Supplemental Materials

Prenatal PFAS and longitudinal neurodevelopmental trajectories in preschoolers aged 3-7: effect modification by bile acid metabolism

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Supplementary Text 1. Sample Collection

To investigate the effects of environmental pollutants on fetal growth, a birth cohort was established at Maoming Children's Health Hospital between 2015 and 2018. Among the 22,200 participants recruited, 9,765 provided 5 mL blood samples (maternal samples collected within 7 days before delivery and infant samples at delivery) and completed the questionnaires. After applying initial exclusion criteria for conditions including pregnancy complications (e.g., gestational hypertension, diabetes) and other serious maternal diseases (as detailed in Supplementary Figure 1), a nested sub-cohort of 1,030 mother-child pairs was selected from this biobank for prospective follow-up, based on the completion of an additional detailed questionnaire and the provision of a third-trimester maternal blood sample after 8 hours of fasting. For the present analysis on prenatal PFAS exposure and neurodevelopment, we applied sequential exclusions to this follow-up sub-cohort for reasons including loss to follow-up, multiple births, lack of neurodevelopmental assessment data, or unavailable PFAS measurements. This process resulted in a cross- sectional sample of 460 children with at least one valid neurodevelopmental assessment between 3 and 7 years of age (used for ancillary analyses not presented in the main manuscript). The primary analysis focused on longitudinal neurodevelopmental trajectories, which required at least two repeated assessments per child for group- based trajectory modeling (GBTM). Therefore, we selected the 278 children who met this criterion. Subsequently, to investigate effect modification by bile acids, the sample was further limited to 225 children with available serum bile acid concentration data from the 3-year follow-up. A detailed flowchart of participant selection is provided in Supplementary Figure 1.

Supplementary Text 2. Rationale for Harmonizing Neurodevelopmental Scores Across Assessment Tools

To model neurodevelopmental trajectories across a broad age range (33–84 months), we harmonized scores from different assessment tools, including the Ages and Stages Questionnaire (ASQ), Wechsler Preschool and Primary Scale of Intelligence-IV (WPPSI-IV), and Wechsler Intelligence Scale for Children-IV (WISC-IV). This approach aligns with established methodologies in longitudinal neurodevelopmental studies, where combining scores from age-appropriate assessments is necessary to capture developmental patterns over time.

Scores from ASQ, WPPSI-IV, and WISC-IV were standardized to a common scale (mean = 100, SD = 15) to ensure comparability. This transformation accounts for differences in raw score ranges and measurement foci (e.g., ASQ emphasizes early developmental milestones, while WPPSI/WISC focuses on cognitive abilities). Similar normalization strategies have been widely adopted in cohort studies[1,2]. For instance, Black and Adjei (2022) used data from the UK Millennium Cohort Study and standardized cognitive test scores from multiple instruments across ages 3 to 14 years to identify group-based developmental trajectories[3]. Also, the RESONANCE cohort study normalized scores from the Mullen Scales of Early Learning (MSEL), WPPSI-IV, and WISC-V into full-scale composite scores to analyze cognitive scores across infancy to adolescence[3]. This method prioritizes relative developmental progress over absolute scores, enabling trajectory modeling despite instrument-specific variations.

Combining distinct assessments is justified when the goal is to classify trajectories (e.g., high *vs.* low) rather than compare absolute scores. Studies frequently merge WPPSI and WISC scores to define intellectual disability (IQ < 70) or track cognitive outcomes[1]. Group-based trajectory modeling (GBTM) is particularly robust to such harmonization, as it identifies latent patterns based on relative trends rather than raw values[4]. Importantly, the goal of our analysis was not to compare raw scores across tools, but rather to identify developmental subgroups (i.e., high *vs.* low trajectories) within a common metric framework. To ensure score comparability, we converted all assessments to a uniform scale (percentage-based), which allowed us to harmonize measurements across tools. This harmonization strategy has precedent in the literature, where researchers have combined different developmental assessments across time points using standardized or unified scoring approaches to enhance continuity and validity in longitudinal modeling.

Supplementary Text 3. Group-based trajectory modeling (GBTM), logistic regression, and grouped weighted quantile sum (GWQS) regression models

The Group-Based Trajectory Modeling (GBTM) was used to further investigate the effects of prenatal PFAS exposure on neurodevelopmental trajectories in preschool children aged 3-7 years. GBTM, implemented through the "traj" package in the STATA software, is an extension of univariate group-based trajectory modeling[5]. This approach allows for identifying subgroups within a population with different developmental trajectories and analyzing individual characteristics within these subgroups. In this study, we constructed a longitudinal dataset of children's neurodevelopment by collecting neurodevelopmental data at multiple time points: 33, 36, 42, 48, 54, 60, 72, and 84 months of age. The GBTM model utilizes the minimum Bayesian information criterion (BIC) to determine the optimal number of trajectory groups and the functional model for each trajectory group[6]. Simultaneously, we explored various parameters of the model, encompassing cubic, quadratic, and linear terms fitted across different numbers of trajectory groups (ranging from 1 to 5 groups), in order to determine the most suitable model for characterizing children's neurodevelopmental trajectories. Posterior group-membership probabilities were employed as an indicator of each participant's likelihood of being assigned to a specific trajectory category, with average posterior probability (AvePP) ($\geqslant 0.7$ for each trajectory category) established to identify final members of trajectory subgroups. Further technical details regarding the statistical foundation for calculating GBTM have been previously described[7]. After excluding 182 participants who had only one neurodevelopmental data point available, a total of 278 participants were included in the trajectory model analysis. It was determined that dividing the trajectories into two distinct groups would be optimal for this study, with the high-risk group defined as children exhibiting lower scores in the model. Subsequently, the results were visually presented after determining the optimal number of trajectory categories and appropriate trajectory shape.

Supplementary Text 4. Rationale for Selecting the GBTM model with two trajectories

The selection of the final group-based trajectory model was guided by established methodological principles, prioritizing the Bayesian Information Criterion (BIC), classification accuracy (as measured by average posterior probabilities, AvePP), and class interpretability [8]. Among the models fitted (1- to 5-class solutions), the two-group solution was identified as optimal.

In terms of model fit, BIC values for the 1- to 5-class models were −3376.66, −2993.14, −2989.13, −2994.77, and −2996.21, respectively. While models with more than two classes showed slight improvements in BIC over the two-class model, the gains were marginal and came at the cost of reduced parsimony and classification accuracy [9]. Critically, the 3-, 4-, and 5-class models each resulted in at least one trajectory class comprising a very small proportion of the sample (<5%) — specifically, the smallest classes accounted for 3.60%, 3.60%, and 2.52% of the sample, respectively. The formation of such small, non-generalizable classes is indicative of overfitting and is not recommended, as it undermines the stability and substantive utility of the model [8,10].

In contrast, the two-group solution provided excellent classification accuracy. The average posterior probabilities (AvePP) for the two classes were 0.89 and 0.97, substantially exceeding the recommended threshold of 0.70 [11], which signifies a clear and reliable distinction between the identified trajectories. This high classification certainty is further supported by an entropy value of 0.863.

Therefore, based on the joint consideration of statistical fit (BIC), class stability (each class >5% of the sample), and diagnostic accuracy (AvePP > 0.70) as per standard practices [8,11], the two-group model was selected as the most robust, interpretable, and parsimonious representation of the neurodevelopmental trajectories in our cohort.

Supplementary Text 5. Random forest model

The random forest (RF) algorithm, introduced by Breiman[12], operates by building a collection of decorrelated decision trees through bootstrap aggregation (bagging) and random feature selection. For our classification task, the final output is the class predicted by the majority of trees. This ensemble strategy significantly improves generalization and reduces the risk of overfitting compared to a single decision tree.

(1) Decision tree construction:

We implemented a permutation-test-enhanced random forest model to identify key BA features predictive of neurodevelopmental outcomes. The model input matrix consisted of log-transformed concentrations of 15 BAs, with neurodevelopmental trajectories grouping as the categorical outcome variable. High-precision modeling was achieved using the rfPermute package (v2.5.1), with model robustness ensured by generating an ensemble of 2,500 decision trees. Statistical significance was determined through 1,500 iterations of feature permutation testing.

Feature importance was quantified using the percentage increase in mean squared error (%IncMSE), which estimates the degradation in model predictive accuracy when each feature is randomly permuted. Higher %IncMSE values indicate greater feature importance in classifying neurodevelopmental outcomes. For statistical inference, we employed significance testing based on node purity improvement (IncNodePurity), with results categorized using a step function to generate significance markers (*$P < 0.05$, **$P < 0.01$).

(2) Evaluation of the feature importance:

The key metrics for feature importance evaluation were the percentage increase in mean squared error (%IncMSE), and permutation-based p-values for node purity improvement (IncNodePurity.pval).

The %IncMSE metric quantifies the relative contribution of each BAs to model prediction accuracy, calculated as:

Where $\mathrm{MSE}_{\mathrm{original}}$ represents the mean squared error of the original model, and $\mathrm{MSE}_{\mathrm{b}}^{(\mathrm{i})}$ denotes the prediction error after 1500 permutations of the i-th BAs. The calculation method is shown in Eq. (S1).

$$\%\mathrm{IncMSE}_{\mathrm{i}} = \frac{1}{1500}\sum_{\mathrm{b}=1}^{1500}\left(\frac{\mathrm{MSE}_{\mathrm{b}}^{(\mathrm{i})} - \mathrm{MSE}_{\mathrm{original}}}{\mathrm{MSE}_{\mathrm{original}}}\right) \times 100 \quad \text{(S1)}$$

IncNodePurity.pval was employed to evaluate statistical significance, determining whether the observed feature importance could be attributed to random noise. The calculation is given by:

Where $\mathrm{Purity}_{\mathrm{observed}}^{(\mathrm{i})}$ represents the total improvement in classification purity (reduction in mean

squared error) achieved by BA's feature i at all node splits in the original model, $\mathrm{Purity}_b^{(i)}$ denotes the purity improvement in the b-th permutation test, and $I(\cdot)$ is the indicative function (1 if the condition is true, 0 otherwise), as shown in Eq. (S2).

$$p_i = \frac{1+\sum_{b=1}^{1500} I\left(\mathrm{Purity}_b^{(i)} \geq \mathrm{Purity}_{observed}^{(i)}\right)}{1501} \quad \text{(S2)}$$

The algorithm parameters of the random forest are: the number of decision trees is 2500.

Supplementary Table 1. Summary of the abbreviation, full name, limit of quantification (LOQ) and detection rate for target 32 maternal PFAS.

Abbreviation	Full name	Precursor Ion (m/z)	Quantitative Product Ion (m/z)	LOD (ng/mL)[a]	LOQ (ng/mL)[b]	LOD/√2 (ng/mL)	Detection rate (%)[c]	Recovery rate (%)[f]
HFPO-DA	Hexafluoro-1-propylene oxide dimer acid	285.0	184.8; 168.8	0.5025	1.6800	0.3553	0.22	94.22 ± 12.36
PFBS	Perfluoro-1-butansulfonic acid	298.9	79.8; 297.9	0.0095	0.01	0.0067	3.91	94.80 ± 3.90
PFBA	Perfluoro-n-nbutanoic acid	213.0	168.9	**0.0081**	0.03	0.0057	72.61	89.38 ± 7.30
PFPeS	Perfluoro-1-pentanesulfonic acid	348.9	79.8; 98.7	0.0029	0.01	0.0021	7.83	95.83 ± 4.18
PFPeA	Perfluoro-n-pentanoic acid	263.0	96.8; 218.8	0.0179	0.1	0.0127	37.83	90.83 ± 3.62
PFHxA	Perfluoro-n-hexanoic acid	313.0	118.7; 268.9	**0.0035**	0.05	0.0025	81.96	86.38 ± 11.19
Total PFHxS[d]	Sum of linear and branched perfluoro-1-hexane sulfonate				-		—	-
linear PFHxS	Linear perfluoro-1-hexane sulfonate	399.0	80.0; 98.9	**0.0011**	0.01	0.0008	98.91	96.57 ± 5.97
Branched-PFHxS	Sum of all branched isomers PFHxS	399.0	80.0; 99.0	0.0011	0.01	0.0008	57.39	99.94 ± 5.56
PFHpS	Perfluoro-1-heptanesulfonic acid	448.9	79.9; 98.8	0.0021	0.01	0.0015	88.70	94.36 ± 6.51
PFHpA	Perfluoro-n-heptanoic acid	363.0	168.9; 319	0.0016	0.02	0.0011	60.43	96.24 ± 3.98
PFOS[e]	Sum of linear and branched perfluoro-1-octane sulfonate				-		—	-
linear PFOS	Perfluoro-1-octane sulfonate	499.0	79.7; 98.9	0.0016	0.01	0.0011	99.78	96.64 ± 6.35
total branched PFOS	Sum of all branched isomers PFOS				-		—	-
1m-PFOS	Linear perfluoro-1-methyl-hptanesulfonate	499.0	419	0.0003	0.01	0.0002	99.35	116.46 ± 5.44
6m-PFOS	Perfluoro-6-methyl-heptanesulfonate	499.0	330.0; 98.9	0.001	0.01	0.0007	98.04	94.75 ± 6.93

