European Society for Paediatric Research
Society for Pediatric Research
www.nature.com/pr

CLINICAL RESEARCH ARTICLE

Check for updates

# Emotional and attention-deficit/hyperactivity disorder symptoms of preterm vs. full-term children during COVID-19 pandemic restrictions

Marion Bailhache[1,2,3]✉, Maeva Monnier[2,3], Flore Moulin[2,3], Xavier Thierry[4], Stéphanie Vandentorren[5], Sylvana M. Côté[6], Bruno Falissard[7], Thierry Simeon[8], Bertrand Geay[8], Laetitia Marchand[9], Marie N. Dufourg[8], Marie A. Charles[8,9], Pierre Y. Ancel[9], Maria Melchior[10], Alexandra Rouquette[7,11], Cédric Galera[2,3,12] and for the SAPRIS study group*



**BACKGROUND:** Preterm children are at higher risk of developing mental health problems than full-term children. Deterioration of children's mental health was observed during COVID-19 pandemic restrictive measures. Our study compared emotional and attention-deficit/hyperactivity disorder (ADHD) symptoms during school closure between preterm and full-term children.
**METHODS:** Data from two French birth cohorts—ELFE and EPIPAGE-2—were used. In 2011, infants born ≥22 weeks' gestation were recruited. Parents completed the Strengths and Difficulties Questionnaire when the children were 9 years old and experiencing school closure. Multivariate multinomial logistic regression models were used.
**RESULTS:** Subjects included 4164 full-term and 1119 preterm children. In univariate analyses, compared to full-term children: extremely and very preterm children more frequently had abnormal and borderline ADHD scores (odds ratio [OR] 1.86, 95% confidence interval [CI] 1.50–2.30, OR 1.42, 95% CI 1.08–1.85, respectively) and abnormal emotional scores (OR 1.86, 95% CI 1.43–2.40); moderate to late preterm children more often had abnormal ADHD scores (OR 1.33, 95% CI 1.01–1.78). The associations did not remain when previous symptoms at 5 years old were considered.
**CONCLUSIONS:** School closure during lockdown did not appear to increase the risk of mental health problems in preterm compared to full-term children.

*Pediatric Research*; https://doi.org/10.1038/s41390-022-02037-4

**IMPACT STATEMENT:**

- Preterm children are at higher risk of developing mental health problems than full-term children. Deterioration in children's mental health was observed during COVID-19 pandemic restrictions. However, whether preterm children were a particularly vulnerable subgroup during school closure is unclear.
- In univariate analyses, extremely and very preterm children more often had abnormal and borderline ADHD symptoms and abnormal emotional symptom scores than full-term children. The associations did not remain significantly associated when previous symptoms were considered.
- Preterm compared to full-term children more often suffer from ADHD and emotional symptoms, but school closure during lockdown did not appear to increase this risk.

## INTRODUCTION

Children born preterm are at higher risk of developing mental health problems than full-term children[1], particularly attention-deficit/hyperactivity disorder (ADHD), mood disorders, anxiety, and behavioral problems[1,2]. These risks are significant for extremely preterm children (i.e., those born at <33 weeks' gestation)[3]. Note that weight at birth plays a role independent of gestational age[1].

The worldwide COVID-19 pandemic led to exceptional public health measures, including lockdowns and school closings. Several studies have assessed children's mental health during lockdowns[4]. Home quarantine and the closing of educational institutions lead

[1]CHU de Bordeaux, Pole de pediatrie, Place Amélie Raba Léon, F-33000 Bordeaux, France. [2]Univ. Bordeaux, Bordeaux, France. [3]Bordeaux Population Health Research Center, INSERM U1219, Bordeaux, France. [4]National Institute for Demographic Studies, Paris, France. [5]Santé Publique France, French National Public Health Agency, F-94415 Saint-Maurice, France. [6]Departement of Social and Preventive Medicine, University of Montreal, Montreal, Canada. [7]CESP, Université Paris-Saclay, UVSQ, Villejuif, France. [8]Ined Inserm EFS joint unit ELFE, Paris, France. [9]Université de Paris, INSERM, INRAE Centre for Research in Epidemiology and Statistics Paris, Paris, France. [10]Sorbonne Université, INSERM, Institut Pierre Louis d'Epidémiologie et de Santé Publique (IPLESP), Equipe de Recherche en Epidémiologie Sociale (ERES), Paris, France. [11]Public Health and Epidemiology Department, AP-HP Paris-Saclay, Bicêtre Hospital, Le Kremlin-Bicêtre, France. [12]Department of Child and Adolescent Psychiatry, CH Charles Perrens, Bordeaux, France. *A list of authors and their affiliations appears at the end of the paper. ✉email: marion.lerouge-bailhache@chu-bordeaux.fr

Received: 7 January 2022 Revised: 4 March 2022 Accepted: 13 March 2022
Published online: 30 March 2022

to isolation, limitations on outdoor and physical activities, and problems meeting friends. Loneliness and limited social relationships are associated with more significant mental health difficulties in adolescents during lockdowns and school closings[4,5]. All around the world, children's mental health problems increased during lockdown[6,7]. Anxiety and depression were the most commonly observed problems, particularly among adolescents and girls[7]. Oppositional-defiant behaviors, ADHD, and sleep disorders were also noticed[6,8]. Existing emotional or ADHD symptoms at the beginning of lockdown appeared to predict deterioration in symptoms[4].

