Supplementary Online Content

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eMethods.

MEASURES

Psychotic-like Experiences. On the 21-item *Prodromal Questionnaire-Brief Child Version* (PQ-BC)[1] children are first asked to respond (yes/no) to whether they experienced a thought/feeling/experience (e.g., do familiar surroundings sometimes seem strange, confusing, threatening, or unreal to you?) before reporting on whether it was distressing and if so, the extent that it bothered them. From these data, *Total* (i.e., the sum of endorsed items) and *Distress* (i.e., 0 = no, 1 = yes [but no distress], 2–6 = yes [1 + score on distress scale]) scores were derived. Due to evidence that the *Total* score is more strongly associated with psychosis risk factors,[2] we focused on this metric but report *Distress* total scores here, in the **Supplemental eResults**. In this sample, the winsorized *Total* scores ranged from 0-13.3 (non-winsorized, 0-21), and the *Distress* scores ranged from 0-38.1 (non-winsorized, 0-104).

CBCL Internalizing and Externalizing Subfacets. On the 113-item Child Behavior Checklist (CBCL),[3] parents rated items representing specific problems in the past six months on a scale from 0 (*not true [as far as you know]*) to 2 (*very true or often true*). The Internalizing problems scale is comprised of three subscales assessing *anxious/depresse*d, *withdrawn/depressed*, and *somatic* problems. Similarly, the CBCL Externalizing problems scale is composed of *rule-breaking* and *aggressive* behavior subscales. In this sample, winsorized internalizing scores ranged from 0-21.6 (non-winsorized, 0-51), externalizing from 0-22.0 (non-winsorized, 0-49), anxious/depressed from 0-11.7 (non-winsorized, 0-26), withdrawn/depressed from 0-6.2 (non-winsorized, 0-15), somatic from 0-7.4 (non-winsorized, 0-16), rule-breaking from 0-6.8 (non-winsorized, 0-20), and aggressive from 0-16.3 (non-winsorized, 0-36).

Cognition Composite. The cognition composite is derived from Fluid and Crystalized Cognition Composites by standardizing raw scores and then averaging these scaled scores.[4]

***Fluid Cognition Composite*.** The fluid cognition composite is composed of 5 measures from the National Institute of Health (NIH) Toolbox (TB): 1) Flanker Test of Executive Function-Inhibitory Control and Attention (*Flanker*),[5] 2) List Sorting Working Memory Test (*List Sorting*),[6] 3) Dimensional Change Card Sort Test of Executive Function-Cognitive Flexibility (*Card Sort*),[7] 4) Picture Sequence Memory (*Picture Sequence*),[8] and 5) Pattern Comparison Processing Speed Test (*Processing Speed*).[9] The *Flanker* assesses participants' ability to inhibit prepotent responses when they interfere with goal achievement and is quantified by summing accuracy (i.e., 0.125*number of correct responses) and reaction time (median RTs to correct incongruent trials). *List Sorting* assesses immediate recall and ordering of visually presented stimuli to index working memory. Raw summed scores of the number of items accurately recalled and sequenced on two lists range from 0-26. The *Card Sort* evaluates one's capacity for cognitive flexibility, or the ability to strategically adapt prepotent responses to new situations. Participants are asked to sort bivalent test cards according to one characteristic (e.g., shape) and then another (e.g., color), and the test is scored in the same way as the Flanker. The *Picture Sequence* task assesses episodic memory by asking participants to recall a series of pictures and objects shown in a particular order on the screen, each accompanied by an audio-recorded phrase. Performance is measured by the total number of correctly recalled adjacent pairs of objects. The *Processing Speed* task measures how

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long it takes participants to identify whether two visual patterns are the same or not. The final score denotes the number of correct responses (out of 130) given in 90 seconds.

***Crystalized Cognition Composite*.** The crystalized cognition composite is composed of 2 measures from the NIH TB: 1) *Picture Vocabulary Test (Picture Vocabulary)* and 2) *Oral Reading Recognition Test (Oral Reading).*[10] *Picture Vocabulary* assesses receptive vocabulary by having participants match the meaning of an audio-recorded word with one of four pictures presented on a screen. *Oral Reading* evaluates participants' language ability as they read and pronounce letters and words as accurately as they are able. In both tests, items are presented adaptively until participants have answered 20-30 items. The total cognition composite ranged from 44-117, flanker from 51-116, list sorting from 36-136., card sort from 50-120, picture sequence from 76-136, processing speed from 30-140, picture vocabulary from 29-119, and oral reading from 59-119. As no scores were ± 3 SDs, no winsorization was applied.

Sleep Problems. The *Sleep Disturbance Scale for Children* (SDSC)[11] is a 27-item questionnaire completed by parents that assesses sleep problems in children. The total score is derived by summing across the 6 subscales that assess symptoms of: 1) disorders of initiating and maintaining sleep, 2) sleep breathing disorders, 3) disorders of arousal, 4) sleep-wake transition disorders, 5) disorders of excessive somnolence, and 6) sleep hyperhidrosis. In this sample, the winsorized total sleep score ranged from 11.1 to 61.8 (non-winsorized, 0-126), disorders of initiating and maintaining sleep from 0.48-23.0 (non-winsorized, 0-35), sleep breathing disorders from 0-7.6 (non-winsorized, 0-15), disorders of arousal from 0.66-6.2 (non-winsorized, 0-15), sleep-wake transition disorders from 0.18-16.1 (non-winsorized, 0-30), disorders of excessive somnolence from 0-14.3 (non-winsorized, 0-25), and sleep hyperhidrosis from 0-6.0 (non-winsorized, 0-10).

Body Mass Index (BMI). BMI, as measured in children at the baseline assessment (ages 9.9±0.6), was calculated as:

$$703 * \frac{weight(lbs)}{height(in)^2}$$

Data with implausible values were set to missing in our analyses according to the following criteria. First, BMI measures based upon impossible values (i.e., height of 4 and 4.25 inches) were set to missing (n=2). Second, BMIs lower than the minimum value on CDC charts[12] (i.e., 10) were set to missing (n=17). The highest observed BMI value was 54.99, which was considered possible. Overall, 8 children were missing height or weight measurements, with 19 BMI values set to missing based on the aforementioned data cleaning. In this sample, winsorized BMI values ranged from 10.1-31.5 (non-winsorized, 10.1-54.99).

Brain Structure. MRI Acquisition and Processing. Casey et al., 2018 provide an in-depth description of the ABCD Study℠ imaging acquisition protocol and parameters.[13] Briefly, 1 mm isotropic T1-weighted structural images were acquired on 3 T (Siemens, Phillips and GE) MRI scanners using either a 32-channel head or 64-channel head-and-neck coil. Scan protocols were carefully harmonized across the three MRI vendor platforms to reduce scanner-caused variability. Head motion is a significant concern for pediatric imaging, so real-time motion detection and correction was implemented (prospective motion correction on the GE and Volumetric Navigators on the Siemens platforms). Structural MRI data was released for 11,556 of the 11,875 participants.

Hagler et al., 2019 provide an in-depth description of the ABCD Study℠ image processing and analysis methods.[14] MRI data were processed with the Multi-Modal Processing Stream

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software package that includes FreeSurfer 5.3. Besides a modified intensity normalization process used by the ABCD processing pipeline, the standard FreeSurfer cortical and subcortical reconstruction pipeline was run to generate structural measures including volume and cortical thickness. A description of the quality-control measures conducted on the processed data is provided in Hagler et al. Only participants whose structural MRI reconstructions passed QC tests (n=11,076) were included in the current analysis. Total intracranial volume (ICV), total gray matter volume (GMV), and total white matter volume (WMV) were extracted from ABCD data release 2.0.1, which corrected an initial problem with data released in data release 2.0 with regard to the laterality of data in some participants.

Covariate Descriptions

All variables were assessed at the ABCD baseline assessment and with the exception of prenatal exposure, birth weight, and gestational age at birth reflect measures taken while children were ages 9.9±0.6.

Child age. Self-reported age was logged in months and converted to years.

Child sex. Child sex is a dichotomous variable indicating whether the child is female (0) or male (1).

Birth weight. Parent/caregiver retrospectively reported on child birth weight in pounds and ounces. We converted to a total in ounces.

Child Race/Ethnicity. Parents/caregivers were allowed to select from 26 categories. We formed dichotomous groups for the most prevalent categories of race (i.e., White, Black, Asian, Pacific Islander, Native American), with remaining participants being assigned to Other. Hispanic ethnicity was also considered. All variables were dummy coded as non-mutually exclusive dichotomous variables; as such, participants could be coded within more than one category.

Child Lifetime Substance Exposure. Children self-reported if they tried alcohol (i.e., ever had a sip), marijuana (e.g., ever had a puff of a cigarette or blunt, etc.), and tobacco (e.g., ever had a puff of a cigarette or hookah, etc.). More substantive self-reported use or positive hair toxicology screens were rare and as such participants were excluded on these metrics in follow-up analyses (for additional information on these variables, please refer to the section entitled ***Post-hoc Analyses with Exclusions: Excluding Uncommon Substances Used by Children and Mothers During Pregnancy as well as Children Born Prematurely and non-Biological Mother Report*** below).

Unplanned Pregnancy. Parent/caregivers retrospectively reported whether the pregnancy was planned.

Maternal Age at Birth. Parents/caregivers retrospectively reported the child's biological mother's age at the time of the child's birth.

Prenatal Vitamin Usage. Parent/caregivers noted whether the mother used prenatal vitamins during the pregnancy.

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Gestational Age at Birth: Parent/caregivers retrospectively reported on child gestation age at birth.

Gestational Age when Mother Learned of Pregnancy. Parent/caregivers retrospectively reported the number of weeks the mother was pregnant before she learned of her pregnancy.

Maternal Education. Maternal education was recoded such that 12th grade, HS grad, and GED =12 years; some college and associates degree = 14 years; Bachelor's degree = 16 years; Master's degree = 18 years; Professional and Doctoral degrees = 20 years.

Household Income. Due to low endorsement of the first five of 10 household income levels, this variable was recoded such that the first five categories were assigned a value of one (i.e., <$50,000; n=3,104). The subsequent categories used were coded as two ($50,000-$74,999, n=1,454), three ($75,000-$99,999, n=1,511), four ($100,000-$199,999, n=3,217), and five ($200,000 or more, n=1,221), respectively (**Table 1**). Analyses treating this measure as a continuous variable across all categories produced identical results.

Family History of Psychopathology. Parent/caregivers reported on whether any 1st degree relatives had a history of problems with psychosis, depression, anxiety, antisocial behavior, or mania.

Prenatal exposure to alcohol and tobacco. Child prenatal exposure to alcohol and tobacco both before (alcohol: n = 2,781; tobacco: n = 1,506) and after (alcohol: n = 290; tobacco: n = 566) maternal knowledge of pregnancy were coded as separate dichotomous variables based upon parent/caregiver retrospective report.

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ANALYSES

Hierarchical Linear Model Specification

Below, we illustrate the general hierarchical linear model form we used across all analyses, where fixed effects estimates are represented by the gamma coefficients (γ):

Level 1 (child)

$$Outcome_{ijk} = \pi_{0jk} + \pi_{1jk}exposure_{1jk} + \pi_{2jk}covariate_{2jk} + \pi_{3jk}covariate_{3jk} \ \ldots + e_{ijk}$$

Level 2 (family)

$$\pi_{0jk} = B_{00k}$$
$$\pi_{1jk} = B_{10k}$$
$$\pi_{2jk} = B_{20k}$$
$$\pi_{3jk} = B_{30k}$$
$$\ldots$$
$$\pi_{ijk} = B_{i0k}$$

Level 3 (research site)

$$B_{ook} = \gamma_{000}$$
$$B_{1ok} = \gamma_{100}$$
$$B_{2ok} = \gamma_{200}$$
$$B_{3ok} = \gamma_{300}$$
$$\ldots$$
$$B_{iok} = \gamma_{i00}$$

All additional analyses reported below were identical to those reported in the main manuscript, with the same covariates and random effects (i.e., family membership nested within site). Unless otherwise noted, analyses were conducted with the inclusion of covariates.

