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Supplemental Material

Perfluoroalkyl Substances and Maternal Thyroid Hormones in Early Pregnancy; Findings in the Danish National Birth Cohort

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Figure S3. Adjusted TSH and fT4 levels in each gestational week according to binary PFAS exposure, mutual adjustment of all six PFAS in the same model.

Table S1. Detection and quantitation limits of the PFAS

	Lower limit of detection (ng/ml)[a]	Lower limit of quantitation (ng/ml) [a]	N (%) >LLOQ		
			Sample 1	**Sample 2**	**Sample 3**
PFOS	0.09	0.28	188 (100%)	97 (100%)	1081 (100%)
PFOA	0.07	0.20	188 (100%)	97 (100%)	1081 (100%)
PFHxS	0.03	0.08	NA	95 (98%)	1081 (100%)
PFNA	0.09	0.27	NA	87 (90%)	1016 (93%)
PFHpS	0.04	0.11	NA	91 (94%)	1074 (99%)
PFDA	0.03	0.09	NA	83 (86%)	1037 (96%)

[a] The limit is for sample 2 and 3 from Aarhus Lab. There was no lower limit reported from 3M lab say because all PFOS and PFOA were detected.

Table S2. Study specific range of the PFAS concentrations in each quartile (ng/ml)

		Sample 1	Sample 2	Sample 3
PFOS				
	Quartile 1	≤27.3	≤18.7	≤22.2
	Quartile 2	27.4-33.9	18.8-29.6	22.3-28.5
	Quartile 3	34.0-43.5	29.7-37.0	28.6-36.4
	Quartile 4	43.6-71.9	37.1-61.6	36.5-91.4
PFOA				
	Quartile 1	≤3.88	≤2.86	≤3.33
	Quartile 2	3.89-5.40	2.87-4.12	3.34-4.43
	Quartile 3	5.41-7.07	4.13-5.84	4.44-5.62
	Quartile 4	7.08-41.5	5.85-9.30	5.63-13.3
PFHxS				
	Quartile 1	NA	≤0.57	≤0.84
	Quartile 2	NA	0.58-0.93	0.85-1.12
	Quartile 3	NA	0.94-1.23	1.13-1.40
	Quartile 4	NA	1.24-3.22	1.41-12.8
PFNA				
	Quartile 1	NA	≤0.33	≤0.36
	Quartile 2	NA	0.34-0.41	0.37-0.45
	Quartile 3	NA	0.42-0.51	0.46-0.57
	Quartile 4	NA	0.52-1.03	0.58-2.16
PFHpS				
	Quartile 1	NA	≤0.19	≤0.27
	Quartile 2	NA	0.20-0.30	0.28-0.37
	Quartile 3	NA	0.31-0.43	0.38-0.49
	Quartile 4	NA	0.44-0.77	0.50-1.52
PFDA				
	Quartile 1	NA	≤0.10	≤0.13
	Quartile 2	NA	0.11-0.16	0.14-0.17
	Quartile 3	NA	0.17-0.23	0.18-0.21
	Quartile 4	NA	0.24-0.43	0.22-0.90

Table S3. Pearson Correlation Coefficients between the PFAS (ng/ml) [a]

	PFOS	**PFOA**	**PFHxS**	**PFNA**	**PFHpS**
PFOA	0.65	-	-	-	-
PFHxS	0.32	0.32	-	-	-
PFNA	0.46	0.45	0.27	-	-
PFHpS	0.89	0.66	0.43	0.53	-
PFDA	0.42	0.24	0.18	0.75	0.43

[a] Based on 1178 samples with values of all six PFAS. The correlation coefficient between PFOS and PFOA in all 1366 samples were 0.60.

Table S4. Distribution of TSH and fT4 in each gestational week.

		TSH (mIU/L)				fT4 (pmol/L)			
Gestational week	**N**	Geometric mean [95% CI]	10^{th} percentile	50^{th} percentile	90^{th} percentile	Geometric mean [95% CI]	10^{th} percentile	50^{th} percentile	90^{th} percentile
5-6	285	1.56 [1.44-1.68]	0.88	1.54	3.32	14.4 [14.2-14.6]	12.5	14.4	16.4
7	248	1.27 [1.16-1.39]	0.52	1.23	2.93	14.2 [14.0-14.4]	12.3	14.1	16.5
8	260	0.99 [0.89-1.11]	0.37	1.09	2.49	14.2 [14.0-14.4]	12.2	14.0	16.9
9	208	0.93 [0.81-1.07]	0.28	1.05	2.52	14.4 [14.2-14.7]	12.4	14.3	16.7
10	149	0.97 [0.86-1.10]	0.40	1.01	2.22	14.4 [14.1-14.6]	12.3	14.5	16.5
11	111	1.04 [0.89-1.21]	0.43	1.13	2.42	13.9 [13.6-14.2]	12.3	13.8	16.1
12-19	105	1.02 [0.86-1.23]	0.43	1.09	2.64	13.7 [13.4-14.0]	11.6	13.9	15.7

Table S5. Association between maternal thyroid hormones and PFAS levels (ng/ml) additionally adjusted for fish intake, geographical residence, and alcohol intake during pregnancy.

