

This is a pre-copyedited, author-produced version of an article accepted for publication in Archives of Women's Mental Health following peer review. The version of record Ahun MN, Consoli A, Pingault JB, Falissard B, Battaglia M, Boivin M, Tremblay RE, Côté SM. Maternal depression symptoms and internalising problems in the offspring: the role of maternal and family factors. *Eur Child Adolesc Psychiatry*. 2018 Jul;27(7):921-932. doi: 10.1007/s00787-017-1096-6, is available online at: <https://doi.org/10.1007/s00787-017-1096-6>

Maternal depression symptoms and internalising problems in the offspring: the role of maternal and family factors

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BACKGROUND

Depressive and anxiety disorders are among the top ten leading causes of disability in the world [1, 2]. Children with high levels of internalising problems (i.e. depressive and anxiety symptoms) are twice as likely to suffer from depression as adults [3, 4], and are at significant risk for other problems such as substance use and abuse, suicidal behaviours, and premature death [5, 6]. Internalising problems (IP) during middle childhood are a significant public health issue given their relatively high prevalence (3-10% in middle childhood) [7], their tendency to increase with age [8], and their impact on child functioning and mental health in adolescence and young adulthood [4, 9, 10]. Maternal depression symptoms (MDS) have been identified as a risk factor for child psychopathology, including IP [11-15], with predictions extending into middle childhood [16], adolescence [17, 18] and early adulthood [19, 20]. However, it is not clear whether MDS per se are the main factors involved in the development of children's IP, or whether the maternal and family factors highly correlated with MDS are the main explanatory variables.

Other factors within the family of depressed mothers, such as mother-child interactions, parenting practices, family functioning, and socioeconomic factors have also been identified as potential risk factors for child psychopathology [14, 15]. First, with respect to mother-child interactions, depressed mothers tend to be less responsive to their child's emotional and affective states, and to express more anger, criticism and sadness than non-depressed mothers [21-23]. Second, families with a depressed mother differ from those of non-depressed mothers. Poor parenting practices, family conflicts, [21-26] and harsh discipline [27] were shown to be more prevalent among families with depressed

mothers. These factors also forecasted IP in children [28]. Accounting for mother-child interactions and/or parenting and family functioning could have an impact on the predictive association between MDS and children's IP.

Maternal depression symptoms also tend to co-occur with other psychopathology such as anxiety [29] and antisocial behaviours [30], and other forms of psychopathology could account for part of the association between MDS and child outcomes. For example, antisocial personality disorder symptoms in depressed mothers accounted for 18 to 29% of the effect of MDS on children's antisocial behaviours at ages 5 and 7 years [30]. Additionally, accounting for comorbid maternal mental health problems – and other contextual variables – attenuated the strength of the association between MDS and children's antisocial behaviour [31] and verbal abilities [32]. These results point to the importance of accounting for and addressing maternal comorbidity and its influence on child outcomes in MDS studies.

Previous studies provide evidence that associations between MDS and elevated levels of children's IP appear as early as the preschool years [33, 34]. Specifically, in a previous investigation, we found that child difficult temperament and maternal lifetime major depression at 5 months were associated with a high-rising (mother-rated) depression and anxiety symptom trajectory between 1½ and 5 years [33]. Recent studies have reported similar findings between MDS and membership in high IP trajectories in early childhood [35-37]. These studies rely on multiple assessments of child IP over time, a methodological strength which allows us to understand the development of symptoms. However, none of these studies accounted for a major methodological challenge in this line of research – the common rater bias.

The common rater bias has hampered the study of the associations between MDS and child outcomes in population-based samples. Population-based (non-clinical) studies typically rely on maternal ratings of both MDS and child behaviours and such ratings can be tainted by maternal depressive/negative cognitions [38]. Reliance on an additional source of evaluation may provide a better estimation. In non-clinical samples, teachers are often used as raters of children's behaviours as they have a good sense of normative versus atypical behaviours.

The objectives of the present study were 1) to identify a group of children with high levels of IP between 6 and 12 years using combined maternal and teacher assessments 2) to quantify the associations between trajectories of MDS during early childhood and children's internalising developmental trajectories before and after controlling for family factors associated with MDS.

