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Supplemental Material

Birth Outcomes in Relation to Prenatal Exposure to Per- and Polyfluoroalkyl Substances and Stress in the Environmental Influences on Child Health Outcomes (ECHO) Program

Amy M. Padula, Xuejuan Ning, Shivani Bakre, Emily S. Barrett, Tracy Bastain, Deborah H. Bennett, Michael S. Bloom, Carrie V. Breton, Anne L. Dunlop, Stephanie M. Eick, Assiamira Ferrara, Abby Fleisch, Sarah Geiger, Dana E. Goin, Kurunthachalam Kannan, Margaret R. Karagas, Susan Korrick, John D. Meeker, Rachel Morello-Frosch, Thomas G. O'Connor, Emily Oken, Morgan Robinson, Megan E. Romano, Susan L. Schantz, Rebecca J. Schmidt, Anne P. Starling, Yeyi Zhu, Ghassan B. Hamra, Tracey J. Woodruff, and the program collaborators for Environmental influences on Child Health Outcomes

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References

Table S1. Characteristics of study population among selected ECHO cohorts (N=3339)

Cohort Name	**N**	**Location**	**Years of birth**	**Trimester of PFAS sample**	**Media**	**PFAS lab**	**Perceived Stress Scale**
Chemicals in Our Bodies (CiOB)	402	San Francisco, CA	2014-2019	2nd, 3rd	Serum	California Department of Toxic Substances Control (Eick et al. 2021)	PSS4
Illinois Kids Development Studies (IKIDS)	184	Urbana - Champaign, IL	2014-2016	2nd	Serum		PSS10
Project Viva	842	Boston, MA	1999-2002	1st	Plasma	Centers for Disease Control and Prevention (Kato et al. 2011; Oh et al. 2021; Sagiv et al. 2018)	none
Healthy Start	652	CO	2010-2014	2nd, 3rd	Serum		PSS10
New Hampshire Birth Cohort Study (NHBCS)	324	Lebanon and Concord, NH	2010-2013	2nd, 3rd	Plasma		none
Markers of Autism Risk in Babies Learning Early Signs (MARBLES)	39	Northern CA	2009-2014	1st, 2nd, 3rd	Serum		PSS10
Emory (Atlanta)	424	Atlanta, GA	2015-2018	1st, 2nd	Serum	Human Health Exposure Analysis Resource (HHEAR) (Honda et al. 2018)	PSS14
Maternal And Developmental Risks from Environmental and social Stressors (MADRES)	347	Los Angeles, CA	2016-2019	1st, 2nd, 3rd	Serum		PSS10
Pregnancy and EnvironmenT And Lifestyle Study (PETALS)	124	CA	2014-2016	1st, 2nd	Serum		PSS10
Rochester	35	Rochester, NY	2017-2019	2nd	Serum		PSS14
Kaiser Permanente Research Bank Pregnancy Cohort (KPRB-PC)	13	CA	2014	1st	Serum		none

Table S2. Number of participants with measured PFAS (ng/mL) and percent above limit of detection by analyte by cohort in 11 selected ECHO cohorts

		Cohort										
PFAS	**Total N (%>LOD)**	**CiOB (N=402)**	**IKIDS (N=184)**	**Project Viva (N=842)**	**Healthy Start (N=652)**	**NHBCS (N=324)**	**MARBLES (N=39)**	**Atlanta (N=424)**	**MADRES (N=347)**	**PETALS (N=124)**	**Rochester (N=35)**	**KPRB-PC (N=13)**
PFOA	3954 (88.0%)	474 (99.8%)	184 (100.0%)	842 (100.0%)	652 (99.7%)	648 (51.7%)	65 (100.0%)	437 (97.3%)	347 (65.4%)	244 (95.1%)	35 (100.0%)	26 (50.0%)
PFOS	3954 (99.7%)	474 (100.0%)	184 (100.0%)	842 (100.0%)	652 (99.4%)	648 (100.0%)	65 (100.0%)	437 (98.6%)	347 (100.0%)	244 (100.0%)	35 (100.0%)	26 (100.0%)
PFNA	3605 (95.9%)	474 (98.7%)	184 (98.9%)	842 (98.3%)	652 (98.3%)	324 (100.0%)	65 (100.0%)	437 (96.8%)	347 (70.9%)	232 (100.0%)	35 (100.0%)	13 (100.0%)
PFHxS	3605 (99.2%)	474 (100.0%)	184 (98.9%)	842 (99.3%)	652 (98.6%)	324 (100.0%)	65 (100.0%)	437 (97.5%)	347 (100.0%)	232 (100.0%)	35 (100.0%)	13 (100.0%)
PFDA	3510 (64.2%)	474 (75.7%)	184 (73.9%)	842 (45.8%)	652 (65.3%)	324 (88.0%)	65 (84.6%)	342 (48.5%)	347 (57.6%)	232 (87.9%)	35 (65.7%)	13 (100.0%)
NMFOSAA	3510 (59.8%)	474 (88.0%)	184 (83.7%)	842 (100.0%)	652 (28.8%)	324 (41.7%)	65 (63.1%)	342 (49.7%)	347 (10.4%)	232 (40.1%)	35 (42.9%)	13 (69.2%)
PFUNDA	2016 (55.4%)	474 (80.8%)	184 (71.2%)			324 (43.8%)	65 (55.4%)	342 (43.3%)	347 (9.5%)	232 (92.7%)	35 (57.1%)	13 (69.2%)
PFPEA	597 (67.2%)							342 (47.4%)		220 (99.5%)	35 (57.1%)	
EtFOSAA	2813 (32.8%)	474 (8.2%)	184 (9.2%)	842 (99.6%)	651 (0.8%)		65 (0.0%)	342 (5.0%)		220 (2.3%)	35 (2.9%)	
PFBS	1602 (4.4%)	474 (2.1%)	184 (1.6%)					342 (14.0%)	347 (1.4%)	220 (0.9%)	35 (8.6%)	
PFDODA	1320 (5.9%)	474 (3.8%)	184 (4.9%)				65 (24.6%)	342 (2.0%)		220 (12.3%)	35 (2.9%)	
PFHPA	1602 (10.9%)	474 (15.0%)	184 (19.6%)					342 (14.9%)	347 (0.0%)	220 (5.9%)	35 (11.4%)	
PFHXA	597 (28.1%)							342 (47.4%)		220 (2.7%)	35 (0.0%)	
PFOSA	3096 (3.8%)	474 (3.4%)	184 (14.7%)	842 (8.8%)	652 (0.3%)			342 (0.0%)	347 (0.0%)	220 (0.0%)	35 (0.0%)	

PFAS (14) measured in ECHO cohorts: Perfluorooctanoic acid (PFOA); Perfluorooctanesulfonic acid (PFOS); Perfluorononanoic acid (PFNA); Perfluorohexane sulfonic acid (PFHxS); Perfluorodecanoic acid (PFDA); N-methyl Perfluorooctane sulfonamido acetic acid (NMFOSAA); Perfluroundecanoic acid (PFUnDA); Perfluoro-n-pentanoic acid (PFPEA); 2-(N-Ethyl-perfluorooctane sulfonamido) acetic acid (EtFOSAA); Perfluorobutanesulfonic acid (PFBS); Perfluorooctanesulfonate (PFDODA); Perfluoroheptanoic acid (PFHPA); Perfluorohexanoic acid (PFHXA); Perfluorooctanesulfonamide (PFOSA)
Chemicals in Our Bodies (CiOB); Illinois Kids Development Studies (IKIDS); New Hampshire Birth Cohort Study (NHBCS); Markers of Autism Risk in Babies Learning Early Signs (MARBLES); Emory (Atlanta); Maternal And Developmental Risks from Environmental and social Stressors (MADRES); Pregnancy and EnvironmenT And Lifestyle Study (PETALS); Kaiser Permanente Research Bank Pregnancy Cohort (KPRB-PC).

Table S3. PFAS (ng/mL) distribution by year, cohort, perceived stress scale and limit of detection in 11 selected ECHO cohorts