Post-hoc Analyses with Exclusions: Uncommon Substances Used by Children and Mothers During Pregnancy as well as Children Born Prematurely and non-Biological Mother Report. A series of *post hoc* analyses were conducted to determine whether removing the following individuals from analyses significantly altered results:

a) children who reported using marijuana (n=14), using substances other than alcohol and tobacco (i.e., bath salts, n=1; "sniff" to "get high," n=9; inhalants, n=3; amphetamines not as prescribed, n=2; tranquilizers/anxiolytics/sedatives not as prescribed, n=2; pain medication not as prescribed, n=1; cough medication to "get high," n=1), or having a full drink of alcohol (n=19) or more than a puff of tobacco (n=14), or screened positive for substances based on hair toxicology (methamphetamines, n=4; THC, n=3; EtG, n=4; cotinine, n=5; Adderall, n=6). A total of 80 individuals were excluded for these analyses (Numbers do not sum as some children were positive across multiple indices).

b) individuals whose biological mothers reported using other illicit substances while pregnant (cocaine or crack, n=68; heroin or morphine, n=20; oxycontin, n=33; other, n=100). A total of 185 individuals were excluded (numbers do not sum as some mothers were positive across multiple indices).

c) individuals born more than 8 weeks premature (n=148).

d) individuals whose parent/caregiver in ABCD is not the biological mother (n=1427).

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Exclusion of Children whose Mother Used Cannabis Only Before Knowledge of Pregnancy but Discovered Pregnancy at ≥15 or ≥10 Weeks Gestation. Given variability in gestational age when the mother learned of her pregnancy and our hypotheses with regard to the timing of exposure based on endocannabinoid ontogeny, we conducted supplemental analyses excluding participants who were prenatally exposed only prior to maternal knowledge of pregnancy whose mothers learned of the pregnancy ≥15 (n=25) and ≥10 (n=61) weeks. These analyses were done to minimize the possibility that exposure only prior to knowledge occurred following sufficient fetal endocannabinoid receptor expression.

Evaluation of Covariate Influence. To determine which covariates were responsible for attenuating associations between prenatal marijuana exposure and childhood outcomes, covariates with the lowest p-values were systematically removed from each model until non-significant associations became significant. The following outcomes were examined in this manner with regard to prenatal exposure after maternal knowledge of pregnancy: BMI, sleep problems, internalizing, birth weight, intracranial volume, gray matter volume, and white matter volume. In addition, all outcomes were examined in this manner with respect to prenatal exposure prior to maternal knowledge of pregnancy: psychosis proneness; internalizing, externalizing, attention, thought, social, and sleep problems; cognition; BMI; birth weight; and intracranial, gray matter, and white matter volumes.

Log-transformed Analyses. None of our variables, with the exception of birth weight, had skewness statistics indicative that transformations are needed (i.e., skewness < 2.58). However, with the exception of cognition (post-maternal knowledge use, Levene's test: p=0.25; pre-maternal knowledge use, Levene's test: p=0.25), birth weight (post-maternal knowledge use, Levene's test: p=0.676 pre-maternal knowledge use, Levene's test: p=0.30), psychotic-like experiences (pre-maternal knowledge use, Levene's test: p=0.23), BMI (pre-maternal knowledge use, Levene's test: p=0.37), and gestational age (pre-maternal knowledge use, Levene's test: p=0.07), outcome variables showed evidence of unequal variances across groups (i.e., post-maternal knowledge use vs no post-maternal knowledge use and/or pre-maternal knowledge use vs no pre-maternal knowledge use (all other Levene's test all ps<0.0063). As a result, we repeated all analyses for variables showing unequal variances across groups as well as abnormal skew (i.e., birth weight) using log transformed data.

Including maternal PLEs instead of familial history of psychosis. We calculated an estimate of maternal PLEs from four questions on the Adult Self Report (ASR) of psychopathology as described by Barber and colleagues.[15] We replaced family history of psychosis as a covariate in analyses due to its low endorsement (**Table 1**; <2.3% overall).

Polygenic Score (PGS) Derivation and Analyses.

***Rationale*:** Emerging studies suggest that cannabis use is genetically correlated with several of the outcomes studied here, especially PLE, externalizing and internalizing problems and cognition.[16,17] This observation raises the possibility of confounding, such that any association between prenatal cannabis use and the outcome might be attributable to the greater risk of prenatal cannabis use in women with a genetic susceptibility to cannabis use, and consequently, due to pleiotropic variants shared between maternal cannabis use and psychopathology that segregated to the offspring. While we account for family history, which encompasses both genetic and environmental factors, polygenic scores (PGS) offer an additional genomic index of such shared

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pleiotropic vulnerability. For instance, if the association between prenatal cannabis use and PLEs is attributable to the genetic correlation between schizophrenia and cannabis use, then inclusion of polygenic risk scores for both schizophrenia and cannabis use should adjust for this confounding.

Genotyping, Quality Control, and Imputation. Saliva samples were genotyped on the Smokescreen array[18] by the Rutgers University Cell and DNA repository. Genotyped calls were aligned to GRCh37 (hg19) and all individuals self-reporting ancestral origins other than European were excluded due to our reliance on summary statistics based on GWAS conducted in European ancestral samples and evidence that polygenic risk scores are poorly predictive across ancestral origins.[19]

The following processing steps were conducted using the Ricopili pipeline.[20] Briefly, SNPs with call rates ≥ 0.95 and MAF ≥ 1% were retained. Individuals with high rates of missingness (>5%) and autosomal heterozygosity deviation (F_{HET}) that is not within ± 2 SD were removed; after sample QC, SNPs were further filtered to call rate ≥ 0.98 and Hardy-Weinberg p-values > 1E-6 (founders only), yielding 372,342 SNPs. Sex checks were conducted with follow-up to reconcile mismatches.

Individuals that passed the first phase of QC were then checked for relatedness, both known and cryptic and Mendelian errors were resolved. Next, using data from unrelated individuals (pi-hat ≤ 0.15) and an LD pruned set of common (MAF>0.05) and non-palindromic SNPs (and excluding MHC and chromosome 8 inversion region), we performed principal components analysis (PCA) using the cosmopolitan 1000 Genomes Project phase 3 data in EIGENSTRAT. Only those aligning with ancestral non-Hispanic European ancestry were retained yielding a final sample of 4,737. After selection, a final ancestrally-informative PCA was conducted and the first 10 PCs were projected from founders to other relatives. Imputation to 1000 Genomes and Haplotype Reference Consortium (HRC) data was conducted using strictly QCed SNPs on the Michigan Imputation Server yielding 39,127,678 SNPs. Dosage data were converted to hard-call genotypes using Plink and only SNPs with imputation r^2 scores ≥ 0.3 were carried forward into polygenic scores.[21]

PGS calculation. PGS reflect the weighted additive effect of approximately independent SNPs. Weights are derived from well-powered discovery genome-wide association studies (GWASs) from which effect sizes and effect alleles may be extracted.[19] We used summary statistics generated from the most well-powered GWASs of schizophrenia,[22] educational attainment,[23] and cannabis use.[16] PC-verified non-Hispanic individuals of European ancestry (n=4,644 of those with complete prenatal exposure data) were scored using p-value informed LD clumping and thresholding (P_ts = 0.00000005, 0.0001, 0.001, 0.01, 0.01, 0.10, 0.20, 0.30, 0.40, 0.50, 1.0) with PGSice 2 software.[24]

PGS Analyses. First, linear mixed effect models were run for each outcome variable in the European-only subsample, including all previous fixed effect covariates except race **(eTable 13)**. Second, each outcome of interest was associated with each p-value threshold of the relevant PGS, the first 10 principal components (PCs), and sex **(eTables 15-16)**. Third, models were run for each outcome variable in the European-only subsample, including the same fixed effect covariates as well as the PGS for the most significantly associated threshold and the first 10 PCs (**eTable 14)**. All models nested data by family membership within site.

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Non-Mutually Exclusive Groups Regressions. To test the robustness of our findings across an analogous statistical procedure, we conducted our analyses with non-mutually exclusive exposure groups (n=648 prenatally exposed to cannabis prior to maternal knowledge of pregnancy, n=242 exposed following maternal knowledge of pregnancy). Both exposure groups were entered into linear mixed effects models simultaneously; beta estimates can be interpreted as the difference between each exposure group and no exposure on each outcome, when accounting for the overlap in the rate of exposure. This procedure is analogous to that described in the main text but does not give comparisons between exposures or allow omnibus main effects test of both or each exposure.

Test of Overfitting with 5-Fold Cross-Validation Procedure. With few exceptions, past research on prenatal cannabis exposure has generally been limited to small samples that are unable to include potentially confounding covariates in analytic models. Here, we compared estimates of prenatal exposure before and after knowledge of pregnancy with and without including covariates (e.g., whether the pregnancy was planned, familial history of psychopathology, child substance exposure) that often confound smaller studies (see **Tables 2** and **Table 3** for our estimated beta coefficients).

Many associations with prenatal marijuana exposure following maternal knowledge of pregnancy remained significant when covariates were included, but effect sizes were (expectedly) attenuated downward (please refer to main manuscript). However, this attenuation could be due to a real effect or due to overfitting in our model resulting from the inclusion of covariates. As we are not interpreting the whole model fit here, but rather single beta parameters, the main effect of overfitting would be to increase the variance of our beta parameters and to decrease their generalizability/consistency to predict out of sample. Ideally, we would use a hold-out data set of the ABCD study[SM]. However, because we used the full data to fit the models and due to the relatively small sample size of exposed children, we approximated the degree of difference in a hold-out sample with a 5-fold cross-validation procedure. Our exposure groups here were non-mutually exclusive; because cross-validation of regression estimates are far more common than of mean differences (as the latter often relies on post-hoc tests) and because both mutually exclusive groups and non-mutually exclusive groups give analogous results, we have conducted our cross-validation on a regression analysis. This analysis is not being used to draw conclusions about statistical significance. Instead, it is testing generalizability of prediction given our covariates (or the lack thereof). These tests should perform identically when used via model comparison (which we do below) and when all regression and ANOVA assumptions are met. The latter is not guaranteed across cross-folds, however, giving credence to the regression format.

We did this by estimating the effect of the beta after knowledge of pregnancy marijuana exposure in each cross-fold and comparing it to the beta of this same variable in the hold-out fold. In doing so, we scaled beta estimates to extract the standardized parameter. We then used this comparison to develop a root mean square error of approximation (RMSEA) statistic that serves as a measure of the degree of overfitting. We call this statistic RMSDA (root mean square difference of approximation) to differentiate from the RMSEA used in standard whole model fit statistics).

Essentially, when the beta estimates are the standardized estimates (which in this case they are), this statistic is scaling the Mean Square Error (MSE), set to the same scale as the beta estimates. While there is no accepted cutoff for the MSE in the context of k-fold validation

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procedures, the RMSDA being on the same scale as the beta is a useful indicator of the degree of inconsistency we see in the betas.

More specifically, let b_{at}, and b_{ak} represent the estimated beta of after knowledge of pregnancy in the held out *kth* fold when all covariates are included in the model. In that case our RMSDA statistic would be expressed as:

$$RMSDA = \sqrt{\left(\sum_{K} (b_{at} - b_{ak})^2 \right)}$$

With the RMSDA being the degree of misfit calculated across all k-folds of the data for the after-knowledge variable when covariates are included in the model.

We can then calculate a value for the consistency of the beta estimate when no covariates are included in the model, if b_{nt} is the beta for each *k*th fold when no covariates are included and b_{nk} is the beta value prediction in the kth fold when no covariates are predicted, we can then substitute those variables for b_{at} and b_{ak}, respectively. This provides an estimate of the degree of inconsistency between the betas (the RMSDA) for a model with and without the covariates. If RMSDA*c* is with the covariates, and RMSDA*n* is a model with no covariates, *in order to test whether the model is overfit due to inclusion of covariates*, we simply subtract the difference in the consistencies, i.e. RMSDA*c* – RMSDA*n*, such that we measure the degree of inaccuracy measured by specifically including the covariates and whether it exceeds the absolute value of the beta prediction. This value can then be compared to the beta, as the root of mean square of the standardized beta estimates is on the same scale as the standardized beta estimates themselves. There is no statistical cut off for MSE, and that is true for a scaled MSE (such as RMSDA) as well, but it is a useful approximation to demonstrate the marked consistency of our results.