	TSH (mIU/L)		fT4 (pmol/L)	
	Relative % difference (95% CI) [a,b]	**Absolute % Difference (95% CI) [a,b]**	**Relative % difference (95% CI) [a,b]**	**Absolute % Difference (95% CI) [a,b]**
PFOS (n=1366)				
Per IQR increase	1.03 (0.95, 1.12)	2.9 (-5.5, 12.1)	1.00 (0.99, 1.02)	0.3 (-1.1, 1.7)
Quartile 1	Ref	Ref	Ref	Ref
Quartile 2	0.86 (0.70, 1.05)	-14.2 (-30.2, 5.4)	1.02 (0.99, 1.06)	2.4 (-0.7, 5.7)
Quartile 3	0.96 (0.78, 1.17)	-4.5 (-21.9, 16.9)	1.02 (0.99, 1.05)	1.8 (-1.1, 4.7)
Quartile 4	1.00 (0.82, 1.20)	-0.4 (-17.7, 20.4)	1.01 (0.98, 1.04)	0.6 (-2.5, 3.8)
PFOA (n=1366)				
Per IQR increase	1.00 (0.93, 1.08)	0.3 (-6.9, 8.1)	1.01 (0.99, 1.02)	0.6 (-0.6, 1.8)
Quartile 1	Ref	Ref	Ref	Ref
Quartile 2	0.96 (0.78, 1.18)	-4.2 (-22.1, 17.8)	0.99 (0.97, 1.02)	-0.5 (-3.4, 2.4)
Quartile 3	1.01 (0.83, 1.23)	1.0 (-17.1, 23.1)	1.01 (0.98, 1.04)	1.2 (-1.9, 4.3)
Quartile 4	1.06 (0.86, 1.32)	6.5 (-14.0, 31.9)	1.01 (0.98, 1.04)	0.6 (-2.3, 3.6)
PFHxS (n=1178)				
Per IQR increase	1.02 (0.96, 1.09)	2.3 (-3.6, 8.8)	1.00 (0.98, 1.01)	-0.3 (-1.6, 0.9)
Quartile 1	Ref	Ref	Ref	Ref
Quartile 2	0.98 (0.79, 1.21)	-2.4 (-21.0, 20.7)	0.99 (0.96, 1.02)	-1.0 (-4.1, 2.2)
Quartile 3	0.92 (0.68, 1.24)	-8.0 (-31.8, 24.2)	1.01 (0.97, 1.05)	1.1 (-2.9, 5.2)
Quartile 4	1.04 (0.84, 1.27)	3.6 (-15.9, 27.5)	1.02 (0.99, 1.06)	2.2 (-1.2, 5.9)
PFNA (n=1178)				
Per IQR increase	1.01 (0.95, 1.07)	0.8 (-4.9, 6.8)	1.00 (0.99, 1.01)	-0.1 (-1.2, 0.9)
Quartile 1	Ref	Ref	Ref	Ref
Quartile 2	0.96 (0.75, 1.24)	-3.8 (-25.4, 23.9)	1.00 (0.96, 1.04)	-0.2 (-3.8, 3.6)
Quartile 3	1.01 (0.81, 1.25)	0.9 (-18.7, 25.1)	1.00 (0.97, 1.04)	0.4 (-3.1, 3.9)
Quartile 4	1.03 (0.83, 1.28)	2.9 (-17.1, 27.8)	1.00 (0.96, 1.03)	-0.6 (-3.9, 2.8)
PFHpS (n=1178)				
Per IQR increase	1.02 (0.93, 1.12)	2.0 (-6.8, 11.5)	1.00 (0.99, 1.02)	0.1 (-1.3, 1.5)
Quartile 1	Ref	Ref	Ref	Ref
Quartile 2	0.95 (0.74, 1.21)	-5.4 (-26.4, 21.4)	1.00 (0.96, 1.03)	-0.4 (-3.7, 3.0)
Quartile 3	1.00 (0.81, 1.23)	-0.5 (-19.1, 22.5)	1.02 (0.99, 1.05)	1.7 (-1.5, 5.0)
Quartile 4	1.06 (0.85, 1.31)	5.8 (-14.9, 31.3)	1.00 (0.96, 1.03)	-0.4 (-3.7, 2.9)
PFDA (n=1178)				
Per IQR increase	0.98 (0.95, 1.09)	-1.9 (-7.7, 4.2)	1.01 (1.00, 1.02)	0.8 (-0.4, 1.9)
Quartile 1	Ref	Ref	Ref	Ref
Quartile 2	0.96 (0.78, 1.18)	-3.7 (-21.6, 18.1)	1.01 (0.98, 1.04)	0.9 (-2.4, 4.2)
Quartile 3	1.00 (0.79, 1.27)	0.0 (-21.2, 26.9)	1.01 (0.98, 1.05)	1.2 (-2.6, 5.1)
Quartile 4	1.04 (0.84, 1.30)	4.3 (-16.5, 30.1)	0.99 (0.96, 1.03)	-0.7 (-4.0, 2.6)

[a] Adjusted for maternal age, parental socio-occupational status, pre-pregnancy BMI, parity, maternal smoking, birth year, fish intake, geographical residence, and alcohol intake during pregnancy. Study sample (1, 2, 3) was included in the model for continuous exposure and study-specific distribution was used to define PFAS quartiles.

[b] Relative % difference was calculated as exp(beta). Absolute % difference was calculated as (exp(beta)−1)×100%.

Table S6. Association between maternal thyroid hormones and PFAS levels in multiple PFAS models.

A) TSH (mIU/L)

Per IQR increase of each PFAS (ng/ml)	Model 1 [a]		Model 2 [b]		Model 3 [c]	
	Relative % difference (95% CI) [d]	Absolute % Difference (95% CI) [d]	Relative % difference (95% CI)	Absolute % Difference (95% CI)	Relative % difference (95% CI)	Absolute % Difference (95% CI)
PFOS	1.04 (0.96, 1.14)	4.3 (-4.3, 13.8)	1.04 (0.94, 1.15)	3.9 (-6.5, 15.4)	1.03 (0.89, 1.18)	2.6 (-10.7, 17.9)
PFOA	NA	NA	0.99 (0.91, 1.08)	-1.0 (-9.3, 8.1)	1.00 (0.86, 1.16)	-0.4 (-14.4, 15.9)
PFHxS	NA	NA	NA	NA	1.01 (0.95, 1.09)	1.5 (-5.3, 8.7)
PFNA	NA	NA	NA	NA	NA	NA
PFHpS	NA	NA	NA	NA	NA	NA
PFDA	NA	NA	NA	NA	NA	NA

Per IQR increase of each PFAS (ng/ml)	Model 4 [d]		Model 5 [e]		Model 6 [f]	
	Relative % difference (95% CI)	Absolute % Difference (95% CI)	Relative % difference (95% CI)	Absolute % Difference (95% CI)	Relative % difference (95% CI)	Absolute % Difference (95% CI)
PFOS	1.03 (0.89, 1.19)	2.8 (-10.9, 18.6)	1.06 (0.82, 1.37)	6.1 (-17.6, 36.8)	1.09 (0.85, 1.39)	8.5 (-15.0, 38.6)
PFOA	1.00 (0.86, 1.16)	-0.2 (-14.3, 16.2)	1.00 (0.86, 1.17)	0.0 (-14.3, 16.7)	0.98 (0.84, 1.14)	-2.1 (-16.1, 14.3)
PFHxS	1.02 (0.95, 1.09)	1.5 (-5.2, 8.7)	1.02 (0.96, 1.09)	1.9 (-4.4, 8.6)	1.02 (0.96, 1.08)	1.8 (-4.4, 8.5)
PFNA	1.00 (0.93, 1.07)	-0.4 (-7.0, 6.6)	1.00 (0.93, 1.06)	-0.2 (-6.5, 6.5)	1.04 (0.95, 1.15)	4.2 (-5.4, 14.7)
PFHpS	NA	NA	0.96 (0.77, 1.20)	-3.7 (-22.7, 20.1)	0.96 (0.77, 1.20)	-3.8 (-22.7, 19.7)
PFDA	NA	NA	NA	NA	0.94 (0.86, 1.03)	-6.1 (-14.5, 3.0)