	PFOA, median (IQR) [range of LOD [a]]	**PFOS, median (IQR) [range of LOD [a]]**	**PFNA, median (IQR) [range of LOD [a]]**	**PFHxS, median (IQR) [range of LOD [a]]**	**PFDA, median (IQR) [range of LOD [a]]**
Cohort					
CiOB	0.8 (0.5, 1.2) (n=397)	1.9 (1.1, 3.1) (n=397)	0.3 (0.2, 0.4) (n=397)	0.4 (0.2, 0.6) (n=397)	0.1 (0.1, 0.2) (n=397)
	[0.06, 0.13]	[0.06, 0.07]	[0.04, 0.06]	[0.02]	[0.06, 0.08]
IKIDS	0.9 (0.5, 1.4) (n=184)	2.6 (1.6, 4.1) (n=184)	0.3 (0.2, 0.5) (n=184)	0.6 (0.3, 0.9) (n=184)	0.1 (0.0, 0.2) (n=184)
	[0.06]	[0.06]	[0.06]	[0.02]	[0.06]
Project Viva	5.7 (4.2, 7.9) (n=842)	25.7 (18.4, 35.6) (n=842)	0.7 (0.5, 0.9) (n=842)	2.5 (1.6, 3.8) (n=842)	0.1 (0.1, 0.3) (n=842)
	[0.1]	[0.2]	[0.1]	[0.1]	[0.1]
Healthy Start	1.2 (0.8, 1.7) (n=652)	2.4 (1.5, 3.7) (n=652)	0.4 (0.3, 0.6) (n=652)	0.7 (0.5, 1.2) (n=652)	0.1 (0.1, 0.2) (n=652)
	[0.1]	[0.1]	[0.1]	[0.1]	[0.1]
NHBCS	1.4 (1.0, 2.0) (n=300)	2.3 (1.5, 3.2) (n=300)	0.6 (0.4, 0.8) (n=300)	0.7 (0.5, 1.1) (n=300)	0.2 (0.1, 0.2) (n=300)
	[0.1]	[0.1]	[0.1]	[0.1]	[0.1]
MARBLES	0.9 (0.7, 1.4) (n=37)	2.8 (2.3, 4.8) (n=37)	0.5 (0.4, 0.8) (n=37)	0.5 (0.3, 1.0) (n=37)	0.1 (0.1, 0.2) (n=37)
	[0.1]	[0.1]	[0.1]	[0.1]	[0.1]
Atlanta	0.7 (0.5, 1.1) (n=424)	2.2 (1.4, 3.2) (n=424)	0.3 (0.2, 0.4) (n=424)	1.1 (0.7, 1.5) (n=424)	<LOD (<LOD, 0.1) (n=342)
	[0.04, 0.05]	[0.02, 0.2]	[0.02, 0.1]	[0.02, 0.2]	[0.04]
MADRES	0.1 (<LOD, 0.4) (n=331)	1.3 (1.0, 1.9) (n=331)	0.1 (<LOD, 0.2) (n=331)	1.1 (0.8, 1.5) (n=331)	<LOD (<LOD, 0.1) (n=331)
	[0.04]	[0.02]	[0.02]	[0.02]	[0.04]
PETALS	0.8 (0.5, 1.2) (n=124)	2.4 (1.7, 3.2) (n=124)	0.4 (0.3, 0.5) (n=124)	1.2 (0.9, 1.5) (n=124)	0.1 (<LOD, 0.1) (n=124)
	[0.02, 0.1]	[0.02, 0.1]	[0.03, 0.1]	[0.02, 0.1]	[0.02, 0.1]
Rochester	0.5 (0.4, 0.7) (n=35)	2.3 (1.4, 3.1) (n=35)	0.2 (0.2, 0.3) (n=35)	1.8 (1.3, 2.3) (n=35)	<LOD (<LOD, 0.1) (n=35)
	[0.02]	[0.02]	[0.03]	[0.02]	[0.02]
KPRB-PC	1.2 (1.0, 1.5) (n=13)	1.7 (1.5, 2.2) (n=13)	0.6 (0.5, 0.7) (n=13)	0.5 (0.4, 0.9) (n=13)	0.1 (0.1, 0.2) (n=13)
	[0.1]	[0.1]	[0.1]	[0.1]	[0.1]
Year					
1999	5.1 (3.8, 6.8) (n=28)	28.1 (19.5, 36.9) (n=28)	0.7 (0.4, 0.8) (n=28)	2.0 (1.5, 3.7) (n=28)	0.1 (0.1, 0.3) (n=28)
2000	6.0 (4.4, 8.2) (n=330)	28.7 (20.8, 38.1) (n=330)	0.7 (0.5, 1.0) (n=330)	2.6 (1.8, 3.9) (n=330)	0.1 (0.1, 0.3) (n=330)
2001	5.8 (4.2, 8.5) (n=310)	24.8 (18.6, 35.5) (n=310)	0.7 (0.5, 0.9) (n=310)	2.6 (1.7, 4.0) (n=310)	0.1 (0.1, 0.3) (n=310)
2002	5.3 (3.5, 7.3) (n=170)	21.3 (14.2, 29.0) (n=170)	0.6 (0.4, 0.9) (n=170)	2.2 (1.3, 3.2) (n=170)	0.1 (0.1, 0.3) (n=170)
2003	5.3 (2.5, 7.3) (n<5)	25.0 (12.5, 35.5) (n<5)	0.6 (0.3, 1.0) (n<5)	2.3 (1.6, 2.7) (n<5)	0.2 (0.1, 0.3) (n<5)

2009	1.5 (0.9, 2.5) (n=9)	4.1 (3.7, 5.6) (n=9)	0.7 (0.6, 0.8) (n=9)	0.7 (0.4, 1.2) (n=9)	0.2 (0.1, 0.3) (n=9)
2010	1.7 (1.1, 2.2) (n=122)	3.2 (2.1, 5.2) (n=122)	0.5 (0.4, 0.8) (n=122)	0.9 (0.5, 1.5) (n=122)	0.2 (0.1, 0.2) (n=122)
2011	1.4 (0.9, 1.9) (n=225)	2.7 (1.7, 3.8) (n=225)	0.5 (0.4, 0.7) (n=225)	0.8 (0.5, 1.4) (n=225)	0.2 (0.1, 0.2) (n=225)
2012	1.2 (0.8, 1.7) (n=283)	2.3 (1.5, 3.3) (n=283)	0.5 (0.3, 0.7) (n=283)	0.7 (0.4, 1.2) (n=283)	0.1 (0.1, 0.2) (n=283)
2013	1.0 (0.8, 1.6) (n=243)	2.0 (1.4, 2.9) (n=243)	0.4 (0.3, 0.6) (n=243)	0.7 (0.4, 1.0) (n=243)	0.1 (0.1, 0.2) (n=243)
2014	1.1 (0.7, 1.6) (n=204)	2.3 (1.4, 3.6) (n=204)	0.4 (0.2, 0.6) (n=204)	0.6 (0.4, 1.1) (n=204)	0.1 (0.1, 0.2) (n=204)
2015	0.8 (0.5, 1.2) (n=278)	2.5 (1.6, 3.7) (n=278)	0.4 (0.3, 0.5) (n=278)	0.8 (0.4, 1.4) (n=278)	0.1 (0.1, 0.2) (n=278)
2016	0.8 (0.5, 1.3) (n=287)	2.2 (1.4, 3.3) (n=287)	0.3 (0.2, 0.5) (n=287)	0.8 (0.4, 1.3) (n=287)	0.1 (<LOD, 0.2) (n=255)
2017	0.5 (0.3, 0.9) (n=283)	1.6 (1.0, 2.5) (n=283)	0.2 (0.1, 0.3) (n=283)	0.8 (0.3, 1.3) (n=283)	0.1 (<LOD, 0.2) (n=263)
2018	0.4 (0.1, 0.6) (n=286)	1.4 (1.0, 2.0) (n=286)	0.2 (0.1, 0.3) (n=286)	0.9 (0.5, 1.3) (n=286)	0.1 (<LOD, 0.1) (n=286)
2019	0.1 (<LOD, 0.4) (n=98)	1.2 (0.8, 1.8) (n=98)	0.1 (<LOD, 0.2) (n=98)	1.0 (0.7, 1.4) (n=98)	<LOD (<LOD, 0.1) (n=98)
Missing	0.7 (0.4, 1.0) (n=179)	2.1 (1.5, 3.1) (n=179)	0.3 (0.2, 0.4) (n=179)	1.1 (0.7, 1.5) (n=179)	<LOD (<LOD, 0.1) (n=149)
Perceived Stress Scale T-score					
Below median	0.7 (0.4, 1.2) (n=1003)	2.0 (1.3, 3.2) (n=1003)	0.3 (0.2, 0.4) (n=1003)	0.9 (0.5, 1.4) (n=1003)	0.1 (<LOD, 0.1) (n=961)
Above median	0.8 (0.5, 1.3) (n=1006)	2.1 (1.3, 3.2) (n=1006)	0.3 (0.2, 0.5) (n=1006)	0.7 (0.4, 1.2) (n=1006)	0.1 (0.1, 0.2) (n=971)
Missing PSS	3.9 (1.7, 6.6) (n=1330)	17.3 (3.1, 29.2) (n=1330)	0.6 (0.4, 0.9) (n=1330)	1.8 (0.9, 3.0) (n=1330)	0.1 (0.1, 0.3) (n=1325)

[a] Multiple limits of detection (LOD) presented where batches had different LODs with the same cohort and lab. PFAS, per- and polyfluoroalkyl substances; PFOA, perfluorooctanoic acid; PFOS, perfluorooctanesulfonic acid; PFNA, perfluorononanoic acid; PFHxS, perfluorohexane sulfonic acid; PFDA, perfluorodecanoic acid. Chemicals in Our Bodies (CiOB); Illinois Kids Development Studies (IKIDS); New Hampshire Birth Cohort Study (NHBCS); Markers of Autism Risk in Babies Learning Early Signs (MARBLES); Emory (Atlanta); Maternal And Developmental Risks from Environmental and social Stressors (MADRES); Pregnancy and EnvironmenT And Lifestyle Study (PETALS); Kaiser Permanente Research Bank Pregnancy Cohort (KPRB-PC).

Table S4. Spearman correlation coefficients of PFAS by trimester in 3 selected ECHO cohorts (CiOB, MARBLES, PETALS)

PFAS	**1st-2nd (N=63)**	**2nd-3rd (N=82)**	**1st-3rd (N=11)**
PFOA	0.96	0.90	0.95
PFOS	0.94	0.90	0.92
PFNA	0.92	0.84	0.92
PFHxS	0.90	0.85	0.85
PFDA	0.91	0.82	0.53

PFAS, per- and polyfluoroalkyl substances; PFOA, perfluorooctanoic acid; PFOS, perfluorooctanesulfonic acid; PFNA, perfluorononanoic acid; PFHxS, perfluorohexane sulfonic acid; PFDA, perfluorodecanoic acid. Chemicals in Our Bodies (CiOB); Markers of Autism Risk in Babies Learning Early Signs (MARBLES); Pregnancy and EnvironmenT And Lifestyle Study (PETALS).