METHODS

Participants

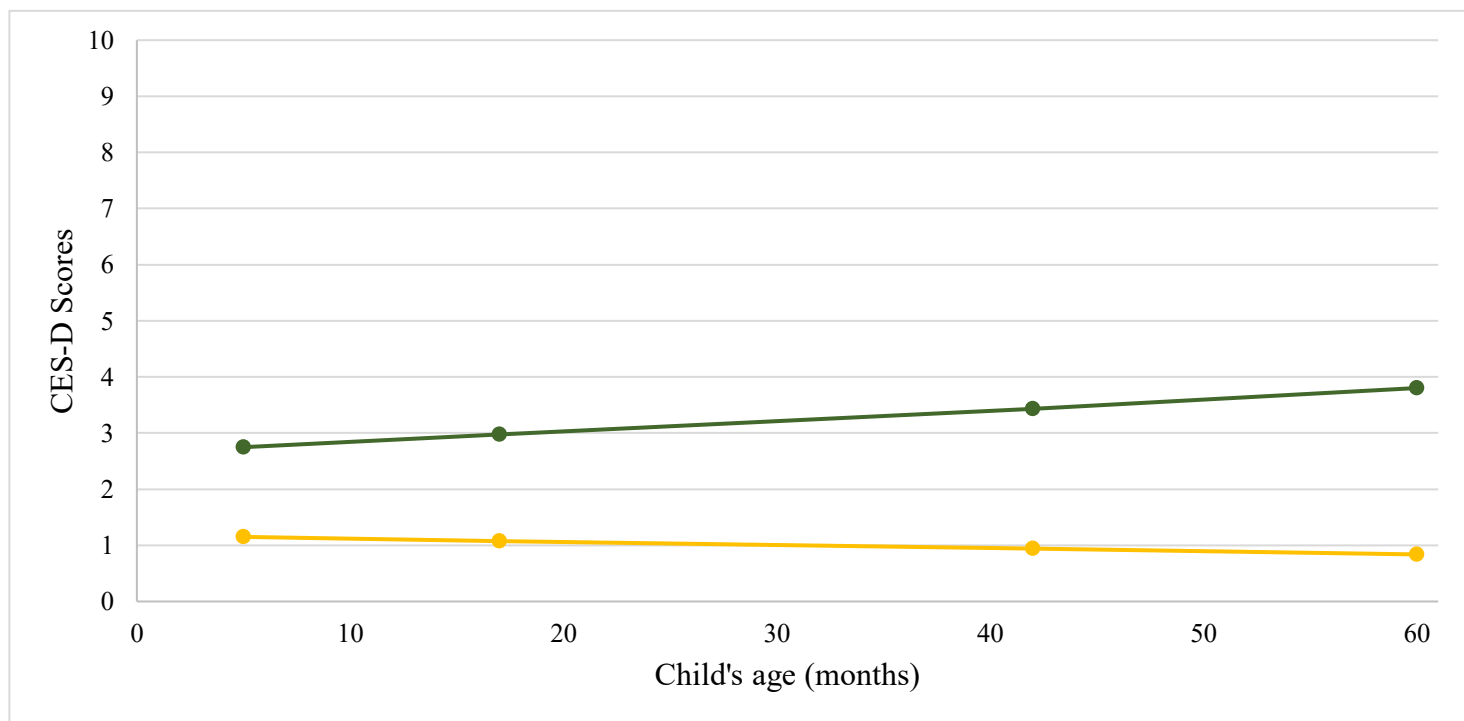
Data were drawn from the Quebec Longitudinal Study of Child Development, whose protocol was approved by the Quebec Institute of Statistics (Quebec City, Canada) and the Ste-Justine Hospital Research Centre (Montreal) ethics committees. Participants were selected via the Quebec Birth Registry using a stratified procedure based on living area and birth rate. The initial sample included a total of $n=2120$ infants representative of children born in the province of Quebec in 1997-1998 and followed yearly from 5 months to 7 years and every two years from 7 to 12 years. Informed written consent was obtained from all participants. Trained interviewers conducted home interviews with the mothers/fathers (and/or spouses) about family characteristics, parental, and child behaviours. The average response rate over 11 years of data collection was 82.22% (range:65.8%–100%). The study sample included $n=1537$ participants for whom the estimation of trajectories of depression and anxiety symptoms from 6 to 12 years-old was possible (data for at least one IP assessment by both informants). This sample was reduced to $n=1218$ in regression analyses due to missing data for confounders. Multiple imputation was used to test whether the results were sensitive to loss of confounder data [39]. The pattern of results with and without imputed data were similar, therefore only the former is reported. In our sample of $n=1537$, fifty-two percent (51.9%) of children were females, six percent (6.1%) came from single-mother homes, the majority of mothers were employed (71.8%) and were 21 years or older at the birth of the target child (94.3%) (Table 1).

Measures

Main exposure variable: maternal depression symptoms (MDS) in early childhood

MDS were assessed at 5 months, 1½, 3½ and 5 years using a short version of the Centre for Epidemiologic Studies Depression Scale (CES-D) [40]. Specifically, 5 to 12 CES-D questions were asked between 5 months and 5 years. Responses were converted to a score varying between 0 and 10. The CES-D is a valid and reliable measure of depressive symptoms assessing the occurrence and severity of depression symptoms during the previous week (e.g. “I felt alone”, “I felt depressed”, “I had the blues”, “what I did was an effort”). Response categories range between 0 (none) to 3 (all the time). Short versions of the CES-D are highly correlated with the original CES-D, and have been used in several studies [41]. A threshold of 2.67 (out of 10) was used to approximate the conventional cut-off (16/60) for elevated MDS from the original CES-D [42, 43]. To maximize our repeated measurements of MDS, we calculated trajectories using group-based trajectory modelling [44]. The estimation of MDS trajectories in this cohort has been previously reported [45]. The model had two trajectories of MDS: a high symptom group (18.3%) and low symptom group (81.7%). All mothers in the high symptom group had a CES-D score $\geq 2.67/10$. Membership to the high symptom trajectory was dummy-coded as 1 and membership in the low trajectory as 0. The two stable trajectories of MDS are presented in Figure 1.

Figure 1. Maternal depression symptoms trajectories (5 months – 5 years)



*This line represents a threshold of 2.67/10 on the short CES-D scale. It is the equivalent of the cut-off of 16/60 used to indicate elevated depressive symptoms on the full length CES-D scale.

Outcome: children's trajectories of internalising problems (IP) during the elementary school years rated by teachers and mothers.

When the children were aged 6, 7, 8, 10 and 12 years, their home room teacher was asked to rate whether the child never (0), sometimes (1) or often (2) exhibited the following IP (in the past 12 months): “unhappy, sad, depressed”, “not as happy as other children”, “has difficulties having fun”, “lack of energy”, “appears fearful or anxious”, “appears worried” and “is nervous or very tense”. Mother-reported IP were also assessed at ages 6 and 8 years. Items were added up to create a total score for each age which was then re-scaled to a range of 0 to 10. Children therefore had five teacher-rated and two mother-rated IP scores. These symptoms were selected from the Preschool Behaviour Questionnaire[46]. They have been used to assess anxious/depressed symptoms[47] in large population studies and shown adequate psychometric properties[48]. The internal consistencies ranged between 0.79 and 0.83 for teacher-reported symptoms and 0.68 and 0.69 for mother-reported symptoms.

To maximize our repeated measurements of child IP we estimated multi-group trajectories [49] of mother-reported and teacher-reported IP using group-based trajectory modelling [44]. For the purpose of the present study, we distinguished a group of children with high levels of IP according to both mother and teachers.