Most of the available research on children's mental health during COVID-19 school closures relies on population-based samples, and very few studies have focused on children born preterm. One study conducted in Switzerland with 54 very preterm children found no increase in the severity of the pandemic's impact on well-being compared to 73 typically developing children[9]. However, the study was limited by the small sample size. The question remains whether premature children were particularly vulnerable to the effects of school closure during COVID. Here we compared 9-years-old preterm and full-term French children in terms of emotional and ADHD symptoms during school closures related to the first lockdown.

## METHODS

### Setting and study design

In the context of the SARS-COV2 pandemic, the Santé, Pratiques, Relations et Inégalités Sociales en population générale pendant la crise COVID-19 (SAPRIS) survey was implemented in mid-March 2020 to evaluate the main challenges of the pandemic in France[10]. Several French population-based cohorts participated, including two national birth cohorts: ELFE and EPIPAGE-2. Participation in the SAPRIS survey was only offered to families with whom contact by email was possible because the survey relied on Web-based questionnaires.

### Sample

In 2011, 344 randomly selected private and public maternity units in metropolitan France participated in the ELFE cohort[11]. Children with parents who were minors or who were not able to give their consent were excluded; Children were also excluded if their mother did not read French, Arabic, Turkish, or English; in cases of multiple pregnancies (≥3) or birth at <33 weeks' of gestation; and if the family planned to move out of metropolitan France in the next 3 years.

In the EPIPAGE-2 cohort, all infants born after the completion of 22–34 weeks of amenorrhea were eligible for inclusion. The beginning date for inclusion was in March 2011, and all maternity units in 25 French regions participated. The recruitment period was 8 months for infants born at 22–26 weeks, 6 months for those born at 27–31 weeks and 5 weeks for those born at 32–34 weeks.

### Outcome

Parents completed two subscales of the French version of the Strengths and Difficulties Questionnaire (SDQ) when the child was 9 years old, during the first French lockdown (from April 16 to May 4, 2020) or immediately thereafter (May 5–June 21, 2020), thus encompassing the whole period of continuous school closure. The first strict French lockdown for the COVID-19 pandemic occurred from March 17 to May 11, 2020. The SDQ is a brief behavioral questionnaire containing 25 questions divided among five subscales[12]. Parents completed the subscales addressing emotional symptoms ("Often complains of headaches, stomach-aches or sickness", "Many worries or often seems worried", "Often unhappy, depressed or tearful", "Nervous or clingy in new situations, easily loses confidence", "Many fears, easily scared") and hyperactivity/inattention ("Restless, overactive, cannot stay still for long", "Constantly fidgeting or squirming", "Easily distracted, concentration wanders", "Thinks things out before acting" [reverse score], "Good attention span, sees work through to the end" [reverse score]). Scores on the two scales range from 0 (no symptoms) to 10 (the most symptoms). On the emotional problems scale, 4 is considered a borderline state and ≥5 abnormal. On the hyperactivity scale, 6 is considered borderline and ≥7 abnormal. The questionnaire has been validated in several languages, including French[12,13].

### Main exposure

Preterm children were children born alive before 37 weeks of amenorrhea. We distinguished three categories based on gestational age: extremely and very preterm (<32 weeks), moderate to late preterm (32–36 weeks + 6 days), and full-term (≥37 weeks).

### Covariates

To choose appropriate covariates, we reviewed factors associated with emotional or ADHD symptoms in childhood and those reported during the the lockdown. Female sex increases the risk for emotional symptoms[14], whereas boys are reportedly at greater risk for ADHD symptoms[14]. Family financial difficulties have been associated with poor mental health, that is, emotional symptoms, suicide attempts, ADHD symptoms, and anxiety[8,15]. Furthermore, adults with less education and those young in age were at greater risk for anxiety and depression during lockdown[16], and parents' mental health can reportedly influence children's well-being[6,8]. Low birth weight is associated with a risk of developing ADHD[17]. Finally, preexisting mental health problems increase the risk of having these symptoms again[18]. Therefore, we chose as covariates maternal age at the child's birth, low weight at birth (defined as birth weight below the 10th percentile for gestational age), child sex, previous parental ratings on the two SDQ subscales at 5 years old, and maternal education and household income when the child was 1 year old. We used standardized French intrauterine growth curves to determine intrauterine growth restrictions[19].

### Ethics

Ethical approval and written informed consent were obtained from each participant before enrolment in the original cohort. Regulatory authorities that oversee ethical data collection in France approved the ELFE and EPIPAGE-2 studies: Comité de Protection des Personnes (CPP no. IDFIX-11-024, CPP SC-2873, respectively); Comité National Informatique et Libertés (CNIL no. 910504, CNIL no. 91009); and CNIS no. 2011X716AU for ELFE, CCTIRS no. 10.626 for EPIPAGE-2. According to French law, specific additional written consent was not required for the present nested survey. The Inserm ethics evaluation committee approved the SAPRIS survey (approval #20-672 dated March 30, 2020).

### Statistical analyses

Children's characteristics were described, and the characteristics of children included in the study were compared to those of children lost to follow-up with chi-square tests.