B) fT4 (pmol/L)

Per IQR increase of each PFAS (ng/ml)	Model 1 [a]		Model 2 [b]		Model 3 [c]	
	Relative % difference (95% CI)	Absolute % Difference (95% CI)	Relative % difference (95% CI)	Absolute % Difference (95% CI)	Relative % difference (95% CI)	Absolute % Difference (95% CI)
PFOS	1.00 (0.99, 1.02)	0.4 (-1.0, 1.8)	1.00 (0.98, 1.02)	0.1 (-1.8, 1.9)	1.00 (0.98, 1.03)	0.3 (-2.3, 2.9)
PFOA	NA	NA	1.01 (0.99, 1.02)	0.6 (-1.0, 2.2)	1.00 (0.97, 1.03)	0.0 (-3, 3.2)
PFHxS	NA	NA	NA	NA	1.00 (0.98, 1.01)	-0.4 (-1.8, 1)
PFNA	NA	NA	NA	NA	NA	NA
PFHpS	NA	NA	NA	NA	NA	NA
PFDA	NA	NA	NA	NA	NA	NA

Per IQR increase of each PFAS (ng/ml)	Model 4 [d]		Model 5 [e]		Model 6 [f]	
	Relative % difference (95% CI)	Absolute % Difference (95% CI)	Relative % difference (95% CI)	Absolute % Difference (95% CI)	Relative % difference (95% CI)	Absolute % Difference (95% CI)
PFOS	1.00 (0.98, 1.03)	0.3 (-2.3, 3.1)	1.00 (0.96, 1.04)	-0.3 (-4.4, 3.9)	0.99 (0.95, 1.03)	-1.0 (-5.0, 3.1)
PFOA	1.00 (0.97, 1.03)	0.1 (-2.9, 3.2)	1.00 (0.97, 1.03)	0.0 (-3.0, 3.2)	1.01 (0.98, 1.04)	0.7 (-2.4, 3.9)
PFHxS	1.00 (0.98, 1.01)	-0.4 (-1.8, 1.1)	1.00 (0.98, 1.01)	-0.4 (-1.8, 1.0)	1.00 (0.98, 1.01)	-0.4 (-1.8, 1.0)
PFNA	1.00 (0.99, 1.01)	-0.1 (-1.4, 1.1)	1.00 (0.99, 1.01)	-0.2 (-1.5, 1.1)	0.98 (0.97, 1.00)	-1.5 (-3.1, 0.1)
PFHpS	NA	NA	1.01 (0.97, 1.05)	0.8 (-2.9, 4.6)	1.01 (0.97, 1.05)	0.8 (-2.8, 4.5)
PFDA	NA	NA	NA	NA	1.02 (1.00, 1.04)	2.0 (0.2, 3.7)

[a] Model included maternal age, parental socio-occupational status, BMI, parity, maternal smoking, birth year, an indicator of study sample as covariate, and adjusted for PFOS.

[b] Included all covariate in model 1 and co-adjusted for PFOS, and PFOA in the same model.

[c] Included all covariate in model 1 and co-adjusted for PFOS, PFOA, and PFHxS in the same model.

[d] Included all covariate in model 1 and co-adjusted for PFOS, PFOA, PFHxS, and PFNA in the same model.

[e] Included all covariate in model 1 and co-adjusted for PFOS, PFOA, PFHxS, PFNA, and PFHpS in the same model.

[f] Included all covariate in model 1 and co-adjusted for PFOS, PFOA, PFHxS, PFNA, PFHpS and PFDA in the same model.

[d] Relative % difference was calculated as exp(beta). Absolute % difference was calculated as (exp(beta)−1)×100%.

Table S7. Association between maternal thyroid hormones and PFAS levels (ng/ml) stratified by socio-economic status, parity, smoking, birth year, and geographical residence, maternal age, and alcohol intake.