Inverse Probability Weighted Propensity Scores. To test whether covariates could be used to account for non-random assignment to exposed and unexposed conditions, we used inverse probability weighted propensity scores (IPW).[26] These analyses can be considered an alternative to the covariate adjustment we used in our main analyses. IPW weights the sample based on the likelihood of exposure associated with particular covariates. For example, if lower household income predicts greater exposure to prenatal cannabis exposure after knowledge of pregnancy, then any individual from a high-income family that was exposed after knowledge of pregnancy would have a higher weight in the analysis. After propensity scores were generated and the sample was weighted, we conducted a balance analysis to determine whether the covariates included in the propensity score weights were still significant predictors of prenatal marijuana exposure in the weighted sample. If so, this means that our propensity score method did not fully account for non-random assignment of prenatal exposure based on that particular covariate. We ran this procedure separately for each category of exposure in our original model (i.e., before knowledge of pregnancy, after knowledge of pregnancy) as well as for any prenatal cannabis exposure. Here, we conducted three models: any before knowledge, any after knowledge, and any exposure. With a three-level unordered factor variable (i.e., mutually exclusive groups), we cannot create single set of weights for exposure easily. While some procedures have been developed, this would involve complex three level interactions, which likely have high false discovery rates when given number of covariates in the model. Instead, we generated our weights predicting three exposures, any exposure, before exposure only, and any after exposure and then conducted three models to

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demonstrate robustness to non-random selection for each exposure, with each analysis retaining its own set of weights to maximally account for non-random exposure.

All necessary variables (outcomes, predictors, nesting factors) were gathered from the dataset, which was reduced to participants with complete data. For each type of exposure (before-knowledge; after-knowledge; any exposure), a correlation matrix was conducted with the exposure variable and all fixed effect covariates used in the original models. All significantly correlated covariates were then used to create weights for each type of exposure. Logistic regression models were used to predict exposure from these covariates. The ipwpoint() function in the IPW package[27] in R was used to create weights based on these covariates. For the balance analysis, the svglm() function from the survey design package[28] was used to run GLM models predicting exposure from the covariates, weighting by the weights created earlier and results were compared to examine whether weighting reduced associations between covariates and exposure. For the final analysis of prenatal cannabis exposure predicting outcomes, weighted data were created with svydesign(), and mixed effect models were run predicting each outcome from the exposure (with analyses of before-knowledge, after-knowledge was included as a covariate, and vice versa) and all other covariates not used to generate weights, using the weighted data.

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eResults

Psychotic-like Experiences Distress. Children prenatally exposed to cannabis after maternal knowledge of pregnancy had significantly higher distress scores relative to those never exposed to cannabis (without fixed effect covariates: b=2.89, p=8.93e-07; with fixed effect covariates: b=1.98, p=0.021) and those exposed only before maternal knowledge (without fixed effect covariates: b=1.16, p=0.109; with fixed effect covariates: b=2.04, p=0.036). Exposure only before maternal knowledge was not significantly more associated with distress scores than no exposure (without fixed effect covariates: b=1.73, p=1.28e-04; with fixed effect covariates: b=-0.057, p=0.917).

Analyses with Exclusions.

Excluding children for uncommon substance use. Results were largely consistent with those reported using the full sample before FDR correction, (**eTable 9**), the only exceptions being that children exposed to cannabis after maternal knowledge of pregnancy weighed significantly lower at birth than those never exposed (b=2.85, p=0.042), and the significant difference between those exposed after knowledge and those only exposed before knowledge was reduced to a trend (b=-1.67, p=0.052).

Excluding children exposed to uncommon substances during pregnancy. Results were largely consistent with those reported using the full sample (**eTable 10).** The only deviation from primary results was that the difference in cognition between those exposed after knowledge and those only exposed before knowledge was reduced to a trend (b=-1.54, p=0.076).

Excluding Children Born Prematurely. Results were consistent with those reported using the full sample (**eTable 11**). The sole exception was that the difference in global cognition scores between those prenatally exposed to cannabis only before maternal knowledge and those never exposed became significant (b=0.955, p=0.046).

Excluding Children Whose Parent/Caregiver Report was not Their Biological Mother. As described in **eTable 12**, results were consistent with those reported using the full sample.

Excluding Children whose Mother Used Cannabis Only Before Knowledge of Pregnancy but Discovered Pregnancy at ≥15 or ≥10 Weeks Gestation. Excluding children who were prenatally exposed to cannabis prior to maternal knowledge only, but whose mothers learned of their pregnancy at ≥ 15 weeks, produces results largely consistent with those reported using the full sample (**eTables 21-22**). The sole exception was that the difference in global cognition scores between those prenatally exposed to cannabis only before maternal knowledge and those never exposed became significant (b=1.04, p=0.033). Further, analyses excluding individuals whose mother used cannabis only before knowledge of pregnancy and who discovered their pregnancy after ≥10 weeks were also consistent, with the same exception (b=1.11, p=0.031).

Covariate Attenuation of Associations Between Prenatal Cannabis Exposure and Child Outcomes. The difference in CBCL Attention scores between those prenatally exposed to cannabis only before maternal knowledge of pregnancy and those never exposed reached significance when removing child sex and familial histories of depression, anxiety, and antisocial behavior (b=0.45, p=0.026). When child age, maternal education, being Black, and household income were removed from the model, the difference in Total Cognition between those exposed after maternal knowledge and those never exposed reached significance (b=-1.85, p=0.015). When

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familial history of depression and twin/triplet status were removed, the difference in Sleep problems between those exposed after knowledge and those never exposed reached significance (*b*=1.47, *p*=0/047), was then reduced to a trend when familial history of anxiety was also removed (*b*=1.28, *p*=0.062), and then again reached significance when familial history of antisocial behavior was removed (*b*=1.78, *p*=0.016). No other non-significant associations were influenced by a single or small number of covariates.

Log-transformed Analyses. Broadly, log-transformation did not meaningfully alter associations between any variables that showed evidence of unequal variances across groups or skewness (**eTable 4**). Notably, the increased internalizing problems associated with cannabis exposure after maternal knowledge of pregnancy relative to those exposed only before knowledge was reduced to a trend *(b*=0.181, *p*=0.062).

Inclusion of Only Significantly Associated Covariates. Restricting fixed effect covariates to only those significantly associated with each outcome produced largely similar results (**eTables 5-7).** The two exceptions were that prenatal exposure post maternal knowledge of pregnancy was no longer associated with significantly more internalizing problems than those exposed only before maternal knowledge (*b*=0.60, *p*=0.20), and the difference in attention problems between those exposed only before knowledge and those never exposed reached significance (*b*=0.37, *p*=0.047).

Including Maternal PLEs Instead of Familial History of Psychosis. Replacing familial history of psychosis with maternal PLEs did not meaningfully alter relationships between child PLEs and prenatal exposure: exposure after maternal knowledge of pregnancy was associated with significantly more PLEs than no exposure (*b*=0.79, *p*=0.012) and exposure only before knowledge (*b*=0.90, *p*=0.012), which did not differ significantly from no exposure (*b*=-0.11, *p*=0.60; **eTable 23).**

Polygenic Score Analyses. In the subsample of individuals of European ancestry with available genetic data (n=4,591), only psychotic-like experiences and social problems remained significantly different in at least one group contrast (**eTable 13**). Associations with externalizing, attention, and thought problems showed the same directionality of group differences and similar effect size but were rendered non-significant (|*b*s|<1.7, *p*s>0.053). We attribute the reductions in significance to the smaller sample size of the European ancestry only sample.

Psychotic-like experiences were not significantly associated with polygenic scores (PGS) for schizophrenia or cannabis use, but were significantly associated with educational attainment, covarying for the first 10 PCs and sex (**eTable 15**). Inclusion of the schizophrenia PGS, educational attainment PGS, and cannabis use PGS that were most significantly associated with PLEs independently, and together, did not alter group differences in PLEs between those prenatally exposed after knowledge and those never exposed (|*b*s|>1.0, *p*s<0.061) and never exposed (|*b*s|>1.5, *p*s<0.016; **eTable 14**). Inclusion of cannabis use PGS, which was not associated with social problems (**eTable 16**), did not alter group differences in social problems between those prenatally exposed after knowledge and those never exposed (*b*=0.86, *p*=0.024) and never exposed (*b*=0.78l, *p*=0.023; **eTable 14**).

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Non-Mutually Exclusive Groups Regressions Results.
When not considering covariates, regressions of non-mutually exclusive exposure groups produced results largely similar to the regression analyses of mutually exclusive ANOVAs presented in the main manuscript (**Table 2**; **eTable 17**). Prenatal exposure after and before knowledge of pregnancy were significantly associated with worse outcomes on all variables except gestational age at birth.

When considering potentially confounding covariates, regressions of non-mutually exclusive exposure groups produced results similar to those reported in the main manuscript (**Table 3**; **eTable 18**). Specifically, prenatal exposure after, but not before, maternal knowledge of pregnancy was significantly associated with higher scores on PLEs and Internalizing, Externalizing, Attention, Thought, and Social problems, and reduced cognition and birth weight.

Test of Overfitting with 5-Fold Cross-Validation Procedure.
When comparing the cross-validated betas from models including the covariates to models excluding the covariates, the standardized mean square difference in the betas (what we call RMSDA values) with the inclusion of covariates was generally small (**eTable 8**). Put in perspective, the empirical standardized difference in the beta estimates by including covariates would alter r^2 values by .1% of the variance in the most extreme cases (the square of RMSDA*c* – RMSDA*n*). For PLES, BMI, Sleep problems, and Birth weight, a model including the covariates had very slightly greater consistency in the beta estimates than a model without them.

Inverse Probability Weighted Propensity Scores.
Balance analyses indicated that for pre-knowledge and any prenatal exposure, inverse probability weights accounted for associations between covariates and exposure (**eTable 19**). With respect to post-knowledge of pregnancy exposure, first-degree familial history of depression and antisocial behavior, as well as unplanned pregnancy and child sex and twin/triplet status still significantly predicted exposure (*p*s<0.05).

Results from IPW analyses, predicting primary outcomes in the weighted sample from each type of exposure, the covariates not included in the generation of weights, and weighting by the weights, yielded similar results to our original analyses with respect to post-knowledge exposure (PLEs, all CBCL scales, and cognition, but not birth weight, were significantly associated with exposure, *p*s <0.01; **eTable 20**). Any exposure was also significantly associated with all outcomes except brain metrics (*p*s<0.01). Here, unlike in our original analyses, pre-knowledge exposure was significantly associated with PLEs, all CBCL scales, BMI, and sleep problems (*p*s<0.01), illustrating the less conservative nature of these analyses.

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Discussion of effect sizes. When not accounting for potentially confounding variables, all studied outcomes, with the exception of gestational age at birth, showed significant differences across those prenatal exposed to cannabis after maternal knowledge of pregnancy and those never exposed and those exposed only before knowledge. The smallest effect was found for birth weight (β=-0.029 and -0.023, R^2=0.001 and 0.001, respectively), with those exposed after knowledge weighing 3.4 and 2.7 ounces less at birth than those not exposed and those exposed only before maternal knowledge of pregnancy. The largest effect was found for externalizing problems (β=0.132 and 0.082, R^2=0.018 and 0.007 respectively), with those exposed only after knowledge scoring 4.8 and 3.0 points higher on the CBCL externalizing scale than those not exposed and those exposed only before knowledge; **Table 2**). All studied outcomes, except gestational age at birth, ICV, and white matter volume, showed significant differences between those exposed only before knowledge and those never exposed. The smallest effect was found for cognition (β=-0.022, R^2=5.0e-04), with those exposed only before knowledge scoring 1.1 points lower than those never exposed. The largest effect was found for attention problems (β=0.071, R^2=0.005), with those exposed only before knowledge scoring 1.3 points higher than those never exposed.

After accounting for potentially confounding covariates, small but significant differences were found between those exposed after knowledge and those not exposed and those exposed only prior to maternal knowledge of pregnancy on PLEs and externalizing, attention, thought, and social problems; nominal/marginally significant findings were present for internalizing problems and birthweight (**Table 3**). The smallest significant difference between those exposed after knowledge and those never exposed was found for PLEs (β=0.030, R^2=0.001), with the former group scoring 0.85 points higher than the latter. The smallest significant difference between those exposed after knowledge and those exposed only before knowledge was found for thought problems (β=0.032, R^2=0.002), with the former group scoring 0.54 points higher than the latter. For both group differences, the largest effect was found for social problems (β=0.058 and 0.054, R^2=0.003 and 0.003, respectively), with those exposed after knowledge scoring 1.0 and 0.94 points higher than those never exposed and those exposed only before knowledge (**Table 3**).