Σ3+4+5m-PFOS	Sum of 3m, 4m and 5m-PFOS	499.0	330.0; 130.0	0.0013	0.01	0.0009	99.57	104.32 ± 3.81
Σm2-PFOS	Sum of all dimethyl isomers PFOS	499.0	130.0; 330.0	0.0008	0.01	0.0006	95.22	83.78 ± 7.14
PFOA	Perfluoro-n-octanoic acid	413.0	168.9; 369	**0.0025**	0.02	0.0018	99.78	98.32 ± 4.08
				0.0011	0.01	0.0008	35.00	102.43 ±
FOSA	Perfluoro-1-octanesulfonamide	497.9	77.8; 310.1					10.02
N-MeFOSAA	N-methylperfluoro-1-octanesulfonamidoacetic acid	573.0	483.1	0.0044	0.01	0.0031	1.30	91.57 ± 1.41
N-EtFOSAA	N-ethylperfluoro-1-octanesulfonamidoacetic acid	589.0	483.1	0.0016	0.01	0.0011	1.96	94.21 ± 3.15
6:2 Cl-PFESA	6:2 chlorinated polyfluorinated ether sulfonate acid	530.9	351	**0.0018**	0.01	0.0013	99.57	94.06 ± 5.11
8:2 Cl-PFESA	8:2 chlorinated polyfluorinated ether sulfonate acid	630.9	451	**0.0015**	0.01	0.0011	79.35	92.36 ± 4.26
PFNS	Perfluoro-1-nonane sulfonic acid	548.9	79.8; 98.7	0.006	0.01	0.0042	3.04	96.14 ± 7.87
PFNA	Perfluoro-n-nonaoic acid	463.1	266.7; 419.1	**0.0024**	0.02	0.0017	99.78	97.42 ± 6.31
PFDS	Perfluoro-1-decane sulfonic acid	598.9	79.9; 98.8	0.0038	0.01	0.0027	3.26	92.53 ± 2.25
PFDA	Perfluoro-n-decanoic acid	513.0	268.9; 469.1	**0.0048**	0.02	0.0034	99.78	97.49 ± 3.49
PFUnDA	Perfluoro-n-undecanoic acid	563.0	268.9; 519.1	**0.0049**	0.02	0.0035	98.70	96.50 ± 4.84
PFDoDA	Perfluoro-n-dodecanoic acid	613.0	268.7; 569.2	**0.0057**	0.02	0.0040	81.96	93.87 ± 3.31
PFTrDA	Perfluoro-n-tridecanoic acid	663.0	364.8; 619.3	**0.0106**	0.03	0.0075	99.57	103.41 ± 6.98
PFTeDA	Perfluoro-n-tetradecanoic acid	713.0	168.7; 669.2	0.0036	0.01	0.0025	65.00	98.93 ± 7.93
4:2FTSA	1H, 1H, 2H, 2H-perfluoro-1-hexanesulfonic acid	327.0	80.3; 307	0.0073	0.03	0.0052	0.43	109.72 ± 4.33
6:2FTSA	1H, 1H, 2H, 2H-perfluoro-1-octanesulfonic acid	427.0	80.4; 407	0.0106	0.03	0.0075	6.52	83.72 ± 2.82
8:2FTSA	1H, 1H, 2H, 2H-perfluoro-1-decanesulfonic acid	527.0	80.7; 507.1	0.0017	0.01	0.0012	0.87	98.40 ± 5.04

Note: [a]: LOD: Limit of Detection; [b]: LOQ: limit of quantification; [c]: n (%) >LOD; [d] Sum of linear and branched perfluorohexanesulfonate (PFHxS); [e] Sum of linear and branched perfluorooctane sulfonate (PFOS). [f]: Recovery rates were determined at a spiking concentration of 5 ng/mL and are presented as mean ± standard deviation (SD) (*n* = 3). **The PFAS compounds marked in black represent the target compounds (with detection rates ⩾70%) analyzed in this study (*n* = 460).**

Supplementary Table 2. Abbreviation, full name, detection rate, and limit of detection (LOD) of 15 bile acids in our study (*n* = 225).

Abbreviation	Full name	Precursor Ion (m/z)	Quantitative Product Ion (m/z)	Internal Standards	LOD (nM)[a]	Detection rate (%)[b]
Primary unconjugated bile acids						
CA	Cholic acid	407.3	407.3	d4-CA	0.04	**100.00%**
HCA	Hyocholic acid	407.3	407.3	d4-CA	0.05	**99.21%**
CDCA	Chenodeoxycholic acid	391.3	391.3	d9-CDCA	0.15	**100.00%**
Primary conjugated bile acids						
GCA	Glycocholic acid	464.3	74	d4-GCA	0.03	**100.00%**
GHCA	Glycohyocholic acid	464.3	74	d4-GCA	0.04	**99.21%**
GCDCA	Glycochenodeoxycholic acid	448.3	74	d4-GUDCA	0.02	**100.00%**
TCDCA	Taurochenodeoxycholic acid	498.3	80/107	d9-TCDCA	0.06	**100.00%**
THCA	Taurohyocholic acid	514.3	80/107	d4-CA	0.08	**100.00%**
TCA	Taurocholic acid	514.3	80/107	d4-CA	0.06	**100.00%**
Secondary unconjugated bile acids						
DCA	Deoxycholic acid	391.3	391.3	d6-DCA	0.04	**89.68%**
UDCA	Ursodeoxycholilc acid	391.3	391.3	d4-UDCA	0.28	**100.00%**
LCA	Lithocholic acid	375.3	375.3	d4-LCA	0.21	74.60%
Secondary conjugated bile acids						
GDCA	Glycodeoxycholic acid	448.3	74	d6-GDCA	0.04	**88.89%**
GHDCA	Glycohyodeoxycholic acid	448.3	74	d4-GUDCA	0.06	71.03%
GLCA	Glycolithocholic acid	432.3	74	d4-GLCA	0.01	**100.00%**
GUDCA	Glycoursodeoxycholilc acid	448.3	74	d4-GUDCA	0.08	**100.00%**
TDCA	Taurodeoxycholic acid	498.3	80	d6-TDCA	0.08	**100.00%**

Note: [a]: LOD: Limit of Detection; [b]: n (%) > LOD. **The bile acids marked in black represent the target compounds (with detection rates ≥75%) analyzed in this study.**

Supplementary Table 3. Fit Statistics and Classification Coefficients[a].

Number of classes	AIC	BIC	Entropy	Probability of class	AvePP
1	-3367.59	-3376.66	-	1	-
2	**-2976.81**	**-2993.14**	**0.863**	**0.1295/0.8705**	**0.89/0.97**
3	-2961.92	-2989.13	0.786	0.0360/0.1763/0.7877	0.96/0.82/0.93
4	-2958.49	-2994.77	0.682	0.0360/0.2338/0.6331/0.0971	0.89/0.68/0.86/0.79
5	-2950.86	-2996.21	0.698	0.0324/0.6475/0.0252/0.0935/0.2014	0.79/0.84/0.93/0.67/0.72

[a] Note: AIC = Akaike information criterion; BIC = Bayesian information criterion; AvePP = Average posterior probability; "Probability of class" represents the actual proportion of individuals classified into each group based on the maximum posterior probability rule (countG/N). Bold font indicates selected model. The Class-2 model was selected as the final GBTM solution. The rationale for this selection is detailed in Text S4.

Supplementary Table 4. Repeated measures of neuropsychological developments at different developmental stages (*n* = 278, 821 repeated measures)

Developmental subscales	33 months (*n* = 62)	36 months (*n* = 163)	42 months (*n* = 51)	48 months (*n* = 121)	54 months (*n* = 84)	60 months (*n* = 157)	72 months (*n* = 124)	84 months (*n* = 59)
	ASQ-3 scores (Mean ± SD)						FSIQ scores (Mean ± SD)	
Total ASQ scores	232.2 ± 40.3	240.7 ± 44.6	249.6 ± 39.3	262.9 ± 31.2	277.6 ± 21.9	277.4 ± 21.6		
FSIQ-WPPSI-IV							109.2 ± 11.3	
FSIQ-WISC-IV								109.2 ± 13

ASQ-3: the Ages and Stages Questionnaires, 3rd edition.

Supplementary Table 5. Comparison between children aged 3-7 years with and study population [Mean ± SD/N(%)][c]

variable		Children aged 3-7 years with at least one neurodevelopmental assessment (n = 460)[e]	Children aged 3-7 years with at least two neurodevelopmental assessments (n = 278)[f]	P-value
mother				
maternal age (years)[a]		29.05 ± 5.28	29.54 ± 5.22	**0.014**
pre-pregnancy BMI (kg/m^2)[a,c]		20.75 ± 3.31	21.13 ± 3.54	**0.004**
parity[b]				
	primiparous	260 (57.0)	153 (55.4)	0.454
	multiparous	196 (43.0)	123 (44.6)	
maternal education[b]				
	≤high school	225 (54.2)	120 (48.0)	**0.002**
	>high school	190 (45.8)	130 (52.0)	
paternal education[b]				
	≤high school	231 (55.5)	133 (53.0)	0.236
	>high school	185 (44.5)	118 (47.0)	
family income (CNY/year)[b,d]				
	<30,000	107 (28.2)	66 (28.4)	0.507
	30,000-100,000	153 (40.4)	98 (42.2)	
	>100,000	119 (31.4)	68 (29.3)	
maternal passive smoking before pregnancy[b]	yes	211 (51.0)	123 (49.2)	0.431
alcohol drinking[b]	yes	11 (2.7)	7 (2.8)	1
folic acid or vitamin supplementation during pregnancy[b]	yes	379 (90.7)	231 (91.7)	0.489
child				
gestational age (weeks)[a]		37.35 ± 2.85	37.42 ± 2.65	0.473
delivery method[b]				
	vaginal delivery	267 (58.6)	152 (55.1)	0.077
	cesarean delivery	189 (41.4)	124 (44.9)	
sex[b]				
	boy	255 (55.4)	145 (52.2)	0.099
	girl	205 (44.6)	133 (47.8)	
birthweight (g)[a]		2829.39 ± 620.95	2852.90 ± 615.81	0.317
breastfeeding duration[b]				
	0 month	27 (6.5)	22 (8.2)	**<0.001**

≤6 months	171 (41.1)	89 (33.2)
>6 months	218 (52.4)	157 (58.6)

Note: [a]: Data are shown as mean ± SD for continuous variables; [b]: Data are shown as n (%) for categorical variables. [c]: Pre-pregnancy BMI was calculated as weight (kg) divided by height squared (m^2). [d]: CNY = Chinese Yuan. [e]: The total population refers to children aged 3-7 years from the Maoming Birth Cohort who had at least one neurodevelopmental assessment and available PFAS data in maternal serum. [f]: A subset of the total population who had at least two neurodevelopmental assessments. Differences between sexes (n = 460) were tested using the $\chi 2$ test for categorical variables and the Wilcoxon rank-sum test for continuous variables.

Supplementary Table 6. Concentrations of maternal PFAS (*n* = 460).

Abbreviation	Lower limit of detection (ng/mL)	Detection rate (%)	PFAS concentrations (ng/mL)		
			25th Percentile	Median	75th Percentile
Alternative PFAS					
6:2 Cl-PFESA	0.0018	99.57%	0.40	0.63	1.02
8:2 Cl-PFESA	0.0015	79.35%	0.00	0.01	0.01
PFBA	0.0081	72.61%	0.01	0.67	1.56
PFHxA	0.0035	81.96%	0.01	0.03	0.08
Σalternative PFAS[a]	-	-	0.86	1.59	2.68
Legacy PFAS					
linear PFHxS	0.0011	98.91%	0.10	0.15	0.24
PFOS[b]	-	-	2.91	4.28	6.61
PFOA	0.0025	99.78%	0.75	1.04	1.46
PFNA	0.0024	99.78%	0.32	0.43	0.59
PFDA	0.0048	99.78%	0.27	0.38	0.55
PFDoDA	0.0057	81.96%	0.02	0.04	0.07
PFTrDA	0.0106	99.57%	0.21	0.34	0.49
PFUnDA	0.0049	98.70%	0.35	0.51	0.72
Σlegacy PFAS[c]	-	-	5.45	7.54	11.01

Note: [a]: Sum of 6:2 Cl-PFESA, 8:2 Cl-PFESA, PFBA, and PFHxA. [b]: Sum of linear and branched perfluorooctane sulfonate (PFOS). [c]: Sum of linear PFHxS, PFOS, PFOA, PFNA, PFDA, PFDoDA, PFTrDA, and PFUnDA.

Supplementary Table 7. Concentrations of bile acids (nM) in children serum (*n* = 225)

Abbreviation	Bile acid concentrations (nM)			
	min	25th Percentile	Median	75th Percentile
Primary unconjugated bile acids				
CA	8.20	32.85	62.00	123.00
HCA	0.23	7.85	13.45	23.50
CDCA	8.65	81.50	170.50	317.00
Primary conjugated bile acids				
GCA	9.00	283.00	595.00	1170.00
GHCA	0.20	17.65	35.30	66.00
GCDCA	41.00	1280.00	2140	3965.00
TCDCA	4.41	223.50	480.50	885.00
THCA	0.85	9.25	18.95	39.85
TCA	2.99	50.00	113.00	270.50
Secondary unconjugated bile acids				
DCA	0.19	20.65	98.50	203.00
UDCA	10.80	55.50	119.50	238.00
Secondary conjugated bile acids				
GDCA	0.18	37.65	187.50	479.00
GLCA	0.23	1.10	2.36	6.25
GUDCA	0.87	274.50	494.00	950.00
TDCA	0.40	10.20	34.40	98.50

Note: Bile acid abbreviations: See Supplementary Table 2.

