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# Selection of environmental risk factors

The selection of environmental risk factors was performed in a two-step approach. First, we included environmental risk factors reported on the recent and comprehensive umbrella review of meta-analyses published by Kim et al. (1). The following environmental risk factors were included in the first step: low maternal education, single-parent family, smoking during pregnancy, use of antidepressants during pregnancy, hypertensive disorders of pregnancy, diabetes mellitus (DM) during pregnancy, maternal stress during pregnancy, cesarean delivery, preterm birth, and breastfeeding (Table S1). Environmental risk factors identified by Kim et al. (1) but not included in our risk score can be found in Table S2.

In the second step, we performed a literature review on Medline to identify potentially relevant meta-analyses published after October 2019 (date of search by Kim et al. (1)). The search was conducted on Medline on September 16th by one author (DTL). The following search terms were used:

(("attention deficit disorder with hyperactivity"[MeSH Terms] OR ("attention"[All Fields] AND "deficit"[All Fields] AND "disorder"[All Fields] AND "hyperactivity"[All Fields]) OR "attention deficit disorder with hyperactivity"[All Fields] OR "adhd"[All Fields]) AND ("meta analysis"[Publication Type] OR "meta analysis as topic"[MeSH Terms] OR "meta analysis"[All Fields])) AND (2019:2021[pdat])

The study selection and inclusion were performed based on title and abstract, followed by a full-text analysis. Both were conducted by one author (DTL) and discussed with a second author (LAR). The initial search identified a total of 362 studies, and 35 were selected for a full-text review. From those, maternal age was included as a new environmental risk in our score (Table S2). Moreover, the study of Leshem et al. (2) was selected as a reference for the use of antidepressants during pregnancy, and the study of Zeng et al. (3) was chosen as a reference for DM during pregnancy (Table S2). A detailed description of studies excluded after the full-text review can be found in Table S3.

# Detailed description of environmental factors

In our sample, all environmental factors described below were assessed during a comprehensive household parent interview performed at baseline. The parent household interview included a detailed evaluation of general risk factors for mental disorders, including selected demographic variables, prenatal and perinatal factors, and early life stressors. All were chosen after a careful literature review (4). From the 2,511 participants assessed at baseline, the household parent interview was performed with the biological mother in 2,298, with the birth father in 115, and with both the biological mother and biological father in 98.

*Low maternal education*

Lower maternal education was considered a risk factor for ADHD according to the meta-analyses published by Russell et al. (5). According to the authors, mothers with no educational qualifications, or high school qualifications only, were more likely to have a child with ADHD when compared to children whose mothers had higher education (finished college with or without postgraduate degrees) with a pooled odds ratio (OR) of 1.91 (95% CI 1.21, 3.03) (5). In the studies included in the meta-analysis (5), the rate of mothers with completed higher education varied between 26-52% (6–10). In our sample, however, only 73 mothers (3.54%) had completed higher education. In this sense, instead of comparing children from mothers with no educational or high school only with mothers with higher education, we compared mothers with no education or elementary school only (less than nine years of study) with mothers with high school or higher education (more than nine years of study). Therefore, children whose mothers had no education or elementary school only received a beta of 0.647, and children whose mothers had high school or higher education received a beta of 0. Moreover, although the study of Russel et al. (5) suggests that paternal education would also increase the odds of ADHD, we decided to include only maternal education in our ERSs. This approach was selected since information regarding paternal education was missing for 583 (30.45%) individuals out of 2,046, mostly from children who had no contact with their fathers anymore.

*Low maternal age*

Low maternal age at birth has been suggested as a risk factor for ADHD, with an adjusted OR of 1.49 (95% CI 1.19, 1.87), according to the meta-analysis published by Min et al. (11). Most studies included in this meta-analysis compared the risk of ADHD in children whose mothers were in the lowest tercile versus middle tercile for age at birth (11). Authors also compared the risk in children whose mothers were in the highest tercile versus middle tercile but found no significant differences (11). In our sample, children whose mothers were at the lowest tercile for age at birth received a beta of 0.398, while mothers in the middle and highest terciles received a beta of 0.

*Single parent family*

Being raised by a single-parent family was considered as a risk factor for ADHD according to the meta-analysis published by Russell et al. (5), with a pooled adjusted OR of 1.28 (95% CI 1.08, 1.52) (5). In our sample, the interviewee answered the following questions: “Did the biological mother live with the child at the child’s first month of child’s life?”, “Did the biological mother live with the child from 2nd to 6th month of child’s life?”, “Did the biological mother live with the child from 7th to 11th month of child’s life?”, “Did the biological mother live with the child from 1st to 3rd year of child’s life?” and “Did the biological mother lives with the child from 4th to 6th year of child’s life?”. The same questions were asked regarding the biological father. To be more conservative, we considered that the children were raised in a single-parent family if the answer was “no” for all five questions (either mother or father). Moreover, if the mother was living together with another partner, we considered the child was not living in a single-parent family. Therefore, children raised by a single-family received a beta of 0.246.

*Smoking during gestation*

Smoking during gestation was considered a risk factor for ADHD, according to the meta-analysis of Huang et al. (12). In this meta-analysis, authors observed that children whose mothers were heavy smokers (10 or more cigarettes per day) had an increased risk of ADHD (OR = 1.75; 95% CI 1.51, 2.02) when compared to children from nonsmoker mothers (12). The risk was also increased in children whose mothers were light smokers (10 or fewer cigarettes per day, OR=1.54; 95% CI 1.40, 1.70) (12). In our sample, information regarding smoking during pregnancy was collected at baseline according to the following classification: nonsmokers, light smokers (up to 14 cigarettes per day), and heavy smokers (more than 14 cigarettes per day). Therefore, children whose mothers were light smokers received a beta of 0.431, children whose mothers were heavy smokers received a beta of 0.559, and children whose mothers did not smoke received a beta of 0.

*Use of antidepressants during pregnancy*

The use of antidepressants, including selective serotonin reuptake inhibitors (SSRIs) and serotonin and norepinephrine reuptake inhibitors (SNRIs) during gestation has been suggested to increase the risk of ADHD (2,13). In the more comprehensive meta-analysis published by Leshem et al. (2), authors reported an OR of 1.26 (95% CI 1.07, 1.49). In the household parent interview, parents were asked the following question “Has the biological mother used any medication for emotional or behavioral problems during pregnancy?”. If the answer was “yes”, the name of each medication was obtained. In our sample, three mothers were taking fluoxetine, two paroxetine, two sertraline, and one fluvoxamine. Children whose mothers reported the use of SSRIs or SNRIs received a beta of 0.23.