Prenatal exposure to cannabis after maternal knowledge of pregnancy was associated with higher scores on indices of psychopathology relative to those never exposed and those exposed only before knowledge, when accounting for potentially confounding covariates. These children on average scored 0.85/0.95 points higher on PLEs and 2.1/1.9, 1.3/1.2, 0.65/0.54, and 1.0/0.94 points higher on CBCL scales assessing externalizing, attention, thought, and social problems, respectively. Although these effect sizes are objectively small, it is important to consider that these are independent effects of prenatal exposure after accounting for a large number of important covariates.

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eTable 1. Full Regression Results From Models Examining Associations Between Prenatal Cannabis Exposure and CBCL Outcomes When Including Potentially Confounding Covariates

	CBCL Internalizing		CBCL Externalizing		CBCL Attention		CBCL Thought		CBCL Social	
Covariate	*b*	*p*	*b*	*p*	*b*	*p*	*b*	*p*	*b*	*p*
Cannabis Post vs. No[a]	1.092	**0.025**	2.045	**2.03E-05**	1.338	**2.28E-05**	0.646	**0.001**	1.010	**2.57E-07**
Cannabis Pre vs. No[a]	-0.088	0.775	0.146	0.632	0.183	0.363	0.110	0.359	0.066	0.597
Cannabis Post vs. Pre[a]	1.180	**0.032**	1.900	**4.70E-04**	1.155	**1.25E-03**	0.537	**0.012**	0.944	**2.13E-05**
Alcohol Post	0.492	0.196	0.070	0.851	0.032	0.897	0.138	0.347	-0.137	0.370
Alcohol Pre	0.470	**0.001**	0.376	**0.006**	0.244	**0.006**	0.169	**0.001**	0.055	0.319
Tobacco Post	-0.022	0.948	0.738	**0.027**	-0.129	0.557	0.245	0.060	0.065	0.635
Tobacco Pre	0.424	0.050	0.653	**0.002**	0.316	**0.025**	0.172	**0.040**	0.238	**0.006**
White	1.054	**5.06E-07**	0.661	**0.001**	0.376	**0.006**	0.311	**1.18E-04**	0.148	0.079
Black	-0.105	0.629	0.221	0.300	0.325	**0.020**	-0.058	0.483	0.142	0.103
Asian	0.039	0.876	-0.225	0.361	0.059	0.718	0.248	**0.010**	-0.049	0.630
Native American	0.116	0.734	0.090	0.790	0.266	0.227	0.274	**0.037**	0.114	0.404
Pacific Islander	-0.724	0.318	-0.447	0.531	-0.010	0.983	-0.205	0.463	-0.080	0.785
Other Race	1.140	**6.93E-05**	0.757	**0.007**	0.283	0.128	0.310	**0.005**	0.243	**0.035**
Hispanic	-0.101	0.576	-0.462	**0.010**	-0.134	0.248	-0.273	**9.51E-05**	-0.067	0.353
Child Sex	0.040	0.713	-1.228	**5.07E-30**	-1.185	**1.58E-61**	-0.410	**2.18E-22**	-0.191	**1.29E-05**
Child Age	0.025	**4.52E-04**	-0.012	0.086	-0.006	0.205	0.001	0.811	-0.005	0.116
Income $50-74	-0.520	**0.008**	-0.687	**3.85E-04**	-0.247	0.051	-0.030	0.690	-0.332	**2.79E-05**
Income $75-99	-0.547	**0.008**	-0.624	**0.002**	-0.161	0.224	0.010	0.904	-0.283	**0.001**
Income $100-199	-0.787	**5.68E-05**	-0.776	**5.46E-05**	-0.239	0.058	-0.063	0.400	-0.405	**2.57E-07**
Income $200+	-1.224	**9.98E-07**	-0.897	**2.67E-04**	-0.444	**0.006**	-0.246	**0.011**	-0.472	**2.71E-06**
Maternal Education	-0.012	0.681	-0.094	**0.002**	-0.037	0.058	-0.026	**0.023**	-0.035	**0.004**
Maternal Age at Birth	-0.015	0.156	-0.022	**0.036**	-0.008	0.228	-0.008	0.057	-0.006	0.196
Unplanned Pregnancy	0.048	0.713	0.347	**0.007**	0.242	**0.004**	0.055	0.280	0.127	**0.016**
Week Learned Pregnant	-0.003	0.760	0.002	0.868	-0.001	0.930	-0.004	0.331	0.000	0.913
Prenatal Vitamin Use	-0.273	0.344	-0.094	0.742	0.131	0.484	0.047	0.673	0.021	0.857
Birth Weight	-0.006	0.138	-0.003	0.377	-0.007	**0.007**	-0.002	0.310	-0.001	0.750
Fam Hx Depression	1.563	**1.18E-32**	1.156	**3.42E-19**	0.698	**1.80E-16**	0.493	**1.53E-22**	0.384	**3.42E-13**
Fam Hx Mania	0.597	**0.027**	0.010	0.969	0.243	0.166	0.151	0.148	0.141	0.196
Fam Hx Psychosis	-0.253	0.540	-0.232	0.567	-0.469	0.079	-0.118	0.459	0.099	0.552
Fam Hx Antisocial	0.762	**1.16E-04**	1.743	**4.35E-19**	0.822	**1.41E-10**	0.267	**4.62E-04**	0.522	**5.89E-11**
Fam Hx Anxiety	1.606	**9.16E-19**	1.161	**8.04E-11**	0.830	**1.64E-12**	0.492	**1.88E-12**	0.480	**4.68E-11**
Child Alcohol Try	0.079	0.545	0.357	**0.006**	0.156	0.070	0.058	0.255	0.102	0.054
Child Tobacco Try	0.335	0.534	1.941	**2.84E-04**	1.039	**0.003**	0.469	**0.025**	0.419	0.054
Twin/Triplet	-0.604	**0.005**	-0.347	0.104	-0.450	**0.001**	-0.270	**0.001**	-0.084	0.322

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eTable 1 Note. Post = post-maternal knowledge of pregnancy exposure. Pre = pre-maternal knowledge of pregnancy exposure. No = no prenatal exposure. Income = annual household income. Fam Hx = family history. CBCL = Child Behavior Checklist. Excluding children with uncommon substance use, children who were prenatally exposed to other illicit substances prenatally, children born at extreme prematurity, or who had non-biological mothers participate in the study does not alter results (**eTables 9-12**). *b* = unstandardized beta estimates. Bolded values indicate significant associations. Log transforming outcomes or including only covariates significantly associated with the outcomes in the full regression models did not meaningfully alter any observed associations (**eTables 4-7**).
[a] Group contrasts were orthogonal and thus independent of each other.

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eTable 2. Full Regression Results From Models Examining Associations Between Prenatal Cannabis Exposure and Psychotic-Like Experiences, BMI, Cognition, Sleep Problems, and Birth Weight When Including Potentially Confounding Covariates

	Psychotic-like Exp.		Body Mass Index		Cognition		Total sleep problems		Birth Weight	
Covariates	*b*	*p*	*b*	*p*	*b*	*p*	*b*	*p*	*b*	*p*
Cannabis Post vs. No[a]	0.850	**0.007**	0.430	0.247	-0.817	0.276	1.236	0.094	-2.564	0.063
Cannabis Pre vs. No[a]	-0.095	0.637	-0.056	0.812	0.907	0.056	0.403	0.390	0.906	0.301
Cannabis Post vs. Pre[a]	0.945	**8.17E-03**	0.486	0.248	-1.723	**0.0428**	0.833	0.319	-3.470	**0.027**
Alcohol Post	0.329	0.184	-0.321	0.268	0.256	0.664	1.091	0.058	0.184	0.864
Alcohol Pre	-0.031	0.732	-0.218	**0.039**	0.642	**0.003**	0.663	**0.002**	0.490	0.213
Tobacco Post	0.171	0.434	0.399	0.121	-0.660	0.205	1.785	**4.91E-04**	-2.790	**0.003**
Tobacco Pre	0.228	0.105	0.594	**3.30E-04**	0.256	0.442	0.495	0.132	-0.965	0.115
White	-0.498	**2.52E-04**	-0.691	**1.66E-05**	1.601	**7.30E-07**	0.687	**0.031**	2.656	**8.33E-06**
Black	0.328	**0.019**	0.995	**2.23E-09**	-2.924	**2.38E-18**	0.522	0.112	-1.832	**0.003**
Asian	-0.303	0.063	-0.667	**0.001**	2.549	**4.23E-11**	0.764	**0.045**	-1.772	**0.013**
Native American	0.233	0.293	-0.109	0.676	-0.021	0.967	1.010	0.051	0.274	0.778
Pacific Islander	0.466	0.317	1.035	0.064	0.622	0.578	-0.003	0.998	0.696	0.740
Other Race	-0.021	0.911	-0.215	0.323	0.036	0.935	1.157	**0.008**	1.552	0.054
Hispanic	0.095	0.430	1.106	**2.20E-15**	-0.844	**0.002**	-0.694	**0.012**	-1.164	**0.022**
Child Sex	-0.386	**5.14E-08**	0.277	**0.001**	0.653	**9.63E-05**	-0.539	**0.001**	-2.795	**5.64E-21**
Child Age	-0.028	**4.73E-09**	0.058	**1.26E-27**	0.358	**1.45E-217**	0.013	0.218	-0.040	**0.032**
Income $50-74	-0.071	0.576	-0.466	**0.002**	1.471	**1.13E-06**	-0.482	0.107	1.295	**0.023**
Income $75-99	0.022	0.867	-0.626	**7.16E-05**	2.274	**5.87E-13**	-0.317	0.308	1.262	**0.033**
Income $100-199	-0.368	**0.004**	-0.939	**4.01E-10**	2.427	**7.03E-16**	-0.829	**0.005**	2.117	**1.71E-04**
Income $200+	-0.580	**3.35E-04**	-1.209	**3.43E-10**	3.046	**2.43E-15**	-1.373	**3.02E-04**	1.729	**0.017**
Maternal Education	-0.066	**0.001**	-0.116	**6.64E-07**	0.677	**2.41E-47**	-0.045	0.322	-0.075	0.391
Maternal Age at Birth	-0.008	0.238	0.026	**0.002**	0.014	0.404	0.032	0.052	0.015	0.638
Unplanned Pregnancy	0.158	0.064	0.065	0.512	-0.626	**0.002**	0.548	**0.006**	-0.172	0.638
Week Learned Pregnant	-0.004	0.585	0.037	**1.73E-05**	-0.053	**0.002**	0.011	0.523	-0.077	**0.014**
Prenatal Vitamin Use	0.250	0.181	0.028	0.899	0.301	0.499	0.180	0.680	1.467	0.071
Birth Weight	-0.004	0.121	0.031	**1.04E-24**	0.028	**5.61E-06**	-0.012	**0.042**	------	------
Fam Hx Depression	0.162	0.055	-0.018	0.860	0.051	0.800	1.911	**7.42E-22**	-0.221	0.556
Fam Hx Mania	0.051	0.772	-0.149	0.469	-0.291	0.482	1.147	**0.005**	-0.858	0.262
Fam Hx Psychosis	0.482	0.070	0.141	0.656	1.492	**0.020**	0.575	0.358	-0.322	0.786
Fam Hx Antisocial	0.237	0.064	-0.028	0.853	-0.721	**0.018**	1.193	**6.98E-05**	-0.565	0.318
Fam Hx Anxiety	0.128	0.273	0.039	0.778	-0.263	0.345	1.331	**1.26E-06**	0.101	0.845
Child Alcohol Try	0.693	**9.71E-16**	0.094	0.340	0.576	**0.004**	0.114	0.565	-0.005	0.988
Child Tobacco Try	0.813	**0.022**	-0.177	0.659	-1.974	**0.017**	0.618	0.446	-1.175	0.406
Twin/Triplet	-0.189	0.196	0.103	0.541	-0.802	**0.015**	-2.129	**1.71E-10**	-23.423	**2.70E-133**

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eTable 2 Note. Post = post-maternal knowledge of pregnancy exposure. Pre = pre-maternal knowledge of pregnancy exposure. No = no prenatal exposure. Fam Hx = family history. BMI = Body mass index Excluding children with uncommon substance use, children who were prenatally exposed to other illicit substances prenatally, children born at extreme prematurity, or who had non-biological mothers participate in the study does not alter results (**eTables 9-12**). *b* = ustandardized beta estimates. Bolded values indicate significant associations. Log transforming outcomes or including only covariates significantly associated with the outcomes in the full regression models did not meaningfully alter any observed associations (**eTables 4-7**).