Table S5. Serum concentrations of PFAS (ng/ml) study population among selected ECHO cohorts (N=3339) and comparison to the National Health And Nutrition Examination Surveys (NHANES) during the study period.

	ECHO 1999-2019								NHANES	
			Percentiles						2011-2012 Geometric Mean (95% CI)	2017-2018 Geometric Mean (95% CI)
PFAS	**Percent detected**	**Highest LOD[a]**	**5th**	**25th**	**50th**	**75th**	**95th**	**Geometric Mean (95% CI)**		
PFOA	96	0.1	0.1	0.6	1.2	2.9	8.7	1.15 (1.12, 1.22)	2.08 (1.95, 2.22)	1.42 (1.33, 1.52)
PFOS	100	0.2	0.7	1.6	2.8	9.8	38.7	3.86 (3.70, 4.03)	6.31 (5.84, 6.82)	4.25 (3.90, 4.62)
PFNA	96	0.1	0.1	0.2	0.4	0.7	1.2	0.35 (0.34, 0.36)	0.88 (0.80, 0.97)	0.41 (0.36, 0.46)
PFHxS	99	0.1	0.2	0.6	1.0	1.9	4.8	1.02 (0.99, 1.05)	1.28 (1.15, 1.43)	1.08 (1.00, 1.18)
PFDA	63	0.1	<LOD	0.1	0.1	0.2	0.4	0.11 (0.10, 0.11)	0.199 (1.15, 1.43)	0.19 (0.18, 0.21)

[a]Multiple LOD are presented in Table S3 where batches had different LODs with the same cohort and lab.

CI, confidence interval; LOD, limit of detection; NHANES, National Health and Nutrition Examination Survey; proportion of results below limit of detection was too high to provide a valid result; PFAS, per- and polyfluoroalkyl substances; PFOA, perfluorooctanoic acid; PFOS, perfluorooctanesulfonic acid; PFNA, perfluorononanoic acid; PFHxS, perfluorohexane sulfonic acid; PFDA, perfluorodecanoic acid.

Table S6. Distribution of Perceived Stress Scale (PSS) by race/ethnicity

Factor	Non-Hispanic White	Non-Hispanic Black	Non-Hispanic Asian	Non-Hispanic other	Hispanic/Latina	Missing/Unknown
N	1687	509	193	96	653	201
PSS t-score category						
<Median (50.6)	362 (48.3%)	186 (50.1%)	48 (35.0%)	24 (41.4%)	285 (54.4%)	98 (57.6%)
>=Median (50.6)	387 (51.7%)	185 (49.9%)	89 (65.0%)	34 (58.6%)	239 (45.6%)	72 (42.4%)
Missing/Unknown	938	138	56	38	129	31

Table S7. Associations of prenatal natural log-transformed PFAS concentrations (ng/mL) and risk of adverse birth outcomes stratified by trimester of exposure in selected ECHO cohorts

	Birthweight-for-gestational-age z-scores		Small-for-gestational-age[a]		Large-for-gestational-age[a]		Term low birth weight		Preterm birth		Gestational age at birth (weeks)	
PFAS	**N**	**β (95% CI)**	**N**	**OR (95% CI)**	**N**	**OR (95% CI)**	**N**	**OR (95% CI)**	**N**	**OR 95% CI**	**N**	**β (95% CI)**
PFOA												
1st	1195	-0.18 (-0.38, 0.02)	1035	1.21 (0.61, 2.39)	1082	0.87 (0.47, 1.61)	978	2.57 (0.39, 17.05)	1176	0.90 (0.48, 1.69)	1197	-0.28 (-0.67, 0.12)
2nd	1181	-0.16 (-0.35, 0.04)	1050	0.96 (0.50, 1.84)	1066	0.77 (0.41, 1.45)	951	1.00 (0.23, 4.42)	1081	1.78 (0.90, 3.54)	1182	-0.33 (-0.66, 0.01)
3rd	854	-0.12 (-0.34, 0.11)	782	0.87 (0.40, 1.86)	762	0.53 (0.21, 1.32)	606	1.83 (0.26, 12.94)	836	2.28 (0.89, 5.87)	854	-0.01 (-0.33, 0.30)
PFOS												
1st	1195	-0.29 (-0.55, -0.03)	1035	2.03 (0.89, 4.62)	1082	0.99 (0.46, 2.13)	978	5.30 (0.81, 34.74)	1176	1.24 (0.54, 2.85)	1197	-0.38 (-0.89, 0.13)
2nd	1181	-0.04 (-0.25, 0.16)	1050	0.67 (0.34, 1.31)	1066	1.07 (0.53, 2.16)	951	0.92 (0.16, 5.40)	1081	1.48 (0.66, 3.30)	1182	-0.17 (-0.53, 0.19)
3rd	854	-0.20 (-0.46, 0.06)	782	0.88 (0.38, 2.04)	762	0.43 (0.16, 1.22)	606	0.63 (0.12, 3.42)	836	0.81 (0.22, 2.90)	854	0.21 (-0.16, 0.57)
PFNA												
1st	1195	-0.35 (-0.55, -0.15)	1035	1.45 (0.75, 2.81)	1082	0.44 (0.24, 0.80)	978	2.33 (0.48, 11.22)	1176	1.08 (0.57, 2.05)	1197	-0.18 (-0.58, 0.22)
2nd	1181	-0.18 (-0.38, 0.02)	1050	0.84 (0.43, 1.61)	1066	0.72 (0.38, 1.37)	951	1.48 (0.29, 7.56)	1081	1.26 (0.62, 2.57)	1182	-0.14 (-0.48, 0.20)
3rd	854	-0.09 (-0.31, 0.14)	782	0.74 (0.35, 1.56)	762	0.60 (0.25, 1.44)	606	2.24 (0.35, 14.18)	836	2.20 (0.88, 5.48)	854	-0.12 (-0.43, 0.19)
PFHxS												
1st	1195	-0.01 (-0.21, 0.20)	1035	1.78 (0.88, 3.60)	1082	1.22 (0.69, 2.18)	978	2.26 (0.55, 9.30)	1176	1.05 (0.51, 2.14)	1197	-0.08 (-0.49, 0.32)
2nd	1181	-0.12 (-0.31, 0.07)	1050	0.94 (0.49, 1.82)	1066	0.60 (0.32, 1.11)	951	0.85 (0.15, 4.74)	1081	1.21 (0.58, 2.54)	1182	-0.05 (-0.38, 0.28)
3rd	854	-0.06 (-0.29, 0.16)	782	1.17 (0.56, 2.44)	762	0.60 (0.25, 1.45)	606	0.96 (0.19, 4.79)	836	0.66 (0.21, 2.06)	854	0.16 (-0.16, 0.47)
PFDA												
1st	1154	-0.38 (-0.56, -0.20)	995	1.17 (0.66, 2.06)	1046	0.29 (0.16, 0.53)	942	2.21 (0.66, 7.39)	1135	1.36 (0.75, 2.44)	1156	-0.15 (-0.51, 0.21)
2nd	1170	-0.19 (-0.39, -0.00)	1039	1.02 (0.54, 1.94)	1055	0.82 (0.43, 1.58)	951	4.27 (0.93, 19.57)	1070	1.12 (0.55, 2.28)	1171	-0.21 (-0.55, 0.12)
3rd	854	-0.08 (-0.32, 0.17)	782	1.11 (0.48, 2.55)	762	1.05 (0.43, 2.60)	606	4.83 (0.75, 31.02)	836	0.67 (0.21, 2.10)	854	0.19 (-0.15, 0.53)

[a] Appropriate-for-gestational-age is the referent from both small- and large-for-gestational age estimates.

Models were adjusted for cohort (dummy variables), maternal race/ethnicity (Hispanic, non-Hispanic White, Black, Asian, other), for maternal educational attainment (<high school, high school degree/GED, some college, Bachelor's degree or higher), maternal age at delivery (<25, 25-29, 30-34, ≥35 years), parity (0, 1+).

PFAS, per- and polyfluoroalkyl substances; PFOA, perfluorooctanoic acid; PFOS, perfluorooctanesulfonic acid; PFNA, perfluorononanoic acid; PFHxS, perfluorohexane sulfonic acid; PFDA, perfluorodecanoic acid.