We used classification and regression tree methods to handle missing data[20]. These methods are attractive for imputation because they are robust against outliers, can be applied to mixed data (both continuous and categorical), and can handle multicollinearity[21]. In addition, we tested the association between prematurity and the child's mental health using unadjusted and adjusted multinomial logistic regression to estimate odds ratios (ORs) and 95% confidence intervals (CIs). Estimates were adjusted based on maternal age at the child's birth, low weight at birth, child sex, previous parental assessments of hyperactivity/inattention and emotional symptoms in the child at 5 years old, and maternal education and monthly household income when the child was 1 year old.

For sensitivity analyses, we conducted these same multinomial logistic regression analyses on a larger sample ($n = 5564$). Instead of including only individuals with hyperactivity/inattention and emotional disturbances at both 5 and 9 years ($n = 5283$), we examined individuals with these problems at age 9 and imputed scores for missing data at age 5.

## RESULTS

### Description of the population

Figure 1 shows participation in the study from birth to the 9-year follow-up, which included 5283 children. Children with incomplete data, that is, without ADHD and emotional symptom assessments at 9 and/or 5 years old, were more frequently full term (92.5% vs. 78.8%, $p < 0.05$) and small for gestational age (89.0% vs. 87.2%, $p < 0.05$) compared to the 5283 included children with ADHD and emotional symptom data at both time points. They more

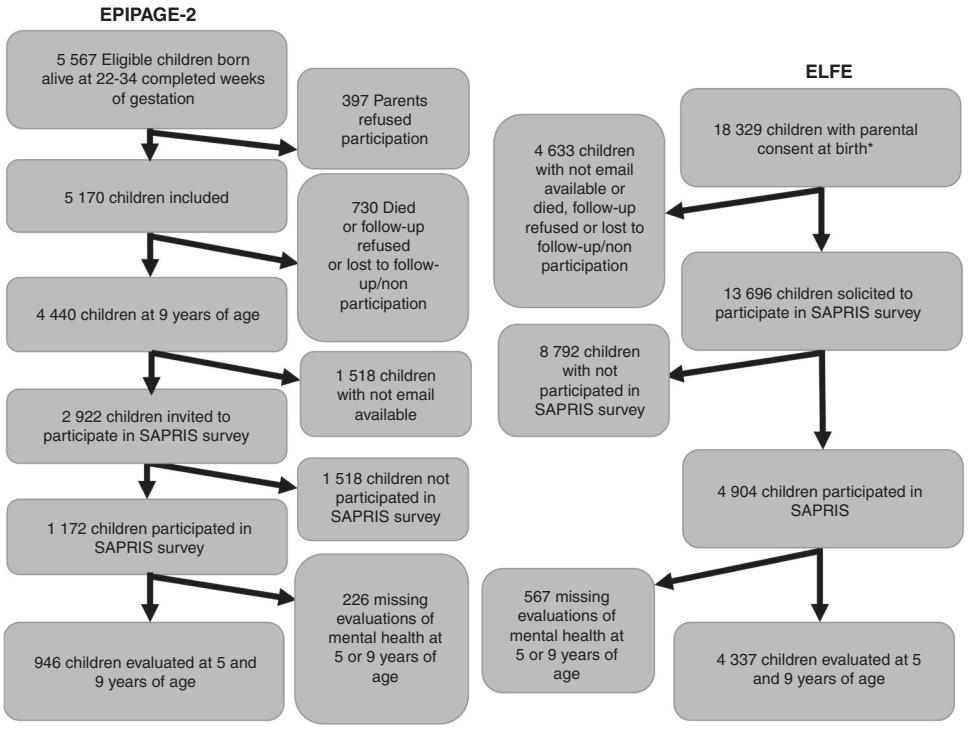


**Fig. 1** Cohort selection flow diagram.

frequently had borderline scores for hyperactivity/inattention symptoms at 5 years old (11.1% vs. 8.2%, $p < 0.05$). They were also more likely to have mothers with less education (46.5% vs. 22.1%, $p < 0.05$) and who were young (<25 years) at their birth (16.0% vs. 5.3%, $p < 0.05$). Finally, this group had a lower household income when the child was 1 year old (56.0% vs. 71.9% with monthly income ≥3000 euros, $p < 0.05$). The children's characteristics are described in Table 1.

When schools were closed, 701 (13.3%) and 411 (7.8%) children, respectively, had abnormal scores for ADHD and emotional symptoms, and 475 (9.0%) and 295 (5.6%) children, respectively, had borderline scores for ADHD and emotional symptoms. Table 2 shows the ADHD and emotional symptom scores at 5 and 9 years old among preterm and full-term children. Supplemental Tables S1 and S2 show changes in these scores between ages 5 and 9.

### Association with hyperactivity/inattention symptoms during school closure

In univariate analyses, compared to full-term children, extremely and very preterm children more often showed abnormal (OR 1.86, 95% CI 1.50–2.30) or borderline (OR 1.42, 95% CI 1.08–1.85) ADHD symptom scores. Moderate to late preterm children showed an increased risk for abnormal ADHD symptom scores (OR 1.33, 95% CI 1.01–1.78; Table 3).

However, these differences were not found after adjustment for covariates. In multivariate analyses, boys were more likely than girls to have high (OR 1.91, 95% CI 1.61–2.28) or intermediate (OR 1.55, 95% CI 1.28–1.89) ADHD symptom scores. Children with abnormal or borderline ADHD symptom scores before the pandemic were more likely than children with scores in the normal range to have abnormal (OR 5.18, 95% CI 4.12–6.51 and OR 3.55, 95% CI 2.76–4.55) or borderline (OR 2.96, 95% CI 2.22–3.94 and OR 2.20, 95% CI 1.61–3.00) scores on the present measurement. Similarly, compared to children with normal emotional symptom scores at 5 years of age, children with abnormal emotional symptom scores at 5 years more often had abnormal (OR 1.59, 95% CI 1.26–2.01) or borderline (OR 1.42, 95% CI 1.08–1.86) ADHD symptoms.