*Hypertensive disorders of pregnancy*

An association between hypertensive disorders of pregnancy (including chronic hypertension, gestational hypertension, preeclampsia, and eclampsia) and ADHD has been reported in a meta-analysis published by Maher et al. (14). The authors reported an increased risk, with an adjusted OR of 1.29 (95% CI 1.06, 2.72) (14). In our sample, hypertensive disorders of pregnancy were considered present if the interviewee answered “yes” for the following question: “Did the biological mother experience high blood pressure, eclampsia, or preeclampsia during pregnancy?”. Children whose mothers experienced hypertensive disorders of pregnancy received a beta of 0.254.

*Diabetes mellitus during pregnancy*

In the umbrella review published by Kim et al. (1), two meta-analyses evaluating the potential role of maternal DM in ADHD were identified. The first assessed the role of preexisting DM in pregnancy in the risk for ADHD (15). The authors included data from 3 manuscripts in the primary analysis and obtained a pooled adjusted hazard ratio of 1.36 (95% CI 1.19, 1.55) (15). The second included both preexisting DM and gestational DM and performed a separate analysis for studies with case-control designs and cohort designs (16). For the case-control studies, three articles were included, and the pooled data showed no association between maternal DM and ADHD, with an OR of 1.20 (95% CI 0.96, 1.49) (16). For the cohort studies, six studies were included, and authors observed a pooled RR of 1.40 (95% CI 1.27, 1.54) (16).

After our literature review, we identified a meta-analysis including 11 studies evaluating the effects of maternal diabetes mellitus (including pregestational DM and gestational DM) on the risk of ADHD (3). Authors report an adjusted OR of 1.36 (95% CI 1.17, 1.58), showing an increased risk of ADHD in children whose mothers had either pregestational DM or gestational DM (3). We extracted the beta from Zeng et al. (3) study since it included a higher number of studies and the association was reported as OR. In our sample, DM during pregnancy was considered present if the interviewee answered “yes” for the question: “Did the biological mother have diabetes during pregnancy?”. Of note, the question did not differentiate between pregestational DM and gestational DM. Children whose mothers experienced DM during pregnancy received a beta of 0.307.

*Maternal stress during pregnancy*

An association between maternal stress during pregnancy and ADHD was observed in the meta-analysis published by Manzari et al. (17). The authors reported an adjusted OR of 1.72 (95% CI 1.27, 2.34), suggesting an increased risk of ADHD in children whose mothers were exposed to stress during pregnancy (17). In our sample, the interviewee reported the level of stress experienced by the biological mother using a 0 to 10 scale. We considered that maternal stress during pregnancy was present if the answer was 7, 8, 9, or 10 (7 and 8 representing intense stress, 9 representing very intense stress, and 10 representing maximum stress). Children whose mothers were exposed to stress during pregnancy received a beta of 0.542.

*Cesarean delivery*

Increased odds of ADHD after cesarean delivery were observed in a meta-analysis published by Zhang et al. (18). In this study, authors reported an adjusted OR of 1.17 (95% CI 1.09, 1.25) (18). In our sample, the mode of delivery was recorded as “normal” or “cesarean.” Therefore, children born from cesarean delivery received a beta of 0.157.

*Preterm birth*

Preterm birth has been suggested as a risk factor for the development of ADHD (19,20). In the meta-analysis published by Allotey et al. (20), authors reported a pooled OR of 1.3 (95% CI 1.1, 1.5) for children born between 34-37 weeks, a pooled OR of 3.7 (95% CI 1.8, 7.7) for children born between 28-34 weeks, and a pooled OR of 3.3 (95% CI 2.0, 5.6) for children born less than 28 weeks (20). The meta-analysis published by Franz et al. (19) reported a pooled OR of 3.04 (95% CI 2.19, 4.21) for children who were born as very preterm, extremely preterm, with very low birth weight, or extremely low birth weight (19). In our database, preterm birth was reported by the interviewee and also checked in the child’s birth ID. Prematurity was stratified as term (≥ 37 weeks), late preterm (34 weeks to <37 weeks), or moderate/very or extremely preterm (<34 weeks). We decided to use the more conservative OR published by (19) for children born less than 34 weeks. Therefore, children born with less than 34 weeks received a beta of 1.111, children born between 37 and 34 weeks received a beta of 0.262, and children born at term received a beta of 0. It is important to stress that although we had categorical information regarding premature birth (either term or prematurely), the exact number of weeks was not reported for all of them. Therefore, it is likely that the total number of children born less than 34 weeks is underreported.

*Breastfeeding*

According to data from a meta-analysis published by Zeng et al. (21), children who were breastfed had fewer chances of having ADHD when compared to children who were never breastfed, with a pooled adjusted OR of 0.70 (95% CI 0.52, 0.93) (21). In our sample, the interviewee was asked for how long the child was breastfed, in months. The information was stratified as “never breastfed” or “breastfed.” Children who were breastfed for any number of months received a beta of -0.35, and children who were never breastfed received a beta of 0.

# Table S1. Number of single nucleotide polymorphisms included in each polygenic risk score threshold

|  |  |
| --- | --- |
| **Threshold** | **Number of SNPs** |
| 1 | 120,063 |
| 0.8 | 106,125 |
| 0.5 | 77,901 |
| 0.4 | 66,498 |
| 0.3 | 53,738 |
| 0.2 | 39,722 |
| 0.1 | 23,203 |
| 0.05 | 13,517 |
| 0.01 | 3,904 |

Table S1. SNPs = single nucleotide polymorphisms.

