1.67 (1.03-2.68)	1.08 (0.97-1.20)	13.0	1.26 (0.97-1.64)	1.04 (0.97-1.12)	15.4	1.34 (1.07-1.69)	1.05 (0.99-1.12)	14.7
All mediators	1.43 (0.87-2.34	1.23 (1.07-1.43)	37.1	1.18 (0.91-1.53)	1.10 (1.02-1.19)	37.1	1.23 (0.97-1.55)	1.15 (1.03-1.28)	39.9
Parental mental health problems									
Emotional problems				1.67 (1.21-2.31)	1.03 (1.01-1.06)	6.1			
Behavioral problems				1.70 (1.24-2.33)	1.03 (1.00-1.05)	4.9			
Hyperactivity-impulsivity				1.67 (1.22-2.28)	1.05 (1.01-1.08)	8.3			
Peer victimization				1.70 (1.24-2.33)	1.03 (1.00-1.06)	4.7			
Cognitive skills				1.71 (1.25-2.35)	1.02 (0.99-1.04)	2.7			
All mediators				1.62 (1.18-2.23)	1.08 (1.03-1.13)	13.6			

[a]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
[b]Odds Ratios (OR) were pooled using inverse-variance weighted meta-analysis. The reference profile is *Low perinatal risk*.
The indirect is the association between perinatal adversity profiles and suicide attempt through mediators, while the direct effects is the association between perinatal adversity profiles and suicide attempt independently from (i.e., not explained by) the mediators.