Table S8. Associations of quartiles of prenatal PFAS concentrations (ng/mL) and risk of adverse birth outcomes in selected ECHO cohorts

	Birthweight-for-gestational-age z-scores	**Small-for-gestational-age***	**Large-for-gestational-age***	**Term low birth weight**	**Preterm birth**	**Gestational age at delivery (weeks)**
	Beta (95%CI)	OR (95%CI)	OR (95%CI)	OR (95%CI)	OR (95%CI)	Beta (95%CI)
PFOA						
Quartile 1 [-1.61, -0.22]	0 (ref)	1 (ref)	1 (ref)	1 (ref)	1 (ref)	0 (ref)
Quartile 2 [-0.22, 0.08]	-0.07 (-0.19, 0.04)	1.38 (0.95, 2.01)	1.02 (0.70, 1.49)	0.94 (0.39, 2.27)	1.18 (0.76, 1.84)	-0.01 (-0.21, 0.20)
Quartile 3 [0.08, 0.49]	-0.08 (-0.21, 0.04)	1.00 (0.65, 1.53)	0.85 (0.55, 1.31)	0.82 (0.30, 2.19)	1.45 (0.90, 2.35)	-0.02 (-0.25, 0.20)
Quartile 4 [0.49, 0.61]	-0.17 (-0.38, 0.05)	1.62 (0.76, 3.43)	1.08 (0.55, 2.11)	1.29 (0.23, 7.29)	2.87 (1.28, 6.44)	-0.31 (-0.69, 0.07)
	N=3099	N=2752	N=2791	N=2815	N=3063	N=3102
PFOS						
Quartile 1 [-1.84, 0.20]	0 (ref)	1 (ref)	1 (ref)	1 (ref)	1 (ref)	0 (ref)
Quartile 2 [0.20, 0.46]	-0.01 (-0.11, 0.10)	0.86 (0.60, 1.22)	0.89 (0.63, 1.27)	0.87 (0.34, 2.19)	0.89 (0.60, 1.33)	-0.04 (-0.23, 0.14)
Quartile 3 [0.46, 1.08]	-0.12 (-0.23, -0.01)	1.14 (0.80, 1.62)	0.86 (0.58, 1.28)	1.63 (0.69, 3.84)	0.96 (0.62, 1.47)	-0.07 (-0.26, 0.13)
Quartile 4 [1.08, 2.18]	-0.25 (-0.53, 0.02)	1.73 (0.61, 4.92)	0.63 (0.30, 1.34)	2.81 (0.35, 22.34)	2.22 (0.68, 7.17)	-0.42 (-0.90, 0.06)
	N=3099	N=2752	N=2791	N=2815	N=3063	N=3102
PFNA						
Quartile 1 [-1.85, -0.62]	0 (ref)	1 (ref)	1 (ref)	1 (ref)	1 (ref)	0 (ref)
Quartile 2 [-0.62, -0.40]	0.01 (-0.10, 0.13)	0.83 (0.58, 1.20)	0.87 (0.61, 1.26)	0.79 (0.32, 1.94)	1.32 (0.87, 2.01)	0.01 (-0.19, 0.21)
Quartile 3 [-0.40, -0.15]	-0.11 (-0.23, 0.00)	0.89 (0.60, 1.31)	0.70 (0.48, 1.04)	1.10 (0.45, 2.69)	0.96 (0.60, 1.54)	0.09 (-0.12, 0.30)
Quartile 4 [-0.15, 1.13]	-0.24 (-0.37, -0.10)	1.19 (0.77, 1.84)	0.51 (0.33, 0.81)	1.88 (0.70, 5.04)	1.74 (1.05, 2.89)	-0.18 (-0.42, 0.06)
	N=3099	N=2752	N=2791	N=2815	N=3063	N=3102
PFHxS						
Quartile 1 [-1.90, -0.25]	0 (ref)	1 (ref)	1 (ref)	1 (ref)	1 (ref)	0 (ref)
Quartile 2 [-0.25, 0.00]	0.02 (-0.09, 0.13)	1.02 (0.70, 1.49)	0.99 (0.69, 1.42)	0.57 (0.23, 1.44)	1.09 (0.70, 1.70)	0.01 (-0.19, 0.20)
Quartile 3 [0.00, 0.28]	-0.07 (-0.19, 0.05)	1.21 (0.81, 1.79)	0.79 (0.52, 1.20)	0.84 (0.34, 2.06)	0.92 (0.57, 1.49)	0.04 (-0.17, 0.25)
Quartile 4 [0.28, 1.51]	-0.07 (-0.21, 0.08)	1.38 (0.87, 2.19)	0.89 (0.56, 1.42)	1.21 (0.44, 3.38)	1.23 (0.71, 2.15)	-0.09 (-0.34, 0.16)

	N=3099	N=2752	N=2791	N=2815	N=3063	N=3102
PFDA						
Quartile 1 [-1.85, -1.15]	0 (ref)	1 (ref)	1 (ref)	1 (ref)	1 (ref)	0 (ref)
Quartile 2 [-1.15, -1.00]	-0.05 (-0.17, 0.07)	0.77 (0.51, 1.15)	0.78 (0.52, 1.17)	0.70 (0.24, 2.06)	1.44 (0.90, 2.29)	-0.03 (-0.24, 0.18)
Quartile 3 [-1.00, -0.70]	-0.10 (-0.20, 0.00)	0.82 (0.58, 1.15)	0.78 (0.57, 1.07)	0.74 (0.30, 1.81)	1.09 (0.74, 1.61)	0.01 (-0.16, 0.19)
Quartile 4 [-0.70, 0.52]	-0.26 (-0.37, -0.16)	1.28 (0.91, 1.81)	0.58 (0.41, 0.82)	2.28 (1.09, 4.77)	1.36 (0.91, 2.03)	-0.13 (-0.32, 0.06)
	N=3047	N=2701	N=2744	N=2770	N=3011	N=3050

[a]Appropriate-for-gestational-age is the referent from both small- and large-for-gestational age estimates.

Beta coefficients (β) and odds ratios (ORs) represent a difference between stated quartile and lowest (first quartile) in PFAS concentration (ng/mL) and are presented with 95% confidence intervals (CI). Models were adjusted for cohort, maternal race/ethnicity (Hispanic, non-Hispanic White, Black, Asian, other), for maternal educational attainment (<high school, high school degree/GED, some college, Bachelor's degree or higher), maternal age at delivery (<25, 25-29, 30-34, ≥35 years), parity (0, 1+).

PFAS, per- and polyfluoroalkyl substances; PFOA, perfluorooctanoic acid; PFOS, perfluorooctanesulfonic acid; PFNA, perfluorononanoic acid; PFHxS, perfluorohexane sulfonic acid; PFDA, perfluorodecanoic acid.

Table S9. Mixed versus fixed effects models of continuous measures of prenatal natural log-transformed PFAS (ng/mL) concentrations and birthweight-for-gestational age Z-scores in selected ECHO cohorts.

	Birthweight-for-gestational-age z-scores	
PFAS	**N**	**β (95% CI)**
PFOA		
Mixed effects[1]	3099	-0.13 (-0.24, -0.02)
Fixed effects	3099	-0.15 (-0.27, -0.03)
PFOS		
Mixed effects[1]	3099	-0.11 (-0.24, 0.02)
Fixed effects	3099	-0.14 (-0.28, 0.00)
PFNA		
Mixed effects[1]	3099	-0.20 (-0.32, -0.09)
Fixed effects	3099	-0.22 (-0.33, -0.10)
PFHxS		
Mixed effects[1]	3099	-0.07 (-0.18, 0.05)
Fixed effects	3099	-0.06 (-0.18, 0.06)
PFDA		
Mixed effects[1]	3047	-0.24 (-0.36, -0.13)
Fixed effects	3047	-0.25 (-0.37, -0.14)

[a] Mixed models include cohort as a random effect (fixed models are presented as Model 2 in Table 2)

Beta coefficients (β) represent 1 log-unit increase in PFAS concentration (ng/mL) and are presented with 95% confidence intervals (CI).

Models adjusted for cohort, maternal race/ethnicity (Hispanic, non-Hispanic White, Black, Asian, other), for maternal educational attainment (<high school, high school degree/GED, some college, Bachelor's degree or higher), maternal age at delivery (<25, 25-29, 30-34, ≥35 years), parity (0, 1+).

PFAS, per- and polyfluoroalkyl substances; PFOA, perfluorooctanoic acid; PFOS, perfluorooctanesulfonic acid; PFNA, perfluorononanoic acid; PFHxS, perfluorohexane sulfonic acid; PFDA, perfluorodecanoic acid.

Table S10. Associations of prenatal natural log-transformed PFAS concentrations (ng/mL) and risk of adverse birth outcomes additionally adjusted for tobacco smoke exposure (via maternal smoking or second-hand smoke) in selected ECHO cohorts

	Birthweight-for-gestational age z-score		**Large-for-gestational age[a]**	
PFAS	**N**	**β (95% CI)**	**N**	**OR (95% CI)**
PFOA	2702	-0.17 (-0.30, -0.04)	2702	1.15 (0.95, 1.39)
PFOS	2702	-0.16 (-0.31, -0.02)	2702	1.40 (1.15, 1.70)
PFNA	2702	-0.26 (-0.39, -0.14)	2702	0.86 (0.67, 1.11)
PFHxS	2702	-0.09 (-0.22, 0.03)	2702	1.09 (0.84, 1.42)
PFDA	2650	-0.27 (-0.39, -0.14)	2650	0.65 (0.47, 0.89)

[a] Appropriate-for-gestational-age is the referent from large-for-gestational age estimates.
Adjusted for cohort, maternal race/ethnicity (Hispanic, non-Hispanic White, Black, Asian, other), maternal educational attainment (<high school, high school degree/GED, some college, Bachelor's degree or higher), maternal age at delivery (<25, 25-29, 30-34, ≥35 years), parity (0, 1+), prenatal tobacco smoke exposure (either maternal smoking or second-hand smoke).
PFAS, per- and polyfluoroalkyl substances; PFOA, perfluorooctanoic acid; PFOS, perfluorooctanesulfonic acid; PFNA, perfluorononanoic acid; PFHxS, perfluorohexane sulfonic acid; PFDA, perfluorodecanoic acid.