Children whose mothers were 40 years or older at their birth were more likely than children whose mothers were younger to display abnormal ADHD symptoms (ORs for age categories from youngest to oldest: 0.54, 0.46, 0.57, 0.65).

### Association with emotional symptoms during school closure

In univariate analyses, compared to full-term children, extremely and very preterm children more frequently exhibited abnormal emotional symptoms (OR 1.86, 95% CI 1.43–2.40). No significant differences were observed between moderate to late preterm and full-term children (Table 4).

Multivariate analyses revealed no significant differences between full-term and preterm children after adjustment for covariates. Boys were less likely than girls to have abnormal (OR 0.80, 95% CI 0.65–0.99) or borderline (OR 0.68, 95% CI 0.53–0.87) emotional symptom scores. Children with previous abnormal or borderline emotional symptoms were more likely than those with previously normal scores to have abnormal (OR 3.67, 95% CI 2.86–4.69 and OR 2.40, 95% CI 1.76–3.27) or borderline (OR 2.29, 95% CI 1.69–3.12 and OR 1.70, 95% CI 1.17–2.47) emotional symptom scores.

Similarly, children with previous abnormal ADHD symptom scores were more likely than children with previously normal scores to have abnormal (OR 1.50, 95% CI 1.10–2.03) or borderline (OR 1.78, 95% CI 1.24–2.56) emotional symptom scores. Finally, children whose mothers were 40 years or older at their birth were more likely than children whose mothers were 25–34 years old to display abnormal emotional symptoms.

### Sensitivity analyses

When we performed sensitivity analyses and imputed the data in the presence of missing data for scores measured at age 5, the results were similar, with no difference between preterm and full-term children in multivariate analyses.

**Table 1.** Characteristics of children and their families ($n = 5283$).

| Characteristic | *n* (%) |
|---|---|
| Prematurity | 5283 (100) |
| Extremely and very preterm | 698 (13.21) |
| Moderate to late preterm | 421 (7.97) |
| Full-term | 4164 (78.82) |
| Hyperactivity/Inattention symptoms during school closure (≈9 years old) | 5283 (100) |
| Abnormal | 701 (13.27) |
| Borderline | 475 (8.99) |
| Normal | 4107 (77.74) |
| Emotional symptoms during school closure (≈9 years old) | 5283 (100) |
| Abnormal | 411 (7.78) |
| Borderline | 295 (5.58) |
| Normal | 4577 (86.64) |
| Hyperactivity/Inattention symptoms at 5 years old | 5283 (100) |
| Abnormal | 522 (9.88) |
| Borderline | 433 (8.20) |
| Normal | 4328 (81.92) |
| Emotional symptoms at 5 years old | 5283 (100) |
| Abnormal | 677 (12.81) |
| Borderline | 478 (9.05) |
| Normal | 4128 (78.14) |
| Sex | 5279 (99.92) |
| Male | 2687 (50.90) |
| Female | 2592 (49.10) |
| Small for gestational age | 5230 (99.00) |
| Yes | 668 (12.77) |
| No | 4562 (87.23) |
| Maternal age at birth (in year) | 5272 (99.79) |
| ≤24 | 281 (5.33) |
| 25–29 | 1649 (31.28) |
| 30–34 | 2184 (41.43) |
| 35–39 | 961 (18.23) |
| ≥40 | 197 (3.74) |
| Maternal educational level when the child was 1 year old | 5210 (98.62) |
| Secondary school or less | 1149 (22.05) |
| First cycle of higher education program | 1295 (24.86) |
| Second or higher cycle of higher education program | 2766 (53.09) |
| Monthly household when the child was 1 year old (in euros) | 5119 (96.90) |
| <2000 | 354 (6.92) |
| [2000; 3000] | 1086 (21.22) |
| ≥3000 | 3679 (71.87) |

Small for gestational age was defined as birth weight below the 10th percentile for gestational age and sex based on French intrauterine growth curves.

**Table 2.** Emotional and hyperactivity/inattention symptoms at 5 and 9 years old among preterm and full-term children ($n = 5283$).

| | Full-term | | | Moderate to late preterm | | | Extremely and very preterm | | |
|---|---|---|---|---|---|---|---|---|---|
| | Normal | borderline | Abnormal | Normal | Borderline | Abnormal | Normal | Borderline | Abnormal |
| Hyperactivity/inattention symptoms at 5 years old | 3510 | 357 | 297 | 333 | 31 | 57 | 485 | 45 | 168 |
| Hyperactivity/inattention symptoms at 9 years old | 3308 | 355 | 501 | 312 | 46 | 63 | 487 | 74 | 137 |
| Emotional symptoms at 5 years old | 3348 | 353 | 463 | 310 | 46 | 65 | 470 | 79 | 149 |
| Emotional symptoms at 9 years old | 3646 | 227 | 291 | 357 | 29 | 35 | 574 | 39 | 85 |