Supplementary Table 8. Associations between maternal PFAS and neurodevelopment scores at 33 months of age (adjusted models)(*n* = 90)[a]

Exposure	Total ASQ	Communication	Gross-motor	Fine-motor	Problem-solving	Personal-social
	Adjusted β (95%CI)					
Alternative PFAS						
6:2 Cl-PFESA	-8.08 (-24.79, 8.64)	-2.05 (-6.39, 2.29)	0.88 (-2.24, 4.01)	-2.87 (-10.11, 4.37)	-1.01 (-6.25, 4.22)	-3.02 (-6.74, 0.69)
8:2 Cl-PFESA	0.15 (-9.08, 9.38)	-0.99 (-3.37, 1.39)	-0.28 (-1.99, 1.44)	-1.07 (-5.05, 2.91)	1.75 (-1.08, 4.58)	0.74 (-1.33, 2.81)
PFBA	-2.74 (-6.99, 1.52)	-0.65 (-1.75, 0.46)	-0.32 (-1.12, 0.47)	-0.31 (-2.17, 1.55)	-0.57 (-1.91, 0.76)	-0.88 (-1.83, 0.06)
PFHxA	0.90 (-6.06, 7.85)	-0.37 (-2.18, 1.43)	0.90 (-0.38, 2.17)	-0.44 (-3.44, 2.56)	0.88 (-1.27, 3.03)	-0.07 (-1.63, 1.50)
Legacy PFAS						
linear PFHxS	0.12 (-8.77, 9.01)	0.36 (-1.95, 2.66)	0.88 (-0.76, 2.51)	-2.16 (-5.96, 1.63)	1.44 (-1.30, 4.18)	-0.39 (-2.39, 1.61)
PFOS[b]	-9.87 (-27.14, 7.39)	-2.79 (-7.26, 1.68)	1.01 (-2.22, 4.25)	-3.68 (-11.16, 3.80)	-1.44 (-6.86, 3.98)	-2.98 (-6.84, 0.87)
PFOA	-6.46 (-19.99, 7.08)	-1.78 (-5.29, 1.73)	0.61 (-1.92, 3.14)	0.25 (-5.64, 6.14)	-2.27 (-6.47, 1.93)	**-3.26 (-6.21, -0.31)**
PFNA	-18.57 (-41.02, 3.89)	-5.09 (-10.90, 0.72)	-1.20 (-5.46, 3.06)	-4.49 (-14.36, 5.37)	-2.91 (-10.02, 4.21)	-4.88 (-9.89, 0.14)
PFDA	**-18.69 (-37.19, -0.18)**	**-5.07 (-9.86, -0.28)**	-2.57 (-6.06, 0.93)	-5.28 (-13.44, 2.88)	-2.70 (-8.62, 3.22)	-3.07 (-7.31, 1.17)
PFDoDA	-1.13 (-9.96, 7.70)	-1.13 (-3.40, 1.15)	1.12 (-0.49, 2.73)	-3.22 (-6.94, 0.49)	2.15 (-0.54, 4.84)	-0.05 (-2.04, 1.94)
PFTrDA	2.78 (-13.52, 19.07)	-1.43 (-5.64, 2.79)	1.84 (-1.16, 4.83)	0.26 (-6.79, 7.30)	2.98 (-2.03, 7.99)	-0.87 (-4.54, 2.80)
PFUnDA	**-9.19 (-17.55, -0.83)**	-1.97 (-4.17, 0.23)	-0.62 (-2.23, 0.99)	-1.45 (-5.20, 2.29)	-2.24 (-4.88, 0.41)	**-2.91 (-4.71, -1.11)**
Total PFAS	-13.34 (-33.15, 6.48)	-3.09 (-8.25, 2.07)	1.18 (-2.55, 4.91)	-3.56 (-12.21, 5.08)	-2.89 (-9.11, 3.32)	**-4.97 (-9.31, -0.63)**

Note: [a]: Adjusted by maternal age, Pre-pregnancy BMI, parity, maternal education, family income, maternal passive smoking before pregnancy, alcohol drinking, folic acid or vitamin supplementation during pregnancy, child sex, and gestational age. [b]: Sum of linear and branched perfluorooctane sulfonate (PFOS). Bold font indicates statistical significance.

Supplementary Table 9. Associations between maternal PFAS and neurodevelopment scores at 36 months of age (adjusted models) (*n* = 248)[a]

Exposure	Total ASQ	Communication	Gross-motor	Fine-motor	Problem-solving	Personal-social
	Adjusted β (95%CI)					
Alternative PFAS						
6:2 Cl-PFESA	8.68 (-0.61, 17.97)	2.44 (-0.43, 5.30)	0.74 (-1.27, 2.75)	2.44 (-0.46, 5.34)	2.17 (-0.58, 4.91)	0.89 (-1.52, 3.31)
8:2 Cl-PFESA	**7.49 (1.86, 13.12)**	1.57 (-0.19, 3.32)	1.16 (-0.06, 2.38)	1.35 (-0.43, 3.12)	**2.24 (0.58, 3.89)**	1.18 (-0.29, 2.65)
PFBA	0.81 (-1.83, 3.45)	0.23 (-0.58, 1.04)	0.29 (-0.27, 0.86)	0.44 (-0.38, 1.27)	-0.21 (-0.98, 0.57)	0.05 (-0.63, 0.73)
PFHxA	-2.07 (-6.35, 2.21)	-0.97 (-2.28, 0.35)	0.12 (-0.80, 1.05)	-0.74 (-2.07, 0.59)	0.02 (-1.25, 1.28)	-0.50 (-1.61, 0.60)
Legacy PFAS						
linear PFHxS	5.33 (-2.57, 13.24)	1.27 (-1.17, 3.71)	0.05 (-1.66, 1.75)	1.77 (-0.69, 4.24)	1.50 (-0.83, 3.84)	0.74 (-1.31, 2.78)
PFOS[b]	8.98 (-0.57, 18.53)	2.78 (-0.16, 5.72)	0.77 (-1.30, 2.83)	**3.27 (0.31, 6.24)**	1.48 (-1.35, 4.32)	0.68 (-1.81, 3.16)
PFOA	-0.76 (-10.58, 9.06)	-1.35 (-4.36, 1.67)	0.49 (-1.61, 2.60)	-0.55 (-3.61, 2.50)	0.86 (-2.03, 3.76)	-0.22 (-2.75, 2.32)
PFNA	7.61 (-3.48, 18.71)	**3.61 (0.21, 7.00)**	-0.11 (-2.50, 2.28)	2.29 (-1.17, 5.75)	0.39 (-2.90, 3.67)	1.44 (-1.43, 4.31)
PFDA	9.73 (-2.42, 21.88)	**4.22 (0.50, 7.93)**	-0.13 (-2.75, 2.50)	3.62 (-0.15, 7.39)	0.33 (-3.28, 3.94)	1.69 (-1.46, 4.83)
PFDoDA	3.94 (-2.48, 10.36)	1.30 (-0.68, 3.28)	0.05 (-1.34, 1.43)	1.37 (-0.63, 3.36)	0.62 (-1.28, 2.52)	0.61 (-1.05, 2.27)
PFTrDA	8.73 (-1.25, 18.70)	2.51 (-0.57, 5.58)	-0.23 (-2.39, 1.92)	**3.47 (0.37, 6.56)**	1.49 (-1.47, 4.45)	1.50 (-1.09, 4.08)
PFUnDA	10.16 (-1.97, 22.29)	**3.73 (0.01, 7.46)**	-0.35 (-2.97, 2.27)	**4.15 (0.40, 7.91)**	1.15 (-2.45, 4.75)	1.47 (-1.68, 4.61)
Total PFAS	10.45 (-2.04, 22.93)	2.77 (-1.08, 6.62)	0.95 (-1.74, 3.65)	**4.71 (0.85, 8.57)**	1.39 (-2.31, 5.10)	0.62 (-2.63, 3.86)

Note: [a]: Adjusted by maternal age, Pre-pregnancy BMI, parity, maternal education, family income, maternal passive smoking before pregnancy, alcohol drinking, folic acid or vitamin supplementation during pregnancy, child sex, and gestational age. [b]: Sum of linear and branched perfluorooctane sulfonate (PFOS). Bold font indicates statistical significance.

Supplementary Table 10. Associations between maternal PFAS and neurodevelopment scores at 42 months of age (adjusted models) (*n* = 79)[a]

Exposure	Total ASQ	Communication	Gross-motor	Fine-motor	Problem-solving	Personal-social
	Adjusted β (95%CI)					
Alternative PFAS						
6:2 Cl-PFESA	10.19 (-6.56, 26.95)	0.77 (-4.56, 6.10)	1.20 (-1.13, 3.53)	1.82 (-4.28, 7.92)	3.96 (-2.68, 10.59)	2.44 (-1.42, 6.31)
8:2 Cl-PFESA	2.23 (-6.50, 10.96)	0.01 (-2.73, 2.75)	0.10 (-1.11, 1.31)	-0.05 (-3.20, 3.10)	1.08 (-2.38, 4.53)	1.09 (-0.90, 3.09)
PFBA	-3.46 (-7.60, 0.68)	-0.79 (-2.10, 0.53)	-0.02 (-0.61, 0.57)	-0.06 (-1.59, 1.48)	-1.59 (-3.21, 0.03)	**-1.01 (-1.95, -0.07)**
PFHxA	1.48 (-5.13, 8.10)	-0.49 (-2.56, 1.58)	-0.61 (-1.51, 0.29)	0.14 (-2.25, 2.52)	1.52 (-1.06, 4.10)	0.93 (-0.58, 2.43)
Legacy PFAS						
linear PFHxS	5.02 (-11.99, 22.03)	1.64 (-3.68, 6.97)	-0.44 (-2.80, 1.92)	-2.23 (-8.34, 3.87)	3.32 (-3.37, 10.00)	2.74 (-1.12, 6.59)
PFOS[b]	-7.09 (-31.31, 17.12)	-0.30 (-7.92, 7.31)	-1.98 (-5.29, 1.34)	-3.22 (-11.91, 5.47)	-2.13 (-11.73, 7.47)	0.53 (-5.07, 6.14)
PFOA	1.78 (-17.28, 20.85)	-0.03 (-6.00, 5.94)	-0.89 (-3.51, 1.74)	0.74 (-6.12, 7.59)	1.29 (-6.25, 8.83)	0.67 (-3.72, 5.07)
PFNA	10.00 (-20.41, 40.41)	3.47 (-6.05, 12.98)	-0.58 (-4.81, 3.64)	-0.85 (-11.83, 10.14)	4.18 (-7.85, 16.22)	3.77 (-3.19, 10.73)
PFDA	-4.65 (-28.57, 19.27)	-0.57 (-8.08, 6.93)	-1.54 (-4.82, 1.75)	-4.79 (-13.29, 3.71)	1.17 (-8.31, 10.65)	1.08 (-4.44, 6.60)
PFDoDA	-2.16 (-12.80, 8.47)	-1.58 (-4.89, 1.72)	-0.49 (-1.96, 0.98)	-2.17 (-5.95, 1.60)	0.30 (-3.91, 4.52)	1.78 (-0.62, 4.18)
PFTrDA	-4.92 (-19.81, 9.97)	0.41 (-4.27, 5.10)	-0.50 (-2.57, 1.56)	-3.78 (-9.04, 1.48)	-3.48 (-9.32, 2.35)	2.44 (-0.93, 5.81)
PFUnDA	-6.97 (-30.94, 17.00)	0.01 (-7.53, 7.55)	-1.98 (-5.26, 1.29)	-6.11 (-14.57, 2.35)	-2.22 (-11.73, 7.28)	3.33 (-2.13, 8.80)
Total PFAS	-6.62 (-35.51, 22.28)	-0.76 (-9.83, 8.31)	-1.54 (-5.52, 2.44)	-2.97 (-13.35, 7.41)	-1.36 (-12.82, 10.10)	0.02 (-6.66, 6.70)

Note: [a]: Adjusted by maternal age, Pre-pregnancy BMI, parity, maternal education, family income, maternal passive smoking before pregnancy, alcohol drinking, folic acid or vitamin supplementation during pregnancy, child sex, and gestational age. [b]: Sum of linear and branched perfluorooctane sulfonate (PFOS). Bold font indicates statistical significance.