Putative confounding variables. The following variables are factors within the family environment that are associated with both the outcome (MDS) and exposure (children's IP) variables and have the potential to bias the association between them.

Mother-child interactions were observed at home by a trained research assistant at age 5 months using the Home Observation Measurement of the Environment [50]. Two

dimensions reflected the quality of mothers' early interactions with their infant: verbalisation (e.g. mother responds verbally to her child; mother expresses positive emotions to the child; mother praises her child, etc.) and stimulation (e.g. mother encourages progress of the child; mother uses educational toys/games).

Parenting. The Parental Cognitions and Conduct toward the Infant Scale PACOTIS [51] was used to assess maternal parenting practices at 5 months. The PACOTIS consists of six dimensions of parenting practices: self-efficacy (e.g. "I feel that I am able to calm my child"), parental impact (e.g. "I have little effect on the development of my child's personality"), coercion (e.g. "I have gotten angry at my child when he/she has been particularly difficult"), affection (e.g. "I often play with my child. For example, I regularly take time to have fun with him/her"), overprotection (e.g. "I want my baby to be close to me at all times"), perception of child's qualities (e.g. "I feel that my child is very curious compared to other children"). Responses to each item ranged from 0 (not at all what I think or did) to 10 (exactly what I think or did), with higher scores indicating greater endorsement of a given parenting dimension.

Family functioning. The General Functioning scale (a sub-scale of the McMaster Family Assessment Device) is a validated instrument completed by the parents at baseline and including 8 items measuring how well the family operates on a daily basis (e.g. planning family activities is difficult because we misunderstand each other, in times of crisis we can turn to each other for support)[52] . Responses to each item range from 1 (totally agree) to 4 (totally disagree). Scores from all items are summed up (positive items are reverse-coded) and re-scaled to produce a final overall score on a range from 0 to 10. Higher values indicate higher levels of relationship difficulties in the family.

Maternal anxiety and antisocial behaviours. To isolate the role of MDS in children's IP, we controlled for two main types of maternal psychopathology symptoms that may co-occur with MDS. General, trait-like maternal anxiety was assessed when the target child was 4½ years using validated items inspired by DSM-IV criteria[53]. The reliability coefficient of these items was 0.87. The presence of maternal antisocial behaviours in adolescence was assessed via a questionnaire to the mother when the child was 5 months. Mothers were asked whether they had exhibited five different conduct problems [54]. The scale ranged from 0 to 5 and the internal consistency of items was 0.33.

Child and family characteristics. Child sex, and mother-rated difficult temperament at 5 months were considered as potential control variables[8]. Child temperament was assessed with items from the difficult temperament scale of the well-validated Infant Characteristics Questionnaire ICQ [55]. Internal consistency of items was 0.80.

Socio-economic status (SES) of the family was derived from five variables including maternal education (years of schooling), spouse's education and occupational status, maternal occupational status and household income. The final SES composite was standardised for all families (mean = 0, SD = 1) .[56]

Family status at 5 months was coded as 1 for single-parent families and 0 for biparental families (including blended families). The age of the mother was treated as a binary variable reflecting 21 years or younger at the birth of the target child (0) or older than 21 years (1). Becoming a mother before age 21 was previously shown to be a valid indicator of risk in the Québec population [57]. The mother's professional activity at baseline was coded as 0 for mother has a job (full time or part-time) and 0 for not.

Data analyses

Data analyses included 2 steps. In the first, we estimated multi-group trajectories of mother and teacher IP ratings. In the second, we estimated regression models of the association between MDS trajectories and child IP trajectories.

We used group-based trajectory modeling [44], a statistical method designed to identify groups of individuals that are following similar trajectories based on a single outcome variable. Multi-trajectory modeling [49] extends the basic model by defining trajectory groups in terms of multiple outcome variables. Both the basic model and the multi-trajectory generalisation are applications of finite mixture modeling. The multi-trajectory method applied here combined the trajectories of IP based on maternal reports (6 to 8 years) with trajectories of IP based on teacher reports (from age 6 to 13 years). Thus, the multi-trajectories are the product of combined estimation procedures for each group's trajectories across both raters. Two criteria were used to determine the number of groups to include in the multi-trajectory modeling, BIC and substantive significance [44].

Multinomial logistic regression models were used to estimate the association between MDS and children's IP while controlling for family factors and other confounders. We selected putative confounders on the basis of a) previous literature indicating a link between a given risk factor and children's IP and b) epidemiological guidelines for modelling longitudinal data, whereby potential confounders are selected at baseline and not at subsequent time points [58, 59]. 2. Two models were estimated: (I) testing the unadjusted association between MDS trajectory and childhood IP trajectory and (II) including confounders in a subsequent model.