	TSH (mIU/L)			fT4 (pmol/L)		
	Relative % difference (95% CI) [a,b]			Relative % difference (95% CI) [a,b]		
	Low socio-occupational status (N=425)	High socio-occupational status (N=941)	*P for interaction* [c]	Low socio-occupational status (N=425)	High socio-occupational status (N=941)	*P for interaction* [c]
PFOS [b]	0.96 (0.81, 1.14)	1.06 (0.97, 1.17)	0.32	1.01 (0.99, 1.03)	1.00 (0.98, 1.01)	0.47
PFOA	0.99 (0.85, 1.15)	1.01 (0.92, 1.11)	0.85	1.01 (0.98, 1.04)	1.00 (0.99, 1.01)	0.47
PFHxS	1.01 (0.86, 1.18)	1.03 (0.97, 1.09)	0.56	1.01 (0.98, 1.03)	0.99 (0.98, 1.01)	0.21
PFNA	0.95 (0.84, 1.08)	1.06 (1.00, 1.13)	0.11	1.01 (0.99, 1.03)	0.99 (0.98, 1.01)	0.29
PFHpS	0.89 (0.74, 1.07)	1.08 (0.98, 1.19)	0.09	1.01 (0.99, 1.04)	0.99 (0.97, 1.01)	0.13
PFDA	0.98 (0.79, 1.22)	1.01 (0.96, 1.06)	0.45	1.01 (0.98, 1.04)	1.01 (1.00, 1.02)	0.80
	Nulliparous (N=712)	**Multiparous (N=648)**	***P for interaction***	**Nulliparous (N=712)**	**Multiparous (N=648)**	***P for interaction***
PFOS	1.02 (0.92, 1.13)	1.04 (0.90, 1.20)	0.99	1.00 (0.99, 1.02)	1.01 (0.99, 1.03)	0.54
PFOA	0.99 (0.91, 1.07)	1.03 (0.86, 1.23)	0.66	1.00 (0.99, 1.02)	1.02 (0.99, 1.04)	0.52
PFHxS	1.05 (1.00, 1.11)	0.89 (0.76, 1.05)	0.07	0.99 (0.98, 1.00)	1.03 (1.00, 1.06)	0.01
PFNA	1.05 (0.97, 1.13)	0.97 (0.88, 1.06)	0.41	1.00 (0.98, 1.01)	1.00 (0.99, 1.02)	0.57
PFHpS	1.06 (0.95, 1.19)	0.98 (0.85, 1.12)	0.33	0.99 (0.98, 1.01)	1.02 (0.99, 1.04)	0.12
PFDA	1.01 (0.93, 1.10)	0.95 (0.86, 1.04)	0.30	1.01 (0.99, 1.03)	1.01 (0.99, 1.03)	0.77
	Smoker (N=444)	**Non-Smoker (N=922)**	***P for interaction***	**Smoker (N=444)**	**Non-Smoker (N=922)**	***P for interaction***
PFOS	1.04 (0.91, 1.19)	1.03 (0.92, 1.15)	0.70	1.02 (0.99, 1.04)	1.00 (0.98, 1.02)	0.19
PFOA	1.10 (0.95, 1.26)	0.98 (0.90, 1.07)	0.61	1.00 (0.98, 1.03)	1.01 (0.99, 1.02)	0.76
PFHxS	1.06 (0.98, 1.14)	1.02 (0.94, 1.10)	0.79	1.00 (0.98, 1.01)	1.00 (0.98, 1.01)	0.89
PFNA	1.11 (0.97, 1.26)	0.98 (0.91, 1.05)	0.39	1.00 (0.98, 1.03)	1.00 (0.99, 1.01)	0.81
PFHpS	1.12 (0.94, 1.34)	0.98 (0.88, 1.10)	0.84	1.01 (0.98, 1.03)	1.00 (0.98, 1.02)	0.58
PFDA	0.99 (0.90, 1.08)	0.98 (0.91, 1.06)	0.82	1.02 (1.00, 1.05)	1.00 (0.99, 1.02)	0.15
	Birth year < 2000 (N=402)	**Birth year ≥ 2000 (N=964)**	***P for interaction***	**Birth year < 2000 (N=402)**	**Birth year ≥ 2000 (N=964)**	***P for interaction***
PFOS	1.13 (0.91, 1.40)	1.03 (0.93, 1.13)	0.54	1.00 (0.97, 1.03)	1.00 (0.99, 1.02)	0.81
PFOA	1.20 (0.97, 1.48)	0.98 (0.91, 1.07)	0.23	1.01 (0.98, 1.04)	1.00 (0.99, 1.02)	0.65
PFHxS	0.95 (0.77, 1.16)	1.03 (0.96, 1.10)	0.73	1.02 (0.99, 1.05)	0.99 (0.98, 1.01)	0.19
PFNA	0.97 (0.80, 1.19)	1.03 (0.97, 1.10)	0.48	1.00 (0.98, 1.03)	1.00 (0.98, 1.01)	0.60
PFHpS	1.07 (0.89, 1.28)	1.03 (0.92, 1.14)	0.60	1.01 (0.98, 1.03)	1.00 (0.98, 1.02)	0.85
PFDA	1.06 (0.82, 1.35)	0.98 (0.92, 1.05)	0.80	0.99 (0.96, 1.02)	1.01 (1.00, 1.02)	0.63
	East (N=484)	**West (N=882)**	***P for interaction***	**East (N=484)**	**West (N=882)**	***P for interaction***
PFOS	1.12 (0.94, 1.33)	0.98 (0.89, 1.08)	0.33	1.01 (0.98, 1.04)	1.00 (0.99, 1.02)	0.68
PFOA	1.13 (0.92, 1.38)	0.97 (0.91, 1.05)	0.26	1.01 (0.97, 1.04)	1.00 (0.99, 1.02)	0.83
PFHxS	1.04 (0.94, 1.15)	1.01 (0.93, 1.09)	0.29	0.99 (0.97, 1.01)	1.00 (0.99, 1.02)	0.17
PFNA	1.07 (0.90, 1.26)	1.00 (0.93, 1.06)	0.59	1.00 (0.98, 1.02)	1.00 (0.99, 1.01)	0.67
PFHpS	1.06 (0.89, 1.27)	1.00 (0.90, 1.10)	0.51	1.00 (0.97, 1.03)	1.00 (0.99, 1.02)	0.90
PFDA	1.07 (0.87, 1.30)	0.97 (0.92, 1.03)	0.77	1.00 (0.98, 1.03)	1.01 (1.00, 1.02)	0.94
	Maternal age <30 (N=607)	**Maternal age ≥30 (N=759)**	***P for interaction***	**Maternal age <30 (N=607)**	**Maternal age ≥30 (N=759)**	***P for interaction***
PFOS	1.09 (0.96, 1.23)	0.99 (0.89, 1.10)	0.28	1.00 (0.98, 1.02)	1.01 (0.99, 1.03)	0.70
PFOA	1.02 (0.91, 1.14)	0.96 (0.84, 1.09)	0.46	1.00 (0.99, 1.02)	1.01 (0.99, 1.04)	0.89
PFHxS	1.03 (0.95, 1.12)	1.02 (0.96, 1.09)	0.63	0.99 (0.98, 1.01)	1.00 (0.99, 1.01)	0.51

PFNA	1.00 (0.89, 1.13)	1.02 (0.96, 1.09)	0.78	1.01 (0.99, 1.03)	1.00 (0.98, 1.01)	0.72
PFHpS	1.05 (0.92, 1.20)	1.00 (0.90, 1.12)	0.41	1.00 (0.98, 1.02)	1.01 (0.99, 1.03)	0.40
PFDA	0.98 (0.88, 1.09)	0.99 (0.93, 1.05)	0.82	1.02 (0.99, 1.04)	1.00 (0.99, 1.01)	0.70