Figure 1. Perinatal profiles identified using latent class analysis in QLSCD[a] and ALSPAC
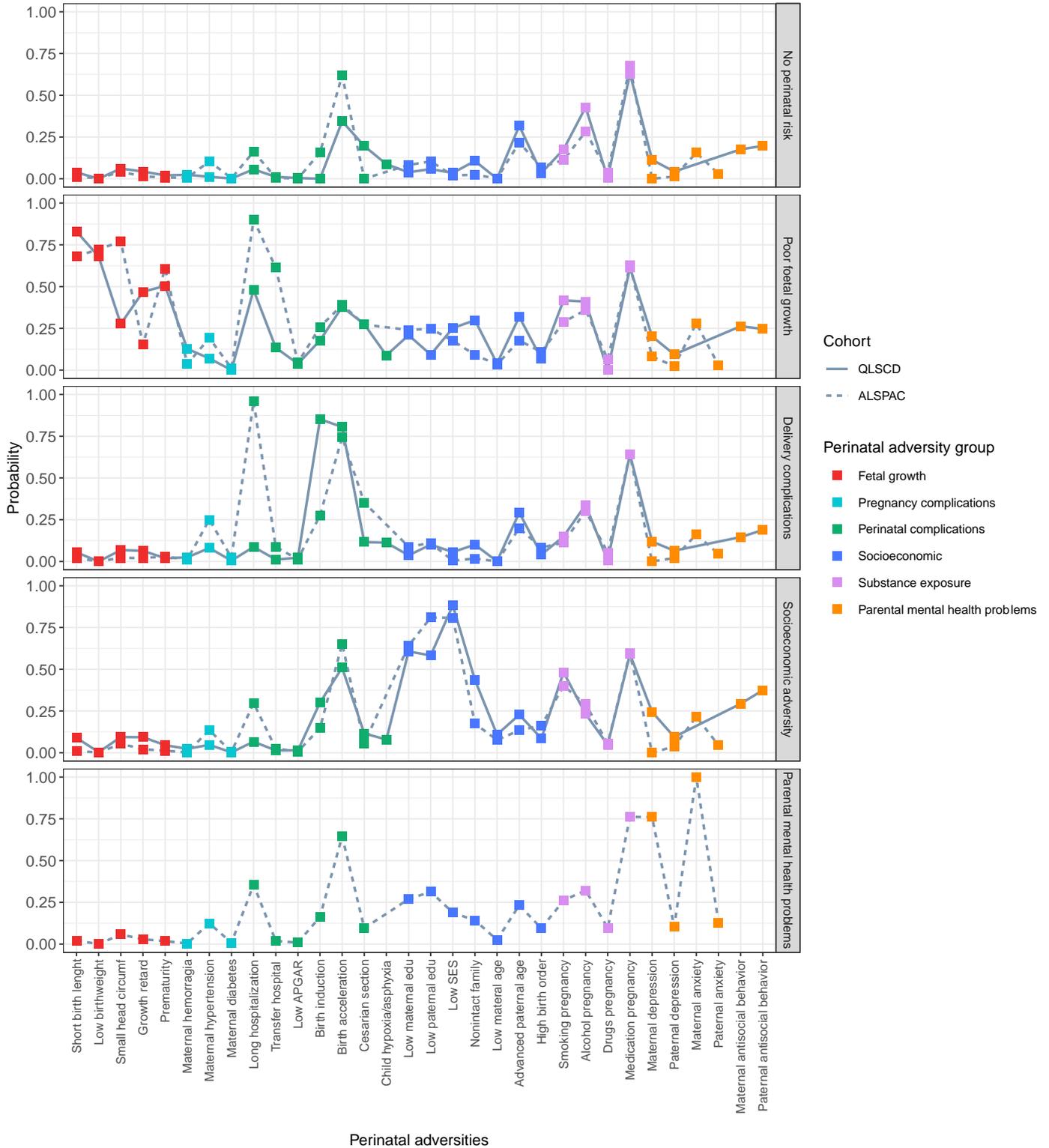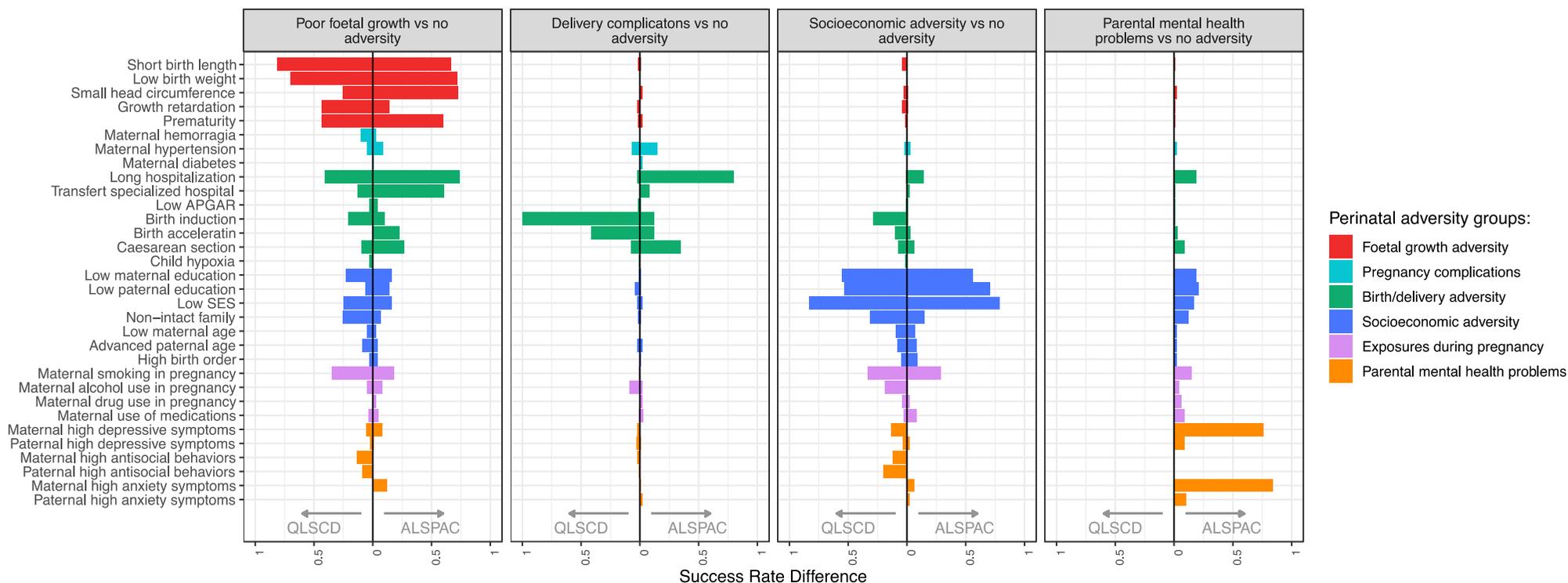