Supplementary Table 11. Associations between maternal PFAS and neurodevelopment scores at 48 months of age (adjusted models) (*n* = 151)[a]

Exposure	Total ASQ	Communication	Gross-motor	Fine-motor	Problem-solving	Personal-social
	Adjusted β (95%CI)					
Alternative PFAS						
6:2 Cl-PFESA	4.47 (-4.16, 13.10)	0.58 (-2.33, 3.48)	0.41 (-2.17, 3.00)	0.97 (-1.99, 3.94)	2.62 (-0.25, 5.50)	-0.12 (-1.94, 1.71)
8:2 Cl-PFESA	2.57 (-3.22, 8.36)	0.34 (-1.61, 2.29)	-0.42 (-2.15, 1.31)	0.99 (-0.99, 2.97)	1.15 (-0.80, 3.09)	0.51 (-0.71, 1.73)
PFBA	1.95 (-0.39, 4.29)	0.56 (-0.23, 1.35)	**0.79 (0.10, 1.48)**	-0.04 (-0.85, 0.77)	0.66 (-0.13, 1.45)	-0.02 (-0.52, 0.48)
PFHxA	-2.76 (-6.55, 1.03)	**-1.90 (-3.13, -0.68)**	-0.02 (-1.16, 1.13)	-0.73 (-2.03, 0.57)	-0.38 (-1.67, 0.91)	0.26 (-0.54, 1.07)
Legacy PFAS						
linear PFHxS	5.22 (-0.99, 11.42)	0.38 (-1.73, 2.49)	0.29 (-1.58, 2.17)	1.79 (-0.33, 3.92)	**2.44 (0.38, 4.50)**	0.31 (-1.01, 1.64)
PFOS[b]	4.27 (-4.28, 12.82)	2.72 (-0.11, 5.54)	-0.63 (-3.19, 1.92)	-0.10 (-3.04, 2.84)	1.80 (-1.06, 4.67)	0.48 (-1.33, 2.29)
PFOA	3.07 (-7.36, 13.50)	0.63 (-2.87, 4.13)	0.46 (-2.65, 3.57)	1.00 (-2.57, 4.57)	0.33 (-3.19, 3.84)	0.65 (-1.54, 2.85)
PFNA	2.25 (-7.38, 11.89)	-0.32 (-3.55, 2.92)	1.02 (-1.84, 3.89)	1.15 (-2.14, 4.45)	0.86 (-2.38, 4.10)	-0.47 (-2.50, 1.56)
PFDA	0.84 (-9.80, 11.48)	-0.75 (-4.32, 2.82)	1.10 (-2.06, 4.26)	-0.67 (-4.31, 2.98)	0.57 (-3.01, 4.15)	0.59 (-1.65, 2.83)
PFDoDA	0.44 (-4.86, 5.75)	-0.32 (-2.09, 1.46)	0.04 (-1.54, 1.62)	0.23 (-1.58, 2.05)	0.52 (-1.26, 2.31)	-0.03 (-1.15, 1.08)
PFTrDA	6.58 (-2.96, 16.11)	3.11 (-0.06, 6.27)	0.47 (-2.40, 3.33)	0.45 (-2.85, 3.74)	2.52 (-0.68, 5.72)	0.04 (-1.99, 2.06)
PFUnDA	0.99 (-6.63, 8.61)	0.49 (-2.07, 3.04)	-0.16 (-2.43, 2.11)	0.53 (-2.07, 3.14)	0.44 (-2.12, 3.01)	-0.32 (-1.92, 1.28)
Total PFAS	4.95 (-6.18, 16.07)	2.76 (-0.94, 6.46)	-0.33 (-3.66, 3.00)	-0.16 (-3.99, 3.66)	2.03 (-1.71, 5.77)	0.65 (-1.69, 3.00)

Note: [a]: Adjusted by maternal age, Pre-pregnancy BMI, parity, maternal education, family income, maternal passive smoking before pregnancy, alcohol drinking, folic acid or vitamin supplementation during pregnancy, child sex, and gestational age. [b]: Sum of linear and branched perfluorooctane sulfonate (PFOS). Bold font indicates statistical significance.

Supplementary Table 12. Associations between maternal PFAS and neurodevelopment scores at 54 months of age (adjusted models) (*n* = 117)[a]

Exposure	Total ASQ	Communication	Gross-motor	Fine-motor	Problem-solving	Personal-social
	Adjusted β (95%CI)					
Alternative PFAS						
6:2 Cl-PFESA	-3.84 (-9.27, 1.58)	**-2.26 (-4.43, -0.08)**	-0.25 (-1.00, 0.50)	0.30 (-1.86, 2.45)	-0.90 (-2.93, 1.13)	-0.73 (-1.93, 0.47)
8:2 Cl-PFESA	0.53 (-3.82, 4.88)	-0.57 (-2.33, 1.20)	-0.18 (-0.77, 0.41)	0.28 (-1.43, 1.98)	0.14 (-1.47, 1.75)	0.85 (-0.08, 1.79)
PFBA	0.30 (-1.89, 2.48)	-0.03 (-0.92, 0.86)	-0.11 (-0.41, 0.19)	0.11 (-0.75, 0.96)	0.36 (-0.45, 1.17)	-0.03 (-0.51, 0.45)
PFHxA	2.11 (-1.48, 5.69)	0.45 (-1.02, 1.92)	0.23 (-0.26, 0.72)	0.34 (-1.08, 1.75)	1.17 (-0.14, 2.48)	-0.09 (-0.89, 0.71)
Legacy PFAS						
linear PFHxS	2.06 (-5.93, 10.06)	0.87 (-2.38, 4.13)	0.77 (-0.30, 1.85)	1.51 (-1.61, 4.62)	-0.31 (-3.27, 2.66)	-0.78 (-2.53, 0.97)
PFOS[b]	0.99 (-8.64, 10.63)	-0.74 (-4.66, 3.18)	-0.34 (-1.66, 0.97)	1.47 (-2.28, 5.23)	0.94 (-2.63, 4.51)	-0.34 (-2.46, 1.78)
PFOA	-3.94 (-11.28, 3.40)	-2.83 (-5.76, 0.10)	-0.89 (-1.88, 0.09)	0.01 (-2.89, 2.91)	-0.22 (-2.97, 2.52)	-0.00 (-1.63, 1.62)
PFNA	-0.99 (-9.66, 7.67)	-2.19 (-5.68, 1.30)	0.30 (-0.88, 1.48)	1.27 (-2.11, 4.64)	-0.73 (-3.94, 2.47)	0.36 (-1.55, 2.26)
PFDA	1.55 (-9.29, 12.38)	-0.62 (-5.03, 3.80)	0.07 (-1.41, 1.55)	1.32 (-2.91, 5.55)	0.15 (-3.86, 4.17)	0.63 (-1.75, 3.01)
PFDoDA	-0.05 (-5.03, 4.94)	-1.78 (-3.76, 0.20)	0.32 (-0.36, 1.00)	1.31 (-0.62, 3.23)	0.45 (-1.39, 2.30)	-0.34 (-1.44, 0.75)
PFTrDA	-0.06 (-9.01, 8.89)	-1.50 (-5.13, 2.12)	-0.19 (-1.41, 1.03)	**3.82 (0.45, 7.20)**	-1.00 (-4.31, 2.31)	-1.19 (-3.14, 0.76)
PFUnDA	-5.76 (-17.26, 5.74)	-4.07 (-8.68, 0.54)	-0.15 (-1.73, 1.43)	2.07 (-2.43, 6.57)	-2.43 (-6.68, 1.82)	-1.18 (-3.71, 1.35)
Total PFAS	-2.58 (-14.20, 9.05)	-3.35 (-8.02, 1.31)	-0.56 (-2.14, 1.02)	1.45 (-3.10, 5.99)	0.50 (-3.81, 4.82)	-0.62 (-3.17, 1.94)

Note: [a]: Adjusted by maternal age, Pre-pregnancy BMI, parity, maternal education, family income, maternal passive smoking before pregnancy, alcohol drinking, folic acid or vitamin supplementation during pregnancy, child sex, and gestational age. [b]: Sum of linear and branched perfluorooctane sulfonate (PFOS). Bold font indicates statistical significance.

Supplementary Table 13. Associations between maternal PFAS and neurodevelopment scores at 60 months of age (adjusted models) (*n* = 205)[a]

Exposure	Total ASQ	Communication	Gross-motor	Fine-motor	Problem-solving	Personal-social
	Adjusted β (95%CI)					
Alternative PFAS						
6:2 Cl-PFESA	2.54 (-1.60, 6.68)	0.51 (-0.96, 1.98)	0.01 (-0.59, 0.61)	0.18 (-1.68, 2.05)	0.87 (-0.55, 2.29)	**0.97 (0.13, 1.80)**
8:2 Cl-PFESA	1.40 (-1.84, 4.65)	0.22 (-0.93, 1.37)	-0.05 (-0.52, 0.41)	1.25 (-0.19, 2.70)	-0.47 (-1.58, 0.64)	0.45 (-0.21, 1.11)
PFBA	-0.26 (-1.60, 1.07)	0.26 (-0.21, 0.73)	-0.01 (-0.20, 0.18)	-0.25 (-0.84, 0.35)	-0.18 (-0.64, 0.27)	-0.08 (-0.36, 0.19)
PFHxA	-1.33 (-3.57, 0.92)	-0.46 (-1.25, 0.34)	-0.15 (-0.47, 0.18)	-0.34 (-1.35, 0.67)	-0.36 (-1.13, 0.41)	-0.03 (-0.49, 0.43)
Legacy PFAS						
linear PFHxS	3.42 (-0.69, 7.54)	0.33 (-1.14, 1.80)	-0.12 (-0.71, 0.48)	0.46 (-1.40, 2.32)	1.18 (-0.23, 2.59)	**1.57 (0.76, 2.37)**
PFOS[b]	1.01 (-2.86, 4.89)	-0.27 (-1.65, 1.10)	0.01 (-0.55, 0.56)	0.36 (-1.38, 2.10)	0.04 (-1.29, 1.37)	**0.88 (0.10, 1.66)**
PFOA	-0.42 (-5.76, 4.91)	-0.52 (-2.41, 1.37)	0.39 (-0.37, 1.16)	-0.77 (-3.16, 1.62)	-0.76 (-2.58, 1.07)	**1.22 (0.15, 2.30)**
PFNA	1.87 (-3.60, 7.34)	0.48 (-1.46, 2.42)	0.13 (-0.66, 0.91)	-0.33 (-2.79, 2.13)	0.85 (-1.02, 2.72)	0.74 (-0.37, 1.85)
PFDA	1.04 (-4.24, 6.33)	0.96 (-0.91, 2.82)	-0.02 (-0.78, 0.74)	-0.67 (-3.04, 1.70)	0.44 (-1.36, 2.25)	0.33 (-0.75, 1.41)
PFDoDA	-0.12 (-3.24, 3.00)	0.07 (-1.03, 1.18)	-0.09 (-0.54, 0.35)	-0.28 (-1.67, 1.12)	-0.01 (-1.08, 1.06)	0.18 (-0.45, 0.82)
PFTrDA	1.11 (-3.59, 5.80)	0.33 (-1.34, 1.99)	-0.07 (-0.74, 0.60)	-0.29 (-2.40, 1.81)	1.08 (-0.52, 2.68)	0.06 (-0.89, 1.02)
PFUnDA	-0.63 (-4.09, 2.83)	-0.82 (-2.04, 0.40)	-0.16 (-0.66, 0.33)	0.14 (-1.41, 1.69)	0.13 (-1.05, 1.32)	0.07 (-0.63, 0.78)
Total PFAS	0.90 (-5.49, 7.29)	-0.36 (-2.62, 1.90)	0.26 (-0.66, 1.17)	0.25 (-2.61, 3.12)	-0.59 (-2.77, 1.60)	**1.34 (0.05, 2.63)**

Note: [a]: Adjusted by maternal age, Pre-pregnancy BMI, parity, maternal education, family income, maternal passive smoking before pregnancy, alcohol drinking, folic acid or vitamin supplementation during pregnancy, child sex, and gestational age. [b]: Sum of linear and branched perfluorooctane sulfonate (PFOS). Bold font indicates statistical significance.

Supplementary Table 14. Associations between maternal PFAS and neurodevelopment scores at 72 months of age (Adjusted) (*n* = 151)[a]

Exposure	FSIQ	VCI	VSI	FRI	WMI	PSI
	Adjusted β (95%CI)					
Alternative PFAS						
6:2 Cl-PFESA	-0.74 (-3.69, 2.21)	0.90 (-2.37, 4.17)	-1.39 (-4.56, 1.78)	-1.68 (-5.07, 1.71)	-1.93 (-5.49, 1.63)	-0.48 (-3.94, 2.97)
8:2 Cl-PFESA	-1.77 (-4.08, 0.53)	-1.20 (-3.77, 1.38)	-2.09 (-4.57, 0.39)	-1.68 (-4.35, 0.99)	-1.59 (-4.40, 1.22)	-0.08 (-2.81, 2.65)
PFBA	0.12 (-0.79, 1.03)	-0.12 (-1.13, 0.89)	0.00 (-0.98, 0.98)	-0.04 (-1.09, 1.01)	0.54 (-0.56, 1.63)	0.31 (-0.75, 1.37)
PFHxA	-0.28 (-1.65, 1.08)	-1.20 (-2.69, 0.30)	0.53 (-0.94, 2.00)	0.42 (-1.16, 1.99)	-0.84 (-2.48, 0.81)	0.01 (-1.59, 1.61)
Legacy PFAS						
linear PFHxS	1.41 (-0.59, 3.41)	2.08 (-0.12, 4.28)	0.87 (-1.31, 3.04)	0.96 (-1.37, 3.28)	1.39 (-1.05, 3.82)	0.31 (-2.05, 2.67)
PFOS[b]	-0.45 (-3.25, 2.34)	0.45 (-2.65, 3.55)	-0.34 (-3.35, 2.68)	-2.10 (-5.30, 1.10)	-0.68 (-4.06, 2.71)	0.24 (-3.04, 3.51)
PFOA	-1.36 (-4.81, 2.09)	1.53 (-2.30, 5.36)	-1.96 (-5.67, 1.75)	-2.70 (-6.66, 1.25)	-3.46 (-7.60, 0.68)	1.74 (-2.30, 5.77)
PFNA	-2.18 (-5.91, 1.56)	-0.25 (-4.42, 3.92)	-2.60 (-6.62, 1.43)	**-4.94 (-9.16, -0.71)**	-1.42 (-5.96, 3.13)	-0.50 (-4.90, 3.90)
PFDA	-3.25 (-6.90, 0.39)	-0.77 (-4.88, 3.33)	-3.73 (-7.66, 0.19)	**-4.84 (-9.00, -0.68)**	-2.86 (-7.31, 1.59)	-2.00 (-6.32, 2.32)
PFDoDA	-0.20 (-2.10, 1.70)	0.58 (-1.52, 2.68)	-0.61 (-2.65, 1.44)	0.53 (-1.66, 2.72)	-0.63 (-2.93, 1.67)	-0.18 (-2.40, 2.05)
PFTrDA	-0.48 (-4.08, 3.13)	0.68 (-3.32, 4.68)	-0.63 (-4.52, 3.26)	-3.54 (-7.64, 0.57)	0.48 (-3.90, 4.85)	-0.62 (-4.85, 3.60)
PFUnDA	**-3.17 (-6.02, -0.32)**	-1.74 (-4.96, 1.48)	-2.31 (-5.43, 0.81)	**-3.37 (-6.68, -0.06)**	**-3.54 (-7.01, -0.07)**	-1.84 (-5.24, 1.56)
Total PFAS	-1.58 (-5.84, 2.69)	0.42 (-4.32, 5.16)	-1.90 (-6.50, 2.70)	**-5.32 (-10.14, -0.50)**	-0.44 (-5.62, 4.75)	0.26 (-4.74, 5.27)

Note: [a]: Adjusted by maternal age, Pre-pregnancy BMI, parity, maternal education, family income, maternal passive smoking before pregnancy, alcohol drinking, folic acid or vitamin supplementation during pregnancy, child sex, gestational age. [b]: Sum of linear and branched perfluorooctane sulfonate (PFOS). Bold font indicates statistical significance. Abbreviations: FSIQ, Full-Scale Intelligence Quotient; VCI, Verbal Comprehension Index; VSI, Visual Spatial Index; FRI, Fluid Reasoning Index; WMI, Working Memory Index; PSI, Processing Speed Index. These are the primary index scores from the Wechsler Preschool and Primary Scale of Intelligence-Fourth Edition (WPPSI-IV).