	Alcohol intake in pregnancy (N=1144)	**No alcohol intake in pregnancy (N=222)**	***P for interaction***	**Alcohol intake in pregnancy (N=1144)**	**No alcohol intake in pregnancy (N=222)**	***P for interaction***
PFOS	1.03 (0.94, 1.12)	1.12 (0.92, 1.35)	0.82	1.00 (0.99, 1.02)	1.00 (0.97, 1.03)	0.61
PFOA	0.99 (0.92, 1.06)	1.14 (0.89, 1.47)	0.93	1.01 (1.00, 1.02)	1.00 (0.96, 1.04)	0.41
PFHxS	0.99 (0.94, 1.04)	1.02 (0.90, 1.17)	0.81	1.00 (0.99, 1.01)	0.99 (0.97, 1.02)	0.91
PFNA	1.03 (0.97, 1.10)	0.98 (0.85, 1.13)	0.46	0.99 (0.98, 1.00)	1.01 (1.00, 1.03)	0.04
PFHpS	1.00 (0.92, 1.10)	1.09 (0.89, 1.35)	0.77	1.00 (0.99, 1.02)	1.00 (0.97, 1.04)	0.49
PFDA	0.97 (0.92, 1.03)	0.98 (0.86, 1.12)	0.96	1.00 (0.99, 1.02)	1.02 (1.00, 1.04)	0.33

[a] Relative % difference in thyroid hormones was calculated per interquartile range (IQR) increase in continuous variables.
[b] Adjusted for maternal age, parental socio-occupational status, BMI, parity, maternal smoking, birth year, and an indicator of study sample.
[c] Tests of heterogeneity were also performed by assessing the p-value of the interaction term for each PFAS and potential modifying factors in the regression models

Table S8. Estimated maternal TSH and fT4 levels in each gestational week according to high or low PFAS exposure

	TSH (mIU/L)			fT4 (pmol/L)		
Gestational week	PFAS ≤75th	PFAS >75th	Difference [a]	PFAS ≤75th	PFAS >75th	Difference [a]
a) PFOS	N=1024	N=342		N=1024	N=342	
5-6	1.44 (1.15, 1.74)	1.61 (1.33, 1.88)	+0.17	14.5 (14.1, 15.0)	14.0 (13.4, 14.6)	-0.5
7	1.16 (1.03, 1.29)	1.31 (1.12, 1.49)	+0.15	14.5 (14.2, 14.7)	14.2 (13.8, 14.6)	-0.3
8	1.00 (0.88, 1.12)	1.14 (0.93, 1.36)	+0.14	14.4 (14.1, 14.6)	14.3 (14.0, 14.7)	-0.1
9	0.93 (0.80, 1.06)	1.07 (0.85, 1.29)	+0.14	14.2 (14.0, 14.5)	14.4 (14.0, 14.8)	+0.2
10	0.94 (0.81, 1.06)	1.08 (0.88, 1.29)	+0.14	14.1 (13.8, 14.3)	14.3 (13.9, 14.7)	+0.2
11	1.01 (0.88, 1.14)	1.17 (0.96, 1.39)	+0.16	13.8 (13.6, 14.1)	14.1 (13.6, 14.6)	+0.3
12-19	1.18 (0.95, 1.41)	1.37 (0.98, 1.75)	+0.19	13.5 (13.1, 14.0)	13.8 (13.0, 14.6)	+0.3
b) PFOA	N=1024	N=342		N=1024	N=342	
5-6	1.44 (1.14, 1.75)	1.60 (1.35, 1.85)	+0.16	14.4 (14.0, 14.9)	14.3 (13.8, 14.7)	-0.1
7	1.15 (1.01, 1.29)	1.34 (1.18, 1.50)	+0.19	14.4 (14.2, 14.7)	14.4 (14.1, 14.7)	±0.0
8	0.99 (0.87, 1.11)	1.18 (0.96, 1.40)	+0.19	14.3 (14.1, 14.6)	14.5 (14.1, 14.8)	+0.2
9	0.93 (0.80, 1.06)	1.09 (0.85, 1.33)	+0.16	14.2 (14.0, 14.5)	14.4 (14.0, 14.8)	+0.2
10	0.95 (0.82, 1.07)	1.05 (0.83, 1.28)	+0.10	14.1 (13.8, 14.3)	14.3 (13.9, 14.7)	+0.2
11	1.04 (0.92, 1.17)	1.07 (0.84, 1.30)	+0.03	13.9 (13.6, 14.1)	14.0 (13.5, 14.5)	+0.1
12-19	1.24 (1.01, 1.48)	1.13 (0.77, 1.49)	-0.11	13.6 (13.2, 14.1)	13.6 (12.9, 14.4)	±0.0
c) PFHxS	N=883	N=295		N=883	N=295	
5-6	1.46 (1.11, 1.82)	1.60 (1.30, 1.90)	+0.14	14.2 (13.7, 14.7)	14.6 (14.0, 15.2)	+0.4
7	1.17 (1.01, 1.33)	1.32 (1.15, 1.49)	+0.15	14.3 (14.0, 14.5)	14.7 (14.3, 15.0)	+0.4
8	1.01 (0.87, 1.14)	1.14 (0.93, 1.35)	+0.13	14.2 (14.0, 14.5)	14.6 (14.2, 15.0)	+0.4
9	0.94 (0.79, 1.08)	1.04 (0.82, 1.26)	+0.10	14.2 (13.9, 14.5)	14.5 (14.0, 14.9)	+0.3
10	0.94 (0.80, 1.08)	0.99 (0.78, 1.21)	+0.05	14.0 (13.8, 14.3)	14.3 (13.8, 14.8)	+0.3
11	1.02 (0.88, 1.16)	1.00 (0.77, 1.23)	-0.02	13.8 (13.6, 14.1)	13.9 (13.3, 14.6)	+0.1
12-19	1.20 (0.95, 1.45)	1.05 (0.68, 1.42)	-0.15	13.6 (13.1, 14.0)	13.6 (12.5, 14.6)	±0.0
d) PFNA	N=883	N=295		N=883	N=295	
5-6	1.52 (1.14, 1.90)	1.47 (1.27, 1.66)	-0.05	14.3 (13.8, 14.8)	14.4 (13.8, 15.0)	+0.1
7	1.18 (1.02, 1.34)	1.28 (1.12, 1.45)	+0.10	14.4 (14.1, 14.7)	14.3 (14.0, 14.7)	-0.1
8	1.00 (0.86, 1.14)	1.15 (0.93, 1.37)	+0.15	14.4 (14.1, 14.6)	14.2 (13.9, 14.6)	-0.2
9	0.93 (0.78, 1.08)	1.06 (0.83, 1.29)	+0.13	14.3 (14.0, 14.6)	14.2 (13.8, 14.6)	-0.1
10	0.94 (0.79, 1.08)	1.00 (0.80, 1.19)	+0.06	14.1 (13.8, 14.4)	14.2 (13.7, 14.6)	+0.1
11	1.03 (0.89, 1.17)	0.96 (0.79, 1.13)	-0.07	13.8 (13.5, 14.1)	14.2 (13.7, 14.6)	+0.4
12-19	1.24 (0.98, 1.50)	0.95 (0.71, 1.19)	-0.29	13.5 (13.0, 13.9)	14.2 (13.5, 14.8)	+0.7
e) PFHpS	N=884	N=294		N=884	N=294	
5-6	1.45 (1.09, 1.80)	1.68 (1.34, 2.01)	+0.23	14.5 (14.0, 15.0)	13.8 (13.2, 14.5)	-0.7
7	1.14 (0.99, 1.29)	1.39 (1.20, 1.59)	+0.25	14.4 (14.2, 14.7)	14.1 (13.7, 14.5)	-0.3
8	0.97 (0.83, 1.11)	1.21 (0.99, 1.43)	+0.24	14.4 (14.1, 14.6)	14.3 (13.9, 14.7)	-0.1
9	0.90 (0.76, 1.05)	1.11 (0.88, 1.34)	+0.21	14.2 (13.9, 14.5)	14.3 (13.9, 14.8)	+0.1
10	0.92 (0.78, 1.06)	1.06 (0.85, 1.27)	+0.14	14.0 (13.7, 14.3)	14.3 (13.8, 14.7)	+0.3
11	1.01 (0.87, 1.15)	1.06 (0.85, 1.28)	+0.05	13.8 (13.5, 14.1)	14.1 (13.6, 14.5)	+0.3
12-19	1.21 (0.94, 1.48)	1.12 (0.77, 1.46)	-0.09	13.5 (13.0, 14.0)	13.8 (13.0, 14.5)	+0.3
f) PFDA	N=883	N=295		N=883	N=295	
5-6	1.49 (1.12, 1.85)	1.54 (1.26, 1.83)	+0.05	14.5 (14.0, 15.0)	13.9 (13.4, 14.5)	-0.6
7	1.16 (1.00, 1.31)	1.34 (1.13, 1.55)	+0.18	14.5 (14.2, 14.7)	14.1 (13.8, 14.5)	-0.4
8	0.99 (0.86, 1.12)	1.18 (0.94, 1.43)	+0.19	14.4 (14.1, 14.6)	14.2 (13.8, 14.6)	-0.2
9	0.93 (0.78, 1.08)	1.05 (0.81, 1.29)	+0.12	14.2 (13.9, 14.5)	14.3 (13.9, 14.8)	+0.1
10	0.96 (0.82, 1.11)	0.95 (0.75, 1.15)	-0.01	14.0 (13.7, 14.3)	14.3 (13.9, 14.8)	+0.3
11	1.10 (0.95, 1.25)	0.87 (0.71, 1.03)	-0.23	13.7 (13.4, 14.0)	14.3 (13.9, 14.7)	+0.6
12-19	1.37 (1.09, 1.66)	0.80 (0.60, 1.01)	-0.57	13.3 (12.8, 13.8)	14.2 (13.6, 14.8)	+0.9