[a]Data were compiled from the final master file of the Québec Longitudinal Study of Child Development (1998–2018), ©Gouvernement du Québec, Institut de la statistique du Québec

Perinatal adversity profiles estimated using Latent Class Analysis in the Québec Longitudinal Study of Child Development (QLSCD, N=1623; solid lines) and in the Avon Longitudinal Study of Parents and Children (ALSPAC, N=5735; dotted lines). For each profile (indicated in the right-end panel label). The y-axis represents the estimated probability for each perinatal adversity (reported in the x-axis), that we color coded according to the groups of perinatal adversities. Entropy was 0.813 in QLSCD and 0.732 in ALSPAC.

SES, Socioeconomic status

Figure 2. Comparison between the prevalence of perinatal adversities in each adversity profile compared to the reference profile in QLSCD[a] and ALSPAC

For each perinatal adversity profile (panel), the figure shows the difference between the prevalence of each perinatal factor (y-axis) in each perinatal adversity profile vs. the reference profile (*Low perinatal risk* profile) in the Québec Longitudinal Study of Child Development (QLSCD, N=1623; left side of each panel) and in the Avon Longitudinal Study of Parents and Children (ALSPAC, N=5735; right side). Comparison of the prevalence was done using the Success Rate Difference (SRD), a measure of effect size computed as follows: SRD= (rate group 1 – rate reference group). For example, in QLSCD, the difference in short birth length rate between children in the *Poor fetal growth* profiles vs *No perinatal* risk profile was 81% (see first panel, left side), while for children in the *Socioeconomic adversity* profile, this difference was 4% (see third panel, left side). SES, Socioeconomic status

Perinatal adversity profiles and suicide attempt in adolescence and young adulthood: Longitudinal analyses from two 20-year birth cohort studies

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Table S1. Rate of each perinatal factor and sex in the analysis sample and in the nonincluded sample, for QLSCD[a] and ALSPAC