[a] Group contrasts were orthogonal and thus independent of each other.

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eTable 3. Full Regression Results From Models Examining Associations Between Prenatal Cannabis Exposure and Brain Structure Metrics When Including Potentially Confounding Covariates

	Intracranial Volume		White Matter Volume		Gray Matter Volume	
Covariate	*b*	*p*	*b*	*p*	*b*	*p*
Cannabis Post vs. No[a]	0.032	0.511	-0.037	0.286	0.035	0.235
Cannabis Pre vs. No[a]	0.040	0.604	-0.066	0.234	0.017	0.718
Cannabis Post vs. Pre[a]	8.13E-03	0.927	-0.029	0.643	-0.018	0.732
Alcohol Post	0.196	**0.001**	0.008	0.848	0.089	**0.015**
Alcohol Pre	0.038	0.091	0.012	0.440	0.011	0.419
Tobacco Post	-0.083	0.126	-0.024	0.530	0.019	0.569
Tobacco Pre	0.022	0.518	0.030	0.218	-0.040	0.058
White	0.204	**1.77E-09**	0.043	0.067	0.076	**2.29E-04**
Black	-0.103	**0.003**	0.009	0.716	-0.226	**1.81E-26**
Asian	-0.060	0.141	0.080	**0.004**	-0.041	0.102
Native American	-0.027	0.616	0.014	0.708	0.023	0.483
Pacific Islander	-0.032	0.783	0.159	0.051	-0.131	0.064
Other Race	0.098	**0.031**	0.071	**0.028**	0.020	0.463
Hispanic	-0.107	**3.28E-04**	-0.004	0.833	-0.065	**2.89E-04**
Child Sex	-0.822	**0.00E+00**	-0.036	**0.009**	-0.059	**8.85E-07**
Child Age	0.008	**1.49E-12**	0.004	**6.27E-08**	-0.012	**2.88E-63**
Income $50-74	0.036	0.249	0.003	0.877	0.033	0.084
Income $75-99	0.101	**0.002**	0.016	0.481	0.073	**2.52E-04**
Income $100-199	0.111	**3.92E-04**	0.023	0.299	0.057	**0.003**
Income $200+	0.159	**8.06E-05**	0.057	**0.040**	0.075	**0.002**
Maternal Education	0.023	**1.53E-06**	-0.007	**0.047**	0.005	0.085
Maternal Age at Birth	0.000	0.814	-0.006	**4.98E-07**	0.003	**0.004**
Unplanned Pregnancy	-0.039	0.063	0.009	0.541	0.022	0.078
Week Learned Pregnant	-0.003	0.144	0.001	0.302	-0.001	0.477
Prenatal Vitamin Use	0.075	0.105	-0.029	0.362	0.063	**0.026**
Birth Weight	0.010	**3.31E-54**	-0.001	0.229	0.001	**0.001**
Fam Hx Depression	0.034	0.105	0.002	0.893	0.024	0.057
Fam Hx Mania	-0.007	0.876	0.011	0.720	-0.025	0.344
Fam Hx Psychosis	-0.026	0.702	0.080	0.095	0.085	**0.036**
Fam Hx Antisocial	-0.081	**0.010**	-0.051	**0.021**	-0.045	**0.019**
Fam Hx Anxiety	-0.019	0.519	-0.001	0.973	-0.001	0.977
Child Alcohol Try	0.001	0.944	-0.019	0.196	0.002	0.860
Child Tobacco Try	-0.165	**0.048**	0.012	0.847	-0.016	0.765
Twin/Triplet	0.118	**0.002**	0.017	0.513	-0.054	**0.015**
Intracranial Volume	-----	-----	0.893	**0.00E+00**	0.894	**0.00E+00**

eTable 3 Note. Post = post-maternal knowledge of pregnancy exposure. Pre = pre-maternal knowledge of pregnancy exposure. No = no prenatal exposure. Fam Hx = family history. Excluding children with non-prevalent substance use, children who were prenatally exposed to other illicit substances prenatally, children born at extreme prematurity, or who had non-biological mothers participate in the study does not alter results (**eTables 9-12**). Total intracranial volume was included as an additional covariate in the white and gray matter models; however, excluding this as a covariate did not alter associations between exposure and gray and white matter volumes (all $|b|$s<0.069, all *p*s>0.19). *b* = unstandardized beta estimates. Bolded values indicate significant associations. Log transforming outcomes or including only covariates significantly associated with the outcomes in the full regression models did not meaningfully alter any observed associations (**eTables 4-7**).

[a] Group contrasts were orthogonal and thus independent of each other.

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eTable 4. Regression Results From Models Examining Associations Between Prenatal Cannabis Exposure and Log-Transformed Outcomes When Including Potentially Confounding Covariates

	Cannabis exposure post-knowledge vs. no exposure		Cannabis exposure pre-knowledge vs. no exposure		Cannabis exposure post-knowledge vs. pre-knowledge	
Outcome	*b*	*p*	*b*	*p*		
PLEs	0.205	**0.0106**	-5.18e-03	0.919	0.210	**0.0208**
CBCL Internalizing	0.195	**0.0228**	0.014	0.799	0.181	0.0622
CBCL Externalizing	0.352	**1.04e-04**	6.31e-03	0.913	0.345	**7.69e-04**
CBCL Attention	0.307	**1.57e-04**	0.043	0.405	0.264	**4.14e-03**
CBCL Thought	0.193	**2.78e-03**	0.026	0.525	0.166	**0.0225**
CBCL Social	0.321	**1.48e-06**	0.039	0.358	0.282	**1.91e-04**
Body Mass Index	0.022	0.220	1.28e-03	0.913	0.021	0.307
Total sleep problems	0.023	0.226	0.010	0.408	0.013	0.546
Birth Weight (oz)	-0.023	0.0673	8.11e-03	0.300	-0.031	**0.0282**
Gestational Age	3.58e-03	0.442	5.29e-04	0.857	3.05e-03	0.564
Intracranial Volume	5.40e-03	0.481	4.15e-03	0.389	1.25e-03	0.885
White Matter Volume	-6.93e-03	0.282	-3.12e-03	0.669	-3.81e-03	0.344
Gray Matter Volume	2.78e-03	0.547	4.40e-03	0.130	-1.62e-03	0.757

eTable 4 Note. Skewness statistics did not indicate evidence of substantial skew among any outcomes. Linear mixed effect models were used to analyze the group differences between mutually exclusive exposure groups and each log-transformed outcome, nesting data by research site and family ID. Fixed-effect covariates included (1-4) prenatal exposure to alcohol or tobacco before or after knowledge of pregnancy; (5) household income; (6) maternal education level; (7) maternal age at birth; (8) whether the pregnancy was planned (0 = planned, 1 = unplanned); (9) length of time (weeks) pregnant before maternal knowledge of pregnancy; (10) prenatal vitamin use; (11-17) child race/ethnicity: Caucasian, African American, Asian, Native American, Pacific Islander, Hispanic, other; (18) birth weight (not included in model with birth weight as the outcome); (19) child sex (0 = male, 1 = female); (20) child age; (21-22) child substance use: alcohol sip, tobacco puff; (23-27) first-degree familial history of mental illness: depression, psychosis, anxiety, mania, antisocial behavior; (28) whether the child has a twin or triplet in the study (0 = singleton or sibling, 1 = twin or triplet). Models with white and gray matter as outcomes included total intracranial volume as a covariate. *b* = unstandardized beta estimates. PLEs = Psychotic-like Experiences; CBCL = Child Behavior Checklist.

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eTable 5. Full Regression Results From Models Examining Associations Between Prenatal Cannabis Exposure and CBCL Outcomes When Including Potentially Confounding Covariates Associated With the Outcome Only

	CBCL Internalizing		CBCL Externalizing		CBCL Attention		CBCL Thought		CBCL Social	
Covariate	*b*	*p*	*b*	*p*	*b*	*p*	*b*	*p*	*b*	*p*
Cannabis Post vs. No	0.887	**0.024**	2.10	**1.35E-06**	1.08	**2.99E-05**	0.602	3.18E-04	0.842	**1.30E-06**
Cannabis Pre vs. No	0.290	0.301	0.032	0.914	0.370	**0.047**	0.071	0.530	0.119	0.297
Cannabis Post vs. Pre	0.597	0.196	2.07	**3.37E-05**	0.714	**0.018**	0.531	**5.73E-03**	0.722	**2.88E-04**
Alcohol Pre	0.521	**2.06E-05**	0.435	**6.76E-04**	0.269	**0.001**	0.184	1.68E-04	-----	-----
Tobacco Post	-----	-----	0.854	**0.007**	-----	-----	-----	-----	-----	-----
Tobacco Pre	-----	-----	0.712	**4.75E-04**	0.366	**0.001**	0.307	7.45E-06	0.328	**2.38E-06**
White	1.02	**1.08e-12**	0.525	**5.67E-04**	0.284	**0.010**	0.325	2.92E-08	-----	-----
Black	-----	-----	-----	-----	0.262	**0.026**	------	------	-----	-----
Asian	-----	-----	-----	-----	-----	-----	0.244	**0.006**	-----	-----
Native American	-----	-----	-----	-----	-----	-----	0.188	0.121	-----	-----
Other Race	0.815	**3.50e-04**	0.571	**0.026**	-----	-----	0.257	**0.009**	0.120	0.182
Hispanic	-----	-----	-0.479	**0.004**	-----	-----	-0.227	4.61E-04	-----	-----
Child Sex	-----	-----	-1.23	**2.27E-33**	-1.19	**6.55E-71**	-0.413	7.77E-26	-0.192	**1.66E-06**
Child Age	0.025	**1.07E-04**	-----	-----	-----	-----	-----	-----	-----	-----
Income $50-74	-0.620	**3.55e-04**	-0.764	**2.96E-05**	-0.330	**0.004**	-0.073	0.297	-0.342	**1.48E-06**
Income $75-99	-0.652	**2.33e-04**	-0.708	**2.04E-04**	-0.258	**0.027**	-0.023	0.751	-0.348	**2.09E-06**
Income $100-199	-0.920	**1.96e-09**	-0.875	**1.35E-06**	-0.340	**0.001**	-0.103	0.133	-0.453	**3.00E-11**
Income $200+	-1.34	**1.35e-11**	-1.02	**1.17E-05**	-0.596	**7.54E-06**	-0.272	0.002	-0.522	**3.41E-09**
Maternal Education	-----	-----	-0.104	**2.03E-04**	-----	-----	-0.021	**0.049**	-0.031	**0.004**
Maternal age at Birth	-----	-----	-0.018	**0.077**	-----	-----	-----	-----	-----	-----
Unplanned Pregnancy	-----	-----	0.259	**0.033**	0.171	**0.029**	-----	-----	0.110	**0.019**
Birth Weight	-----	-----	-----	-----	-0.007	**0.005**	-----	-----	-----	-----
Fam Hx Depression	1.51	**7.18E-36**	1.09	**2.35E-19**	0.711	**8.33E-20**	0.502	1.60E-26	0.414	**5.14E-18**
Fam Hx Mania	0.711	**3.19e-03**	-----	-----	-----	-----	-----	-----	-----	-----
Fam Hx Antisocial	0.805	**3.82E-06**	1.75	**5.73E-22**	0.805	**2.26E-12**	0.340	9.25E-07	0.518	**5.03E-13**
Fam Hx Anxiety	1.64	**1.57E-22**	1.19	**1.60E-12**	0.781	**4.89E-13**	0.505	8.72E-15	0.502	**4.38E-14**
Child Alcohol Try	-----	-----	0.345	**0.005**	------	------	-----	-----	-----	-----
Child Tobacco Try	-----	-----	1.56	**0.002**	0.896	**0.005**	0.408	0.039	-----	-----
Twin/Trip	-0.461	**0.0120**	-----	-----	-0.509	**7.02E-05**	-0.253	4.58E-04	-----	-----

eTable 5 Note. Results for the effect of each covariate and the main cannabis exposure during pregnancy results. Post hoc analyses including only covariates significantly associated with outcomes in the full regression. Income = annual household income. Fam Hx = family history. *b* = unstandardized beta estimates. CBCL = Child Behavior Checklist. Bolded values indicate significant associations.