## DISCUSSION

To the best of our knowledge, this is the first study to report emotional and ADHD symptoms among preterm children during school closures caused by the COVID-19 pandemic and to compare these results to those for full-term children in a large

**Table 3.** Factors associated with hyperactivity/inattention symptoms during school closure: multinomial adjusted logistic regression ($n = 5283$).

| Variable | Abnormal vs. normal scores | | Borderline vs. normal scores | |
|---|---|---|---|---|
| | OR [95% CI] | ORa [95% CI] | OR [95% CI] | ORa [95% CI] |
| *Prematurity* | | | | |
| Extremely and very preterm | 1.86 [1.50–2.30] | 1.09 [0.85–1.41] | 1.42 [1.08–1.85] | 1.10 [0.81–1.47] |
| Moderate to late preterm | 1.33 [1.01–1.78] | 1.02 [0.75–1.38] | 1.37 [0.99–1.91] | 1.19 [0.85–1.68] |
| Full term | Reference | Reference | Reference | Reference |
| *Maternal age at birth (in years)* | | | | |
| ≤24 | 1.03 [0.65–1.63] | 0.54 [0.33–0.90] | 0.96 [0.51–1.81] | 0.68 [0.35–1.30] |
| 25–29 | 0.55 [0.38–0.82] | 0.46 [0.31–0.70] | 0.85 [0.51–1.41] | 0.77 [0.46–1.29] |
| 30–34 | 0.57 [0.39–0.83] | 0.57 [0.38–0.85] | 0.79 [0.48–1.31] | 0.80 [0.48–1.33] |
| 35–39 | 0.61 [0.40–0.91] | 0.65 [0.42–0.99] | 0.92 [0.54–1.55] | 0.96 [0.57–1.64] |
| ≥40 | Reference | Reference | Reference | Reference |
| *Small for gestational age* | | | | |
| Yes | 1.43 [1.14–1.78] | 1.16 [0.91–1.49] | 1.10 [0.83–1.46] | 0.96 [0.71–1.30] |
| No | Reference | Reference | Reference | Reference |
| *Sex* | | | | |
| Male | 2.00 [1.69–2.36] | 1.91 [1.61–2.28] | 1.59 [1.31–1.93] | 1.55 [1.28–1.89] |
| Female | Reference | Reference | Reference | Reference |
| *Hyperactivity/inattention symptoms at 5 years old* | | | | |
| Abnormal | 6.39 [5.15–7.93] | 5.18 [4.12–6.51] | 3.36 [2.55–4.41] | 2.96 [2.22– 3.94] |
| Borderline | 3.93 [3.09–5.01] | 3.55 [2.76–4.55] | 2.33 [1.71–3.16] | 2.20 [1.61–3.00] |
| Normal | Reference | Reference | Reference | Reference |
| *Emotional symptoms at 5 years old* | | | | |
| Abnormal | 2.06 [1.67–2.55] | 1.59 [1.26–2.01] | 1.62 [1.24–2.11] | 1.42 [1.08–1.86] |
| Borderline | 1.63 [1.26–2.11] | 1.53 [1.16–2.01] | 1.24 [0.90–1.72] | 1.20 [0.86–1.68] |
| Normal | Reference | Reference | Reference | Reference |

Multinomial adjusted logistic regression was also adjusted for maternal education level when the child was 1 year old and monthly household income, when the child was 1 year old. Small for gestational age was defined as birth weight below the 10th percentile for gestational age and sex based on French intrauterine growth curves.
*OR [05%CI]* unadjusted odds ratios (95% confidence interval), *ORa [95%CI]* adjusted odds ratios (95% confidence interval).

epidemiological sample. Although extremely and very preterm children more often had abnormal ADHD scores during school closure compared to full-term children, the association did not remain when previous symptoms were considered. These results suggest that prematurity is a risk factor for mental health problems but school closure during lockdown did not confer an increased risk of mental health in preterm children compared to full-term children. It is interesting that preexisting mental health problems were associated with a greater risk for symptoms during school closure.

These results are in accordance with the results of other available studies. We found only one study in which child well-being before and during the lockdown was compared across three groups of children: 54 children born very preterm, 73 children with congenital heart disease, and 73 typically developing children[9]. Children's psychological well-being decreased significantly during the pandemic but without differences among the three groups. Previous studies on ADHD symptoms conducted outside the COVID-19 pandemic have shown that preterm children are at greater risk for ADHD symptoms from the first years of life, but there does not seem to be any further deterioration in this group over time compared to full-term children[2,22–24]. An Australian study comparing attention profiles at 7 and 13 years between children born before 30 weeks' gestation and those born full term showed that the very preterm children were at greater risk of developing stable low attention or improving attention patterns, but they did not differ in patterns of declining attention[2]. Likewise, in another study Breeman et al. showed that very preterm children (<32 weeks) had an increased risk for attention problems in childhood and adulthood[22]. However, the trajectories of attention development were similar between very preterm and full-term children between 6 and 8 years old[22]. A study conducted in the United Kingdom and the Republic of Ireland comparing extremely preterm (<26 weeks) and full-term children also showed that extremely preterm children had a greater risk of developing ADHD and emotional symptoms at 6, 11, 16, and 19 years of age. However, ADHD symptoms decreased slightly over time, and the difference declined[23]. By contrast, with respect to emotional symptoms, the difference and thus the risk increased over time[23]. However, the results of relevant studies of emotional symptoms before the COVID-19 pandemic are inconsistent. In a Bavarian cohort of very preterm and/or very low-birth-weight children, very preterm children (<32 weeks) were more at risk for emotional problems, with relative stability between 6 and 8.5 years old[25].