Table S11. Associations of non-log transformed prenatal PFAS concentrations (ng/mL) and birthweight in selected ECHO cohorts

PFAS	**N**	**β (95% CI)**
PFOA	3102	-5.48 (-24.22, 13.27)
PFOS	3102	-12.77 (-30.60, 5.05)
PFNA	3102	-15.99 (-29.77, -2.22)
PFHXS	3102	-1.36 (-12.44, 9.73)
PFDA	3050	-15.76 (-26.81, -4.71)

Beta coefficients (β) represent a change in birthweight (grams) for a difference in interquartile range of PFAS concentration (ng/mL, not log transformed) and are presented with 95% confidence intervals (CI). Models were adjusted for cohort, maternal race/ethnicity (Hispanic, non-Hispanic White, Black, Asian, other), for maternal educational attainment (<high school, high school degree/GED, some college, Bachelor's degree or higher),), maternal age at delivery (<25, 25-29, 30-34, ≥35 years), parity (0, 1+), and gestational age at delivery. PFAS, per- and polyfluoroalkyl substances; PFOA, perfluorooctanoic acid; PFOS, perfluorooctanesulfonic acid; PFNA, perfluorononanoic acid; PFHxS, perfluorohexane sulfonic acid; PFDA, perfluorodecanoic acid.

Figure S1. Flow chart for eligibility of study population of selected ECHO cohorts

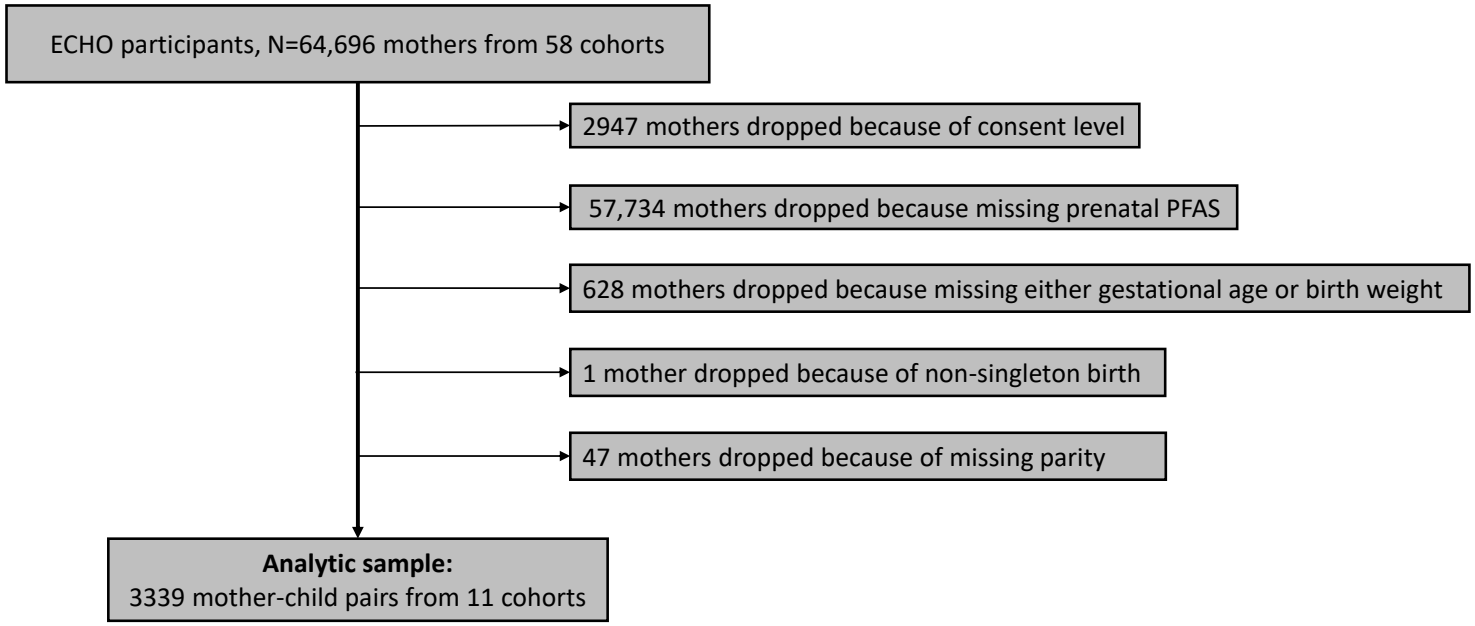
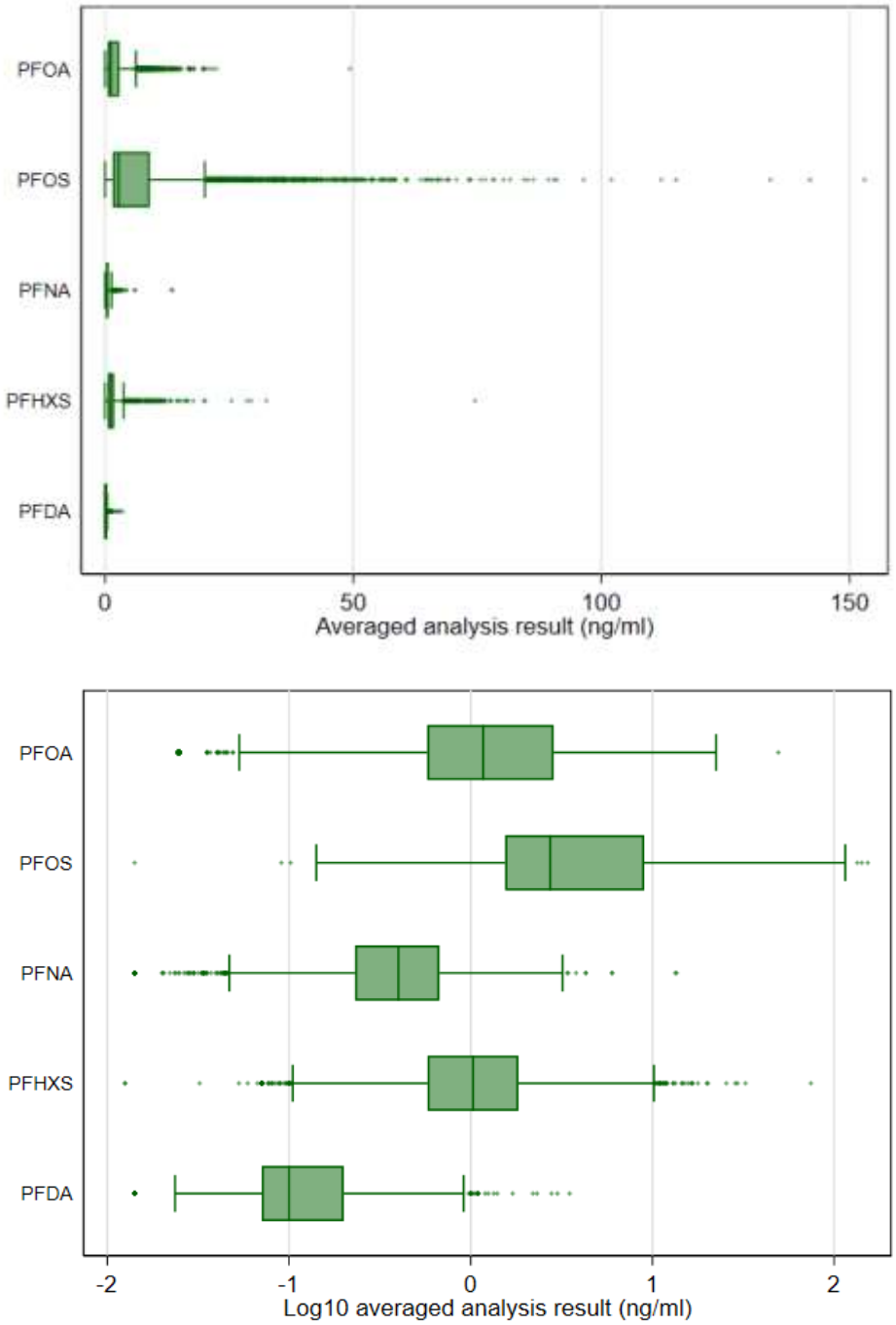


Figure S2. Raw (above) and natural log transformed (below) distributions of PFAS (ng/mL) in selected ECHO cohorts (N=3339). See Table S5 for corresponding numeric data.



PFAS, per- and polyfluoroalkyl substances; PFOA, perfluorooctanoic acid; PFOS, perfluorooctanesulfonic acid; PFNA, perfluorononanoic acid; PFHxS, perfluorohexane sulfonic acid; PFDA, perfluorodecanoic acid.