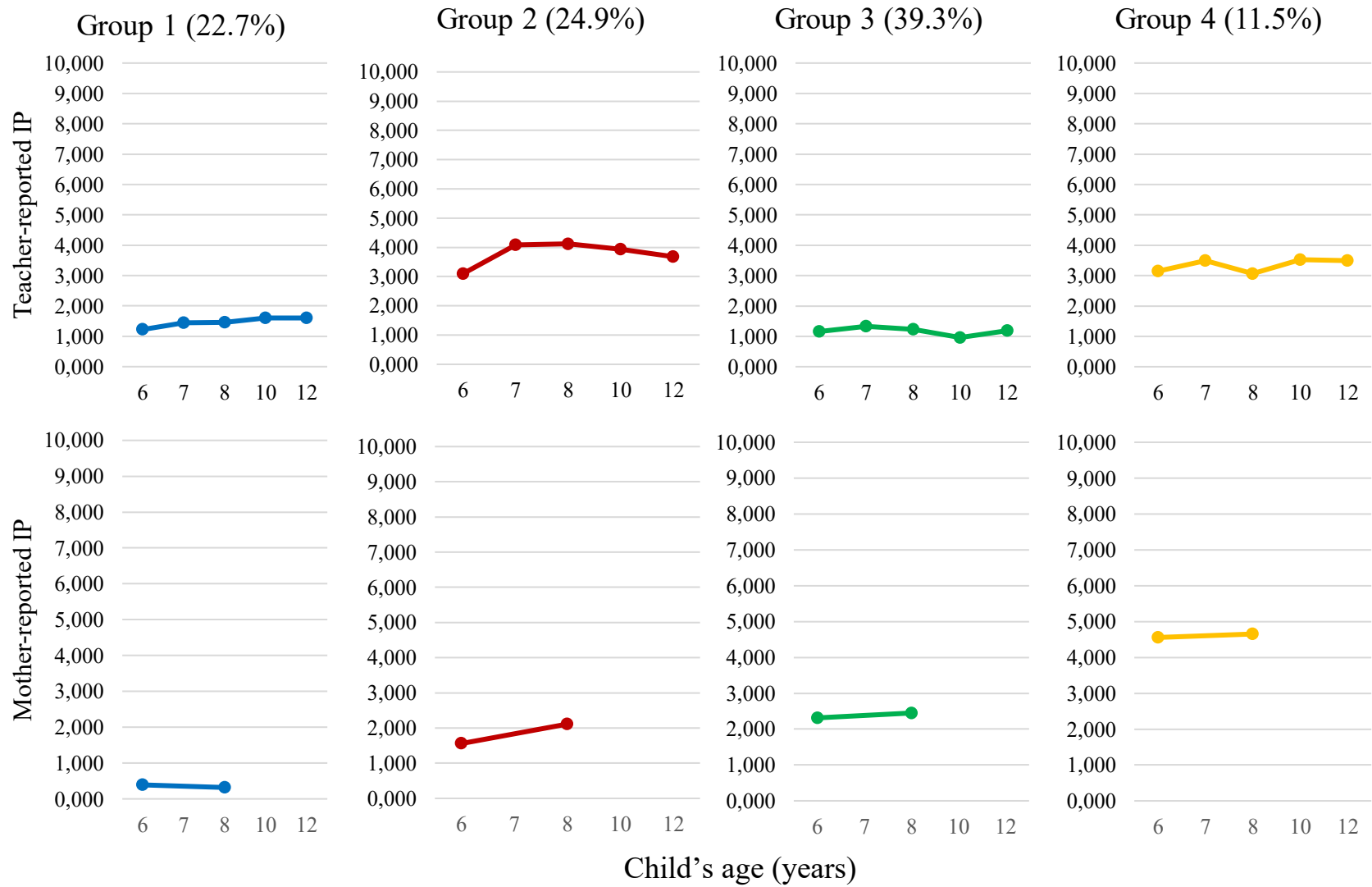
To account for attrition, we estimated the regression analyses using the fully conditional specification (FCS) imputation method [39] (number of imputations = 10) in the n=1537 sample to address missing data in confounders. Imputation was based on the assumption that data were missing at random. We also repeated analysis on a data set without imputation. We report only results obtained on the imputed data sets.

RESULTS

Multi-group trajectories of mother and teacher rated internalising problems (IP).

We identified 4 groups of children following distinct IP trajectories: 1) low IP by both mothers and teachers (low; 22.8%), 2) high IP by teachers and increasing IP by mothers (high-increasing; 24.5%), 3) low IP by teachers and moderate by mothers (low-moderate; 41.3%), and 4) high by both mothers and teachers (high; 11.5%). The trajectories of IP are presented in figure 2.

Figure 2. Multi-trajectory model of teacher- and mother-reported internalizing problems in middle childhood (6-12 years).



Multinomial logistic regression models estimating the association between maternal depression symptoms (MDS) and children's internalising problems (IP).

Selection of confounding variables. Table 1 presents the bivariate associations between childhood IP trajectory groups and study variables. Child's sex, levels of MDS, maternal psychopathology (anxiety and antisocial behaviour), stimulation in mother-child interactions, maternal overprotection and perception of parental impact, whether or not the mother was employed, socioeconomic status, and family functioning differed significantly across childhood IP trajectory groups. Specifically, compared to children in the 3 lowest IP trajectory groups, children in the high IP trajectory group were more likely to: be exposed to MDS (32.2%) and to high levels of maternal anxiety, come from a low SES family, have an unemployed mother (38.4%), live in families with the highest reported levels of family dysfunction, have lower levels of stimulating interactions with their mother (e.g. encouraging progress of child), and to be exposed to mothers who exhibited more antisocial behaviours during their youth, were overprotective, and were less likely to believe that their actions had an impact on their child's development.

Table 1. Sample characteristics according to teacher- and mother-reported childhood internalising problems (IP) trajectory groups

Variable [n, (%)] or [mean (SD)]	Children's Internalising problems (IP) Trajectory Group between 6 and 12 years				Total sample (n=1537)	p-value on χ^2 test or ANOVA F-test
	Low (n=350 22.8%)	High-increasing (n=376 24.5%)	Low-high (n=634 41.3%)	High (n=177 11.5%)		
Child Characteristics						
Sex [n, (%)]						0.006
<i>Boys</i>	166(22.4)	206(27.8)	271(36.7)	97(13.1)	740(48.1)	
<i>Girls</i>	184(23.1)	170(21.3)	363(45.6)	80(10.0)	797(51.9)	
Difficult temperament [mean (SD)]	2.62(1.6)	2.74(1.6)	2.67(1.5)	2.88(1.7)	2.70 (1.6)	0.310
Maternal Characteristics						
Maternal depression symptoms [n, (%)]						<.0001
<i>Low</i>	314 (25.0)	299 (23.8)	523 (41.6)	120 (9.6)	1256 (81.7)	
<i>High</i>	36 (12.8)	77 (27.4)	111 (39.5)	57 (20.3)	281 (18.3)	
Age at birth [n, (%)]						0.192
< 21 years-old	14(15.9)	29(33.0)	35(39.8)	10(11.4)	88(5.73)	