Variable	QLSCD [a]						ALSPAC					
	n (%) among included participants (max N=1623)		n (%) among non-included participants (max N=497)		*P*-value χ^2	Risk more common in analysis sample?	n (%) among included participants (max N=5765)		n (%) among non-included participants (max N=8023)		*P*-value χ^2	Risk more common in analysis sample?
	Yes	No	Yes	No			Yes	No	Yes	No		
Fetal growth adversities												
Short birth length	130 (8.7)	1368 (91.3)	43 (9.9)	392 (90.1)	0.583		163 (4.4)	3533 (95.6)	251 (5.4)	4424 (94.6)	0.045	No
Low birth weight	51 (3.1)	1571 (96.9)	20 (4.0)	477 (96.0)	1.000		240 (4.2)	5457 (95.8)	427 (5.4)	7490 (4.6)	0.002	No
Short head circumference	133 (8.2)	1490 (91.8)	39 (7.8)	458 (92.2)	0.070		360 (7.9)	4211 (92.1)	523 (8.8)	5445 (91.2)	0.103	
Growth restriction	129 (8.0)	1493 (92)	43 (8.7)	454 (91.3)	0.539		101 (2.9)	3435 (97.1)	188 (4.0)	4532 (96.0)	0.006	No
Prematurity	78 (4.8)	1545 (95.2)	26 (5.2)	471 (94.8)	0.385		275 (4.8)	5490 (95.2)	491 (6.1)	7532 (93.9)	0.001	No
Pregnancy complications												
Mother hemorrhage	47 (2.9)	1576 (97.1)	14 (2.8)	483 (97.2)	0.458		25 (0.8)	3312 (99.8)	46 (1.0)	4437 (99.0)	0.202	
Mother hypertension	62 (3.8)	1561 (96.2)	27 (5.4)	470 (94.6)	1.000		812 (14.5)	4804 (85.5)	1114 (14.5)	6550 (85.5)	0.901	
Mother diabetes	5 (0.3)	1618 (99.7)	<5 (<1.6)	<5 (<1.0)	NA		33 (0.9)	3503 (99.1)	53 (1.1)	4667 (98.9)	0.401	
Birth/delivery adversities												
Long hospitalization	130 (8.2)	1458 (91.8)	49 (10.5)	419 (89.5)	0.703		1477 (44.3)	1855 (55.7)	1804 (40.6)	2640 (59.4)	0.001	Yes
Transfer hospital	24 (1.9)	1224 (98.1)	6 (1.6)	376 (98.4)	0.738		326 (5.9)	5212 (94.1)	484 (7.4)	6040 (92.6)	0.001	No
low APGAR	25 (1.6)	1579 (98.4)	<5 (<1.6)	≥460 (≥98.0)	1.000		28 (0.8)	3360 (99.2)	84 (1.9)	4419 (98.1)	<0.001	No
Birth induction	495 (31.3)	1088 (68.7)	143 (30.6)	324 (69.4)	0.810		667 (19.3)	2798 (80.8)	916 (19.8)	3721 (80.3)	0.571	
Delivery acceleration	756 (51.9)	700 (48.1)	202 (49.3)	208 (50.7)	1.000		1994 (63.8)	1134 (36.3)	2777 (67.2)	1355 (32.8)	0.002	No
Caesarean section	242 (15)	1373 (85.0)	90 (19.0)	383 (81.0)	0.538		588 (10.4)	5050 (89.6)	834 (10.8)	6882 (89.2)	0.483	
Child hypoxia/asphyxia	154 (9.5)	1469 (90.5)	41 (8.2)	456 (91.8)	1.000							
Socioeconomic adversities												
Low maternal education	273 (16.8)	1348 (83.2)	112 (22.6)	384 (77.4)	0.453		1134 (20.3)	4452 (79.7)	2547 (38.2)	4118 (61.8)	<0.001	No
Low paternal education	251 (16.8)	1244 (83.2)	88 (20.1)	349 (79.9)	0.043	No	1348 (24.7)	4107 (75.3)	2723 (43.1)	3597 (56.9)	<0.001	No
Low socioeconomic status	370 (23)	1239 (77)	153 (31.5)	333 (68.5)	0.029	No	515 (14.1)	3138 (85.9)	1072 (30.1)	2492 (69.9)	<0.001	No
Nonintact family	300 (18.6)	1317 (81.4)	106 (21.4)	389 (78.6)	0.045	No	347 (6.2)	5219 (93.8)	838 (14.1)	5113 (85.9)	<0.001	No
Low maternal age	39 (2.4)	1583 (97.6)	20 (4)	477 (96)	0.452		105 (1.8)	5660 (98.2)	544 (6.8)	7479 (93.2)	<0.001	No