# Table S2. Environmental risk factors included in our score

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| **Environmental factor** | **Reference study** | **OR (95% CI)** | **Number of studies** | **Total number of individuals** | **Individuals with ADHD** | **I-squared (p-value)** |
| Mother education | Russell et al. (5) | 1.91 (1.21, 3.03) | 6 | 108,812 | 6,960 | 91% (<.0001) |
| Low maternal age | Min et al. (11) | 1.49 (1.19, 1.87) | 8 | 4,337,610 | 97,816 | 97.1% (<.0001) |
| Single parent family | Russell et al. (5) | 1.28 (1.08, 1.52) | 6 | 99,305 | 7,838 | 0% |
| Smoking during gestation | Huang et al. (12) |  |  |  |  |  |
| Light |  | 1.54 (1.40, 1.70) | 6 | NA | NA | 58.9% (.3) |
| Heavy |  | 1.75 (1.51, 2.02) | 6 | NA | NA | 77% (.001) |
| Use of antidepressants during pregnancy | Leshem et al. (2) | 1.26 (1.07, 1.49) | 4 (6 estimates) | NA | NA | 48% |
| Hypertensive disorders during pregnancy | Maher et al. (14) | 1.29 (1.06, 2.72) | 6 (8 estimates) | 1,395,605 | 37,128 | 0% |
| Diabetes mellitus during pregnancy | Zeng et al. (3) | 1.36 (1.17, 1.58) | 7 (11 estimates) | 5,052,397 | 111,039 | 82% (.00001) |
| Maternal stress during pregnancy | Manzari et al. (17) | 1.72 (1.27, 2.34) | 7 (8 estimates) | 1,758,906 | 25,547 | 85% (<.00001) |
| Cesarean delivery | Zhang et al. (18) | 1.17 (1.09, 1.25) | 13 (14 estimates) | 3,711,607 | 92,426 | 79.2% (<.001) |
| Preterm birth |  |  |  |  |  |  |
| <34 weeks | Franz et al. (19) | 3.04 (2.19, 4.21) | 12 | 6,163 | 592 | 17% (.27) |
| 34-37 weeks | Allotey et al. (20) | 1.3 (1.1, 1.5) | 2 (3 estimates) | 41,842 | 1,343 | 0% |
| Breastfeeding | Zeng et al. (21) | .70 (.52, .93). | 6 (7 estimates) | 40,053 | 1,305 | 74.3% (.001) |

Table S2. OR = odds ratio; ADHD = attention-deficit/hyperactivity disorder; CI = confidence interval; NA = not available.

# Table S3. Environmental risk factors not included in our score

|  |  |  |
| --- | --- | --- |
| Risk factor | Reference | Reason for exclusion |
| From: Kim et al. (1) | | |
| Maternal pre-pregnancy obesity | Jenabi et al. (22) | Data not collected in our database |
| Childhood eczema | Schans et al. (23) | Data not collected in our database |
| Maternal acetaminophen exposure during pregnancy | Gou et al. (24) | Data not collected in our database |
| Childhood asthma | Cortese et al. (25) | Data not collected in our database |
| Mother pre-pregnancy overweight | Jenabi et al. (22) | Data not collected in our database |
| Maternal high-frequency cell phone use during pregnancy | Birks et al. (26) | Data not collected in our database |
| Breach/transverse presentation | Zhu et al. (27) | Data not collected in our database |
| Childhood TBI | Adeyemo et al. (28) | Data not collected in our database |
| Childhood allergic conjunctivitis | Miyazaki et al. (29) | Data not collected in our database |
| Childhood allergic rhinitis | Miyazaki et al. (29) | Data not collected in our database |
| Low perinatal vitamin D concentration | Khoshbakht et al. (30) | Data not collected in our database |
| Childhood obesity | Cortese et al. (31) | Data not collected in our database |
| Children younger than school classmates | Caye et al. (32) | Not considered a risk factor |
| 5-minute Apgar score<7 | Zhu et al. (27) | Missing data for more than 50% of subjects in our database |
| Paternal low education level | Russell et al. (5) | Missing data for more than 30% of subjects in our database |
| Childhood eating disorder | Nazar et al. (33) | Only two estimates |
| Maternal hypothyroidism/subclinical hypothyroidism during pregnancy | Thompson et al. (34) | Not significant |
| Perinatal synthetic oxytocin use | Lønfeldt et al. (35) | Not significant |
| Childhood food allergy | Miyazaki et al. (29) | Not significant |
| Prenatal and early infancy thimerosal exposure | Yoshimasu et al. (36) | Not significant |
| Prenatal alcohol exposure | Porter et al. (37) | Not significant |
| From: Additional search | | |
| Childhood urinary symptoms | Mahjani et al. (38) | Data not collected in our database |
| Maternal polycystic ovary syndrome | Maleki et al. (39) | Data not collected in our database |
| Childhood general anesthesia | Sun et al. (40) | Data not collected in our database |
| Early-life antibiotic exposure | Yu et al. (41) | Data not collected in our database |
| Childhood dietary patterns | Shareghfarid et al. (42) | Data not collected in our database |
| Maternal pre-pregnancy overweight/obesity | Li et al. (43) | Repeated outcome |
| Maternal DM | Guo et al. (44) | Repeated outcome |
| Maternal thyroid disorders | Ge et al. (45) | Repeated outcome |
| Childhood asthma | Kaas et al. (46) | Repeated outcome |
| Maternal acetaminophen exposure during pregnancy | Alemany et al. (47) | Repeated outcome |
| Month of birth | Hsu et al. (48) | Repeated outcome |
| Maternal gestational DM | Rowland & Wilson (49) | Repeated outcome |
| Smoke exposure | Huang et al. (50) | Repeated outcome |
| Childhood TBI | Asarnow et al. (51) | Repeated outcome |
| Childhood sugar consumption | Farsad-Naeimi et al. (52) | Did not evaluate ADHD diagnosis |
| Maternal dietary quality | Polanska et al. (53) | Did not evaluate ADHD diagnosis |
| Prenatal opioid exposure | Schwartz et al. (54) | Did not evaluate ADHD diagnosis |
| Childhood short sleep duration | Lee et al. (55) | Did not evaluate ADHD diagnosis |
| Celiac disease | Clappison et al. (56) | Only two estimates |
| Labor induction | Jenabi et al. (57) | Not significant |
| Maternal perfluoroalkyl substances exposure | Qu et al. (58) | Not significant |
| Gut microbiota | Nikolova et al. (59) | Not significant |
| Necrotising enterocolitis | Matei et al. (60) | Not significant |
| Childhood phthalate exposure | Radke et al. (61) | Not significant |
| ﻿Childhood polycyclic aromatic hydrocarbons exposure | Kalantary et al. (62) | Not significant |
| Toxoplasma gondii | Nayeri et al. (63) | Not significant |
| Air pollutants | Zhang et al. (64) | Not significant |
| Maternal autoimmune disease | Nielsen et al. (65) | Repeated outcome, not significant, only two estimates\* |

Table S3. DM = diabetes mellitus; TBI = traumatic brain injury; ADHD = attention-deficit/hyperactivity disorder.