≥ 21 years old	336(23.2)	347(23.9)	599(41.3)	167(11.5)	1449(94.3)	
Maternal anxiety [mean (SD)]	0.95(1.0)	1.38(1.3)	1.27(1.2)	1.84(1.4)	1.28 (1.3)	<.0001
Maternal youth antisocial behavior [mean (SD)]	0.69(0.9)	0.86(1.0)	0.84(0.9)	0.83(0.9)	0.81 (0.9)	0.046
Mother-child interaction [mean (SD)]						
<i>Stimulation</i>	4.80(2.3)	4.45(2.4)	4.95(2.3)	4.91(2.4)	4.79 (2.4)	0.021
<i>Verbalization</i>	6.72(1.6)	6.54(1.7)	6.79(1.5)	6.85(1.6)	6.72 (1.6)	0.100
Parenting practices [mean (SD)]						
<i>Self-efficacy</i>	9.03(0.9)	9.01(1.0)	8.99(0.9)	8.85(1.0)	8.99 (0.9)	0.234
<i>Parental Impact</i>	8.43(1.8)	8.23(1.8)	8.61(1.7)	8.29(2.0)	8.44 (1.8)	0.008
<i>Coercion</i>	1.03(1.2)	1.12(1.3)	1.00(1.1)	1.21(1.1)	1.06 (1.2)	0.142
<i>Affection</i>	9.66(1.6)	9.69(0.7)	9.67(0.7)	9.70(0.8)	9.68 (0.7)	0.918
<i>Overprotection</i>	4.41(2.2)	4.89(2.2)	4.43(2.2)	4.84(2.2)	4.58 (2.2)	0.002
<i>Perception of child</i>	7.90(1.6)	7.91(1.8)	8.01(1.7)	7.99(1.5)	7.96 (1.7)	0.723
Maternal employment [n, (%)]						<.0001
<i>Yes</i>	89(20.7)	129(30.0)	144(33.5)	68(15.8)	430(28.3)	
<i>No</i>	261(23.9)	239(21.9)	484(44.3)	108(9.9)	1092(71.8)	

Family Environment Characteristics

Family status [n, (%)]						0.878
<i>Intact</i>	329(22.8)	348(24.2)	598(41.5)	165(11.5)	1440(94.9)	
<i>Single-mother</i>	21(22.3)	26(27.7)	36(38.3)	11(11.7)	94(6.1)	
Socioeconomic Status [mean (SD)]	0.15(1.0)	-0.17(0.9)	0.21(1.0)	-0.19(1.0)	0.05 (1.0)	<.0001
Family functioning [mean (SD)]	1.52(1.4)	1.77(1.4)	1.68(1.5)	1.88(1.3)	1.69 (1.4)	0.024

After adjusting for confounders – child’s sex and temperament, maternal anxiety, antisocial behaviour, age at child’s birth, and parenting practices, family SES, status (single-mother vs intact), dysfunction, and mother-child interactions – children in the high IP group were more likely to have mothers with higher levels of MDS compared to those in the low, high-increasing, and low-moderate groups. Children rated as high IP by both mothers and teachers were also more likely to be exposed to higher levels of maternal anxiety and to have mothers who reported lower levels of self-efficacy in their parenting skills. The adjusted odds ratios and their 95% confidence intervals comparing the high group (reference) to all other IP groups are presented in Table 2.

Table 2. Multinomial logistic regression model of the association between maternal depression symptoms trajectories (0 to 5 years) and membership in children’s mother-reported and teacher-reported internalising problems groups (6 to 12 years) adjusted for covariates (n=1537).

Exposure Variable	Child internalising problems group		
	<u>Low</u>	<u>High-Increasing</u>	<u>Low-Moderate</u>
Maternal depression symptoms (high)	2.60 [1.55;4.36]	1.60 [1.02;2.51]	1.60[1.04;2.44]
Confounders			
Child’s sex (boys)	1.21 [0.83;1.76]	0.94 [0.65;1.36]	1.55 [1.10;2.19]
Child difficult temperament (high)	1.06 [0.94;1.20]	1.03 [0.91;1.15]	1.05 [0.94;1.18]
Mother age at birth (< 21 years)	1.17 [0.46;2.93]	0.81 [0.36;1.83]	0.66 [0.30;1.47]
Maternal anxiety (high)	1.52 [1.29;1.80]	1.22 [1.05;1.40]	1.16 [1.01;1.32]
Maternal antisocial behaviour (high)	1.09 [0.88;1.35]	0.95 [0.78;1.17]	0.90 [0.74;1.09]
Stimulation (low)	1.01 [0.92;1.12]	1.06 [0.96;1.17]	0.99 [0.91;1.09]
Verbalisation (low)	1.09 [0.94;1.27]	1.07 [0.93;1.25]	1.09 [0.94;1.25]
Self-efficacy (high)	0.77 [0.60;0.99]	0.81 [0.64;1.03]	0.80 [0.64;1.01]

Parental impact (high)	1.04 [0.93;1.16]	1.03 [0.93;1.14]	0.96 [0.87;1.07]
Coercion (high)	0.99 [0.83;1.17]	1.00 [0.85;1.17]	1.08 [0.93;1.27]
Affection (low)	1.33 [0.95;1.87]	1.17 [0.84;1.63]	1.28 [0.93;1.76]
Overprotection (high)	1.00 [0.91;1.10]	0.97 [0.88;1.06]	1.01 [0.92;1.10]
Perception of child's qualities (high)	1.06 [0.93;1.21]	1.05 [0.93;1.19]	1.03 [0.91;1.16]
Maternal employment (no)	1.34 [0.83;2.19]	1.26 [0.79;2.00]	1.51 [0.97;2.35]
Family status (intact)	0.59 [0.26;1.34]	0.83 [0.38;1.81]	0.69 [0.32;1.45]
High SES	0.84 [0.65;1.10]	1.03 [0.79;1.34]	0.73 [0.57;0.94]
Family dysfunction (high)	1.04 [0.90; 1.20]	1.00 [0.87;1.15]	0.98 [0.86;1.12]