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eTable 6. Psychotic-Like Experiences, BMI, Cognition, Sleep, and Birth Weight Models With Significant Fixed Effect Covariates Only

	Psychotic-like Experiences		Body Mass Index		Cognition		Sleep problems		Birth Weight	
Covariates	*b*	*p*	*b*	*p*	*b*	*p*	*b*	*p*	*b*	*p*
Cannabis Post vs. No	1.165	**1.15E-05**	0.475	0.162	-0.936	0.185	0.887	0.160	-2.33	0.050
Cannabis Pre vs. No	0.274	0.116	-0.037	0.869	0.874	0.055	0.535	0.217	0.404	0.608
Cannabis Post vs. Pre	0.891	**0.004**	0.512	0.189	-1.81	**0.026**	0.352	0.631	-2.73	**0.048**
Alcohol Pre	-----	-----	-0.194	**0.049**	0.662	**0.001**	0.858	**6.25E-06**	-----	-----
Tobacco Post	-----	-----	-----	-----	-----	-----	2.24	**3.80E-08**	-3.03	**7.19E-05**
Tobacco Pre	-----	-----	0.640	**3.81E-06**	-----	-----	-----	-----	-----	-----
White	-0.417	**8.55E-05**	-0.602	**1.64E-05**	1.72	**1.59E-09**	0.302	0.195	2.31	**4.03E-06**
Black	0.429	**1.85E-04**	1.05	**4.81E-12**	-2.79	**4.50E-19**	-----	-----	-2.00	**2.82E-04**
Asian	-----	-----	-0.579	**0.002**	2.57	**5.16E-12**	0.659	0.058	-1.71	**0.010**
Other Race	-----	-----	-----	-----	-----	-----	0.743	0.055	-----	-----
Hispanic	-----	-----	1.05	**1.42E-16**	-0.822	**0.001**	-0.571	**0.024**	-0.683	0.125
Child Sex	-0.331	**1.99E-07**	0.262	**0.001**	0.684	**2.95E-05**	-0.536	**4.81E-04**	-2.87	**9.78E-25**
Child Age	-0.029	**8.01E-12**	0.060	**3.33E-31**	0.354	**1.51E-225**	-----	-----	-0.037	**0.034**
Income $50-74	-0.112	0.322	-0.393	**0.007**	1.540	**1.79E-07**	-0.481	0.078	1.60	**0.002**
Income $75-99	-0.168	0.150	-0.566	**1.58E-04**	2.323	**3.64E-14**	-0.313	0.261	1.51	**0.004**
Income $100-199	-0.529	**9.96E-07**	-0.903	**1.77E-10**	2.488	**1.11E-17**	-0.874	**4.69E-04**	2.50	**6.28E-08**
Income $200+	-0.791	**1.75E-08**	-1.14	**4.53E-10**	3.147	**2.62E-17**	-1.35	**2.60E-05**	1.97	**0.001**
Maternal Education	-0.090	**8.68E-08**	-0.128	**1.09E-08**	0.679	**2.34E-51**	-----	-----	-----	-----
Maternal age at Birth	-----	-----	0.026	**0.001**	-----	-----	-----	-----	-----	-----
Unplanned Pregnancy	-----	-----	-----	-----	-0.630	**0.001**	0.404	**0.026**	-----	-----
Week Learned Pregnant	-----	-----	0.035	**1.75E-05**	-0.057	**0.001**	-----	-----	-0.094	**0.001**
Birth Weight	-----	-----	0.030	**1.24E-28**	0.028	**3.74E-06**	-0.013	**0.021**	-----	-----
Fam Hx Depression	-----	-----	-----	-----	-----	-----	1.84	**3.84E-23**	-----	-----
Fam Hx Mania	-----	-----	-----	-----	-----	-----	1.28	**0.001**	-----	-----
Fam Hx Psychosis	-----	-----	-----	-----	1.36	**0.025**	-----	-----	-----	-----
Fam Hx Antisocial	-----	-----	-----	-----	-0.702	**0.014**	1.24	**5.84E-06**	-----	-----
Fam Hx Anxiety	-----	-----	-----	-----	-----	-----	1.33	**2.26E-07**	-----	-----
Child Alcohol Try	0.697	**3.62E-19**	-----	-----	0.666	**0.001**	-----	-----	-----	-----
Child Tobacco Try	0.919	**0.004**	-----	-----	-1.69	**0.036**	-----	-----	-----	-----
Twin/Trip	-----	-----	-----	-----	-0.736	**0.024**	-2.09	**2.79E-11**	-23.3	**1.07E-135**

eTable 6 Note. Post hoc analyses including only covariates significantly associated with outcomes in the full regression. Income = annual household income. Fam Hx = family history. *b* = unstandardized beta estimates. Bolded values indicate significant associations.

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eTable 7. Brain Structure Models With Significant Fixed Effect Covariates Only

	Intracranial Volume		White Matter Volume		Gray Matter Volume	
Covariate	*b*	*p*	*b*	*p*	*b*	*p*
Cannabis Post vs. No	0.022	0.747	-0.047	0.334	-0.015	0.696
Cannabis Pre vs. No	0.070	0.111	-0.021	0.503	0.021	0.421
Cannabis Post vs. Pre	-0.048	0.538	-0.026	0.647	-0.037	0.425
Alcohol Post	0.140	**0.008**	-----	-----	0.084	**0.008**
White	0.246	**1.18E-16**	-----	-----	0.086	**2.75E-07**
Black	-0.117	**1.62E-04**	-----	-----	-0.222	**1.11E-33**
Asian	-----	-----	0.078	**0.002**	-----	-----
Other Race	0.126	**0.002**	0.065	**0.010**	-----	-----
Hispanic	0.118	**1.28E-05**	-----	-----	0.069	**9.23E-06**
Child Sex	-0.827	**0.00E+00**	-0.036	**0.005**	-0.059	**8.29E-08**
Child Age	0.007	**5.78E-13**	0.005	**1.13E-10**	-0.012	**3.23E-73**
Income $50-74	0.031	0.278	0.003	0.868	0.031	0.073
Income $75-99	0.088	**0.003**	0.003	0.874	0.052	**0.003**
Income $100-199	0.109	**1.05E-04**	0.022	0.259	0.054	**0.001**
Income $200+	0.152	**3.15E-05**	0.049	0.050	0.071	**4.65E-04**
Maternal Education	0.027	**1.01E-09**	-0.005	0.140	-----	-----
Maternal age at Birth	-----	-----	-0.005	**1.26E-05**	0.004	**5.85E-05**
Prenatal Vitamin Use	-----	-----	-----	-----	0.062	**0.013**
Birth Weight	0.010	**4.53E-63**	-----	-----	0.001	**1.27E-04**
Fam Hx Psychosis	-----	-----	-----	-----	0.070	**0.049**
Fam Hx Antisocial	-0.077	**0.005**	-0.041	**0.034**	-0.036	**0.029**
Child Tobacco Try	-0.113	0.137	-----	-----	-----	-----
Twin/Trip	0.122	**4.31E-04**	-----	-----	-0.039	0.058
ICV	-----	-----	0.885	**0.00E+00**	0.891	**0.00E+00**

eTable 7 Note. Post hoc analyses including only covariates significantly associated with outcomes in the full regression. Income = annual household income. Fam Hx = family history. *b* = unstandardized beta estimates. Bolded values indicate significant associations.

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eTable 8. Test of Overfitting Results From 5-Fold Cross Validation

Outcome Variable	**RMSDA*c***	**RMSDA*n***	**RMSDA*c* - RMSDA*n***
PLEs	0.018	0.023	-0.005
CBCL Internalizing	0.059	0.027	0.032
CBCL Externalizing	0.041	0.019	0.022
CBCL Attention	0.024	0.021	0.003
CBCL Thought	0.036	0.021	0.014
CBCL Social	0.027	0.026	0.0004
Body Mass Index	0.035	0.036	-0.0003
Cognition Composite	0.031	0.017	0.015
Total sleep problems	0.019	0.023	-0.003
Birth Weight (oz)	0.030	0.039	-0.009
Gestational age	0.016	0.011	0.005
Intracranial Volume	0.037	0.006	0.031
White Matter Volume	0.027	0.026	0.001
Gray Matter Volume	0.018	0.010	0.008

eTable 8 Note. Estimates of the empirical degree of imprecision in models including all fixed-effects covariates (RMSDAc) vs. models excluding fixed-effects covariates (RMSDAn). Simple difference was used to estimate the degree of added imprecision added via covariance inclusion. PLEs = Psychotic-Like Experiences. CBCL = Child Behavior Checklist.

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eTable 9. Regression Results When Excluding Children With Non-Prevalent Substance Use

	Cannabis exposure post-knowledge vs. no exposure		Cannabis exposure pre-knowledge vs. no exposure		Cannabis exposure post-knowledge vs. pre-knowledge		
Outcome	*b*	*p*	*b*	*p*	*b*	*p*	*N*
PLEs	0.824	**9.87e-03**	-0.045	0.822	0.869	**0.0163**	8118
CBCL Internalizing	0.990	**0.0445**	-0.177	0.571	1.17	**0.0368**	8121
CBCL Externalizing	2.03	**2.90e-05**	0.075	0.807	1.95	**3.86e-04**	8121
CBCL Attention	1.30	**4.90e-05**	0.186	0.358	1.11	**2.16e-03**	8121
CBCL Thought	0.587	**1.98e-03**	0.107	0.372	0.480	**0.0259**	8121
CBCL Social	0.976	**8.64e-07**	0.059	0.640	0.917	**4.57e-05**	8121
Body Mass Index	0.274	0.466	-0.083	0.726	0.357	0.402	8104
Cognition Composite	-0.741	0.328	0.931	0.0521	-1.67	0.0519	7954
Total sleep problems	1.14	0.126	0.301	0.525	0.840	0.321	8122
Birth weight (oz)	-2.85	**0.0418**	0.740	0.402	-3.58	**0.0238**	8122
Gestational age	0.142	0.401	1.52e-03	0.989	0.140	0.464	8094
Intracranial Volume	0.036	0.649	0.043	0.380	-7.61e-03	0.932	7802
White Matter Volume	-0.063	0.263	-0.038	0.277	-0.025	0.699	7391
Gray Matter Volume	0.035	0.466	0.033	0.267	1.41e-03	0.979	7798

eTable 9 Note. Excluded children reported using marijuana (n=14), using substances other than alcohol and tobacco (i.e., bath salts, n=1; "sniff" to "get high," n=9; inhalants, n=3; amphetamines not as prescribed, n=2; tranquilizers/anxiolytics/sedatives not as prescribed, n=2; pain medication not as prescribed, n=1; cough medication to "get high," n=1), or having a full drink of alcohol (n=19) or more than a puff of tobacco (n=14), or screened positive for substances based on hair toxicology (methamphetamines, n=4; THC, n=3; EtG, n=4; cotinine, n=5; Adderall, n=6). A total of 80 individuals were excluded for these analyses (Numbers do not sum as some children were positive across multiple indices). *b* = unstandardized beta estimates. PLEs = Psychotic-Like Experiences. CBCL = Child Behavior Checklist.