Supplementary Table 15. Associations between maternal PFAS and neurodevelopment scores at 84 months of age (Adjusted) (*n* = 66)[a]

Exposure	FSIQ	VCI	PRI	WMI	PSI
	Adjusted β (95%CI)				
Alternative PFAS					
6:2 Cl-PFESA	-2.32 (-6.90, 2.26)	-0.86 (-6.53, 4.81)	-3.76 (-7.64, 0.12)	-2.44 (-6.74, 1.85)	0.27 (-4.71, 5.25)
8:2 Cl-PFESA	-2.26 (-5.90, 1.38)	-3.51 (-7.91, 0.88)	-1.02 (-4.19, 2.15)	-0.13 (-3.63, 3.37)	-2.20 (-6.03, 1.64)
PFBA	-0.70 (-2.80, 1.40)	0.49 (-2.08, 3.07)	-1.36 (-3.16, 0.43)	-1.19 (-3.14, 0.75)	-0.09 (-2.35, 2.18)
PFHxA	**-2.93 (-5.75, -0.10)**	-2.78 (-6.32, 0.75)	**-2.90 (-5.32, -0.48)**	-1.42 (-4.19, 1.35)	-1.16 (-4.32, 2.00)
Legacy PFAS					
linear PFHxS	0.37 (-3.30, 4.04)	2.02 (-2.42, 6.46)	-1.00 (-4.17, 2.17)	-1.41 (-4.83, 2.01)	0.52 (-3.38, 4.42)
PFOS[b]	-2.40 (-6.30, 1.49)	-1.90 (-6.72, 2.92)	-2.76 (-6.08, 0.57)	-1.30 (-5.01, 2.41)	-0.83 (-5.04, 3.38)
PFOA	-1.30 (-8.77, 6.18)	5.70 (-3.25, 14.66)	-5.06 (-10.60, 0.48)	-3.95 (-10.87, 2.97)	-2.34 (-9.37, 4.70)
PFNA	-3.83 (-9.76, 2.10)	-3.02 (-10.37, 4.32)	**-5.08 (-10.12, -0.05)**	-2.29 (-7.93, 3.36)	-0.60 (-7.09, 5.89)
PFDA	-3.94 (-9.70, 1.82)	-3.29 (-10.43, 3.85)	-4.42 (-9.38, 0.55)	-2.44 (-7.93, 3.06)	-0.79 (-7.12, 5.53)
PFDoDA	-0.64 (-4.81, 3.54)	0.06 (-5.05, 5.17)	0.04 (-3.56, 3.64)	-0.89 (-4.81, 3.03)	-2.20 (-6.56, 2.15)
PFTrDA	-3.79 (-10.11, 2.53)	-1.92 (-9.77, 5.93)	-4.04 (-9.37, 1.29)	-3.26 (-9.23, 2.70)	-1.20 (-7.91, 5.51)
PFUnDA	-3.10 (-8.98, 2.79)	-2.13 (-9.40, 5.15)	-4.19 (-9.23, 0.86)	-1.25 (-6.86, 4.35)	-1.04 (-7.43, 5.35)
Total PFAS	-4.61 (-12.16, 2.94)	0.62 (-8.80, 10.03)	**-6.26 (-12.41, -0.12)**	-4.82 (-11.89, 2.24)	-3.53 (-11.38, 4.31)

Note: [a]: Adjusted by maternal age, Pre-pregnancy BMI, parity, maternal education, family income, maternal passive smoking before pregnancy, alcohol drinking, folic acid or vitamin supplementation during pregnancy, child sex, and gestational age. [b]: Sum of linear and branched perfluorooctane sulfonate (PFOS). Bold font indicates statistical significance. Abbreviations: FSIQ, Full-Scale Intelligence Quotient; VCI, Verbal Comprehension Index; PRI, Perceptual Reasoning Index; WMI, Working Memory Index; PSI, Processing Speed Index. These are the primary index scores from the Wechsler Intelligence Scale for Children-Fourth Edition (WISC-IV).

Supplementary Table 16. Adjusted ORs and 95% CIs for neurodevelopmental trajectories (33-84 months, neurodevelopmental scores) from logistic regression and grouped weighted quantile sum (GWQS) regression models (*n* = 278)

PFAS (ng/mL)/ GWQS index	Neurodevelopmental scores from 33 to 84 months of age
	Persistently low *vs.* persistently high
	Adjusted ORs[a] (95% CIs)
Alternative PFAS	
6:2 Cl-PFESA	1.14 (0.65, 2.01)
8:2 Cl-PFESA	0.83 (0.59, 1.19)
PFBA	0.96 (0.82, 1.11)
PFHxA	1.11 (0.86, 1.43)
GWQS index 1[b]	0.63 (0.26, 1.54)
Legacy PFAS	
linear PFHxS	1.13 (0.70, 1.82)
PFOS[c]	1.13 (0.66, 1.94)
PFOA	1.92 (0.99, 3.72)
PFNA	1.57 (0.74, 3.31)
PFDA	**2.38 (1.05, 5.37)**
PFDoDA	**1.66 (1.10, 2.52)**
PFTrDA	1.01 (0.54, 1.91)
PFUnDA	**2.36 (1.00, 5.54)**
GWQS index 2[b]	**2.18 (1.01, 4.73)**

Note: [a]: Adjusted by maternal age, Pre-pregnancy BMI, parity, maternal education, family income, maternal passive smoking before pregnancy, alcohol drinking, folic acid or vitamin supplementation during pregnancy, child sex, gestational age. Bold font indicates statistical significance.

[b]: GWQS index 1 and GWQS index 2 were respectively created using all type of alternative (6:2 Cl-PFESA, 8:2 Cl-PFESA, PFBA and PFHxA) and legacy PFAS (linear PFHxS, PFOS, PFOA, PFNA, PFDA, PFDoDA, PFTrDA and PFUnDA) to reflect their mixture exposure levels. The GWQS indices are unitless weighted summary measures, and the ORs represent the effect per quartile increase in the index.

[c]: Sum of linear and branched perfluorooctane sulfonate (PFOS).

Supplementary Table 17. Adjusted ORs and 95% CIs for low neurodevelopmental trajectories (33-84 months) in 225 children at 3-7 years of age according to maternal PFAS concentrations [per natural-ln unit (ng/mL) increase], stratified by TCA.

PFAS ln-transformed, ng/mL	Neurodevelopmental scores from 33 to 84 months of age (Adjusted OR (95%CI)) [a]		*P* interaction [b]
	High TCA group	Low TCA group	
maternal plasma			
Alternative PFAS			
6:2 Cl-PFESA	0.39 (0.12, 1.22)	0.9 (0.35, 2.27)	0.2339
8:2 Cl-PFESA	0.90 (0.5, 1.62)	0.84 (0.48, 1.47)	0.8692
PFBA	0.92 (0.65, 1.29)	1.08 (0.85, 1.39)	0.4572
PFHxA	1.09 (0.67, 1.78)	1.46 (0.97, 2.19)	0.3657
Legacy PFAS			
linear PFHxS	0.59 (0.27, 1.26)	0.85 (0.44, 1.67)	0.4625
PFOS[c]	**0.20 (0.04, 0.97)**	**2.05 (0.89, 4.7)**	**0.0088**
PFOA	1.34 (0.36, 4.95)	1.29 (0.54, 3.1)	0.9624
PFNA	0.9 (0.22, 3.68)	2.21 (0.62, 7.95)	0.3244
PFDA	0.75 (0.17, 3.31)	2.72 (0.87, 8.47)	0.1553
PFDoDA	1.76 (0.85, 3.62)	1.34 (0.73, 2.46)	0.5569
PFTrDA	0.79 (0.23, 2.66)	0.78 (0.31, 1.98)	0.9855
PFUnDA	0.91 (0.33, 2.52)	2.33 (0.74, 7.4)	0.213

Note: [a]: Adjusted by maternal age, Pre-pregnancy BMI, parity, maternal education, family income, maternal passive smoking before pregnancy, alcohol drinking, folic acid or vitamin supplementation during pregnancy, child sex, gestational age. [b]: Bold font indicates statistical significance for interaction effects ($P < 0.1$). [c]: Sum of linear and branched perfluorooctane sulfonate (PFOS).

Supplementary Table 18. Adjusted ORs and 95% CIs for low neurodevelopmental trajectories (33-84 months) in 225 children at 3-7 years of age according to maternal PFAS concentrations [per natural-ln unit (ng/mL) increase], stratified by TCDCA.

PFAS ln-transformed, ng/mL	Neurodevelopmental scores from 33 to 84 months of age (Adjusted OR (95%CI))[a]		*P* interaction [b]
	High TCDCA group	Low TCDCA group	
maternal plasma			
Alternative PFAS			
6:2 Cl-PFESA	0.46 (0.15, 1.42)	0.8 (0.31, 2.08)	0.4279
8:2 Cl-PFESA	0.92 (0.52, 1.63)	0.84 (0.48, 1.48)	0.8386
PFBA	1.13 (0.76, 1.67)	0.98 (0.77, 1.24)	0.5448
PFHxA	1.2 (0.76, 1.91)	1.37 (0.9, 2.08)	0.6652
Legacy PFAS			
linear PFHxS	0.68 (0.33, 1.41)	0.76 (0.4, 1.43)	0.8231
PFOS[c]	**0.25 (0.06, 1.08)**	**2.7 (1.02, 7.17)**	**0.0063**
PFOA	1.9 (0.41, 8.87)	1.21 (0.52, 2.83)	0.604
PFNA	0.77 (0.21, 2.88)	2.8 (0.72, 10.85)	0.1536
PFDA	0.59 (0.13, 2.68)	**3.26 (0.99, 10.67)**	**0.0667**
PFDoDA	1.53 (0.76, 3.1)	1.47 (0.78, 2.75)	0.9244
PFTrDA	0.44 (0.13, 1.49)	1.08 (0.42, 2.78)	0.2401
PFUnDA	0.9 (0.41, 2)	3.24 (0.93, 11.29)	**0.0804**

Note: [a]: Adjusted by maternal age, Pre-pregnancy BMI, parity, maternal education, family income, maternal passive smoking before pregnancy, alcohol drinking, folic acid or vitamin supplementation during pregnancy, child sex, gestational age. [b]: Bold font indicates statistical significance for interaction effects ($P < 0.1$). [c]: Sum of linear and branched perfluorooctane sulfonate (PFOS).

Supplementary Table 19. Adjusted ORs and 95% CIs for low neurodevelopmental trajectories (33-84 months) in 225 children at 3-7 years of age according to maternal PFAS concentrations [per natural-ln unit (ng/mL) increase], stratified by GCA.

PFAS ln-transformed, ng/mL	Neurodevelopmental scores from 33 to 84 months of age (Adjusted OR (95%CI))[a]		*P* interaction [b]
	High GCA group	Low GCA group	
maternal plasma			
Alternative PFAS			
6:2 Cl-PFESA	0.45 (0.15, 1.37)	0.81 (0.32, 2.07)	0.4043
8:2 Cl-PFESA	1.03 (0.54, 1.95)	0.79 (0.47, 1.34)	0.534
PFBA	1.03 (0.73, 1.44)	1.01 (0.79, 1.29)	0.9347
PFHxA	1.17 (0.75, 1.85)	1.39 (0.9, 2.13)	0.5943
Legacy PFAS			
linear PFHxS	0.55 (0.25, 1.23)	0.87 (0.44, 1.74)	0.3897
PFOS[c]	0.82 (0.23, 2.9)	1.48 (0.61, 3.61)	0.4199
PFOA	1.12 (0.29, 4.34)	1.43 (0.6, 3.39)	0.7544
PFNA	0.76 (0.2, 2.85)	2.79 (0.74, 10.47)	0.1434
PFDA	0.71 (0.18, 2.77)	**3.35 (1.02, 11.03)**	**0.0773**
PFDoDA	1.37 (0.68, 2.72)	1.62 (0.85, 3.07)	0.716
PFTrDA	0.37 (0.11, 1.23)	1.29 (0.48, 3.47)	0.1077
PFUnDA	0.46 (0.11, 1.95)	3.36 (0.98, 11.54)	**0.0314**

Note: [a]: Adjusted by maternal age, Pre-pregnancy BMI, parity, maternal education, family income, maternal passive smoking before pregnancy, alcohol drinking, folic acid or vitamin supplementation during pregnancy, child sex, gestational age. [b]: Bold font indicates statistical significance for interaction effects ($P < 0.1$). [c]: Sum of linear and branched perfluorooctane sulfonate (PFOS).

Supplementary Table 20. Adjusted ORs and 95% CIs for low neurodevelopmental trajectories (33-84 months) in 225 children at 3-7 years of age according to maternal PFAS concentrations [per natural-ln unit (ng/mL) increase], stratified by GCDCA.