DISCUSSION

We used a 12-year longitudinal investigation of a population-based sample ($n=1537$) to determine whether there was a distinctive contribution of maternal depression symptoms (MDS) in early childhood (5 months to 5 years) to membership in a high trajectory of offspring's internalising problems (IP) during middle childhood (6 to 12 years) while controlling for family variables (e.g. parenting, mother-child interactions). Using both teachers' and mothers' assessments of child IP between 6 and 12 years, we identified 4 trajectory groups: 1) low IP by both mothers and teachers (low; 22.8%), 2) high IP by teachers and increasing IP by mothers (high-increasing; 24.5%), 3) low IP by teachers and moderate by mothers (low-moderate; 41.3%), and 4) high by both mothers and teachers (high; 11.5%). This method enabled us to track the development of IP across middle childhood in the home and school environments and to assess how exposure to MDS influenced changes in IP during this time period.

We found that MDS were the main contributors to membership in the high IP trajectory group, even after adjusting for family factors which have been identified as modifiable determinants of child psychopathology. Specifically, children with high levels of mother and teacher reported IP were more likely to have been exposed to MDS than children with low levels of IP. Children in the high group were also exposed to higher levels of maternal anxiety and poorer parenting practices (i.e. perceived self-efficacy in parenting practices). This latter finding supports previous research which suggests that maladaptive parenting practices and exposure to other forms of maternal psychopathology also contribute to the development of IP in the offspring [15, 30]. Overall, these results are in line with earlier studies reporting associations between MDS and elevated levels of

children's IP in early childhood [33-37], but ours is the first study to find this association using IP data from two independent informants.

Our results highlight the importance of being attentive to comorbidity of maternal mental health issues in the prevention of children's IP. Targeting maternal psychopathology and improving the quality of parenting practices, particularly perceived self-efficacy, may represent a promising target for family-based prevention programs. In a family-based randomised controlled intervention including 8-15 years children whose parents were suffering from mood disorders, targeting parent-child interactions and increasing understanding of self and parental illness proved to be useful [60]. Beyond the treatment of maternal psychopathology, the results suggest that a promising intervention strategy should support depressed mothers to improve early parenting processes.

Limitations and strengths

This study presents a number of important strengths. First, it relies on analyses of a large population-based birth cohort with detailed and repeated assessments of the main variables, i.e., yearly IP assessments from 6 to 12 years-old by teachers, combined with two maternal assessments at 6 and 8 years; and 4 repeated assessments of MDS between 5 months and 5 years. The use of repeated assessments allowed us to model group-based developmental trajectories of MDS and IP – a valuable analytical method for examining how exposures and outcomes change over time. Second, distinct informants were used for assessment of different family variables (i.e. research assistant observers of mother child interaction, interviews with the mothers). Furthermore, children's IP were assessed by teachers and mothers. This helped to reduce the impact of the common rater bias and to capture differences in the exhibition of depression and anxiety symptoms at home and at

school. Teachers were independent raters (different teacher every year) with a good sense of normative behaviours. Despite the potential bias of relying on mothers to rate her child's internalising symptoms [61], using mother-report enabled us to account for the exhibition of symptoms in the home environment. Third, we accounted for carefully chosen risk factors which correlated with MDS and children's IP and could confound the associations between them. For instance, we controlled for maternal anxiety and antisocial behaviour, two types of symptoms highly co-morbid with MDS and associated with children's socio-emotional development [15, 30, 31]. Furthermore, the association between exposure to high levels of MDS and children's IP was still significant in sensitivity analyses, supporting the robustness of results.

The study is limited by a number of factors. First, we used maternal ratings of MDS to predict maternal ratings of children's IP which could have biased the results. We minimised the influence of this potential bias by including teachers' independent rating of IP as an additional outcome. Our results showed that children rated as having high IP by mothers were also rated as high by their teachers, indicating that these children were consistently exhibiting high levels of depression and anxiety symptoms across different environments. Second, although our models include information on maternal comorbid conditions, quality of the mother child relationship, and socioeconomic conditions, we cannot rule out the possibility that unmeasured environmental or genetic risk factors explain part of the associations. Genetically informative studies are needed to disentangle the role of genetic from environmental factors in the mechanism linking MDS to children's psychopathology.

In addition, studies investigating whether a) treatment of MDS or b) intervention

aiming at modifying maternal parenting practices modify children's emotional development would provide information on the putatively causal role of MDS and its related behaviours. In light of the present evidence, as well as that from previous studies on the associations between MDS and child internalising and externalising problems, developing interventions aimed at treating maternal psychopathology and buffering its effects on child development appear to be crucial [62]. Finally, we have chosen to focus here on maternal psychopathology, but further studies including fathers' psychopathology could shed light on the joint contribution of symptoms among both parents [63].

CONCLUSION

Maternal depression symptoms during early childhood were related to an increased risk of mother and teacher-reported internalising problems during middle childhood (6 to 12 years) after accounting for maternal psychopathology, parenting, and family functioning in early childhood. Maternal anxiety and parenting are important factors in the family environment which are also associated with children's internalising problems. Experimental studies testing the role of distinct and joint treatment components – reducing maternal psychopathology and/or improving the quality of parenting – would provide information on the putatively causal role of these risk factors on offspring's internalising problems.