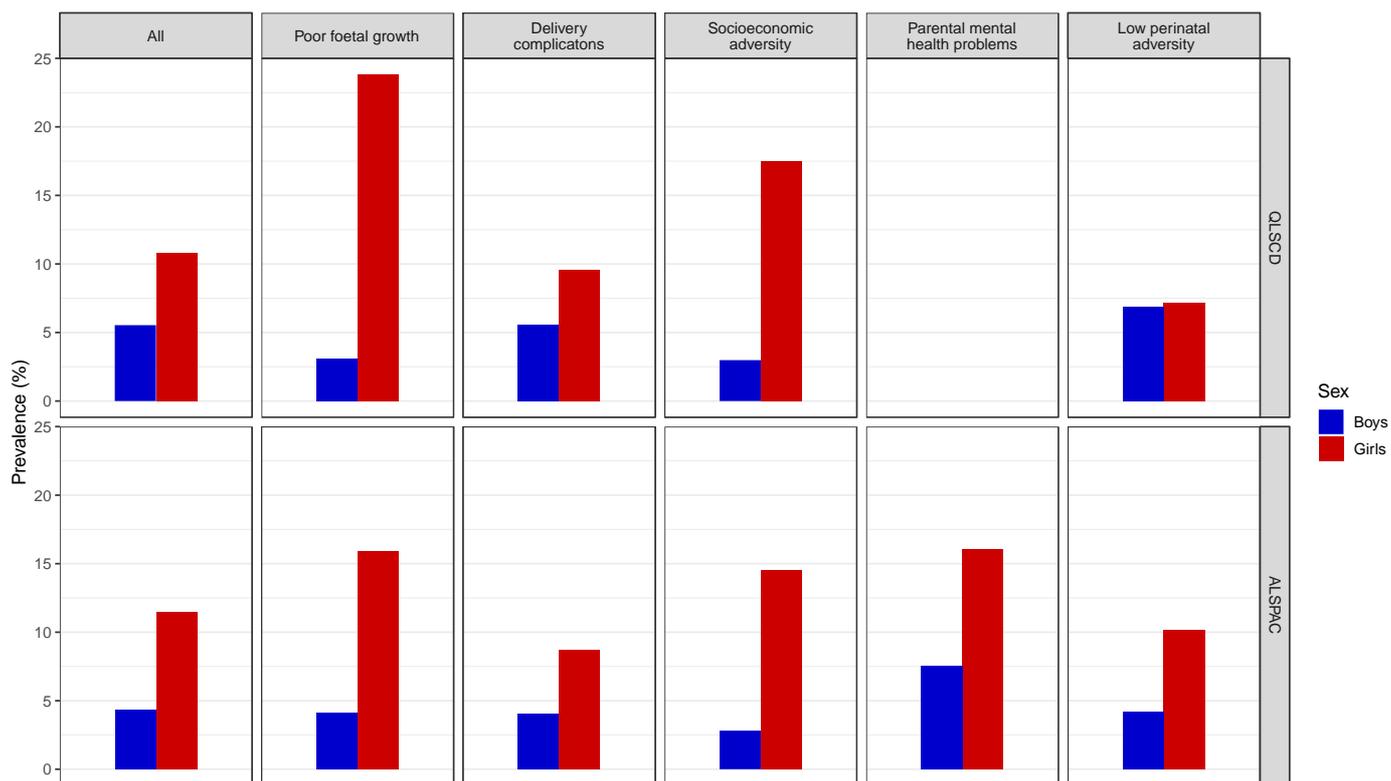|													
Advanced paternal age	444 (29.5)	1063 (70.5)	126 (28.4)	317 (71.6)	0.021	Yes	803 (20.0)	3214 (80.0)	581 (15.5)	3173 (84.5)	<0.001	Yes
High birth order	71 (4.4)	1552 (95.6)	86 (17.3)	411 (82.7)	0.945		515 (9.2)	5086 (90.8)	704 (10.5)	6010 (89.5)	0.017	No
Exposures during pregnancy												
Maternal smoking	393 (24.3)	1221 (75.7)	140 (28.2)	356 (71.8)	0.012	No	1056 (18.4)	4671 (81.6)	2487 (32.6)	5138 (67.4)	<0.001	No
Maternal alcohol use	622 (38.5)	992 (61.5)	130 (26.2)	366 (73.8)	0.499		1687 (29.6)	4012 (70.4)	3226 (41.7)	4513 (58.3)	<0.001	No
Maternal drug use	22 (1.4)	1592 (98.6)	8 (1.6)	488 (98.4)	0.566		288 (5.0)	5450 (95.0)	437 (5.7)	7241 (94.3)	0.088	
Maternal medication use	1026 (63.6)	586 (36.4)	288 (58.1)	208 (41.9)	0.538		3732 (66.2)	1909 (33.8)	4736 (65.5)	2498 (34.5)	0.413	
Parental mental health												
Maternal depression	222 (13.7)	1395 (86.3)	96 (19.4)	400 (80.6)	0.156		406 (7.6)	4957 (92.4)	562 (9.9)	5123 (90.1)	<0.001	No
Paternal depression	80 (5.7)	1315 (94.3)	28 (7.5)	347 (92.5)	0.935		99 (2.6)	3730 (97.4)	107 (3.4)	3058 (96.6)	0.05	No
Maternal anxiety							1354 (25.3)	4009 (74.8)	1679 (29.5)	4006 (70.5)	<0.001	No
Paternal anxiety							166 (4.3)	3705 (95.7)	157 (4.9)	3055 (95.1)	0.228	
Maternal antisocial behavior	315 (20.2)	1248 (79.8)	88 (19)	374 (81)	0.835							
Paternal antisocial behavior	326 (23.4)	1067 (76.6)	79 (21.4)	291 (78.6)	0.034	Yes						
Child sex (female)	845 (52.1)	778 (47.9)	195 (39.2)	302 (60.8)	<0.001	Yes	3356 (58.2)	2409 (41.8)	3311 (41.3)	4712 (58.7)	<0.001	Yes