It is not surprising that in our study, preexisting conditions were particularly associated with the presence of symptoms during school closure. Some studies focusing specifically on the impact of the pandemic on children with ADHD suggest an increase in ADHD symptoms, sometimes with a resultant deterioration in family relationships[26]. However, children with ADHD have also a significantly higher risk of developing major depressive disorder[27].

Within the context of the wider literature, the present results suggest that childhood may not have been the most at-risk age period during the first lockdown. Indeed, a systematic review and

**Table 4.** Factors associated with emotional symptoms during school closure: multinomial adjusted logistic regression ($n = 5283$).

| Variable | Abnormal vs. normal scores | | Borderline vs. normal scores | |
|---|---|---|---|---|
| | OR (95% CI) | ORa (95% CI) | OR (95% CI) | ORa (95% CI) |
| *Prematurity* | | | | |
| Extremely and very preterm | 1.86 [1.43–2.40] | 1.25 [0.93–1.68] | 1.09 [0.77–1.55] | 0.92 [0.63–1.35] |
| Moderate to late preterm | 1.23 [0.85–1.77] | 1.03 [0.70–1.51] | 1.30 [0.87–1.95] | 1.23 [0.81–1.86] |
| Full-term | Reference | Reference | Reference | Reference |
| *Maternal age at birth (in years)* | | | | |
| ≤24 | 1.02 [0.59–1.76] | 0.61 [0.34–1.08] | 1.06 [0.46–2.42] | 0.79 [0.34–1.84] |
| 25–29 | 0.55 [0.35–0.87] | 0.46 [0.29–0.74] | 1.00 [0.51–1.97] | 0.87 [0.44–1.73] |
| 30–34 | 0.54 [0.35–0.85] | 0.51 [0.32–0.82] | 1.05 [0.54–2.04] | 0.95 [0.49–1.85] |
| 35–39 | 0.52 [0.32–0.85] | 0.61 [0.34–1.08] | 1.10 [0.55–2.20] | 1.05 [0.52–2.11] |
| ≥40 | Reference | Reference | Reference | Reference |
| *Small for gestational age* | | | | |
| Yes | 1.56 [1.19–2.04] | 1.24 [0.92–1.65] | 1.04 [0.73–1.48] | 0.96 [0.66–1.40] |
| No | Reference | Reference | Reference | Reference |
| *Sex* | | | | |
| Male | 0.80 [0.66–0.98] | 0.80 [0.65–0.99] | 0.70 [0.55–0.89] | 0.68 [0.53–0.87] |
| Female | Reference | Reference | Reference | Reference |
| *Hyperactivity/inattention symptoms at 5 years old* | | | | |
| Abnormal | 2.07 [1.56–2.75] | 1.50 [1.10–2.03] | 1.86 [1.32–2.62] | 1.78 [1.24–2.56] |
| Borderline | 1.59 [1.14–2.23] | 1.33 [0.94–1.89] | 1.93 [1.34–2.77] | 1.87 [1.29–2.71] |
| Normal | Reference | Reference | Reference | Reference |
| *Emotional symptoms at 5 years old* | | | | |
| Abnormal | 4.12 [3.25–5.23] | 3.67 [2.86–4.69] | 2.49 [1.85–3.35] | 2.29 [1.69–3.12] |
| Borderline | 2.50 [1.85–3.40] | 2.40 [1.76–3.27] | 1.79 [1.23–2.59] | 1.70 [1.17–2.47] |
| Normal | Reference | Reference | Reference | Reference |

Multinomial adjusted logistic regression was also adjusted for maternal education level when the child was 1 year old and monthly household income, when the child was 1 year old. Small for gestational age was defined as birth weight below the 10th percentile for gestational age and sex based on French intrauterine growth curves.
*OR [05%CI]* unadjusted odds ratios (95% confidence interval), *ORa [95%CI]* adjusted odds ratios (95% confidence interval).

meta-analysis of 23 studies assessing the mental health of children and adolescents during the active phase of the COVID-19 pandemic from 2019 to 2020 revealed that adolescents exhibited a higher prevalence of depression than children[7]. Compared to childhood, adolescence is also a higher risk life period for suicidal ideation or suicide attempts independent of the COVID-19 pandemic[28]. Assessing the mental health trajectories of preterm adolescents to determine any age effects would be particularly relevant.

Children of older mothers in the present study were more likely to have ADHD symptoms, contrary to what has been reported in the literature[29]. The same observation was made for emotional symptoms. In a recent study, both younger and older maternal age were linked to depression in offspring[30]. Older mothers may have been less tolerant or more aware of their child's symptoms and thus reported them more. Uncontrolled environmental confounding factors could also be involved.