Figure S3. Directed Acyclic Graph

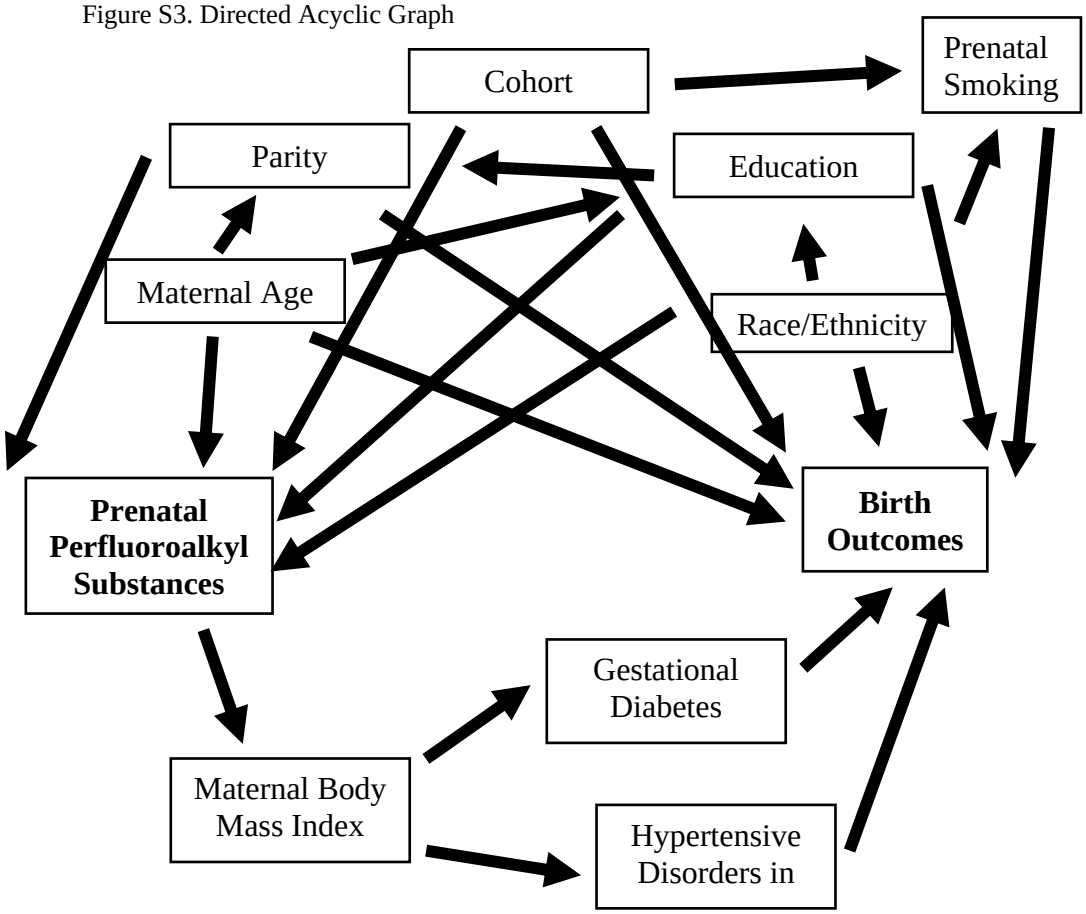
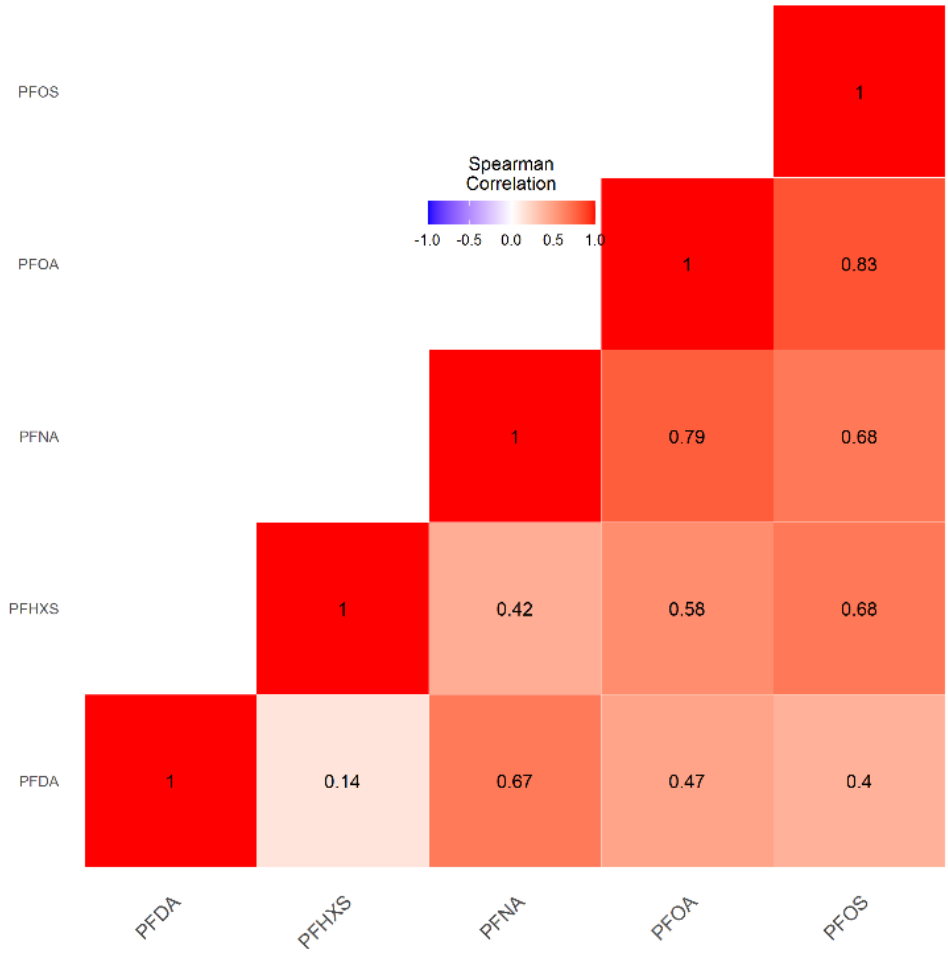
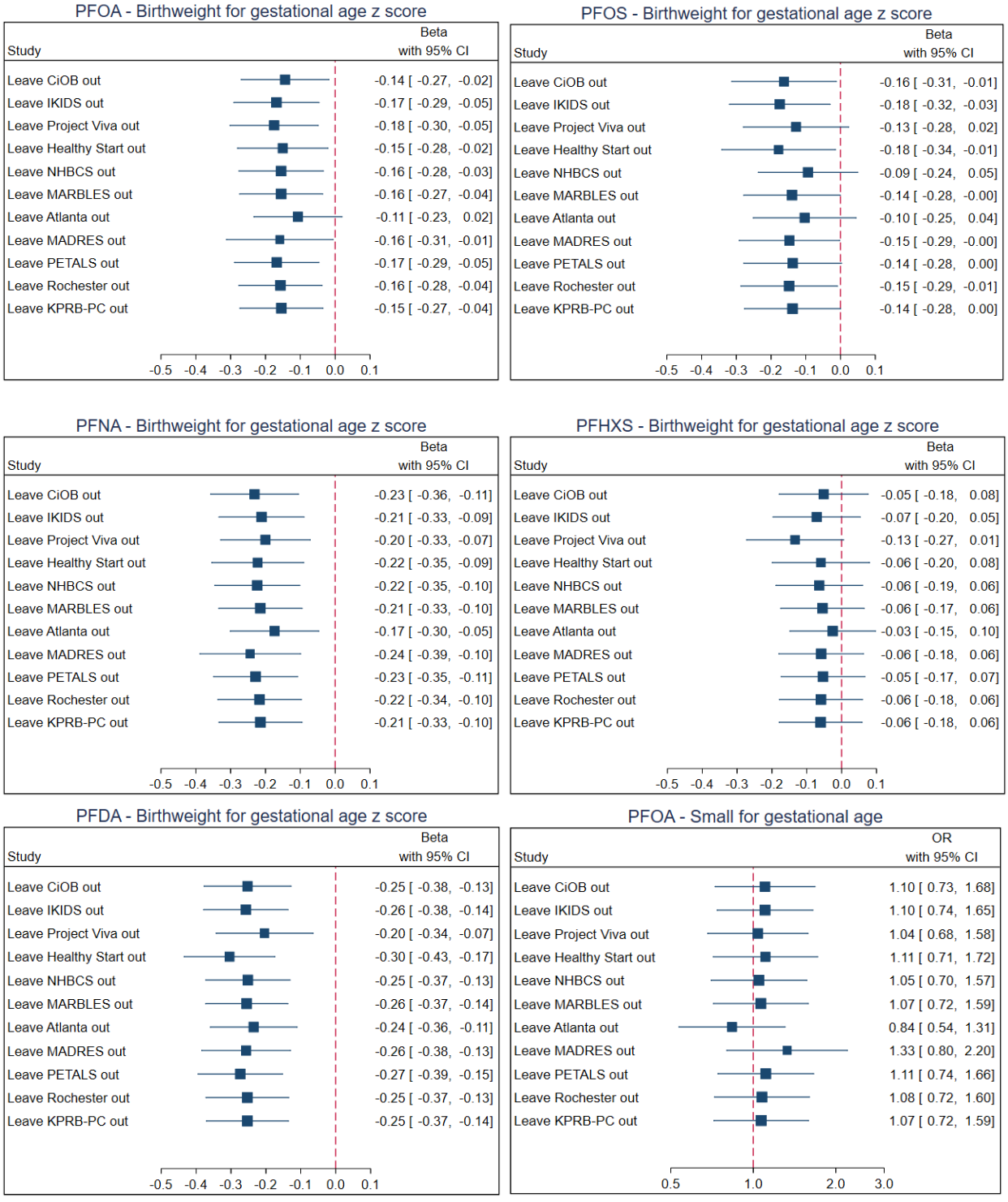


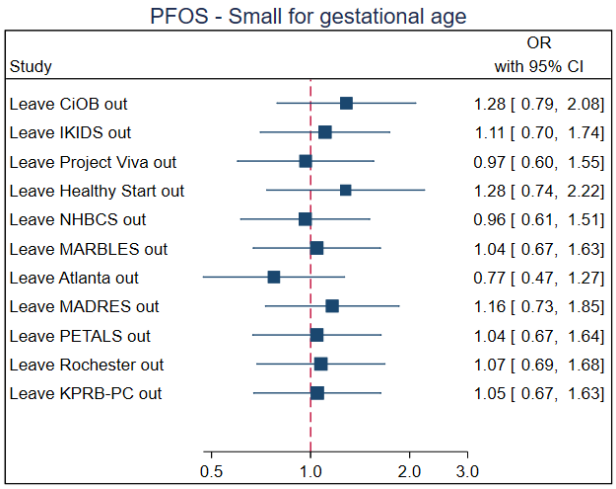
Figure S4. Spearman correlation for PFAS concentrations (ng/mL) in selected ECHO cohorts (N=3339)