[a] We estimated the expected TSH and fT4 value for each gestational week comparing the top PFAS quartile to the lower three quartiles adjusting for maternal age, socio-occupational status, BMI, parity, smoke, and birth year. Study-specific distribution was used to define PFAS quartiles. The model also included the interaction terms between PFAS (binary) and gestational week (continuous value and a square term). Mean difference was calculated as the expected mean among the top PFAS quartile minus the expected mean among the lower three quartiles. Data is shown in Figure 2.

Table S9. Association between maternal thyroid hormones and binary PFAS variables (>75th vs. ≤75th as reference) according to gestational week (<10, ≥10).

	TSH (mIU/L)			fT4 (pmol/L)		
	Relative % difference (95% CI) [a,b]			Relative % difference (95% CI) [a,b]		
	Gestational week <10 (N=1001)	Gestational week ≥10 (N=365)	*P for interaction*	Gestational week <10 (N=1001)	Gestational week ≥10 (N=365)	*P for interaction*
PFOS	1.11 (0.93, 1.31)	1.02 (0.78, 1.32)	0.45	0.98 (0.96, 1.01)	1.02 (0.98, 1.07)	0.16
PFOA	1.14 (0.96, 1.36)	0.92 (0.72, 1.17)	0.15	1.00 (0.97, 1.03)	1.02 (0.97, 1.06)	0.66
PFHxS	1.14 (0.95, 1.36)	0.95 (0.72, 1.26)	0.18	1.03 (1.00, 1.06)	1.01 (0.96, 1.07)	0.84
PFNA	1.11 (0.92, 1.33)	0.81 (0.63, 1.04)	0.10	0.99 (0.96, 1.02)	1.02 (0.97, 1.06)	0.29
PFHpS	1.12 (0.93, 1.36)	0.96 (0.73, 1.27)	0.20	0.98 (0.95, 1.02)	1.02 (0.97, 1.07)	0.29
PFDA	1.22 (1.01, 1.47)	0.72 (0.56, 0.93)	0.003	0.97 (0.94, 1.00)	1.04 (1.00, 1.08)	0.02

[a] Adjusted for maternal age, parental socio-occupational status, BMI, parity, maternal smoking, birth year, and an indicator of study sample.

[b] Relative % difference in thyroid hormones were calculated comparing the three lower PFAS quartiles (reference) to the highest.

Table S10. Gestational week-specific high or low thyroid hormones status according to plasma PFAS levels (ng/ml) among 1,061 women included in study sample 3.