REFERENCES

1. Lopez, A.D. and C.C. Murray, *The global burden of disease, 1990-2020*. Nat Med, 1998. **4**(11): p. 1241-3.
2. Murray, C.J. and A.D. Lopez, *Global mortality, disability, and the contribution of risk factors: Global Burden of Disease Study*. Lancet, 1997. **349**(9063): p. 1436-42.
3. Bittner, A., et al., *What do childhood anxiety disorders predict?* J Child Psychol Psychiatry, 2007. **48**(12): p. 1174-83.
4. Roza, S.J., et al., *Stable prediction of mood and anxiety disorders based on behavioral and emotional problems in childhood: a 14-year follow-up during childhood, adolescence, and young adulthood*. Am J Psychiatry, 2003. **160**(12): p. 2116-21.
5. Briggs-Gowan, M.J., et al., *Prevalence of social-emotional and behavioral problems in a community sample of 1- and 2-year-old children*. J Am Acad Child Adolesc Psychiatry, 2001. **40**(7): p. 811-9.
6. Weissman, M.M., et al., *Children with prepubertal-onset major depressive disorder and anxiety grown up*. Arch Gen Psychiatry, 1999. **56**(9): p. 794-801.
7. Egger, H.L. and A. Angold, *Common emotional and behavioral disorders in preschool children: presentation, nosology, and epidemiology*. J Child Psychol Psychiatry, 2006. **47**(3-4): p. 313-37.
8. Cote, S.M., et al., *Depression and anxiety symptoms: onset, developmental course and risk factors during early childhood*. J Child Psychol Psychiatry, 2009. **50**(10): p. 1201-8.
9. Angold, A., *Childhood and adolescent depression. I. Epidemiological and aetiological aspects*. Br J Psychiatry, 1988. **152**: p. 601-17.
10. Copeland, W.E., et al., *Longitudinal patterns of anxiety from childhood to adulthood: the Great Smoky Mountains Study*. J Am Acad Child Adolesc Psychiatry, 2014. **53**(1): p. 21-33.
11. Weissman, M.M., et al., *Offspring of depressed parents: 20 years later*. Am J Psychiatry, 2006. **163**(6): p. 1001-8.
12. Barker, E.D., *The duration and timing of maternal depression as a moderator of the relationship between dependent interpersonal stress, contextual risk and early child dysregulation*. Psychol Med, 2012. **43**(8): p. 1587-96.
13. Hirshfeld-Becker, D.R., et al., *Psychopathology in adolescent offspring of parents with panic disorder, major depression, or both: a 10-year follow-up*. Am J Psychiatry, 2012. **169**(11): p. 1175-84.
14. Barker, E.D., et al., *Relative impact of maternal depression and associated risk factors on offspring psychopathology*. Br J Psychiatry, 2012. **200**(2): p. 124-9.
15. Goodman, S.H., et al., *Maternal depression and child psychopathology: A meta-analytic review*. Clinical Child and Family Psychology Review, 2011. **14**(1): p. 1-27.
16. Verkuyl, N., et al., *Postnatal depressive symptoms and child psychological development at 10 years: a prospective study of longitudinal data from the South African Birth to Twenty cohort*. Lancet Psychiatry, 2014: p. on line.

17. Halligan, S.L., et al., *Maternal depression and psychiatric outcomes in adolescent offspring: a 13-year longitudinal study*. J Affect Disord, 2007. **97**(1-3): p. 145-54.
18. Murray, L., et al., *Maternal postnatal depression and the development of depression in offspring up to 16 years of age*. J Am Acad Child Adolesc Psychiatry, 2011. **50**(5): p. 460-70.
19. Hammen, C., et al., *Intergenerational transmission and continuity of stress and depression: depressed women and their offspring in 20 years of follow-up*. Psychol Med, 2012. **42**(5): p. 931-42.
20. Pearson, R.M., et al., *Maternal depression during pregnancy and the postnatal period: risks and possible mechanisms for offspring depression at age 18 years*. JAMA Psychiatry, 2013. **70**(12): p. 1312-9.
21. Silk, J.S., et al., *Expressed emotion in mothers of currently depressed, remitted, high-risk, and low-risk youth: links to child depression status and longitudinal course*. J Clin Child Adolesc Psychol, 2009. **38**(1): p. 36-47.
22. Toth, S.L., et al., *The efficacy of toddler-parent psychotherapy to reorganize attachment in the young offspring of mothers with major depressive disorder: a randomized preventive trial*. J Consult Clin Psychol, 2006. **74**(6): p. 1006-16.
23. Goodman, S.H. and I.H. Gotlib, *Risk for psychopathology in the children of depressed mothers: a developmental model for understanding mechanisms of transmission*. Psychol Rev, 1999. **106**(3): p. 458-90.
24. Leckman-Westin, E., P.R. Cohen, and A. Stueve, *Maternal depression and mother-child interaction patterns: association with toddler problems and continuity of effects to late childhood*. J Child Psychol Psychiatry, 2009. **50**(9): p. 1176-84.
25. Stein, D., et al., *Parent-child bonding and family functioning in depressed children and children at high risk and low risk for future depression*. J Am Acad Child Adolesc Psychiatry, 2000. **39**(11): p. 1387-95.
26. Downey, G. and J.C. Coyne, *Children of depressed parents: an integrative review*. Psychol Bull, 1990. **108**(1): p. 50-76.
27. McLearn, K.T., et al., *Maternal depressive symptoms at 2 to 4 months post partum and early parenting practices*. Arch Pediatr Adolesc Med, 2006. **160**(3): p. 279-84.
28. Weiss, B., et al., *Some consequences of early harsh discipline: child aggression and a maladaptive social information processing style*. Child Dev, 1992. **63**(6): p. 1321-35.
29. Carter, A.S., et al., *Maternal depression and comorbidity: predicting early parenting, attachment security, and toddler social-emotional problems and competencies*. J Am Acad Child Adolesc Psychiatry, 2001. **40**(1): p. 18-26.
30. Kim-Cohen, J., et al., *Maternal depression and children's antisocial behaviour: nature and nurture effects*. Archives of General Psychiatry, 2005. **62**(2): p. 173-181.
31. Gajos, J.M. and K.M. Beaver, *Maternal depression and risk for antisocial behaviour in children*. Child and Family Social Work, 2017. **22**: p. 349-363.
32. Ahun, M.N., et al., *Timing and chronicity of maternal depression symptoms and children's verbal abilities*. Journal of Pediatrics, 2017. **in press**.