\* Repeated outcome: type 1 DM, hyperthyroidism, hypothyroidism. Not significant: multiple sclerosis, rheumatoid arthritis, systemic lupus erythematosus, celiac disease, crohn disease, ulcerative colitis, immune thrombocytopenic purpura. Only two estimates: any autoimmune disease, psoriasis.

# Table S4. Demographics at baseline according to attention-deficit/hyperactivity disorder status

|  |  |  |  |
| --- | --- | --- | --- |
|  | No ADHD | ADHD | p-value |
| Sample size | 1811 (88.51%) | 235 (11.49%) | - |
| Female | 850 (46.94%) | 90 (38.30%) | .012 |
| Age, years | 10.20 (1.92) | 9.99 (1.81) | .10 |
| Mother education\* |  |  |  |
| No education or elementary school | 729 (40.25%) | 92 (39.15%) | .74 |
| Maternal age at birth, years | 26.34 (6.62) | 25.63 (6.85) | .12 |
| Single parent family\* | 193 (10.66%) | 23 (9.79%) | .68 |
| Smoking during pregnancy\* | |  |  |
| Light smoker | 201 (11.09%) | 40 (17.03%) | .005 |
| Heavy smoker | 142 (7.84%) | 24 (10.21%) | .11 |
| Antidepressants during pregnancy\* | 8 (.44%) | 0 | .30 |
| Hypertensive disorders of pregnancy\* | 348 (19.22%) | 66 (28.09%) | .001 |
| DM during pregnancy\* | 78 (4.31%) | 9 (3.83%) | .73 |
| Maternal stress during pregnancy\* | 572 (31.58%) | 108 (45.96%) | <.0001 |
| Cesarean birth\* | 704 (38.87%) | 86 (36.60%) | .50 |
| Preterm\* |  |  |  |
| <34 weeks | 64 (3.53%) | 9 (3.83%) | .85 |
| 34-37 weeks | 311(17.17%) | 37 (15.74%) | .59 |
| Never breastfed | 148 (8.17%) | 26 (11.06%) | .13 |
| Depression | 60 (3.31%) | 13 (5.53%) | .08 |
| Anxiety | 183 (10.10%) | 45 (19.15%) | <.0001 |

Table S4. Categorical variables are presented as total number and percentage, and continuous variables are presented as mean and standard deviation.

DM = diabetes mellitus; ADHD = attention-deficit/hyperactivity disorder.

# Table S5. Demographics at wave 1 according to attention-deficit/hyperactivity disorder status

|  |  |  |  |
| --- | --- | --- | --- |
|  | No ADHD | ADHD | p-value |
| Sample size | 1597 (94.78%) | 88 (5.22%) | - |
| Female | 730 (45.71%) | 29 (32.95%) | .019 |
| Age, years | 13.47 (1.92) | 12.96 (1.74) | .01 |
| Mother education\* |  |  |  |
| No education or elementary school | 622 (38.95%) | 27 (30.68%) | .12 |
| Maternal age at birth, years | 26.49 (6.60) | 25.94 (7.55) | .44 |
| Single parent family\* | 151 (9.46%) | 12 (13.64%) | .19 |
| Smoking during pregnancy\* | |  |  |
| Light smoker | 192 (12.02%) | 10 (11.37%) | .85 |
| Heavy smoker | 128 (8.01%) | 7 (7.95%) | .96 |
| Antidepressants during pregnancy\* | 7 (0.44%) | 1 (1.14%) | .35 |
| Hypertensive disorders of pregnancy\* | 323 (20.23%) | 20 (22.73%) | .57 |
| DM during pregnancy\* | 71 (4.45%) | 4 (4.55%) | .96 |
| Maternal stress during pregnancy\* | 517 (32.37%) | 35 (39.77%) | .15 |
| Cesarean birth\* | 617 (38.63%) | 39 (44.32%) | .28 |
| Preterm\* |  |  |  |
| <34 weeks | 60 (3.76%) | 3 (3.41%) | .88 |
| 34-37 weeks | 275 (17.22%) | 16 (18.18%) | .82 |
| Never breastfed\* | 137 (8.51%) | 11 (12.50%) | .18 |
| Depression | 105 (6.57%) | 12 (13.64%) | .01 |
| Anxiety | 200 (12.52%) | 28 (31.82%) | <.0001 |

Table S5. Categorical variables are presented as total number and percentage, and continuous variables are presented as mean and standard deviation.

DM = diabetes mellitus; ADHD = attention-deficit/hyperactivity disorder.

\* Data collected only at baseline

# Table S6. Demographics at wave 2 according to attention-deficit/hyperactivity disorder status

|  |  |  |  |
| --- | --- | --- | --- |
|  | No ADHD | ADHD | p-value |
| Sample size | 1558 (97.19%) | 45 (2.81%) | - |
| Female | 733 (47.05%) | 15 (33.33%) | .069 |
| Age, years | 18.27 (2.00) | 18.08 (2.09) | .53 |
| Mother education\* |  |  |  |
| No education or elementary school | 604 (38.67%) | 18 (40%) | .86 |
| Maternal age at birth, years | 26.45 (6.67) | 25.94 (7.84) | .61 |
| Single parent family\* | 156 (10.01%) | 7 (15.56%) | .22 |
| Smoking during pregnancy\* | |  |  |
| Light smoker | 183 (11.75%) | 5 (11.11%) | .91 |
| Heavy smoker | 125 (8.02%) | 4 (8.89%) | .84 |
| Antidepressants during pregnancy\* | 7 (0.45%) | 0 | .65 |
| Hypertensive disorders of pregnancy\* | 306 (19.64%) | 8 (17.78%) | .75 |
| DM during pregnancy\* | 71 (4.56%) | 2 (4.44%) | .97 |
| Maternal stress during pregnancy\* | 503 (32.28%) | 25 (55.56%) | .001 |
| Cesarean birth\* | 599 (38.45%) | 19 (42.22%) | .60 |
| Preterm\* |  |  |  |
| <34 weeks | 55 (3.53%) | 3 (6.67%) | .18 |
| 34-37 weeks | 271 (17.39%) | 12 (26.67%) | .08 |
| Never breastfed\* | 133 (8.54%) | 4 (8.89%) | .93 |
| Depression | 237 (15.21%) | 12 (26.67%) | .03 |
| Anxiety | 230 (14.76%) | 15 (33.33%) | .001 |

Table S6. Categorical variables are presented as total number and percentage, and continuous variables are presented as mean and standard deviation.