PFAS ln-transformed, ng/mL	Neurodevelopmental scores from 33 to 84 months of age (Adjusted OR (95%CI))[a]		*P* interaction [b]
	High GCDCA group	Low GCDCA group	
maternal plasma			
Alternative PFAS			
6:2 Cl-PFESA	0.5 (0.17, 1.49)	0.75 (0.29, 1.98)	0.5616
8:2 Cl-PFESA	1.03 (0.55, 1.93)	0.79 (0.47, 1.33)	0.5227
PFBA	1.05 (0.75, 1.47)	1 (0.78, 1.27)	0.8099
PFHxA	1.2 (0.76, 1.9)	1.36 (0.89, 2.06)	0.6931
Legacy PFAS			
linear PFHxS	0.69 (0.32, 1.48)	0.75 (0.41, 1.38)	0.8689
PFOS[c]	0.83 (0.24, 2.89)	1.49 (0.61, 3.62)	0.4265
PFOA	1.47 (0.43, 5.04)	1.28 (0.52, 3.12)	0.8488
PFNA	0.82 (0.21, 3.11)	2.64 (0.7, 9.93)	0.1912
PFDA	0.8 (0.19, 3.27)	2.93 (0.91, 9.42)	0.1399
PFDoDA	1.58 (0.76, 3.27)	1.45 (0.78, 2.69)	0.8569
PFTrDA	0.42 (0.13, 1.4)	1.16 (0.43, 3.09)	0.1906
PFUnDA	0.55 (0.12, 2.44)	2.78 (0.82, 9.42)	**0.0788**

Note: [a]: Adjusted by maternal age, Pre-pregnancy BMI, parity, maternal education, family income, maternal passive smoking before pregnancy, alcohol drinking, folic acid or vitamin supplementation during pregnancy, child sex, gestational age. [b]: Bold font indicates statistical significance for interaction effects ($P < 0.1$). [c]: Sum of linear and branched perfluorooctane sulfonate (PFOS).

Supplementary Table 21. Adjusted ORs and 95% CIs for low neurodevelopmental trajectories (33-84 months) in 225 children at 3-7 years of age according to maternal PFAS concentrations [per natural-ln unit (ng/mL) increase], stratified by GHCA.

PFAS ln-transformed, ng/mL	Neurodevelopmental scores from 33 to 84 months of age (Adjusted OR (95%CI))[a]		*P* interaction [b]
	High GHCA group	Low GHCA group	
maternal plasma			
Alternative PFAS			
6:2 Cl-PFESA	0.39 (0.14, 1.1)	1.03 (0.37, 2.82)	0.1551
8:2 Cl-PFESA	0.99 (0.55, 1.76)	0.79 (0.45, 1.38)	0.5849
PFBA	0.85 (0.64, 1.13)	1.15 (0.86, 1.52)	0.1635
PFHxA	1.34 (0.84, 2.12)	1.25 (0.82, 1.9)	0.8235
Legacy PFAS			
linear PFHxS	0.5 (0.22, 1.16)	0.92 (0.45, 1.88)	0.2763
PFOS[c]	0.53 (0.15, 1.85)	1.98 (0.82, 4.8)	**0.0717**
PFOA	2.21 (0.78, 6.24)	0.91 (0.32, 2.61)	0.2233
PFNA	0.89 (0.25, 3.18)	3.32 (0.77, 14.21)	0.146
PFDA	0.89 (0.25, 3.21)	3.63 (1, 13.09)	0.1057
PFDoDA	1.25 (0.68, 2.31)	1.89 (0.88, 4.08)	0.3947
PFTrDA	0.57 (0.21, 1.58)	1.11 (0.37, 3.36)	0.3738
PFUnDA	0.94 (0.38, 2.3)	3.43 (0.9, 13.04)	**0.0984**

Note: [a]: Adjusted by maternal age, Pre-pregnancy BMI, parity, maternal education, family income, maternal passive smoking before pregnancy, alcohol drinking, folic acid or vitamin supplementation during pregnancy, child sex, gestational age. [b]: Bold font indicates statistical significance for interaction effects ($P < 0.1$). [c]: Sum of linear and branched perfluorooctane sulfonate (PFOS).

Supplementary Table 22. Adjusted ORs and 95% CIs for low neurodevelopmental trajectories (33-84 months) in 225 children at 3-7 years of age according to maternal PFAS concentrations [per natural-ln unit (ng/mL) increase], stratified by THCA.

	Neurodevelopmental scores from 33 to 84 months of age (Adjusted OR (95%CI))[a]		*P* interaction [b]
PFAS ln-transformed, ng/mL	High THCA group	Low THCA group	
maternal plasma			
Alternative PFAS			
6:2 Cl-PFESA	**0.32 (0.1, 0.99)**	1.04 (0.4, 2.68)	**0.0942**
8:2 Cl-PFESA	0.98 (0.55, 1.77)	0.76 (0.43, 1.35)	0.5502
PFBA	0.98 (0.73, 1.31)	1.05 (0.81, 1.36)	0.7113
PFHxA	1.3 (0.82, 2.06)	1.28 (0.84, 1.94)	0.9528
Legacy PFAS			
linear PFHxS	0.54 (0.24, 1.21)	0.88 (0.45, 1.72)	0.352
PFOS[c]	0.57 (0.16, 2.11)	1.61 (0.69, 3.78)	0.1641
PFOA	2.26 (0.78, 6.56)	0.9 (0.33, 2.46)	0.2033
PFNA	0.95 (0.24, 3.86)	2.23 (0.57, 8.69)	0.367
PFDA	0.93 (0.25, 3.5)	2.84 (0.82, 9.89)	0.2102
PFDoDA	1.95 (0.92, 4.16)	1.23 (0.68, 2.23)	0.3415
PFTrDA	0.99 (0.31, 3.12)	0.58 (0.21, 1.63)	0.4956
PFUnDA	1.16 (0.36, 3.76)	1.94 (0.55, 6.8)	0.5456

Note: [a]: Adjusted by maternal age, Pre-pregnancy BMI, parity, maternal education, family income, maternal passive smoking before pregnancy, alcohol drinking, folic acid or vitamin supplementation during pregnancy, child sex, gestational age. [b]: Bold font indicates statistical significance for interaction effects ($P < 0.1$). [c]: Sum of linear and branched perfluorooctane sulfonate (PFOS).

Supplementary Table 23. Adjusted odds ratios (ORs) and 95% confidence intervals (CIs) for neurodevelopmental trajectories (33-84 months; neurodevelopmental scores) per unit increase in maternal PFAS concentrations, with sensitivity analyses adjusting for breastfeeding duration and delivery method, in logistic regression (*n* = 278).

Serum PFAS (ng/mL)	Neurodevelopmental scores from 33 to 84 months of age	
	Persistently low vs. persistently high	
	Adjusted ORs[a] (95% CIs)	Adjusted ORs[b] (95% CIs)
Alternative PFAS		
6:2 Cl-PFESA	1.22 (0.57, 2.58)	1.14 (0.65, 2.02)
8:2 Cl-PFESA	0.86 (0.55, 1.34)	0.83 (0.58, 1.19)
PFBA	0.98 (0.81, 1.17)	0.96 (0.82, 1.11)
PFHxA	1.19 (0.88, 1.60)	1.11 (0.86, 1.43)
Legacy PFAS		
linear PFHxS	1.15 (0.69, 1.92)	1.13 (0.70, 1.82)
PFOS[d]	1.01 (0.54, 1.90)	1.13 (0.66, 1.95)
PFOA	**2.41 (1.09, 5.33)**	1.93 (0.99, 3.77)
PFNA	1.24 (0.57, 2.70)	1.57 (0.74, 3.31)
PFDA	1.58 (0.61, 4.05)	**2.38 (1.05, 5.39)**
PFDoDA	**1.69 (1.03, 2.76)**	**1.66 (1.10, 2.52)**
PFTrDA	0.76 (0.36, 1.60)	1.01 (0.54, 1.91)
PFUnDA	1.81 (0.67, 4.89)	**2.37 (1.01, 5.58)**

Note: [a]: Adjusted by maternal age, Pre-pregnancy BMI, parity, maternal education, family income, maternal passive smoking before pregnancy, alcohol drinking, folic acid or vitamin supplementation during pregnancy, child sex, gestational age and **breastfeeding duration**.

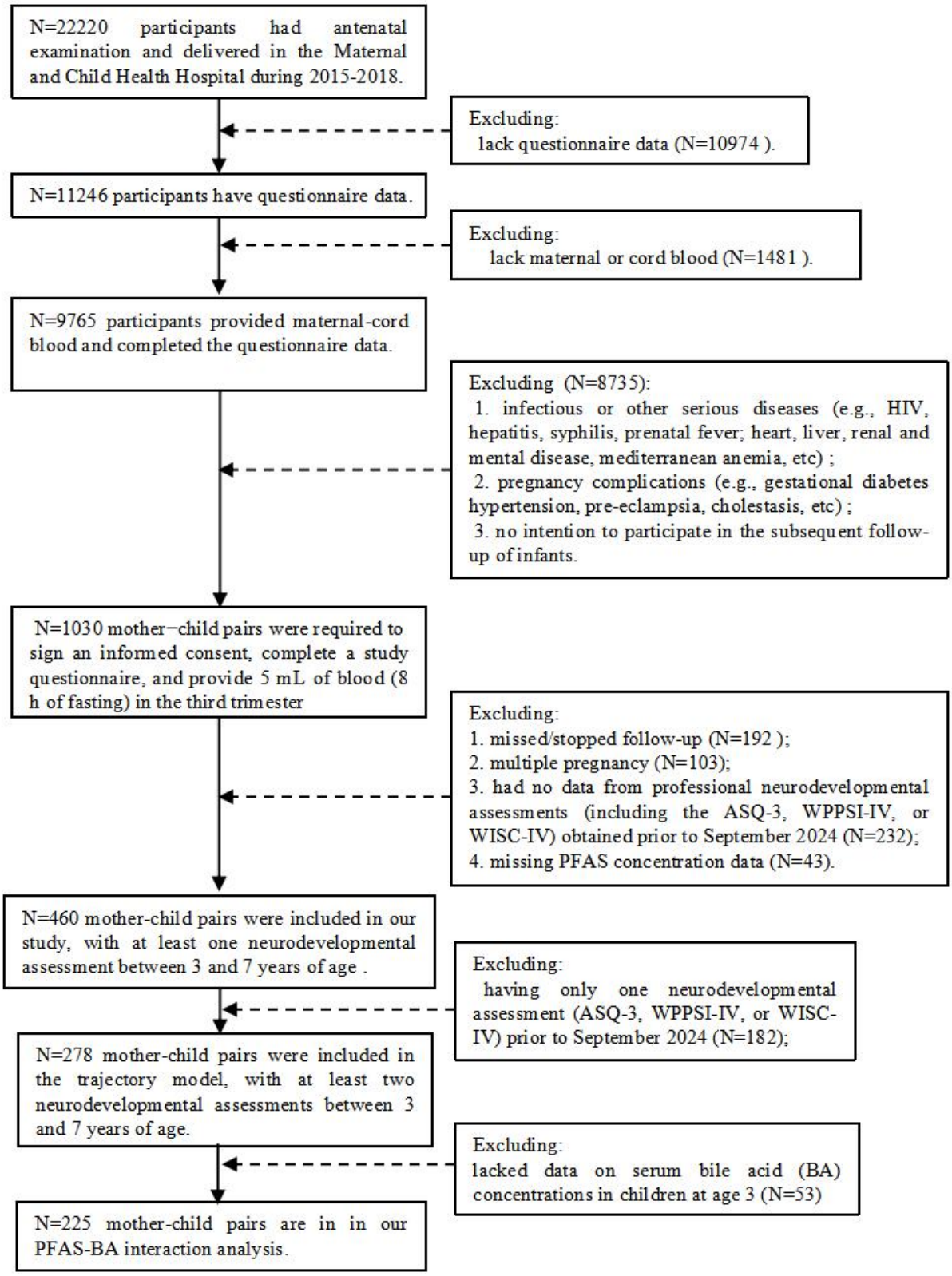
[b]: Adjusted by maternal age, Pre-pregnancy BMI, parity, maternal education, family income, maternal passive smoking before pregnancy, alcohol drinking, folic acid or vitamin supplementation during pregnancy, child sex, gestational age and **delivery method**.

[c]: Sum of linear and branched perfluorooctane sulfonate (PFOS).