Per inter-quartile range increase of each PFAS	Low TSH [a] N=105	High TSH [a] N=109	Low fT4 [a] N=119	High fT4 [a] N=92
	OR and 95% CI [b]			
PFOS	1.16 (0.66, 2.04)	0.83 (0.47, 1.45)	0.87 (0.58, 1.31)	1.23 (0.78, 1.92)
PFOA	0.75 (0.43, 1.32)	0.67 (0.31, 1.46)	1.01 (0.52, 1.96)	1.09 (0.70, 1.69)
PFHxS	1.15 (0.89, 1.47)	1.14 (0.90, 1.45)	1.18 (0.94, 1.50)	1.13 (0.86, 1.49)
PFNA	0.95 (0.69, 1.31)	0.74 (0.52, 1.05)	0.89 (0.65, 1.20)	1.07 (0.84, 1.37)
PFHpS	1.28 (0.78, 2.13)	0.85 (0.54, 1.35)	0.85 (0.58, 1.26)	1.32 (0.85, 2.03)
PFDA	1.05 (0.79, 1.40)	0.81 (0.59, 1.11)	0.81 (0.55, 1.19)	1.30 (0.97, 1.73)

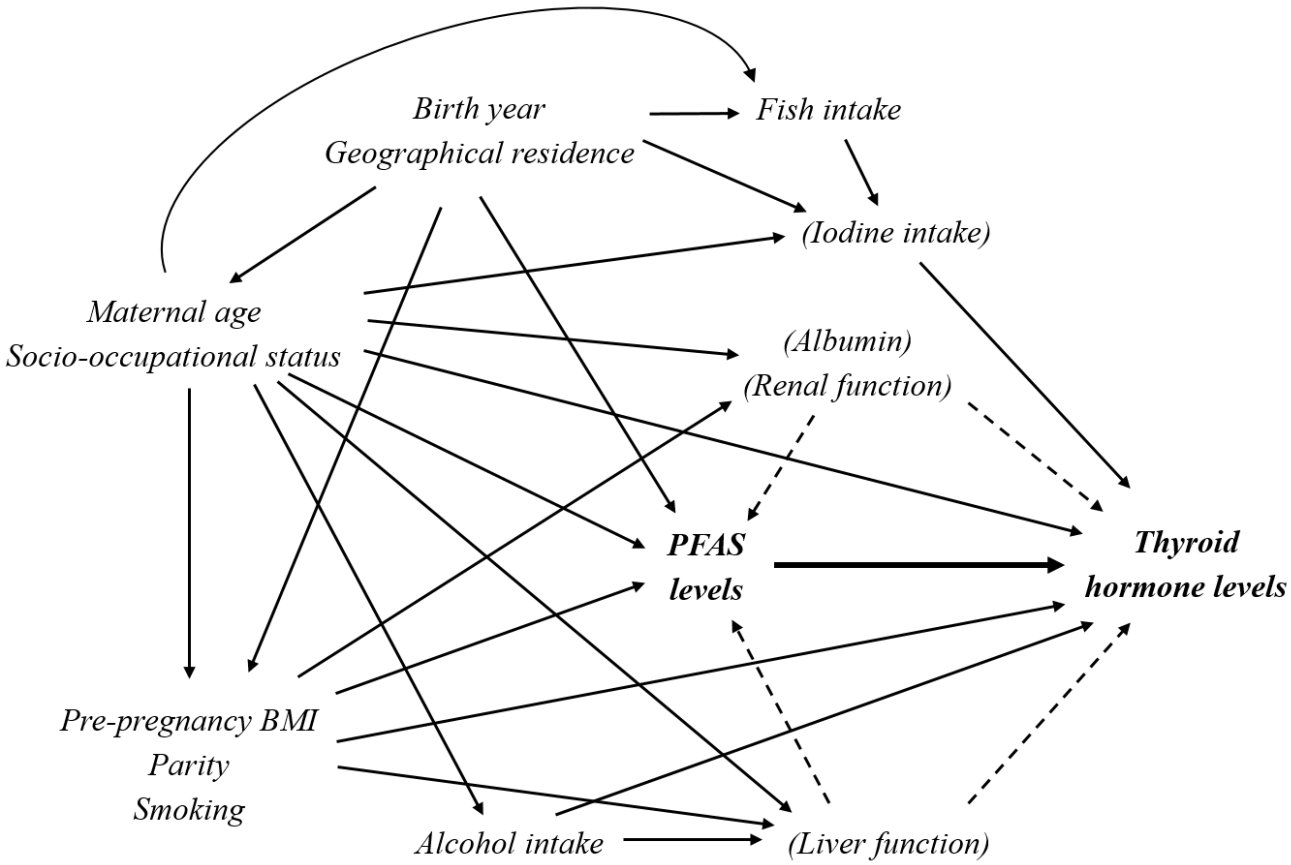
[a] Low or high TSH and fT4 status were defined using the week-specific lowest 10^{th} or highest 90^{th} percentile.
[b] Adjusted for maternal age, parental socio-occupational status, BMI, parity, maternal smoking, and birth year.

Table S11. Gestational week-specific high or low thyroid hormones status according to plasma PFAS levels (ng/ml) excluding women with thyroid diseases (n=1,329).

Per inter-quartile range increase of each PFAS	Low TSH [a] N=133	High TSH [a] N=129	Low fT4 [a] N=137	High fT4 [a] N=127
	OR and 95% CI [b]			
PFOS	1.08 (0.70, 1.68)	0.79 (0.50, 1.23)	0.80 (0.55, 1.16)	1.14 (0.80, 1.63)
PFOA	0.79 (0.53, 1.18)	0.68 (0.40, 1.18)	0.85 (0.48, 1.50)	1.07 (0.87, 1.31)
PFHxS	1.13 (0.89, 1.44)	1.12 (0.88, 1.43)	1.19 (0.94, 1.49)	1.12 (0.87, 1.45)
PFNA	0.92 (0.68, 1.25)	0.72 (0.50, 1.02)	0.90 (0.67, 1.20)	1.06 (0.84, 1.34)
PFHpS	1.27 (0.80, 2.01)	0.81 (0.51, 1.27)	0.85 (0.58, 1.25)	1.21 (0.80, 1.84)
PFDA	1.13 (0.89, 1.44)	0.78 (0.56, 1.07)	0.85 (0.59, 1.23)	1.29 (0.99, 1.68)

[a] Low or high TSH and fT4 status were defined using the week-specific lowest 10^{th} or highest 90^{th} percentile.
[b] Adjusted for maternal age, parental socio-occupational status, BMI, parity, maternal smoking, and birth year.