DM = diabetes mellitus; ADHD = attention-deficit/hyperactivity disorder.

\* Data collected only at baseline

# Table S7. Demographic and clinical characteristics associated with follow-up in waves 1 and 2

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  | Follow-up wave 1 | | Follow-up wave 2 | |
| Baseline demographic/clinical variables | OR (95% CI) | p-value | OR (95% CI) | p-value |
| Female | .81 (.64, 1.02) | .07 | 1.14 (.92, 1.41) | .21 |
| Age, years | .90 (.85, .96) | .001 | 1.04 (.98, 1.10) | .13 |
| Mother education\* |  |  |  |  |
| No education or elementary school | .68 (.54, .86) | .001 | .77 (.62, .96) | .02 |
| Maternal age at birth, years | 1.02 (1.009, 1.04) | .003 | 1.01 (1.003, 1.03) | .01 |
| Single parent family\* | .62 (.44, .86) | .005 | .83 (.59, 1.15) | .27 |
| Smoking during pregnancy\* | |  |  |  |
| Light smoker | 1.11 (.77, 1.61) | .54 | .97 (.70, 1.34) | .87 |
| Heavy smoker | .94 (.62, 1.41) | .76 | .95 (.65, 1.40) | .82 |
| Hypertensive disorders of pregnancy\* | 1.04 (.78, 1.38) | .76 | .83 (.64, 1.07) | .16 |
| DM during pregnancy\* | 1.35 (.72, 2.51) | .33 | 1.46 (.81, 2.61) | .20 |
| Maternal stress during pregnancy\* | .88 (.69, 1.12) | .32 | .94 (.75, 1.17) | .58 |
| Cesarean birth\* | 1.07 (.85, 1.36) | .52 | .98 (.79, 1.22) | .91 |
| Preterm\* |  |  |  |  |
| <34 weeks | 1.39 (.70, 2.74) | .34 | 1.11 (.62, 1.98) | .71 |
| 34-37 weeks | 1.12 (.82, 1.53) | .44 | 1.25 (.93, 1.67) | .13 |
| Never breastfed | 1.07 (.71, 1.63) | .72 | 1.02 (.70, 1.49) | .89 |
| ADHD | 1.08 (.75, 1.56) | .65 | 1.05 (.75, 1.47) | .75 |
| Depression | .99 (.73, 1.34) | .97 | 1.03 (.77, 1.38) | .81 |
| Anxiety | 1.35 (1.09, 1.68) | .006 | 1.28 (1.06, 1.55) | .009 |

Table S7. Logistic regression models were fit with follow-up at waves 1 and 2 (yes = 1) as dependent variable. Therefore, OR > 1 indicate higher odds of following-up at waves 1 and/or 2.

OR = odds ratio; CI = confidence interval; DM = diabetes mellitus; ADHD = attention-deficit/hyperactivity disorder.

# Table S8. Gene-environment correlation between polygenic risk scores and environmental risk factors

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  | Adjusted effects | | | |
|  | OR (95% CI)a | | p-value | |
| Maternal education | 1.10 (.99, 1.22) | | .056 | |
| Low maternal age | 1.07 (.96, 1.18) | | .19 | |
| Single parent family | .98 (.83, 1.15) | | .85 | |
| Smoking during pregnancy | |  | |
| Light smoking | .97 (.83, 1.13) | | .73 | |
| Heavy smoking | 1.07 (.89, 1.28) | | .44 | |
| Use of antidepressants during pregnancy | .96 (.43, 2.15) | | .93 | |
| Hypertensive disorders of gestation | .97 (.86, 1.10) | | .71 | |
| DM during pregnancy | 1.00 (.78, 1.28) | | .97 | |
| Maternal stress during pregnancy | .98 (.89, 1.09) | | .82 | |
| Cesarean delivery | .96 (.87, 1.06) | | .49 | |
| Preterm |  | |  | |
| <34 weeks | 1.07 (.82, 1.40) | | .60 | |
| 34-37 weeks | 1.09 (.95, 1.24) | | .18 | |
| Breastfeeding | 1.07 (.90, 1.28) | | .40 | |
|  | β (95% CI)b | | p-value | |
| ERS | .04 (-.006, .09) | | .09 | |

Table S8. Logistic (model a) and linear (model b) regression models testing for genetic correlation. Only data from baseline were used.

OR = odds ratio; CI = confidence interval; DM = diabetes mellitus; β = regression coefficient from the linear regression model; ADHD-PRS = attention-deficit/hyperactivity disorder polygenic risk score; ERS = environmental risk score; PCs = principal components.

a. Model = Environmental risk factor ~ ADHD-PRS + age + sex + 10 PCs

b. Model = ERS ~ ADHD-PRS + age + sex + 10 PCs

# Table S9. Main effects and interactions between environmental risk scores and polygenic risk scores on dimensional psychopathologic measures while adjusting for sample attrition

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
|  | CBCL/ABCL attention | | | | SDQ Hyperactivity | |
|  | | β (95% CI) | p-value | β (95% CI) | | p-value |
| Main effects adjusting for sample attrition at wave 1 | | | | | |  |
| ADHD-PRSa | | **.08 (.04, .12)** | **<.0001** | **.08 (.04, .12)** | | **<.0001** |
| ERSa | | **.17 (.13, .20)** | **<.0001** | **.16 (.13, .19)** | | **<.0001** |
| Interactions adjusting for sample attrition at wave 1 | | | | | |  |
| ADHD-PRS \* ERSb | | **.04 (.009, .08)** | **.01** | **.04 (.006, .07)** | | **.02** |
| Main effects adjusting for sample attrition at wave 2 | | | | | |  |
| ADHD-PRSa | | **.08 (.04, .12)** | **<.0001** | **.08 (.04, .12)** | | **<.0001** |
| ERSa | | **.17 (.13, .20)** | **<.0001** | **.16 (.13, .19)** | | **<.0001** |
| Interactions adjusting for sample attrition at wave 2 | | | | | |  |
| ADHD-PRS \* ERSb | | **.04 (.009, .08)** | **.01** | **.03 (.006, .07)** | | **.02** |

Table S9. Mixed-effects linear regression models adjusting for sample attrition at waves 1 and 2. We computed inverse probability weights to adjust for demographic and clinical variables associated with follow up rates at waves 1 and 2. The following variables were used to compute inverse probability weights for sample attrition at wave 1: age, maternal education, maternal age, single parent family, diagnosis of anxiety at baseline. For sample attrition at wave 2, the following variables were used to compute inverse probability weights: maternal education, maternal age, diagnosis of anxiety at baseline.