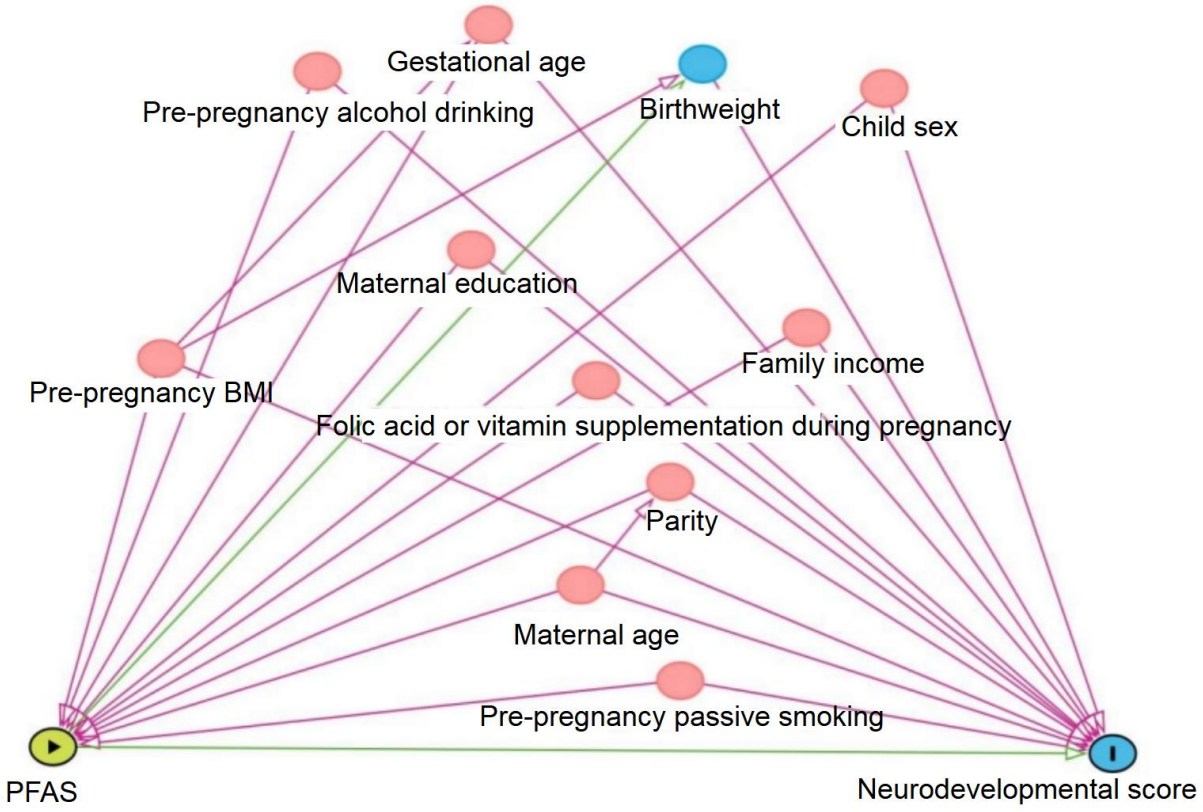
Supplementary Table 24. Consistency of "Low Neurodevelopmental Trajectory" Classification Across Models with Different Assessment Instruments

Model Description	Instruments Included	Age Range (Months)	Total N in Model	N (%) in Low Trajectory	Agreement with Full Model Low Trajectory Group[b]
Primary Full Model[a]	ASQ-3, WPPSI-IV, WISC-IV	33 - 84	278	36 (12.95%)	**Reference**
Sensitivity Model 1	ASQ-3, WPPSI-IV	33 - 72	278	37 (13.3%)	34 / 36 (94.4%)
Sensitivity Model 1	ASQ-3 only	33 - 60	278	34 (12.2%)	33 / 36 (91.6%)

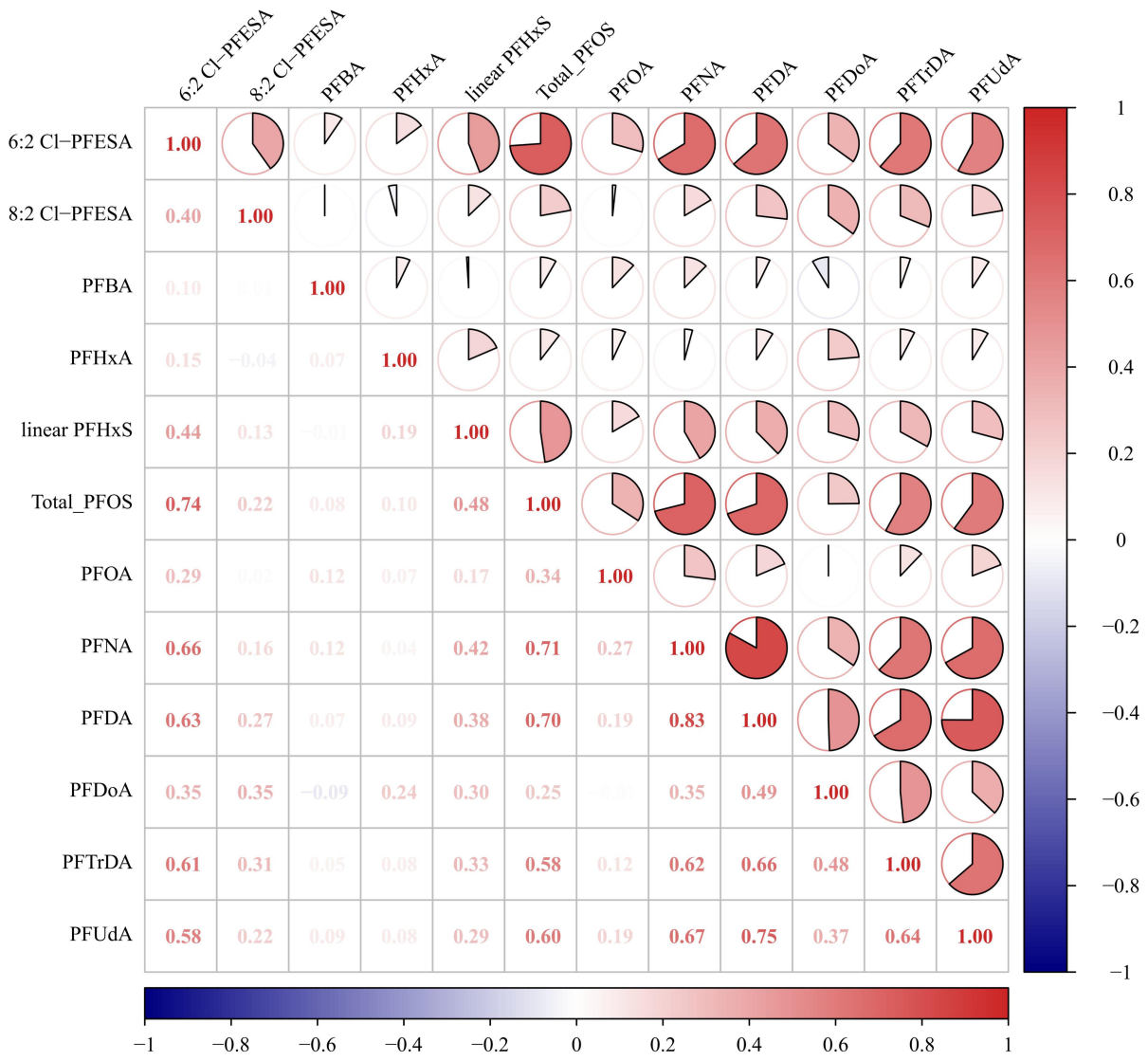
Note: [a]: The "Primary Full Model" served as the reference. [b]: "Agreement with Full Model" is defined as the number and proportion of children classified into the "Low Trajectory" group in the Primary Full Model who were also classified into the "Low Trajectory" group in each sensitivity model. GBTM, group-based trajectory modeling.



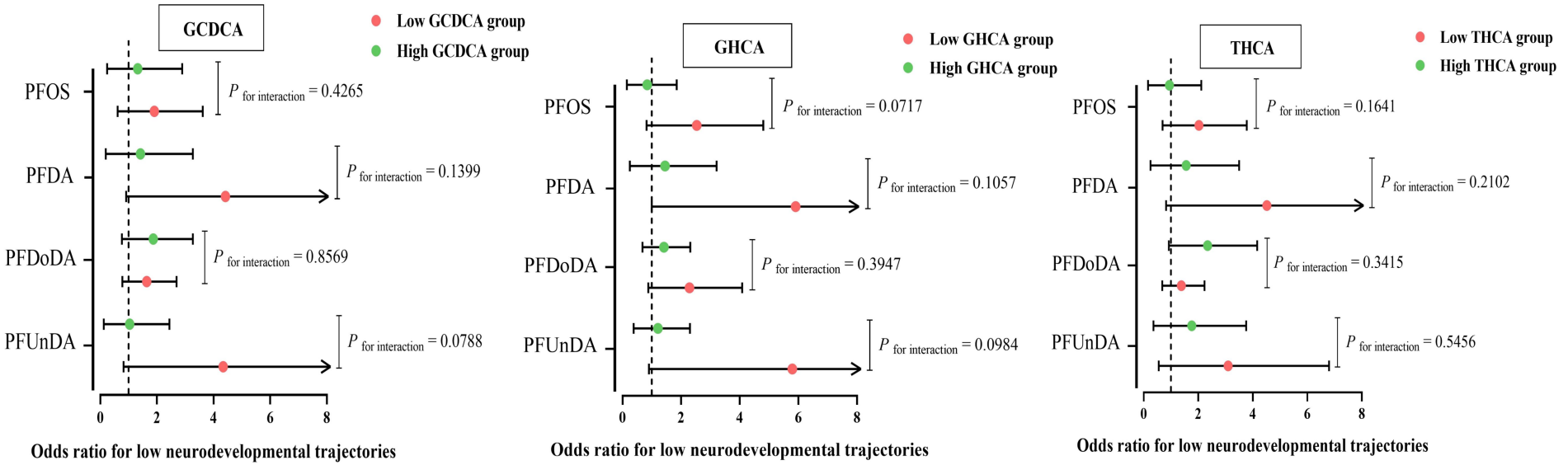
Supplementary Figure 1. Participant selection flowchart for our study (*n* = 278) in the Maoming Birth Cohort (2015-2018).



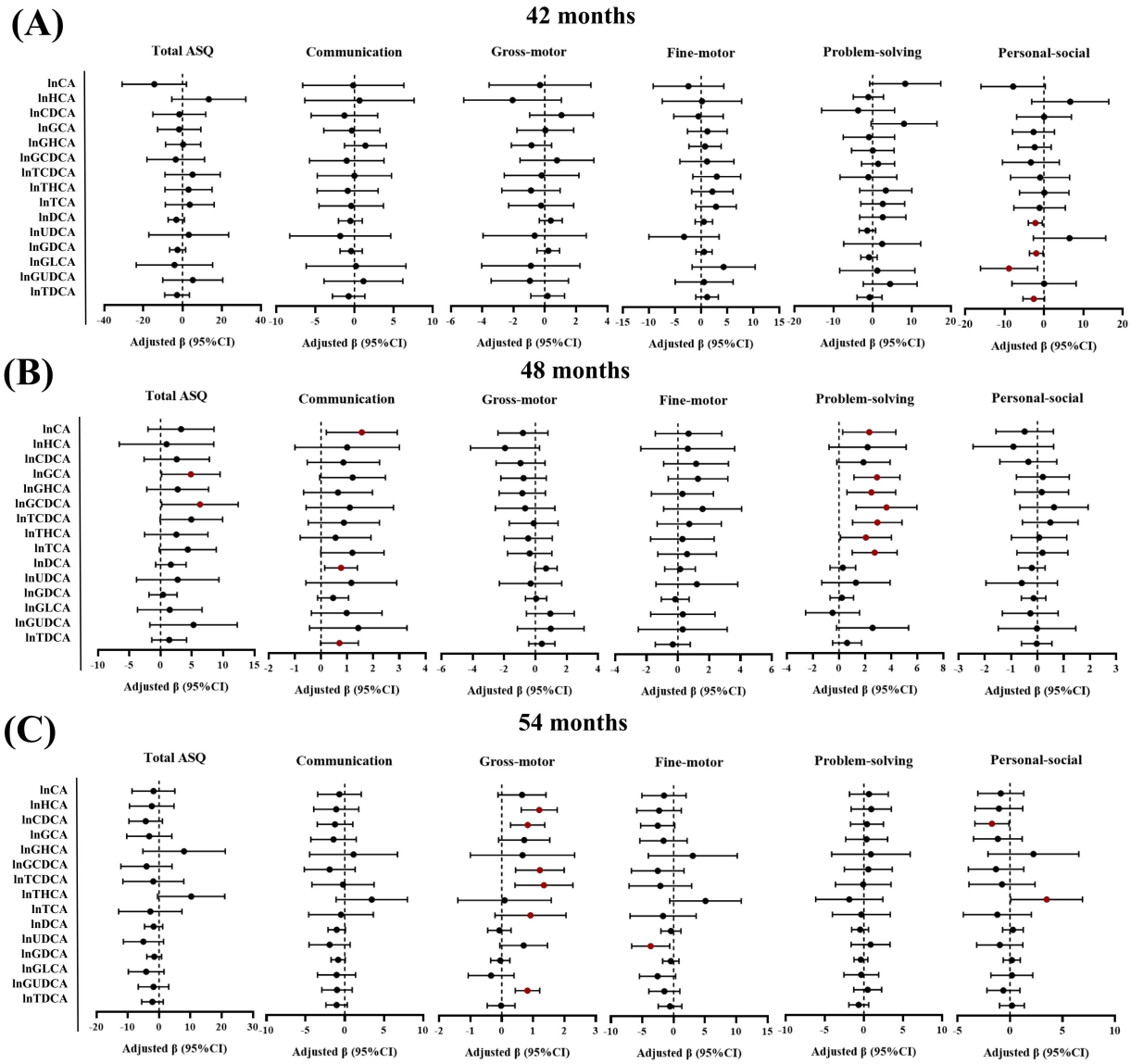
Supplementary Figure 2. The direct acyclic graph (DAG) for the association between maternal PFAS exposure and childhood neurodevelopment. Color legend: Green: exposure; Blue: outcome and variable-related outcome; Red: adjusted variable.