33. Côté, S.M., et al., *Depression and anxiety symptoms: Onset, developmental course and risk factors during early childhood*. . Journal of Child Psychology and Psychiatry, 2009.
34. Sterba, S.K., M.J. Prinstein, and M.J. Cox, *Trajectories of internalising problems across childhood: Heterogeneity, external validity, and gender differences*. Development and Psychopathology, 2007. **19**: p. 345-366.
35. Davis, S., E. Votruba-Drzal, and J.S. Silk, *Trajectories of internalizing symptoms from early childhood to adolescence: Associations with temperament and parenting*. Social Development, 2015. **24**(3): p. 510-520.
36. Nantel-Vivier, A., et al., *Developmental association of prosocial behaviour with aggression, anxiety and depression from infancy to adolescence*. Journal of Child Psychology and Psychiatry, 2014. **55**: p. 1135-1144.
37. Weeks, M., et al., *Early-life predictors of internalizing symptom trajectories in Canadian children*. Depression and Anxiety, 2014. **31**: p. 608-616.
38. Chi, T.C. and S.P. Hinshaw, *Mother-child relationships of children with ADHD: the role of maternal depressive symptoms and depression-related distortions*. Journal of Abnormal Child Psychology, 2002. **30**(4): p. 387-400.
39. van Buuren, S., *Multiple Imputation of discrete and continuous data by fully conditional specification*. Statistical Methods in Medical Research, 2007. **16**: p. 219-242.
40. Radloff, L., *The Center for Epidemiologic Studies Depression Scale (CES-D): a self-report depression scale for research in the general population*. Applied Psychological Measurement, 1977. **1**: p. 385-401.
41. Poulin, C., D. Hand, and B. Boudreau, *Validity of a 12-item version of the CES-D used in the National Longitudinal Study of Children and Youth*. Chronic Dis Can, 2005. **26**(2-3): p. 65-72.
42. Weissman, M.M., et al., *Assessing depressive symptoms in five psychiatric populations: A validation study* American Journal of Epidemiology, 1977. **106**(3): p. 203-214.
43. Comstock, G.W. and K.J. Helsing, *Sympyoms of depression in two communities*. Psychological Medicine, 1976. **6**: p. 551-564.
44. Nagin, D.S., *Group-based modeling of development over the life course*. 2005, Cambridge: MA: Harvard University Press.
45. Herba, C.M., et al., *Maternal depressive symptoms and children's emotional problems. Can early child care help children of depressed mothers?* JAMA Psychiatry 2013. **70**(8): p. 830-838.
46. Behar, L.B. and S. Stringfield, *A behavior rating scale for the preschool child*. Developmental psychology, 1974. **10**: p. 601-610.
47. Achenbach, T., *Child behavior checklist*. 1991: Burlington, VT:Department of Psychiatry, University of Vermont.
48. Boyle, M.H., et al., *Evaluation of the original Ontario Child Health Study scales*. Can J Psychiatry, 1993. **38**(6): p. 397-405.
49. Nagin DS, et al., *Group-based multi-trajectory modeling*. Statistical Methods in Medical Research, 2016. **0**(0): p. 1-9.

50. Caldwell, B. and R. Bradley, *The Home Inventory for Families of Infants and Toddlers (0-3 years)*. 1985, Arkansas: University of Arkansas at Little Rock.
51. Boivin, M., et al., *The genetic-environmental etiology of parents' perceptions and self-assessed behaviours toward their 5-month-old infants in a large twin and singleton sample*. *J Child Psychol Psychiatry*, 2005. **46**(6): p. 612-30.
52. Byles, J., et al., *Ontario Child Health Study: Reliability and validity of the General Functioning Subscale of the McMaster Family Assessment Device*. *Fam Proc*, 1988. **27**: p. 97-104.
53. APA, *Diagnostic and statistical manual of mental disorders IV*. 1994, Washington DC.
54. Zoccolillo, M., D. Paquette, and R.E. Tremblay, *Maternal conduct disorder and the risk for the next generation*, in *Development and treatment of girlhood aggression*, M.K. Pepler D., Webster C. & Levene K. (eds), Editor. 2005, Mahwah, NJ: Lawrence Erlbaum Associates. p. 225-252.
55. Bates, J.E., C.A. Freeland, and M.L. Lounsbury, *Measurement of infant difficultness*. *Child Dev*, 1979. **50**(3): p. 794-803.
56. Willms, J. and M. Shields, *A measure of socioeconomic status for the National Longitudinal Study of Children. Report prepared for the Canadian National Longitudinal Study of Children*. 1996.
57. Tremblay, R.E., et al., *Physical aggression during early childhood: trajectories and predictors*. *Pediatrics*, 2004. **114**(1): p. e43-50.
58. Greenland, S. and H. Morgenstern, *Confounding in health research*. *Annu Rev Public Health*, 2001. **22**: p. 189-212.
59. Pearce, N. and S. Greenland, *Confounding and interaction*, in *Handbook of Epidemiology*, W. Ahrens and I. Pigeot, Editors. 2005, Springer: New York.
60. Beardslee, W.R., et al., *A family-based approach to the prevention of depressive symptoms in children at risk: evidence of parental and child change*. *Pediatrics*, 2003. **112**(2): p. e119-31.
61. Chi, T.C. and S.P. Hinshaw, *Mother-child relationships of children with ADHD: the role of maternal depressive symptoms and depression-related distortions*. *J Abnorm Child Psychol*, 2002. **30**(4): p. 387-400.
62. Wickramaratne, P., et al., *Children of depressed mothers 1 year after remission of maternal depression: findings from the STAR*D-Child study*. *Am J Psychiatry*, 2011. **168**(6): p. 593-602.
63. Wilson, S. and C.E. Durbin, *Effects of paternal depression on fathers' parenting behaviors: a meta-analytic review*. *Clin Psychol Rev*, 2010. **30**(2): p. 167-80.