β = regression coefficient from the mixed-effects linear regression models; CI = confidence interval; CBCL = Child Behavior Checklist; ABCL = Adolescent Behavior Checklist; SDQ = Strength and Difficulties Questionnaire; ADHD = attention-deficit/hyperactivity disorder; PRS = polygenic risk scores; ERS = environmental risk score; PCs = principal components.

a. Model = Dimensional symptoms ~ ADHD-PRS + ERS + age + sex + 10 PCs

b. Model = Dimensional symptoms ~ ADHD-PRS\*ERS + ADHD-PRS + ERS + age + sex + age\*ADHD-PRS + age\*ERS + sex\*ADHD-PRS + sex\*ERS + 10 PCs

# Table S10. Interactions between polygenic risk scores and different environmental risk scores on symptoms of attention-deficit/hyperactivity disorder

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | CBCL/ABCL attention | | | SDQ Hyperactivity | | | | |
| Interaction ADHD-PRS \* ERS | β (95% CI) | p-value | | | | β (95% CI) | p-value | |
| **Variable excluded from ERS** |  | |  | |  | | |  |
| Hypertensive disorders of pregnancy | .04 (.01, .07) | .01 | | | | .03 (.001, .06) | .04 | |
| Smoking during pregnancy | .04 (.01, .08) | .008 | | | | .04 (.007, .07) | .01 | |
| DM during pregnancy | .04 (.01, .08) | .005 | | | | .04 (.007, .07) | .01 | |
| Cesarean birth | .04 (.009, .07) | .01 | | | | .03 (.001, .07) | .03 | |
| Preterm | .05 (.02, .09) | .001 | | | | .04 (.01, .07) | .01 | |
| Maternal stress during pregnancy | .03 (-.003, .06) | .08 | | | | .03 (-.001, .06) | .058 | |
| Mother education | .02 (-.007, .05) | .13 | | | | .02 (-.01, .05) | .23 | |
| Never breastfed | .04 (.01, .08) | .005 | | | | .04 (.007, .07) | .01 | |
| Antidepressants during pregnancy | .04 (.01, .08) | .007 | | | | .03 (.005, .07) | .02 | |
| Single-parent family | .04 (.01, .08) | .005 | | | | .04 (.007, .07) | .01 | |
| Maternal age at birth | .04 (.007, .07) | .01 | | | | .03 (.004, .07) | .02 | |

Table S10. Mixed-effects linear regression models for different ERS. For each model, the ERS was created excluding one environmental risk factor.

Β = regression coefficient from the mixed-effects linear regression models; CI = confidence interval; CBCL = Child Behavior Checklist; ABCL = Adolescent Behavior Checklist; SDQ = Strength and Difficulties Questionnaire; ADHD-PRS = attention-deficit/hyperactivity disorder polygenic risk score; ERS = environmental risk score; PCs = principal components.

Model = Diagnosis ~ ADHD-PRS\*ERS + ADHD-PRS + ERS + age + sex + age\*ADHD-PRS + age\*ERS + sex\*ADHD-PRS + sex\*ERS + 10 PCs

# Table S11. Main effects and interactions between environmental risk scores and polygenic risk scores on psychiatric diagnoses

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | ADHD | | | Depressive disorder | | | Anxiety disorders | |
|  | OR (95% CI) | p-value | OR (95% CI) | | p-value | OR (95% CI) | | p-value |
| Main effects |  |  |  | |  |  | |  |
| ADHD-PRSa | **1.47 (1.22, 1.78)** | **<.0001** | 1.09 (0.94, 1.27) | | .25 | 1.02 (.91, 1.15) | | .69 |
| ERSb | **1.40 (1.19, 1.65)** | **<.0001** | **1.29 (1.13, 1.47)** | | **<.0001** | **1.28 (1.16, 1.42)** | | **<.0001** |
| Additive model ADHD-PRS + ERSc | | |  | |  |  | |  |
| ADHD-PRS | **1.44 (1.19, 1.73)** | **<.0001** | 1.07 (.93, 1.25) | | .32 | 1.01 (.90, 1.14) | | .85 |
| ERS | **1.37 (1.17, 1.62)** | **<.0001** | **1.29 (1.13, 1.47)** | | **<.0001** | **1.28 (1.15, 1.42)** | | **<.0001** |
| Interaction model ADHD-PRS \* ERSd | | |  | |  |  | |  |
| ADHD-PRS \* ERS | 1.15 (.98, 1.35) | .06 | 1.00 (.88, 1.14) | | .92 | 1.08 (.98, 1.20) | | .10 |
| Interaction model ADHD-PRS \* Agee | | |  | |  |  | |  |
| ADHD-PRS \* Age | 1.01 (.97, 1.05) | .49 | .98 (.95, 1.01) | | .34 | 1.0002 (.97, 1.02) | | .98 |
| Interaction model ERS \* Agef | | |  | |  |  | |  |
| ERS \* Age | 0.99 (.96, 1.03) | .96 | .97 (.94, 1.003) | | .08 | .99 (.97, 1.01) | | .72 |

Table S11. Mixed-effects logistic regression models.