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eTable 10. Regression Results When Excluding Children Prenatally Exposed to Illicit Substances Other Than Marijuana

	Cannabis exposure post-knowledge vs. no exposure		Cannabis exposure pre-knowledge vs. no exposure		Cannabis exposure post-knowledge vs. pre-knowledge		
Outcome	*b*	*p*	*b*	*p*	*b*	*p*	*N*
PLEs	0.794	**0.0132**	-0.085	0.681	0.879	**0.0159**	8065
CBCL Internalizing	1.18	**0.0168**	-0.116	0.714	1.30	**0.0209**	8068
CBCL Externalizing	2.16	**8.52e-06**	0.085	0.786	2.08	**1.70e-04**	8068
CBCL Attention	1.32	**3.78e-05**	0.146	0.478	1.18	**1.27e-03**	8068
CBCL Thought	0.646	**6.69e-04**	0.074	0.543	0.572	**8.11e-03**	8068
CBCL Social	1.01	**3.57e-07**	0.071	0.580	0.942	**3.15e-05**	8068
Body Mass Index	0.192	0.613	-0.178	0.462	0.369	0.390	8052
Cognition Composite	-0.661	0.387	0.883	0.0705	-1.54	0.0756	7902
Total sleep problems	1.37	0.0674	0.373	0.437	0.994	0.242	8069
Birth weight (oz)	-2.51	0.0749	0.821	0.362	-3.33	**0.0376**	8069
Gestational age	0.125	0.465	-2.89e-03	0.979	0.128	0.511	8041
Intracranial Volume	0.055	0.491	0.031	0.539	0.024	0.790	7835
White Matter Volume	-0.087	0.120	-0.041	0.248	-0.046	0.467	7343
Gray Matter Volume	4.43e-03	0.927	0.024	0.437	-0.019	0.723	7746

eTable 10 Note. Children who were exposed to other illicit substances prenatally (i.e., cocaine or crack, n=68; heroin or morphine, n=20; oxycontin, n=33; other, n=100) were excluded. A total of 185 individuals were excluded (Numbers do not sum as some mothers were positive across multiple indices). *b* = unstandardized beta estimates. PLEs = Psychotic-Like Experiences. CBCL = Child Behavior Checklist.

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eTable 11. Regression Results When Excluding Children Born at Extreme Prematurity

	Cannabis exposure post-knowledge vs. no exposure		Cannabis exposure pre-knowledge vs. no exposure		Cannabis exposure post-knowledge vs. pre-knowledge		
Outcome	*b*	*p*	*b*	*p*	*b*	*p*	*N*
PLEs	0.844	**7.53e-03**	-0.136	0.502	0.980	**6.25e-03**	8060
CBCL Internalizing	1.09	**0.0250**	-0.069	0.826	1.16	**0.0358**	8063
CBCL Externalizing	2.02	**2.61e-05**	0.141	0.648	1.88	**5.67e-04**	8063
CBCL Attention	1.32	**2.82e-05**	0.164	0.419	1.16	**1.23e-03**	8063
CBCL Thought	0.640	**6.56e-04**	0.112	0.353	0.529	**0.0132**	8063
CBCL Social	1.01	**3.03e-07**	0.061	0.629	0.945	**2.24e-05**	8063
Body Mass Index	0.426	0.250	-0.077	0.746	0.503	0.232	8046
Cognition Composite	-0.817	0.276	0.955	**0.0460**	-1.77	**0.0373**	7898
Total sleep problems	1.23	0.0961	0.382	0.420	0.846	0.312	8064
Birth weight (oz)	-2.67	0.0521	0.928	0.292	-3.60	**0.0212**	8064
Gestational age	7.08e-03	0.961	-0.021	0.822	0.028	0.866	8036
Intracranial Volume	0.039	0.619	0.027	0.583	0.012	0.896	7743
White Matter Volume	-0.066	0.238	-0.036	0.311	-0.030	0.633	7331
Gray Matter Volume	0.019	0.683	0.034	0.256	-0.015	0.782	7739

eTable 11 Note. Children born more than 8 weeks premature (i.e., less than 32 weeks' gestation; n=148) were excluded. *b* = unstandardized beta estimates. PLEs = Psychotic-Like Experiences. CBCL = Child Behavior Checklist.

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eTable 12. Regression Results When Excluding Children Who Had a Non-Biological Mother Report as the Parent/Caregiver Respondent

	Cannabis exposure post-knowledge vs. no exposure		Cannabis exposure pre-knowledge vs. no exposure		Cannabis exposure post-knowledge vs. pre-knowledge		
Outcome	*b*	*p*	*b*	*p*	*b*	*p*	*N*
PLEs	0.806	**0.0127**	-0.114	0.575	0.920	**0.0118**	7638
CBCL Internalizing	1.17	**0.0190**	-0.102	0.747	1.28	**0.0242**	7641
CBCL Externalizing	2.19	**9.68e-06**	0.087	0.781	2.10	**1.72e-04**	7641
CBCL Attention	1.43	**1.14e-05**	0.165	0.421	1.26	**6.02e-04**	7641
CBCL Thought	0.655	**7.07e-04**	0.129	0.289	0.526	**0.0163**	7641
CBCL Social	1.07	**1.08e-07**	0.059	0.643	1.02	**9.11e-06**	7641
Body Mass Index	0.390	0.304	-0.066	0.782	0.456	0.288	7625
Cognition Composite	-0.914	0.235	0.913	0.0586	-1.83	**0.0357**	7480
Total sleep problems	1.25	0.0992	0.381	0.427	0.871	0.311	7642
Birth weight (oz)	-2.55	0.0690	1.01	0.252	-3.56	**0.0248**	7642
Gestational age	0.130	0.443	0.041	0.697	0.089	0.644	7615
Intracranial Volume	0.010	0.897	0.025	0.622	-0.014	0.874	7333
White Matter Volume	-0.079	0.160	-0.049	0.161	-0.030	0.636	6947
Gray Matter Volume	0.019	0.690	0.034	0.266	-0.014	0.794	7329

eTable 12 Note. Children whose parent/caregiver respondent was not their biological mother were excluded (n=1,427). *b* = unstandardized beta estimates. PLEs = Psychotic-Like Experiences. CBCL = Child Behavior Checklist.

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eTable 13. Regression Results Restricted to the Subsample of Individuals With Genomically-Confirmed European Ancestry

	Cannabis exposure post-knowledge vs. no exposure		Cannabis exposure pre-knowledge vs. no exposure		Cannabis exposure post-knowledge vs. pre-knowledge		
Outcome	*b*	*p*	*b*	*p*	*b*	*p*	*N*
PLEs	1.06	0.0589	-0.572	0.115	1.63	**0.0120**	3603
CBCL Internalizing	--------	--------	--------	--------	--------	--------	-------
CBCL Externalizing	1.65	0.0533	0.444	0.425	1.21	0.223	3603
CBCL Attention	0.905	0.114	0.401	0.282	0.504	0.449	3603
CBCL Thought	0.563	0.111	-0.081	0.726	0.644	0.117	3603
CBCL Social	0.863	**0.0138**	-0.085	0.711	0.948	**0.0199**	3603
Body Mass Index	--------	--------	--------	--------	--------	--------	-------
Cognition Composite	--------	--------	--------	--------	--------	--------	-------
Total sleep problems	--------	--------	--------	--------	--------	--------	-------
Birth weight (oz)	--------	--------	--------	--------	--------	--------	-------
Intracranial Volume	--------	--------	--------	--------	--------	--------	-------
White Matter Volume	--------	--------	--------	--------	--------	--------	-------
Gray Matter Volume	--------	--------	--------	--------	--------	--------	-------

eTable 13 Note. Associations with outcomes in the subsample of individuals with genomically-confirmed European ancestry (n=4,644). No genomic variables were entered into these models. Regressions were rerun to determine whether results in the full sample that were significant remain significant in this subsample, following sample size reduction. *b* = unstandardized beta estimates. PLEs = Psychotic-Like Experiences. CBCL = Child Behavior Checklist.

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eTable 14. Regression Results When Including Polygenic Risk Scores and Ancestrally-Informative Principal Components as Additional Covariates

	PGS Covariates	Cannabis exposure post-knowledge vs. no exposure		Cannabis exposure pre-knowledge vs. no exposure		Cannabis exposure post-knowledge vs. pre-knowledge		
Outcome		*b*	*p*	*b*	*p*	*b*	*p*	N
PLEs	SCZ	1.07	0.0561	-0.555	0.126	1.62	**0.0123**	3603
PLEs	EDU	1.06	0.0580	-0.510	0.160	1.57	**0.0154**	3603
PLEs	CU	1.05	0.0600	-0.555	0.126	1.61	**0.0132**	3603
PLEs	EDU + CU	1.05	0.0607	-0.517	0.155	1.56	**0.0157**	3603
PLEs	EDU + CU + SCZ	1.05	0.0596	-0.523	0.150	1.58	**0.0150**	3603
CBCL Social	CU	0.858	**0.0143**	-0.065	0.775	0.924	**0.0233**	3603

eTable 14 Note. All associations that were significant in the genomically-confirmed subsample of European ancestry were robust to the inclusion of relevant polygenic scores and ancestrally-informative principal components. SCZ = PGS for schizophrenia; EDU = PGS for educational attainment; CU = PGS for cannabis use. PGS thresholds selected based on **eTables 16-17.** *b* = unstandardized beta estimates. PLEs = Psychotic-Like Experiences. CBCL = Child Behavior Checklist.

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eTable 15. Associations Between Psychotic-Like Experiences and Polygenic Scores for Schizophrenia, Educational Attainment, and Cannabis Use

	SCZ PGS		EDU PGS		CU PGS	
Threshold	*b*	*p*	*b*	*p*	*b*	*p*
.00000005	11.2	0.164	-750	4.91e-4	**-6.19**	**0.164**
.0001	**83.2**	**0.105**	-2.84e+3	2.01e-05	-25.0	0.577
.001	78	0.482	-4.61e+3	1.59e-05	-40.3	0.576
.01	146	0.581	-1.05e+4	3.95e-08	60.8	0.730
.05	289	0.546	-1.71e+4	7.93e-08	-70.2	0.823
.1	110	0.870	-2.12e+4	1.73e-07	4.34	0.992
.2	229	0.800	**-2.92e+4**	**3.03e-08**	-147	0.786
.3	377	0.728	-3.40e+4	4.39e-08	-163	0.798
.4	275	0.823	-3.72e+4	9.61e-08	-278	0.700
.5	334	0.805	-4.16e+4	4.86e-08	-418	0.598
1	563	0.746	-5.21e+4	6.85e-08	-656	0.516

eTable 15 Note. Linear mixed effect models with PLEs as the outcome and PGS, the first ten PCs, and sex as predictors. Data is nested within families and sites. The bolded line indicates the p-value threshold most significantly associated with the outcome that was used as a covariate in analyses. *b* = unstandardized beta estimates

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eTable 16. Associations Between Social Problems and Polygenic Scores for Cannabis Use

Threshold	*b*	*p*
.00000005	-1.33	0.646
.0001	-34.6	0.236
.001	9.83	0.833
.01	25.8	0.822
.05	-139	0.497
.1	-154	0.560
.2	-308	0.380
.3	-358	0.388
.4	-467	0.318
.5	-534	0.299
1	**-871**	**0.184**

eTable 16 Note.. Linear mixed effect models with social problems as the outcome and PGS, the first ten PCs, and sex as predictors. Data is nested within families and sites. The bolded line indicates the p-value threshold most significantly associated with the outcome that was used as a covariate in analyses. *b* = unstandardized beta estimates

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eTable 17. Non-Mutually Exclusive Groups Regression Results Without Covariates

	Cannabis exposure post-knowledge		Cannabis exposure pre-knowledge		
Outcome	*b*	*p*	*b*	*p*	*N*
PLEs	1.12	**2.21e-07**	0.795	**3.65e-09**	11477
CBCL Internalizing	2.42	**7.00e-13**	1.78	**2.27e-17**	11483
CBCL Externalizing	4.68	**1.17e-42**	2.93	**3.93e-43**	11483
CBCL Attention	2.37	**8.89e-27**	1.71	**2.59e-35**	11483
CBCL Thought	1.36	**1.63e-25**	0.870	**7.75e-27**	11483
CBCL Social	1.54	**3.59e-29**	0.984	**8.87e-31**	11483
Body Mass Index	1.31	**6.58e-07**	0.945	**8.76e-09**	11462
Cognition Composite	-3.83	**1.87e-10**	-2.08	**2.22e-08**	11249
Total sleep problems	4.04	**1.89e-15**	2.88	**9.29e-20**	11489
Birth Weight (oz)	-3.39	**1.23e-03**	-1.75	**6.48e-03**	11113
Gestational age	0.142	0.271	0.076	0.334	11414
Intracranial Volume	-0.273	**8.14e-06**	-0.154	**5.27e-05**	11024
White Matter Volume	-0.295	**2.02e-05**	-0.181	**2.73e-05**	10404
Gray Matter Volume	-0.381	**9.66e-09**	-0.228	**3.77e-08**	11020

eTable 17 Note. Linear mixed effect models were used to analyze the associations between pre- and post-knowledge of pregnancy use of cannabis (analyzed separately) and each outcome, nesting data by research site and family ID (non-imaging analyses) and scanner and family ID (imaging analyses). Results here did not include covariates. *b* = unstandardized beta estimates. PLEs = Psychotic-Like Experiences; CBCL = Child Behavior Checklist.