This study has several limitations. First, our primary outcome was measured only once during the pandemic. Measuring ADHD and emotional symptoms just before the beginning of the lockdown and again afterward would have enabled us to better assess the effects of lockdown and school closure on mental health. Second, the SDQ subscale scores were calculated from only parents' answers, which could have led to measurement bias. The number of children with incomplete data is also important, as it could be related to selection bias. Children with incomplete data were more often male. This could have led to an overestimation of emotional symptoms, as female sex has been associated with depression in several studies[14]. Children with mothers who were young and who had less education more often had incomplete data. This could have resulted in an underestimation of the number of children with emotional and ADHD symptoms, because adults with less education and younger age were themselves more at risk for anxiety and depression during lockdown, and children's well-being is associated with parental mental health[16]. Nonresponders more often reported lower socioeconomic status. However, analyses of the potential association between prematurity and emotional and ADHD symptoms during school closure were adjusted for these variables in children and their families. Hence, these differences should not have affected the comparison of pre- and full-term children. Children with complete data more often had normal ADHD symptom scores at 5 years of age. This could have resulted in an underestimation of the number of children with ADHD symptoms during school closure, because previously existing symptoms were associated with the presence of symptoms during school closure. Finally, our results were for a French sample, and their generalizability may thus be limited to countries with similar characteristics in terms of the health care system and insurance coverage. In the French health care system, premature children benefit from long-term medical and psychological follow-up, which may have helped to reduce the impact of the COVID crisis on their well-being.

## CONCLUSION

Our study suggests that, in the context of the COVID crisis, school closure during the lockdown did not confer an increased risk of mental health problems in preterm children compared to full-term children. It will be important to follow premature children over the long term to fully appreciate the enduring or cumulative effects of the COVID crisis.

## DATA AVAILABILITY

In regards to data availability, data of the study are protected under the protection of health data regulation set by the French National Commission on Informatics and Liberty (Commission Nationale de l'Informatique et des Libertés, CNIL). The data can be available upon reasonable request after a consultation with the steering committee of the Sapris study. The French law forbids us to provide free access to Sapris data; access could however be given by the steering committee after legal verification of the use of the data.

## REFERENCES

1. Hee Chung, E., Chou, J. & Brown, K. A. Neurodevelopmental outcomes of preterm infants: a recent literature review. *Transl. Pediatr.* **9**, S3–S8 (2020).
2. Bogičević, L. et al. Individual attention patterns in children born very preterm and full term at 7 and 13 years of age. *J. Int. Neuropsychol. Soc.* 1–11 https://doi.org/10.1017/S1355617720001411 (2021).
3. Cronin, F. M., Segurado, R., McAuliffe, F. M., Kelleher, C. C. & Tremblay, R. E. Gestational age at birth and "body-mind" health at 5 years of age: a Population Based Cohort Study. *PLoS ONE* **11**, e0151222 (2016).
4. Cooper, K. et al. Loneliness, social relationships, and mental health in adolescents during the COVID-19 pandemic. *J. Affect. Disord.* **289**, 98–104 (2021).
5. Liu, J. J., Bao, Y., Huang, X., Shi, J. & Lu, L. Mental health considerations for children quarantined because of COVID-19. *Lancet Child Adolesc. Health* **4**, 347–349 (2020).
6. Schmidt, S. J., Barblan, L. P., Lory, I. & Landolt, M. A. Age-related effects of the COVID-19 pandemic on mental health of children and adolescents. *Eur. J. Psychotraumatol.* **12**, 1901407 (2021).
7. Ma, L. et al. Prevalence of mental health problems among children and adolescents during the COVID-19 pandemic: a systematic review and meta-analysis. *J. Affect. Disord.* **293**, 78–89 (2021).
8. Moulin, F. et al. Risk and protective factors related to children's symptoms of emotional difficulties and hyperactivity/inattention during the COVID-19-related lockdown in France: results from a community sample. *Eur. Child Adolesc. Psychiatry* https://doi.org/10.1007/s00787-021-01752-3 (2021).
9. Ehrler, M. et al. Impact of the COVID-19 pandemic on children with and without risk for neurodevelopmental impairments. *Acta Paediatr.* **110**, 1281–1288 (2021).
10. Carrat, F. et al. Incidence and risk factors of COVID-19-like symptoms in the French general population during the lockdown period: a multi-cohort study. *BMC Infect. Dis.* **21**, 169 (2021).
11. Charles, M. A. et al. Cohort Profile: The French national cohort of children (ELFE): birth to 5 years. *Int. J. Epidemiol.* **49**, 368–369j (2020).
12. Goodman, R. Psychometric properties of the strengths and difficulties questionnaire. *J. Am. Acad. Child Adolesc. Psychiatry* **40**, 1337–1345 (2021).
13. d'Acremont, M. & Linden, M. Vder Confirmatory factor analysis of the Strengths and Difficulties Questionnaire in a community sample of French-speaking adolescents. *Eur. J. Psychol. Assess.* **24**, 1–8 (2008).
14. Ramirez, S. et al. Brief Research Report: the association between educational experiences and Covid-19 pandemic-related variables, and mental health among children and adolescents. *Front. Psychiatry* **12**, 647456 (2021).
15. Navarro, M. C. et al. Machine learning assessment of early life factors predicting suicide attempt in adolescence or young adulthood. *JAMA Netw. Open* **4**, e211450 (2021).
16. Fancourt, D., Steptoe, A. & Bu, F. Trajectories of anxiety and depressive symptoms during enforced isolation due to COVID-19 in England: a longitudinal observational study. *Lancet Psychiatry* **8**, 141–149 (2021).
17. Perapoch, J. et al. Prematurity and ADHD in childhood: an observational register-based study in Catalonia. *J. Atten. Disord.* **25**, 933–941 (2021).
18. Panchal, U. et al. The impact of COVID-19 lockdown on child and adolescent mental health: systematic review. *Eur. Child Adolesc. Psychiatry* https://doi.org/10.1007/s00787-021-01856-w (2021).
19. Ego, A. et al. Customized and non-customized French intrauterine growth curves. I-Methodology. *J. Gynecol. Obstet. Biol. Reprod.* **45**, 155–164 (2016).
20. Burgette, L. F. & Reiter, J. P. Multiple imputation for missing data via sequential regression trees. *Am. J. Epidemiol.* **72**, 1070–1076 (2010).
21. Buuren, S. V. *Flexible Imputation of Missing Data* 2nd edn. 444 (CRC Press, Boca Raton, FL, 2018).
22. Breeman, L. D., Jaekel, J., Baumann, N., Bartmann, P. & Wolke, D. Attention problems in very preterm children from childhood to adulthood: the Bavarian Longitudinal Study. *J. Child Psychol. Psychiatry* **57**, 132–140 (2016).
23. Linsell, L. et al. Trajectories of behavior, attention, social and emotional problems from childhood to early adulthood following extremely preterm birth: a prospective cohort study. *Eur. Child Adolesc. Psychiatry* **28**, 531–542 (2019).
24. Yates, R. et al. Rates and stability of mental health disorders in children born very preterm at 7 and 13 years. *Pediatrics* **145**, e20192699 (2020).
25. Hall, J. & Wolke, D. A comparison of prematurity and small for gestational age as risk factors for age 6–13 year emotional problems. *Early Hum. Dev.* **88**, 797–804 (2012).
26. Shah, R., Raju, V. V., Sharma, A. & Grover, S. Impact of COVID-19 and lockdown on children with ADHD and their families—an online survey and a continuity care model. *J. Neurosci. Rural Pract.* **12**, 71–79 (2021).
27. Chronis-Tuscano, A. et al. Very early predictors of adolescent depression and suicide attempts in children with attention-deficit/hyperactivity disorder. *Arch. Gen. Psychiatry* **67**, 1044–1051 (2010).
28. Geoffroy, M. C., Orri, M., Girard, A., Perret, L. C., Turecki, G. Trajectories of suicide attempts from early adolescence to emerging adulthood: prospective 11-year follow-up of a Canadian cohort. *Psychol. Med.* 1–11. https://doi.org/10.1017/S0033291720000732 (2020).
29. Hvolgaard Mikkelsen, S., Olsen, J., Bech, B. H. & Obel, C. Parental age and attention-deficit/hyperactivity disorder (ADHD). *Int. J. Epidemiol.* **46**, 409–420 (2017).
30. Filatova, S., Upadhyaya, S., Luntamo, T., Sourander, A. & Chudal, R. Parental age and risk of depression: a nationwide, population-based case-control study. *J. Affect. Disord.* **282**, 322–328 (2021).