OR = odds ratio; CI = confidence interval; ADHD = attention-deficit/hyperactivity disorder; ADHD = attention-deficit/hyperactivity disorder; PRS = polygenic risk score; ERS = environmental risk score; PCs = principal components.

a. Model = Dimensional symptoms ~ ADHD-PRS + age + sex + 10 PCs

b. Model = Dimensional symptoms ~ ERS + age + sex

c. Model = Dimensional symptoms ~ ADHD-PRS + ERS + age + sex + 10 PCs

d. Model = Dimensional symptoms ~ ADHD-PRS\*ERS + ADHD-PRS + ERS + age + sex + age\*ADHD-PRS + age\*ERS + sex\*ADHD-PRS + sex\*ERS + 10 PCs

e. Model = Dimensional symptoms ~ ADHD-PRS\*age + ADHD-PRS + age + sex + sex\*ADHD-PRS + sex\*age + 10 PCs

f. Model = Dimensional symptoms ~ ERS\*time + ERS + age + sex + sex\*ERS + sex\*age

# Table S12. Main effects and interactions between different polygenic risk scores and environmental risk scores on symptoms of attention-deficit/hyperactivity disorder

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  | β (95% CI) | p-value | β (95% CI) | p-value |
|  | Main effect ADHD-PRSa | | Interaction ADHD-PRS \* ERSb | |
|  | CBCL/ABCL Attention | | | |
| ADHD-PRS 08 | .09 (.05, .13) | <.0001 | .04 (.01, 0.08) | .007 |
| ADHD-PRS 05 | .09 (.05, .13) | <.0001 | .04 (.01, 0.08) | .006 |
| ADHD-PRS 04 | .09 (.05, .13) | <.0001 | .04 (.01, 0.08) | .008 |
| ADHD-PRS 03 | .09 (.05, .13) | <.0001 | .04 (.01, 0.07) | .009 |
| ADHD-PRS 02 | .08 (.04, .13) | <.0001 | .04 (.01, 0.08) | .006 |
| ADHD-PRS 01 | .08 (.04, .12) | <.0001 | .03 (.003, 0.07) | .03 |
| ADHD-PRS 005 | .09 (.05, .13) | <.0001 | .04 (.009, 0.07) | .01 |
| ADHD-PRS 001 | .09 (.05, .12) | <.0001 | .04 (.01, 0.08) | .005 |
|  | SDQ Hyperactivity | | | |
| ADHD-PRS 08 | .08 (.04, .12) | <.0001 | .04 (.006, .07) | .02 |
| ADHD-PRS 05 | .09 (.05, .13) | <.0001 | .04 (.007, .07) | .01 |
| ADHD-PRS 04 | .09 (.05, .13) | <.0001 | .04 (.008, .07) | .01 |
| ADHD-PRS 03 | .09 (.05, .13) | <.0001 | .04 (.01, .07) | .01 |
| ADHD-PRS 02 | .09 (.05, .13) | <.0001 | .04 (.01, .07) | .009 |
| ADHD-PRS 01 | .08 (.04, .12) | <.0001 | .03 (.005, .07) | .02 |
| ADHD-PRS 005 | .08 (.04, .12) | <.0001 | .04 (.006, .07) | .01 |
| ADHD-PRS 001 | .06 (.02, .10) | .001 | .04 (.007, .07) | .01 |

Table S12. Mixed-effects linear regression models for different ADHD-PRS thresholds.

Β = regression coefficient from the mixed-effects linear regression models; CI = confidence interval; CBCL = Child Behavior Checklist; ABCL = Adolescent Behavior Checklist; SDQ = Strength and Difficulties Questionnaire; ADHD-PRS = attention-deficit/hyperactivity disorder polygenic risk score; ERS = environmental risk score; PCs = principal components.

a. Model = Dimensional symptoms ~ ADHD-PRS + age + sex + 10 PCs

b. Model = Dimensional symptoms ~ ADHD-PRS\*ERS + ADHD-PRS + ERS + age + sex + age\*ADHD-PRS + age\*ERS + sex\*ADHD-PRS + sex\*ERS + 10 PCs

# Table S13. Main effects and interactions between different polygenic risk scores and environmental risk scores on diagnosis of attention-deficit/hyperactivity disorder

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  | OR (95% CI) | p-value | OR (95% CI) | p-value |
|  | Main effect ADHD-PRSa | | Interaction ADHD-PRS \* ERSb | |
| ADHD-PRS 08 | 1.46 (1.20, 1.76) | <.0001 | 1.15 (.99, 1.34) | .06 |
| ADHD-PRS 05 | 1.49 (1.24, 1.80) | <.0001 | 1.13 (.98, 1.33) | .09 |
| ADHD-PRS 04 | 1.49 (1.23, 1.80) | <.0001 | 1.15 (.99, 1.33) | .07 |
| ADHD-PRS 03 | 1.49 (1.22, 1.80) | <.0001 | 1.15 (.99, 1.34) | .06 |
| ADHD-PRS 02 | 1.44 (1.19, 1.75) | <.0001 | 1.18 (1.01, 1.37) | .03 |
| ADHD-PRS 01 | 1.39 (1.15, 1.68) | <.0001 | 1.12 (.97, 1.30) | .12 |
| ADHD-PRS 005 | 1.37 (1.13, 1.66) | .001 | 1.08 (.93, 1.25) | .30 |
| ADHD-PRS 001 | 1.36 (1.13, 1.64) | .001 | 1.06 (.91, 1.23) | .45 |

Table S13. Mixed-effects logistic regression models for different ADHD-PRS thresholds.

OR = odds ratio; CI = confidence interval; ADHD-PRS = attention-deficit/hyperactivity disorder polygenic risk score; ERS = environmental risk score; PCs = principal components.

a. Model = Diagnosis ~ ADHD-PRS + age + sex + 10 PCs

b. Model = Diagnosis ~ ADHD-PRS\*ERS + ADHD-PRS + ERS + age + sex + age\*ADHD-PRS + age\*ERS + sex\*ADHD-PRS + sex\*ERS + 10 PCs

# Table S14. Main effects and interactions between different polygenic risk scores and environmental risk scores on symptoms of depression/anxiety