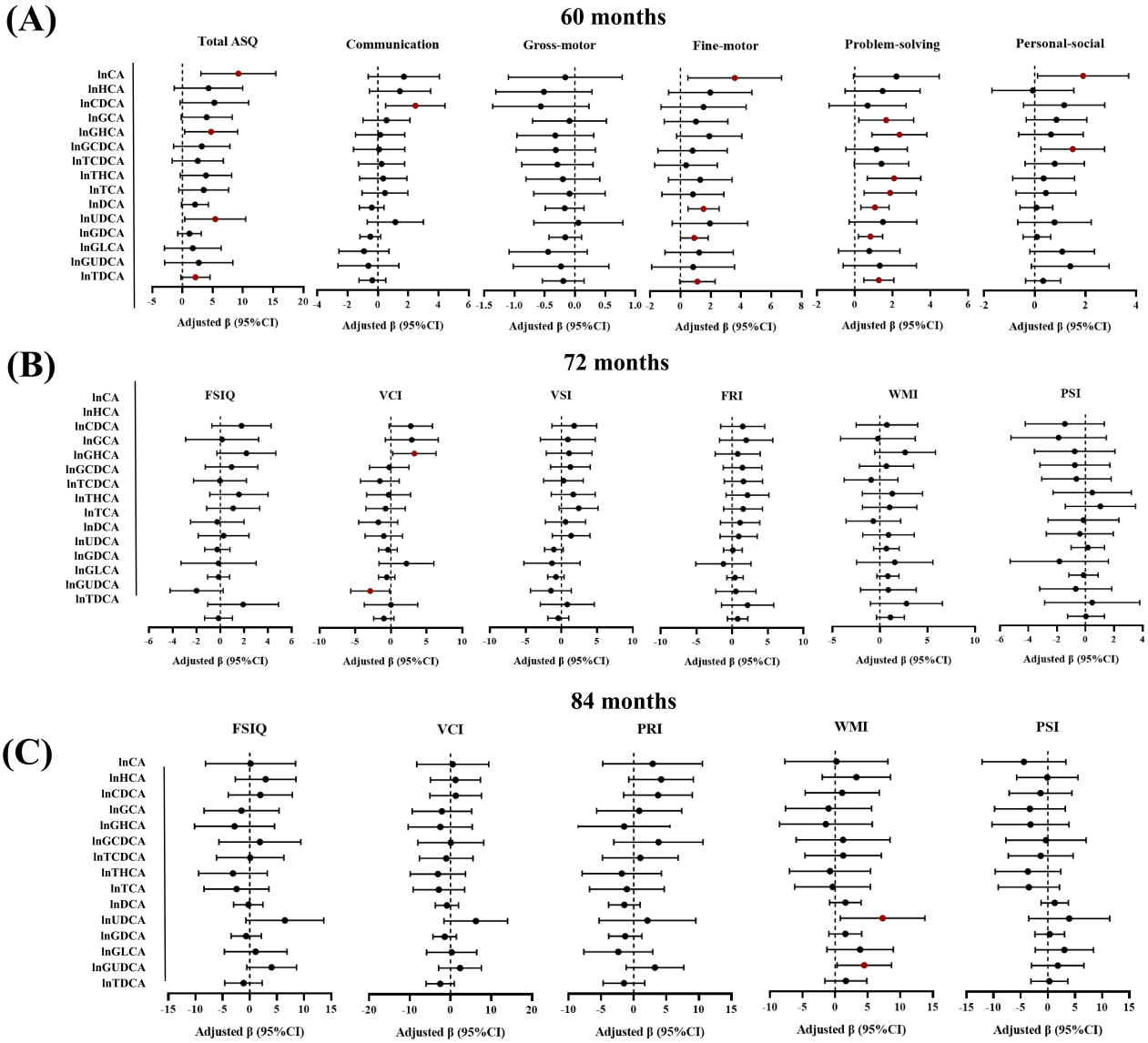
Supplementary Figure 3. Correlation heatmap showing Pearson's partial correlations across maternal PFAS in the full study sample. PFAS concentrations were ln-transformed. Significant correlations at $P < 0.05$ are indicated by asterisks.



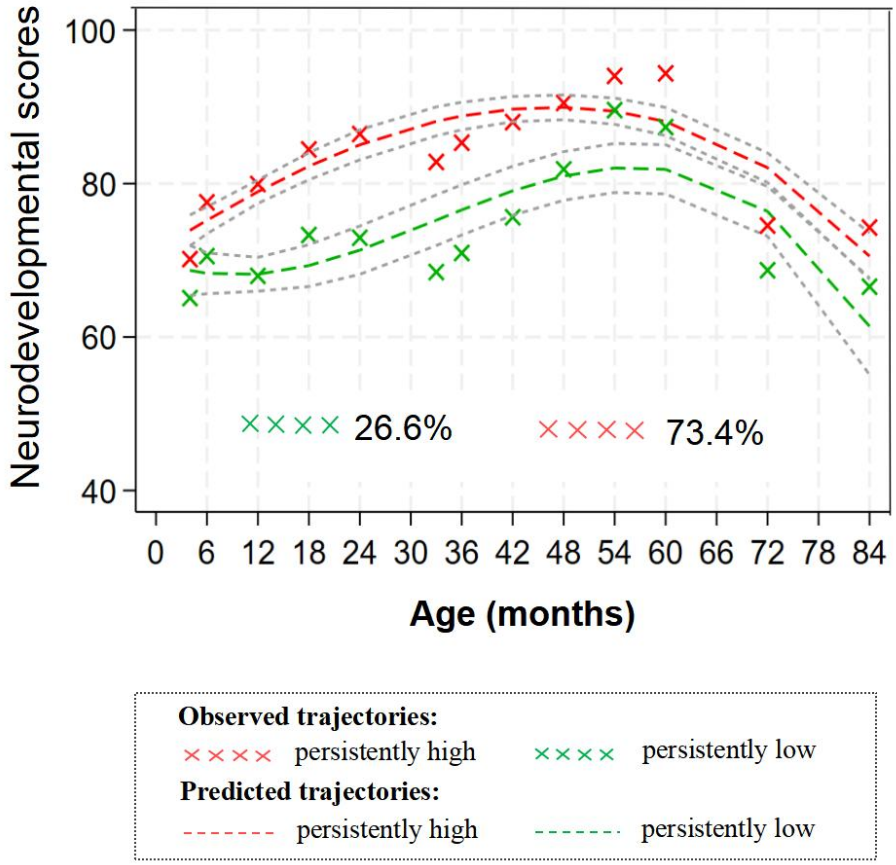
Supplementary Figure 4. Regulatory role of primary conjugated bile acids in the association between prenatal PFAS exposure and neurodevelopmental trajectories (*n* = 225). Logistic regression models were employed to estimate the associations (odds ratios [ORs] and 95% confidence intervals [CIs]) between maternal serum PFAS concentrations during pregnancy and children's neurodevelopmental trajectories, stratified by child GCDCA, GHCA, and THCA levels (high *vs.* low, median split). Interaction *P*-values reflect effect modification. For interaction terms, we considered $P < 0.1$ as nominally significant. The ORs indicate the likelihood of a child being in the persistently low neurodevelopmental trajectory group, with the persistently high group as the reference. All models were controlled for maternal age, pre-pregnancy BMI, parity, maternal education, family income, maternal passive smoking before pregnancy, alcohol drinking, folic acid or vitamin supplementation during pregnancy, child sex, and gestational age. Detailed estimates are presented in Supplementary Tables 20-22.



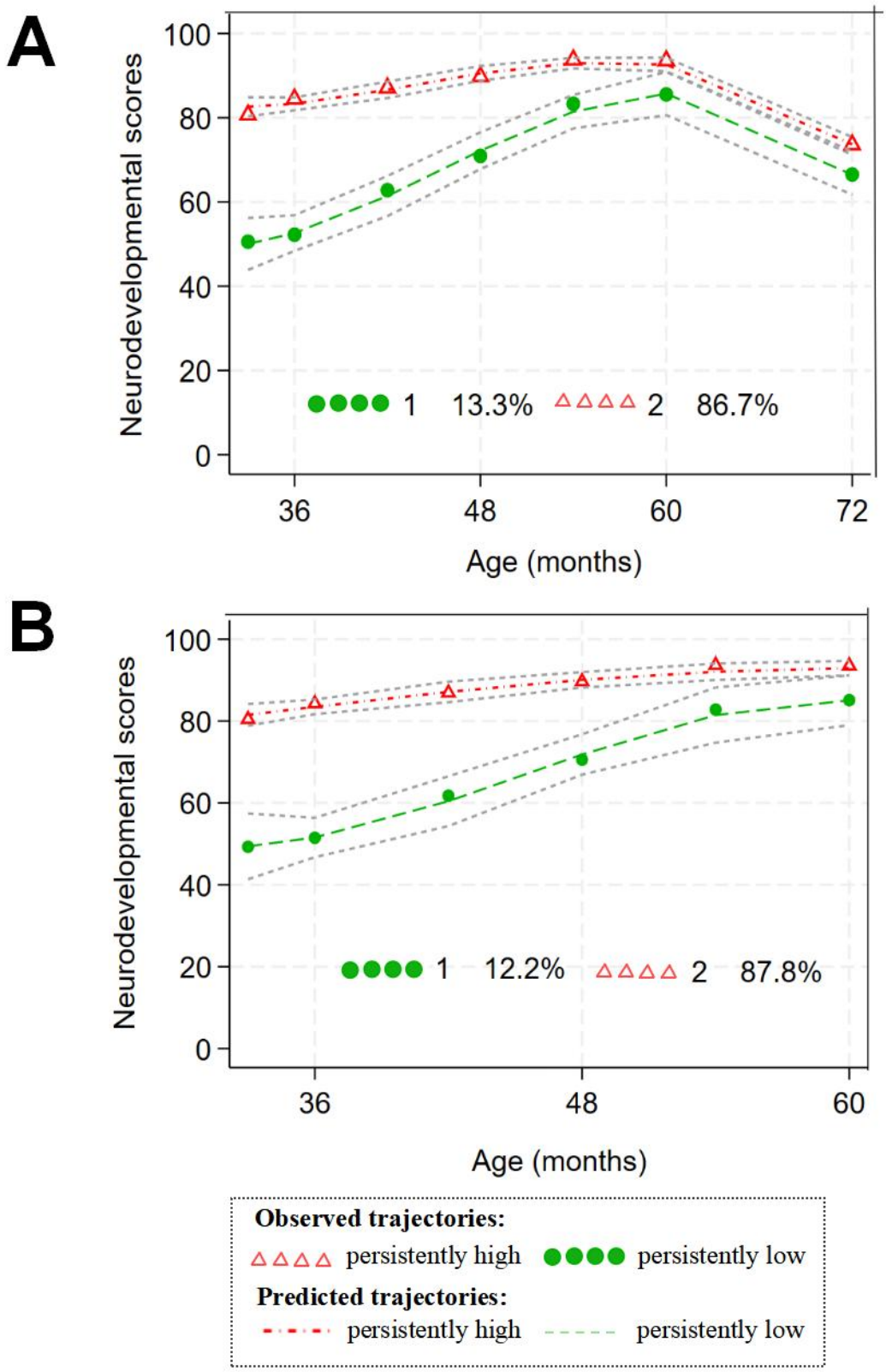
Supplementary Figure 5. Lagged associations of 15 bile acid species with neurodevelopmental changes from 42 to 54 months of age, adjusted for baseline neurodevelopmental score at 33 months. (A) Associations at 42 months of age. (B) Associations at 48 months of age. (C) Associations at 54 months of age. Results are presented as adjusted β coefficients with 95% confidence intervals. All models were adjusted for maternal age, pre-pregnancy BMI, parity, maternal education, family income, maternal passive smoking before pregnancy, alcohol drinking, folic acid or vitamin supplementation during pregnancy, child sex, and gestational age).



Supplementary Figure 6. Lagged associations of 15 bile acid species with neurodevelopmental changes from 60 to 84 months of age, adjusted for baseline neurodevelopmental score at 33 months. (A) Associations at 60 months of age. (B) Associations at 72 months of age. (C) Associations at 84 months of age. Results are presented as adjusted β coefficients with 95% confidence intervals. All models were adjusted for maternal age, pre-pregnancy BMI, parity, maternal education, family income, maternal passive smoking before pregnancy, alcohol drinking, folic acid or vitamin supplementation during pregnancy, child sex, and gestational age).



Supplementary Figure 7. Neurodevelopmental trajectories of children aged from 0 to 84 months (*n* = 278) in group-based trajectory modeling (GBTM). Note: The trajectories represent the latent growth patterns of neurodevelopmental trajectories, which were classified into persistently low and persistently high groups for neurodevelopmental scores. Neurodevelopmental scores are normalized based on the ASQ total score and the Wechsler IQ total score obtained between 33–84 months of age. Trajectory groups were named according to their initial values and subsequent trends. Predicted trajectories (dashed lines: red for high, green for low) and observed data (symbols: red crosses for high, green crosses for low). Note: ASQ-3, Ages & Stages Questionnaires, Third Edition; WPPSI-IV, Wechsler Primary and Preschool Scales of Intelligence-Fourth Edition; WISC-IV, Wechsler Intelligence Scale for Children-Fourth Edition.



Supplementary Figure 8. Sensitivity analysis: stability of neurodevelopmental trajectories across different assessment instruments. Group-based trajectory modeling (GBTM) was conducted to validate the robustness of the identified trajectories against potential

instrument-specific bias. (A) Sensitivity model using data from ASQ-3 and WPPSI-IV only (33–72 months, *n* = 278). (B) Sensitivity model using data from ASQ-3 only (33–60 months, *n* = 278). Harmonized neurodevelopmental scores were used across all models. The trajectories illustrate the consistent identification of a "persistently high" group (red, open triangles, and dashed line) and a "persistently low" group (green, solid circles, and dashed line) across different combinations of assessment tools. The high consistency in group membership across models (detailed in Supplementary Table 23) confirms that the "persistently low" trajectory represents a robust developmental phenotype, not an artifact of the specific instruments used. Note: ASQ-3, Ages & Stages Questionnaires, Third Edition; WPPSI-IV, Wechsler Primary and Preschool Scales of Intelligence-Fourth Edition; WISC-IV, Wechsler Intelligence Scale for Children-Fourth Edition.

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