## ACKNOWLEDGEMENTS

Agence Nationale de la Recherche (ANR, 0009/SAPRIS/997/NB), Fondation pour la Recherche Médicale, Direction Générale de la Recherche et de l'Innovation, Institut Gustave Roussy, the New-Aquitaine region.

## AUTHOR CONTRIBUTIONS

M.B. concept and design the study, interpreted the data and wrote the manuscript. M.M. did the statistical analysis, interpreted the data and revised the manuscript. F.M., X.T., S.V., S.M.C., B.F., T.S., B.G., L.M., M.N.D., M.A.C., P.Y.A., M.M., A.R., interpreted the data, critiqued the manuscript of important intellectual content and approved the final version of manuscript. C.G. concept and design the study, interpreted the data, and revised the manuscript. The SAPRIS group enrolled participants, collected the data, and revised the manuscript. Authors had access to all the data in the study and participated in the decision to submit.

## COMPETING INTERESTS

M.M. has been funded by the New-Aquitaine region (AMI Flash Recherche et Innovations COVID). The other authors have no competing interests to declare.

## CONSENT STATEMENT

A consent form was signed by parents for inclusion.

## ADDITIONAL INFORMATION

**Supplementary information** The online version contains supplementary material available at https://doi.org/10.1038/s41390-022-02037-4.

**Correspondence** and requests for materials should be addressed to Marion Bailhache.

**Reprints and permission information** is available at http://www.nature.com/reprints

**Publisher's note** Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.

**FOR THE SAPRIS STUDY GROUP**

Nathalie Bajos[13], Fabrice Carrat[10], Pierre-Yves Ancel[9], Marie-Aline Charles[8,9], Florence Jusot[14], Claude Martin[15], Laurence Meyer[16], Ariane Pailhé[4], Alexandra Roquette[7,11], Giuanluca Severi[17], Alexis Sprire[15], Mathilde Touvier[18] and Marie Zins[19]

[13]Institut de Recherche Interdisciplinaire sur les enjeux Sociaux – Sciences sociales, politique, santé, IRIS (UMR 8156 CNRS – EHESS-U997 INSERM), Aubervilliers, France. [14]Paris-Dauphine University-PSL, Paris, France. [15]French National Centre for Scientific Research, Paris, France. [16]University of Paris Sud, Paris, France. [17]INSERM, E4N and EN3-cohorts, Paris, France. [18]Sorbonne Paris Cité Epidemiology and Statistics Research Center (CRESS), Inserm U1153, Inra U1125, Cnam, Paris 13 University, Nutritional Epidemiology Research Team (EREN), Bobigny, France. [19]Sorbonne University, Paris, France.