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  | β (95% CI) | p-value | β (95% CI) | p-value |
|  | Main effect ADHD-PRS | | Interaction ADHD-PRS \* ERS | |
|  | CBCL/ABCL Depression/Anxiety | | | |
| ADHD-PRS 08 | .04 (.003, .07) | .03 | .02 (-.006, .31) | .12 |
| ADHD-PRS 05 | .04 (.01, .08) | .01 | .02 (-.006, .05) | .12 |
| ADHD-PRS 04 | .05 (.01, .08) | .009 | .02 (-.009, .05) | .17 |
| ADHD-PRS 03 | .05 (.01, .09) | .003 | .02 (-.008, .05) | .15 |
| ADHD-PRS 02 | .05 (.02, .09) | .002 | .02 (-.008, .05) | .14 |
| ADHD-PRS 01 | .06 (.02, .10) | .001 | .01 (-.01, .04) | .29 |
| ADHD-PRS 005 | .08 (.04, .12) | <.0001 | .01 (-.01, .05) | .23 |
| ADHD-PRS 001 | .05 (.01, .09) | .004 | .01 (-.01, .04) | .34 |
|  | SDQ Emotion | | | |
| ADHD-PRS 08 | .02 (-.009, .06) | .13 | .008 (-.02, .04) | .63 |
| ADHD-PRS 05 | .03 (-.002, .07) | .06 | .009 (-.02, .04) | .57 |
| ADHD-PRS 04 | .04 (.004, .08) | .02 | .008 (-.02, .04) | .59 |
| ADHD-PRS 03 | .04 (.006, .08) | .02 | .009 (-.02, .04) | .58 |
| ADHD-PRS 02 | .05 (.01, .09) | .01 | .005 (-.02, .03) | .73 |
| ADHD-PRS 01 | .05 (.01, .09) | .009 | .003 (-.02, .03) | .85 |
| ADHD-PRS 005 | .05 (.01, .09) | .005 | .007 (-.02, .04) | .64 |
| ADHD-PRS 001 | .03 (-.005, .07) | .09 | .003 (-.03, .03) | .84 |

Table S14. Mixed-effects linear regression models for different ADHD-PRS thresholds.

β = regression coefficient from the mixed-effects linear regression models; CI = confidence interval; CBCL = Child Behavior Checklist; ABCL = Adolescent Behavior Checklist; SDQ = Strength and Difficulties Questionnaire; ADHD-PRS = attention-deficit/hyperactivity disorder polygenic risk score; ERS = environmental risk score; PCs = principal components.

a. Model = Dimensional symptoms ~ ADHD-PRS + age + sex + 10 PCs

b. Model = Dimensional symptoms ~ ADHD-PRS\*ERS + ADHD-PRS + ERS + age + sex + age\*ADHD-PRS + age\*ERS + sex\*ADHD-PRS + sex\*ERS + 10 PCs

# Table S15. Main effects and interactions between different polygenic risk scores and environmental risk scores on diagnosis of depressive disorders

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  | OR (95% CI) | p-value | OR (95% CI) | p-value |
|  | Main effect ADHD-PRS | | Interaction ADHD-PRS \* ERS | |
| ADHD-PRS 08 | 1.08 (.94, 1.25) | .26 | 1.006 (.88, 1.13) | .92 |
| ADHD-PRS 05 | 1.09 (.95, 1.27) | .20 | 0.99 (.87, 1.12) | .94 |
| ADHD-PRS 04 | 1.10 (.96, 1.28) | .17 | 0.99 (.86, 1.11) | .83 |
| ADHD-PRS 03 | 1.12 (.98, 1.30) | .09 | 0.98 (.86, 1.10) | .69 |
| ADHD-PRS 02 | 1.09 (.95, 1.27) | .21 | 0.96 (.84, 1.08) | .49 |
| ADHD-PRS 01 | 1.15 (.99, 1.33) | .06 | 0.98 (.86, 1.10) | .72 |
| ADHD-PRS 005 | 1.17 (1.01, 1.36) | .03 | 0.99 (.87, 1.12) | .93 |
| ADHD-PRS 001 | 1.11 (.97, 1.29) | .12 | 0.99 (.86, 1.11) | .83 |

Table S15. Mixed-effects logistic regression models for different ADHD-PRS thresholds.

OR = odds ratio; CI = confidence interval; ADHD-PRS = attention-deficit/hyperactivity disorder polygenic risk score; ERS = environmental risk score; PCs = principal components.

a. Model = Diagnosis ~ ADHD-PRS + age + sex + 10 PCs

b. Model = Diagnosis ~ ADHD-PRS\*ERS + ADHD-PRS + ERS + age + sex + age\*ADHD-PRS + age\*ERSs + sex\*ADHD-PRS + sex\*ERS + 10 PCs

# Table S16. Main effects and interactions between different polygenic risk scores and environmental risk scores on diagnosis of anxiety disorders

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  | OR (95% CI) | p-value | OR (95% CI) | p-value |
|  | Main effect ADHD-PRS | | Interaction ADHD-PRS \* ERS | |
| ADHD-PRS 08 | 1.02 (.91, 1.15) | .71 | 1.08 (.99, 1.19) | .10 |
| ADHD-PRS 05 | 1.03 (.92, 1.16) | .59 | 1.08 (.99, 1.19) | .09 |
| ADHD-PRS 04 | 1.03 (.93, 1.16) | .51 | 1.07 (.98, 1.18) | .16 |
| ADHD-PRS 03 | 1.06 (.95, 1.19) | .30 | 1.07 (.98, 1.18) | .13 |
| ADHD-PRS 02 | 1.06 (.95, 1.19) | .26 | 1.09 (.99, 1.20) | .06 |
| ADHD-PRS 01 | 1.08 (.97, 1.22) | .15 | 1.10 (1.001, 1.22) | .04 |
| ADHD-PRS 005 | 1.11 (.99, 1.27) | .052 | 1.12 (1.02, 1.24) | .01 |
| ADHD-PRS 001 | 1.03 (.93, 1.16) | .50 | 1.09 (.99, 1.20) | .06 |

Table S16. Mixed-effects logistic regression models for different ADHD-PRS thresholds.

OR = odds ratio; CI = confidence interval; ADHD-PRS = attention-deficit/hyperactivity disorder polygenic risk score; ERS = environmental risk score; PCs = principal components.

a. Model = Diagnosis ~ ADHD-PRS + age + sex + 10 PCs

b. Model = Diagnosis ~ ADHD-PRS\*ERS + ADHD-PRS + ERS + age + sex + age\*ADHD-PRS + age\*ERS + sex\*ADHD-PRS + sex\*ERS + 10 PCs

# Supplementary Figure 1. Symptoms of attention-deficit/hyperactivity disorder according to the genetic and environmental risk for the disorder

Chart, box and whisker chart

Description automatically generated

Supplementary Figure 1. Bars represent the mean ± 95% confidence intervalof symptoms of ADHD (z-scores) in individuals with high/low ADHD-PRS (defined as a z-score **≥** 1 and ≤ -1, respectively) and high/low ERS (defined as a z-score > 1 and < -1, respectively).

CBCL = Child Behavior Checklist; ABCL = Adolescent Behavior Checklist; SDQ = Strength and Difficulties Questionnaire; ADHD = attention-deficit/hyperactivity disorder; PRS = polygenic risk score; ERS = environmental risk score.

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