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eTable 18. Non-Mutually Exclusive Groups Regression Results With Covariates

	Cannabis exposure post-knowledge		Cannabis exposure pre-knowledge		
Outcome	*b*	*p*	*b*	*p*	*N*
PLEs	0.941	**0.00810**	-0.091	0.647	8165
CBCL Internalizing	1.15	**0.0359**	-0.053	0.862	8168
CBCL Externalizing	1.90	**4.63e-04**	0.146	0.630	8168
CBCL Attention	1.14	**0.00136**	0.205	0.305	8168
CBCL Thought	0.523	**0.0134**	0.129	0.277	8168
CBCL Social	0.942	**2.00e-05**	0.070	0.572	8168
Body Mass Index	0.456	0.275	-0.022	0.925	8151
Cognition Composite	-1.69	**0.0457**	0.887	0.0609	8000
Total sleep problems	0.867	0.296	0.370	0.428	8169
Birth weight (oz)	-3.42	**0.0278**	0.871	0.318	8169
Intracranial Volume	0.016	0.858	0.024	0.624	7846
White Matter Volume	-0.037	0.661	-0.040	0.246	7431
Gray Matter Volume	-0.017	0.743	0.035	0.237	7842

eTable 18 Note. Linear mixed effect models were used to analyze the associations between pre- and post-knowledge of pregnancy use of cannabis (entered simultaneously) and each outcome. Results here included all covariates from our original analysis. *b* = unstandardized beta estimates. PLEs = Psychotic-Like Experiences; CBCL = Child Behavior Checklist.

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eTable 19. Inverse Probability Weighting Balance Analysis Results

Covariates	Post-knowledge exposure		Pre-knowledge exposure		Any exposure	
	b	*p*	*b*	*p*	*b*	*p*
Alcohol pre-knowledge	0.089	0.181	0.061	0.274	0.058	0.294
Alcohol post-knowledge	0.169	0.155	-0.021	0.827	-0.021	0.826
Tobacco pre-knowledge	0.159	0.119	0.035	0.488	0.035	0.491
Tobacco post-knowledge	0.223	0.094	0.055	0.456	0.055	0.451
White	-0.046	0.584	-0.051	0.463	-0.049	0.477
Black	0.050	0.568	-0.071	0.259	-0.073	0.246
Fam Hx Depression	0.141	**0.020**	0.028	0.658	0.026	0.683
Fam Hx Mania	-0.070	0.454	-0.120	0.089	-0.118	0.095
Fam Hx Psychosis	---	---	0.036	0.711	0.031	0.745
Fam Hx Antisocial	0.155	**0.036**	0.093	0.078	0.095	0.073
Fam Hx Anxiety	-0.017	0.845	0.087	0.277	0.091	0.259
Child Alcohol Try	---	---	0.080	0.217	0.080	0.215
Unplanned pregnancy	0.161	**0.045**	-0.081	0.137	0.085	0.121
Twin/Triplet	-0.110	**0.021**	-0.044	0.510	-0.043	0.516
Combined Income	-0.035	0.238	0.013	0.562	0.013	0.571
Maternal Education	0.011	0.424	0.002	0.878	0.003	0.806
Maternal Age at Birth	-0.001	0.835	0.001	0.761	0.001	0.771
Week Learned Pregnant	---	---	0.001	0.767	0.001	0.773
Child Sex	0.119	**0.024**	---	---	---	---

eTable 19 Note. Before conducting inverse probability weighting (IPW) by the propensity scores, analyses were conducted to determine whether propensity scores accounted for the non-random confounding by outcomes of interest. The results here are for logistic models predicting exposure. Significant values are bolded and represent the degree to which non-random assignment is not being accounted for by the IPW analysis. Separate propensity scores were calculated for each exposure variable. In contrast to original analyses where combined income was measured as an ordinal predictor, here, due to necessities of the IPW analysis, combined income was measured continuously. *b* = unstandardized beta estimates.

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eTable 20. Inverse Probability Weighting Regression Results

Outcome Variable	Post-knowledge exposure (n = 93)		Pre-knowledge exposure (n = 345)		Any exposure (n = 347)	
	b	*p*	*b*	*p*	*b*	*p*
PLEs	1.23	**2.80e-05**	0.485	**0.002**	0.784	**9.46e-09**
CBCL Internalizing	1.29	**0.009**	0.793	**0.002**	1.18	**2.28e-07**
CBCL Externalizing	2.58	**8.30e-08**	1.55	**4.26e-09**	2.25	**<2.22e-16**
CBCL Attention	1.41	**5.04e-06**	0.982	**3.73e-09**	1.37	**<2.22e-16**
CBCL Thought	0.640	**5.38e-04**	0.370	**2.10e-04**	0.568	**9.28e-11**
CBCL Social	1.14	**4.36e-09**	0.544	**2.04e-07**	0.865	**<2.22e-16**
Body Mass Index	-0.234	0.526	0.892	**1.29e-05**	0.941	**1.30e-07**
Cognition Composite	-2.59	**5.67e-04**	-0.664	0.102	-1.37	**1.17e-04**
Total sleep problems	2.36	0**.002**	1.88	**2.89e-06**	2.56	**3.38e-13**
Birth Weight (oz_	-3.10	0.059	-1.18	0.169	-1.99	**0.008**
Intracranial Volume	-0.167	0.060	-0.045	0.295	-0.068	0.064
Gray Matter Volume	-0.039	0.387	-0.027	0.265	-0.037	0.081
White Matter Volume	-0.037	0.409	-0.026	0.284	-0.035	0.101

eTable 20 Note. Results from a mixed effect model in which a synthetic sample was generated from propensity scores to account for non-random assignment of prenatal exposure. Analyses were run separately for each outcome and each exposure. *b* = unstandardized beta estimates. PLEs = Psychotic-Like Experiences. CBCL = Child Behavior Checklist. Gestational age was not included in the propensity score analyses due to non-significant associations with any measure of exposure, and thus is not reported as an outcome here.

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eTable 21. Regression Results When Excluding Children Whose Mother Used Cannabis Only Prior to Pregnancy Knowledge and Discovered Pregnancy After 15 Weeks

	Cannabis exposure post-knowledge vs. no exposure		Cannabis exposure pre-knowledge vs. no exposure		Cannabis exposure post-knowledge vs. pre-knowledge		
Outcome	*b*	*p*	*b*	*p*	*b*	*p*	*N*
PLEs	0.841	**7.62e-03**	-0.148	0.473	0.989	**6.08e-03**	8146
CBCL Internalizing	1.10	**0.0237**	-0.039	0.904	1.14	**0.0408**	8149
CBCL Externalizing	2.04	**2.08e-05**	0.283	0.367	1.76	**1.36e-03**	8149
CBCL Attention	1.34	**2.25e-05**	0.217	0.294	1.12	**1.91e-03**	8149
CBCL Thought	0.645	**5.79e-04**	0.133	0.280	0.513	**0.0169**	8149
CBCL Social	1.01	**2.44e-07**	0.071	0.581	0.940	**2.72e-05**	8149
Body Mass Index	0.423	0.254	-0.102	0.675	0.525	0.216	8132
Cognition Composite	-0.833	0.266	1.04	**0.0329**	-1.88	**0.0288**	7982
Total sleep problems	1.23	0.0951	0.586	0.224	0.643	0.445	8150
Birth weight (oz)	-2.60	0.0599	1.01	0.264	-3.60	**0.0225**	8150
Gestational age	0.115	0.489	-0.010	0.928	0.125	0.513	8122
Intracranial Volume	0.039	0.613	0.025	0.621	0.014	0.871	7828
White Matter Volume	-0.066	0.233	-0.034	0.346	-0.033	0.606	7416
Gray Matter Volume	0.018	0.705	0.030	0.326	-0.012	0.821	7824

eTable 21 Note. Children whose mother used cannabis only prior to pregnancy knowledge and discovered pregnancy after 15 weeks (n=25). *b* = unstandardized beta estimates. PLEs = Psychotic-Like Experiences. CBCL = Child Behavior Checklist.

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eTable 22. Regression Results When Excluding Children Whose Mother Used Cannabis Only Prior to Pregnancy Knowledge and Discovered Pregnancy After 9 Weeks

	Cannabis exposure post-knowledge vs. no exposure		Cannabis exposure pre-knowledge vs. no exposure		Cannabis exposure post-knowledge vs. pre-knowledge		
Outcome	*b*	*p*	*b*	*p*	*b*	*p*	*N*
PLEs	0.837	**7.83e-03**	-0.152	0.481	0.990	**6.79e-03**	8119
CBCL Internalizing	1.10	**0.0234**	-0.062	0.853	1.16	**0.0393**	8122
CBCL Externalizing	2.03	**2.18e-05**	0.309	0.347	1.72	**1.94e-03**	8122
CBCL Attention	1.32	**2.74e-05**	0.189	0.382	1.13	**1.98e-03**	8122
CBCL Thought	0.642	**6.15e-04**	0.109	0.398	0.533	**0.0143**	8122
CBCL Social	1.01	**2.83e-07**	0.090	0.503	0.916	**5.71e-05**	8122
Body Mass Index	0.418	0.260	-0.052	0.839	0.469	0.276	8106
Cognition Composite	-0.831	0.267	1.11	**0.0310**	-1.94	**0.0261**	7955
Total sleep problems	1.23	0.0943	0.628	0.214	0.606	0.479	8123
Birth weight (oz)	-2.56	0.0637	1.07	0.256	-3.63	**0.0235**	8123
Gestational age	0.116	0.486	0.053	0.635	0.063	0.746	8095
Intracranial Volume	0.038	0.625	0.023	0.664	0.015	0.866	7803
White Matter Volume	-0.062	0.256	-0.028	0.446	-0.034	0.591	7391
Gray Matter Volume	0.017	0.714	0.020	0.531	-2.72e-03	0.961	7799

eTable 22 Note. Children whose mother used cannabis only prior to pregnancy knowledge and discovered pregnancy after 9 weeks (n=61). *b* = unstandardized beta estimates. PLEs = Psychotic-Like Experiences. CBCL = Child Behavior Checklist.

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eTable 23. Psychotic-Like Experiences and Prenatal Cannabis Exposure: Regression Results When Including Maternal Psychotic-Like Experiences as a Covariate

	Psychotic-like Experiences	
Covariates	*b*	*p*
Cannabis Post vs. No	0.793	**0.012**
Cannabis Pre vs. No	-0.106	0.597
Cannabis Post vs. Pre	0.899	**0.012**
Alcohol Post	0.297	0.227
Alcohol Pre	-0.037	0.682
Tobacco Post	0.180	0.410
Tobacco Pre	0.214	0.127
White	-0.503	**2.12E-04**
Black	0.322	**0.021**
Asian	-0.318	0.050
Native American	0.225	0.305
Pacific Islander	0.466	0.317
Other Race	-0.030	0.873
Hispanic	-0.102	0.393
Child Sex	-0.382	**6.77E-08**
Child Age	-0.028	**4.88E-09**
Income $50-74	-0.087	0.492
Income $75-99	0.013	0.919
Income $100-199	-0.371	**0.003**
Income $200+	-0.566	**4.46E-04**
Maternal Education	-0.066	**0.001**
Maternal Age at Birth	-0.008	0.262
Unplanned Pregnancy	-0.157	0.064
Week Learned Pregnant	-0.003	0.672
Prenatal Vitamin Use	0.254	0.174
Birth Weight	-0.004	0.127
Fam Hx Depression	0.158	0.062
Fam Hx Mania	0.113	0.509
Maternal PLEs	0.069	0.155
Fam Hx Antisocial	0.250	**0.049**
Fam Hx Anxiety	0.138	0.235
Child Alcohol Try	0.687	**1.39E-15**
Child Tobacco Try	0.786	**0.027**
Twin/Triplet	-0.185	0.205

eTable 23 Note. Associations between prenatal cannabis exposure and child psychotic-like experiences (PLEs) when substituting first-degree familial history of psychosis with maternal psychotic-like experiences as measured by four questions from the Adult Self Report (ASR) of psychopathology. Post = post-maternal knowledge of pregnancy exposure. Pre = pre-maternal knowledge of pregnancy exposure. Fam Hx = family history. Bolded values indicate significant associations. *b* = unstandardized beta estimates.

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