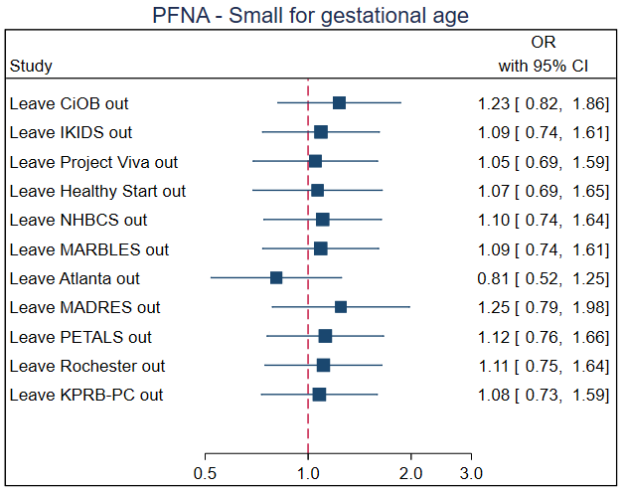


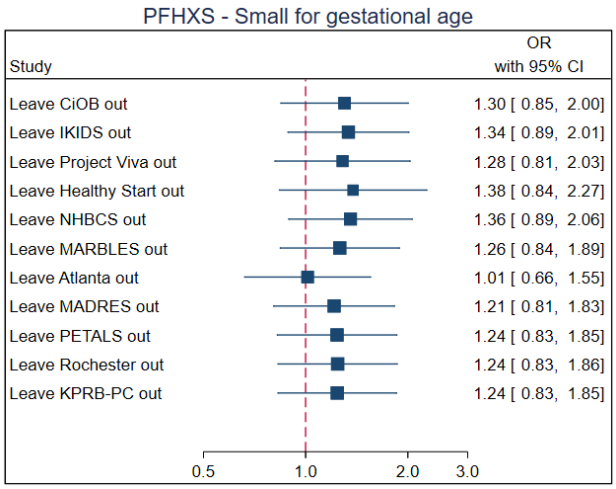
PFAS, per- and polyfluoroalkyl substances; PFOA, perfluorooctanoic acid; PFOS, perfluorooctanesulfonic acid; PFNA, perfluorononanoic acid; PFHxS, perfluorohexane sulfonic acid; PFDA, perfluorodecanoic acid

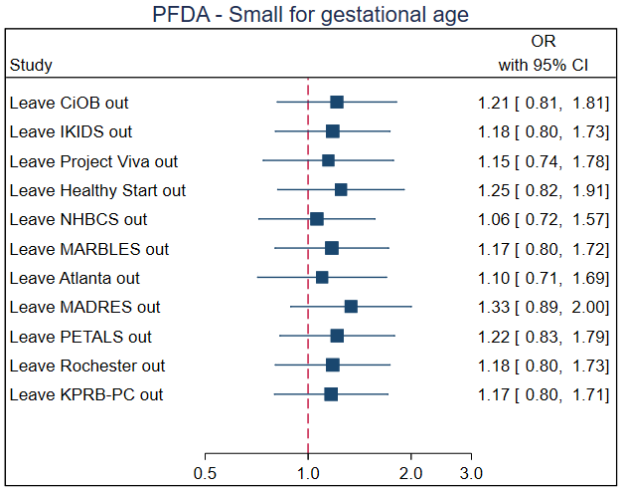
Figure S5. Associations of prenatal natural log transformed PFAS concentrations (ng/mL) and risk of adverse birth outcomes with each cohort removed one at a time in selected ECHO cohorts (N=3339)

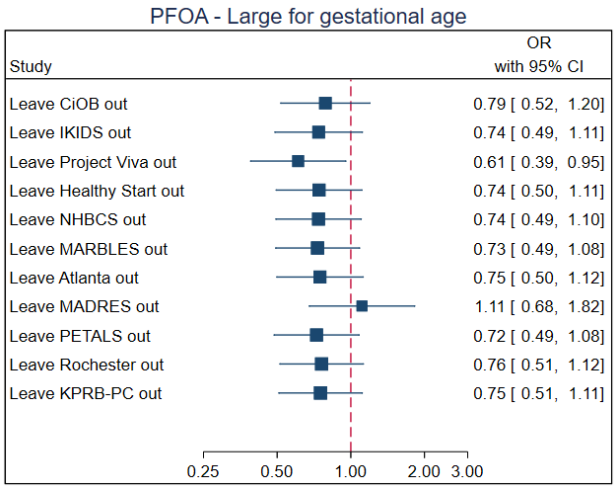


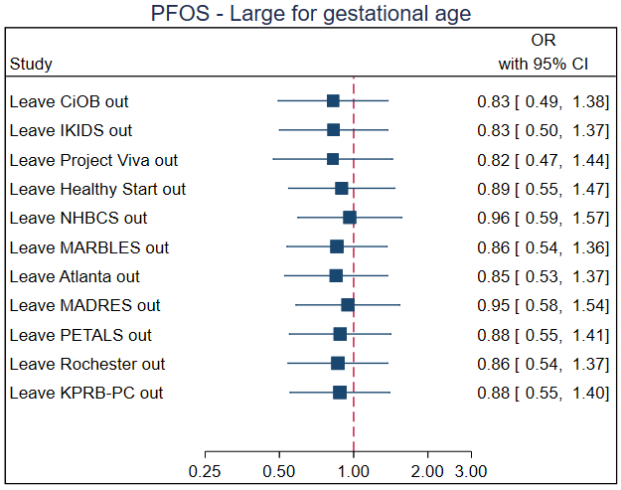

PFOS - Small for gestational age
Study
OR with 95% CI
Leave CiOB out 1.28 [0.79, 2.08]
Leave IKIDS out 1.11 [0.70, 1.74]
Leave Project Viva out 0.97 [0.60, 1.55]
Leave Healthy Start out 1.28 [0.74, 2.22]
Leave NHBCS out 0.96 [0.61, 1.51]
Leave MARBLES out 1.04 [0.67, 1.63]
Leave Atlanta out 0.77 [0.47, 1.27]
Leave MADRES out 1.16 [0.73, 1.85]
Leave PETALS out 1.04 [0.67, 1.64]
Leave Rochester out 1.07 [0.69, 1.68]
Leave KPRB-PC out 1.05 [0.67, 1.63]
0.5
1.0
2.0
3.0

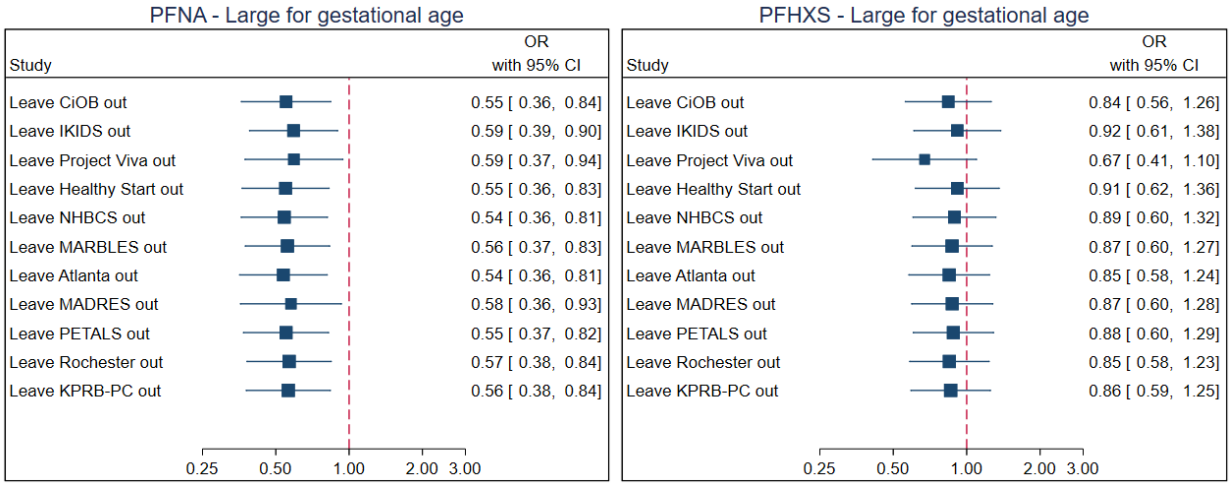

PFNA - Small for gestational age
Study
OR with 95% CI
Leave CiOB out 1.23 [0.82, 1.86]
Leave IKIDS out 1.09 [0.74, 1.61]
Leave Project Viva out 1.05 [0.69, 1.59]
Leave Healthy Start out 1.07 [0.69, 1.65]
Leave NHBCS out 1.10 [0.74, 1.64]
Leave MARBLES out 1.09 [0.74, 1.61]
Leave Atlanta out 0.81 [0.52, 1.25]
Leave MADRES out 1.25 [0.79, 1.98]
Leave PETALS out 1.12 [0.76, 1.66]
Leave Rochester out 1.11 [0.75, 1.64]
Leave KPRB-PC out 1.08 [0.73, 1.59]
0.5
1.0
2.0
3.0


PFHXS - Small for gestational age
Study
OR with 95% CI
Leave CiOB out 1.30 [0.85, 2.00]
Leave IKIDS out 1.34 [0.89, 2.01]
Leave Project Viva out 1.28 [0.81, 2.03]
Leave Healthy Start out 1.38 [0.84, 2.27]
Leave NHBCS out 1.36 [0.89, 2.06]
Leave MARBLES out 1.26 [0.84, 1.89]
Leave Atlanta out 1.01 [0.66, 1.55]
Leave MADRES out 1.21 [0.81, 1.83]
Leave PETALS out 1.24 [0.83, 1.85]
Leave Rochester out 1.24 [0.83, 1.86]
Leave KPRB-PC out 1.24 [0.83, 1.85]
0.5
1.0
2.0
3.0