[a]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
Number below 5 and associated proportion have been rounded at <5. This may contain zero.

Table S2. Assessment of behavioral, emotional, interpersonal problems and cognitive skills in QLSCD and ALSPAC

	QLSCD[a]	ALSPAC
Behavioral problems	**Assessment:** Assessed with the Social Behavioral Questionnaire. E.g., "get into many fights", "physically attack people" **Rating:** teacher-report **Time points (child age, y):** 6, 7, 8, 10, 12 **Number of items:** 9 (3-point scale) **Alpha range:** 0.87-0.88	**Assessment:** Assessed with the Strengths and Difficulties Questionnaires. E.g., "Often fights with other children or bullies them", "Picked on or bullied by other children" **Rating:** teacher-report **Time points (child age, y):** 7/8, 10/11 **Number of items:** 5 (3-point scale) **Alpha range:** 0.73-0.78
Hyperactivity/impulsivity	**Assessment:** Assessed with the Social Behavioral Questionnaire. E.g., "can't sit still, restless", "cannot stop fidgeting" **Rating:** teacher-report **Time points (child age, y):** 6, 7, 8, 10, 12 **Number of items:** 4 (3-point scale) **Alpha range:** 0.82-0.84	**Assessment:** Assessed with the Strengths and Difficulties Questionnaires E.g., "Restless, overactive, cannot stay still for long", "Fidgetiness, restlessness or overactivity" **Rating:** teacher-report **Time points (child age, y):** 7/8, 10/11 **Number of items:** 5 (3-point scale) **Alpha range:** 0.89-0.90
Emotional problems	**Assessment:** Assessed with the Social Behavioral Questionnaire. E.g., "not as happy as other children", "too fearful/anxious" **Rating:** teacher-report **Time points (child age, y):** 6, 7, 8, 10, 12 **Number of items:** 7 (3-point scale) **Alpha range:** 0.79-0.81	**Assessment:** Assessed with the Strengths and Difficulties Questionnaires E.g., "Often unhappy, depressed or tearful", "Many fears, easily scared" **Rating:** teacher-report **Time points (child age, y):** 7/8, 10/11 **Number of items:** 5 (3-point scale) **Alpha range:** 0.83-0.83
Peer victimization	**Assessment:** Self-report victimization scale (modified version) **Rating:** self-report **Time points (child age, y):** 6, 7, 8, 10, 12 **Number of items:** 7 (3-point scale) **Alpha range:** 0.70-0.80	**Assessment:** Assessed with the Bullying and Friendship Interview Schedule **Rating:** self-report **Time points (child age, y):** 7/8, 10/11 **Number of items:** 5 **Alpha range:** 0.59-0.61
Cognitive skills	**Assessment:** Peabody Picture Vocabulary Test **Rating:** direct assessment performed by a research professional **Time points (child age, y):** 4, 7, 10 **Number of items:** NA **Alpha range:** NA	**Assessment:** Wechsler Preschool & Primary Scale of Intelligence (full battery) and the Wechsler Intelligence Scale for Children (short form of the measure was employed where alternate items were used for all subtests, with the exception of the coding subtest which was administered in its full form) **Rating:** direct assessment performed by a research professional **Time points (child age, y):** 4, 8 **Number of items:** NA **Alpha range:** NA

[a]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

Figure S1. Prevalence of suicide attempt by profile and sex in QLSCD[a] and ALSPAC

[a]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