PFDA - Small for gestational age
Study
OR with 95% CI
Leave CiOB out 1.21 [0.81, 1.81]
Leave IKIDS out 1.18 [0.80, 1.73]
Leave Project Viva out 1.15 [0.74, 1.78]
Leave Healthy Start out 1.25 [0.82, 1.91]
Leave NHBCS out 1.06 [0.72, 1.57]
Leave MARBLES out 1.17 [0.80, 1.72]
Leave Atlanta out 1.10 [0.71, 1.69]
Leave MADRES out 1.33 [0.89, 2.00]
Leave PETALS out 1.22 [0.83, 1.79]
Leave Rochester out 1.18 [0.80, 1.73]
Leave KPRB-PC out 1.17 [0.80, 1.71]
0.5
1.0
2.0
3.0

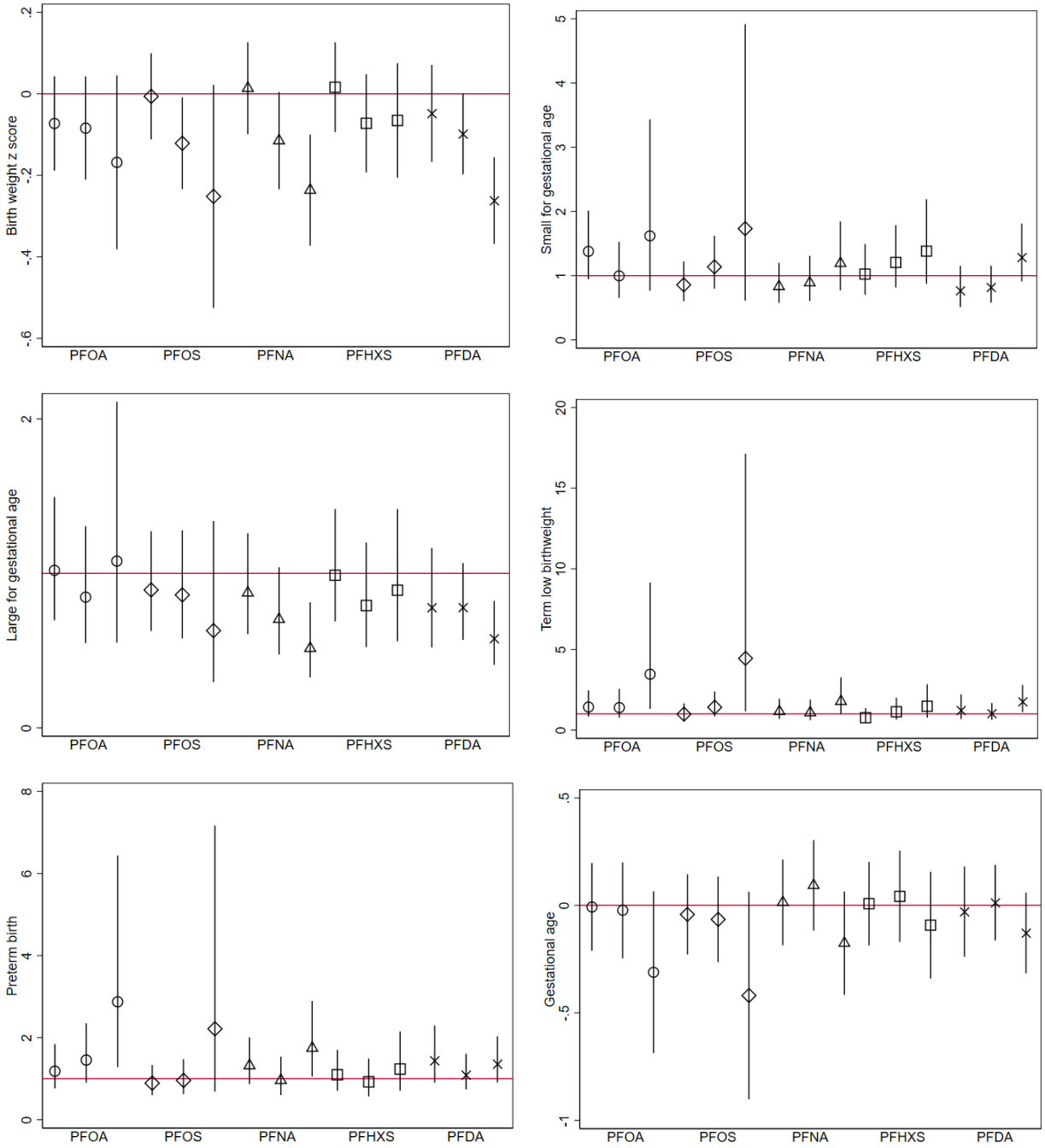

PFOA - Large for gestational age
Study
OR with 95% CI
Leave CiOB out 0.79 [0.52, 1.20]
Leave IKIDS out 0.74 [0.49, 1.11]
Leave Project Viva out 0.61 [0.39, 0.95]
Leave Healthy Start out 0.74 [0.50, 1.11]
Leave NHBCS out 0.74 [0.49, 1.10]
Leave MARBLES out 0.73 [0.49, 1.08]
Leave Atlanta out 0.75 [0.50, 1.12]
Leave MADRES out 1.11 [0.68, 1.82]
Leave PETALS out 0.72 [0.49, 1.08]
Leave Rochester out 0.76 [0.51, 1.12]
Leave KPRB-PC out 0.75 [0.51, 1.11]
0.25
0.50
1.00
2.00
3.00


PFOS - Large for gestational age
Study
OR with 95% CI
Leave CiOB out 0.83 [0.49, 1.38]
Leave IKIDS out 0.83 [0.50, 1.37]
Leave Project Viva out 0.82 [0.47, 1.44]
Leave Healthy Start out 0.89 [0.55, 1.47]
Leave NHBCS out 0.96 [0.59, 1.57]
Leave MARBLES out 0.86 [0.54, 1.36]
Leave Atlanta out 0.85 [0.53, 1.37]
Leave MADRES out 0.95 [0.58, 1.54]
Leave PETALS out 0.88 [0.55, 1.41]
Leave Rochester out 0.86 [0.54, 1.37]
Leave KPRB-PC out 0.88 [0.55, 1.40]
0.25
0.50
1.00
2.00
3.00



PFAS, per- and polyfluoroalkyl substances; PFOA, perfluorooctanoic acid; PFOS, perfluorooctanesulfonic acid; PFNA, perfluorononanoic acid; PFHxS, perfluorohexane sulfonic acid; PFDA, perfluorodecanoic acid
Chemicals in Our Bodies (CiOB); Illinois Kids Development Studies (IKIDS); New Hampshire Birth Cohort Study (NHBCS); Markers of Autism Risk in Babies Learning Early Signs (MARBLES); Emory (Atlanta); Maternal And Developmental Risks from Environmental and social Stressors (MADRES); Pregnancy and EnvironmenT And Lifestyle Study (PETALS); Kaiser Permanente Research Bank Pregnancy Cohort (KPRB-PC)
Sample size (n) for analyses of birthweight-for-gestational age z-score with leaving out the following cohorts: CiOB, IKIDS, Project Viva, Healthy Start, NHBCS, MARBLES, Atlanta, MADRES, PETALS, Rochester, KPRB-PC for the analytes PFOA, PFOS, PFNA, PHFXS are 2711, 2915, 2282, 2448, 2812, 3063, 2856, 2769, 2975, 3067, 3092, respectively, and for PFDA are 2659, 2863, 2230, 2396, 2760, 3011, 2856, 2717, 2923, 3015, 3040, respectively.
Sample size (n) for analyses of SGA with leaving out the following cohorts: CiOB, IKIDS, Project Viva, Healthy Start, NHBCS, MARBLES, Atlanta, MADRES, PETALS, Rochester, KPRB-PC for the analytes PFOA, PFOS, PFNA, PHFXS are 2411, 2608, 2068, 2130, 2497, 2722, 2519, 2456, 2641, 2722, 2746, respectively, and for PFDA are 2360, 2557, 2017, 2079, 2446, 2671, 2519, 2405, 2590, 2671, 2695, respectively.
Sample size (n) for analyses of LGA with leaving out the following cohorts: CiOB, IKIDS, Project Viva, Healthy Start, NHBCS, MARBLES, Atlanta, MADRES, PETALS, Rochester, KPRB-PC for the analytes PFOA, PFOS, PFNA, PHFXS are 2436, 2614, 2034, 2231, 2523, 2757, 2596, 2491, 2675, 2767, 2786, respectively, and for PFDA are 2389, 2567, 1987, 2184, 2476, 2710, 2596, 2444, 2628, 2720, 2739, respectively.

Figure S6. Associations between second, third and fourth quartiles of maternal PFAS (ng/mL) compared to the first quartile (lowest) and risk of adverse birth outcomes in 11 selected ECHO cohorts. Shapes represent point estimate, and lines represent corresponding 95% confidence intervals. See Table S8 for corresponding numeric data.



PFAS, per- and polyfluoroalkyl substances; PFOA, perfluorooctanoic acid; PFOS, perfluorooctanesulfonic acid; PFNA, perfluorononanoic acid; PFHxS, perfluorohexane sulfonic acid; PFDA, perfluorodecanoic acid.

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