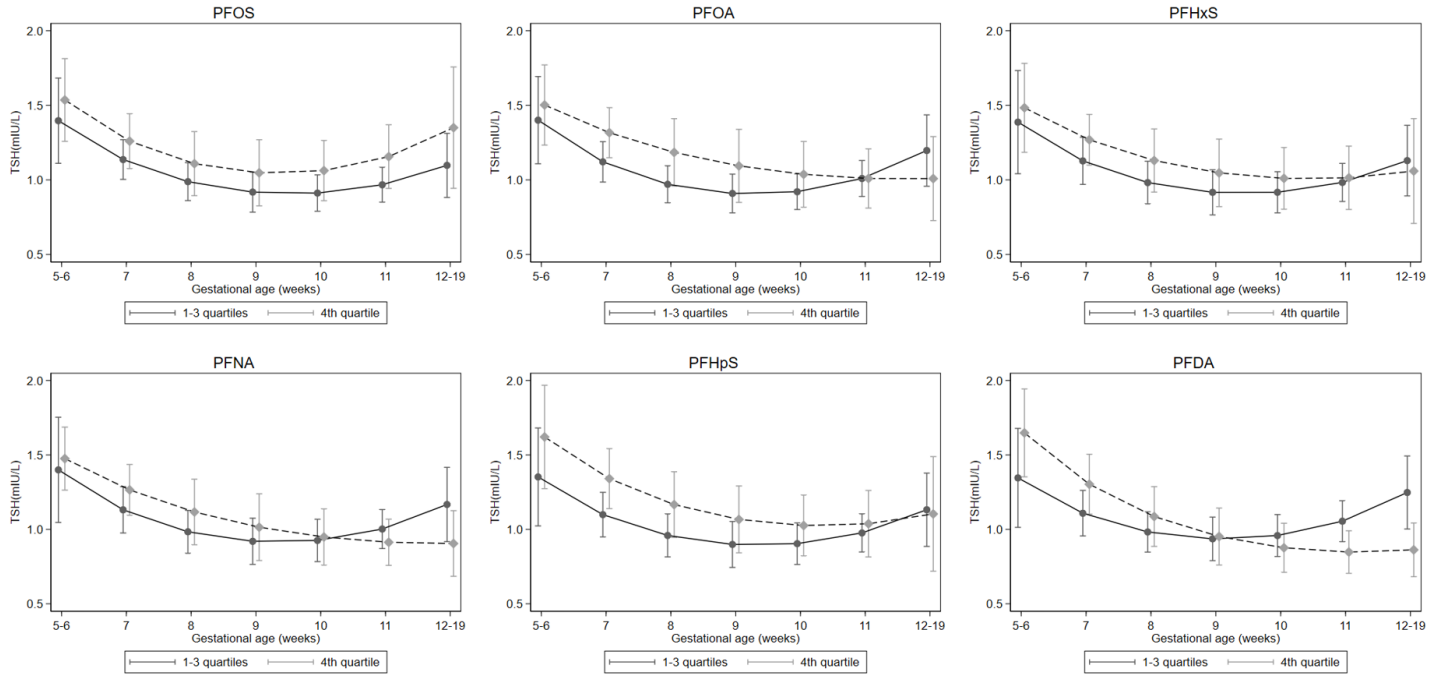
Figure S1. The directed acyclic graph constructed for this study.



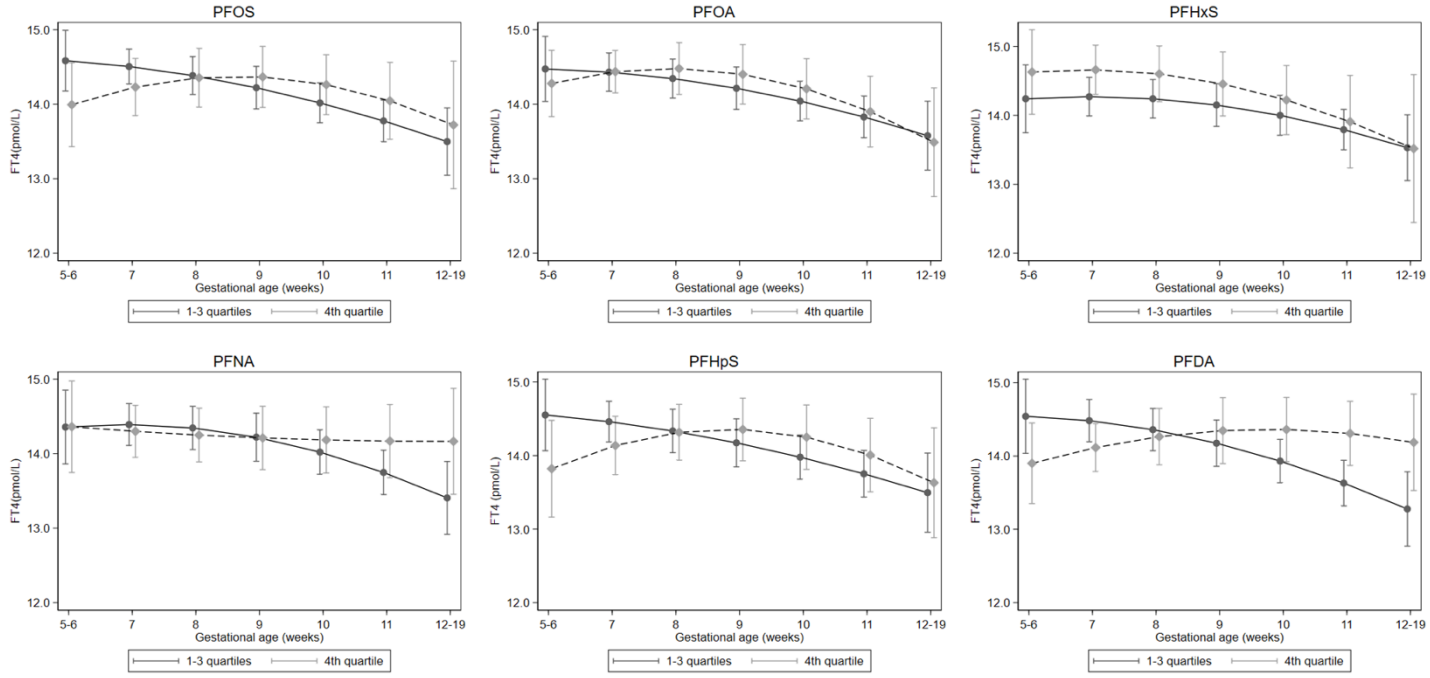
*Variables with parenthesis (and dash arrows pointing to exposure and outcome) indicate potential unmeasured/uncontrolled confounders that should be evaluated for their potential impacts in future studies.

Figure S2. Adjusted TSH and fT4 levels in each gestational week according to PFAS levels (the 1st quartile vs the 4th quartile).

A) TSH



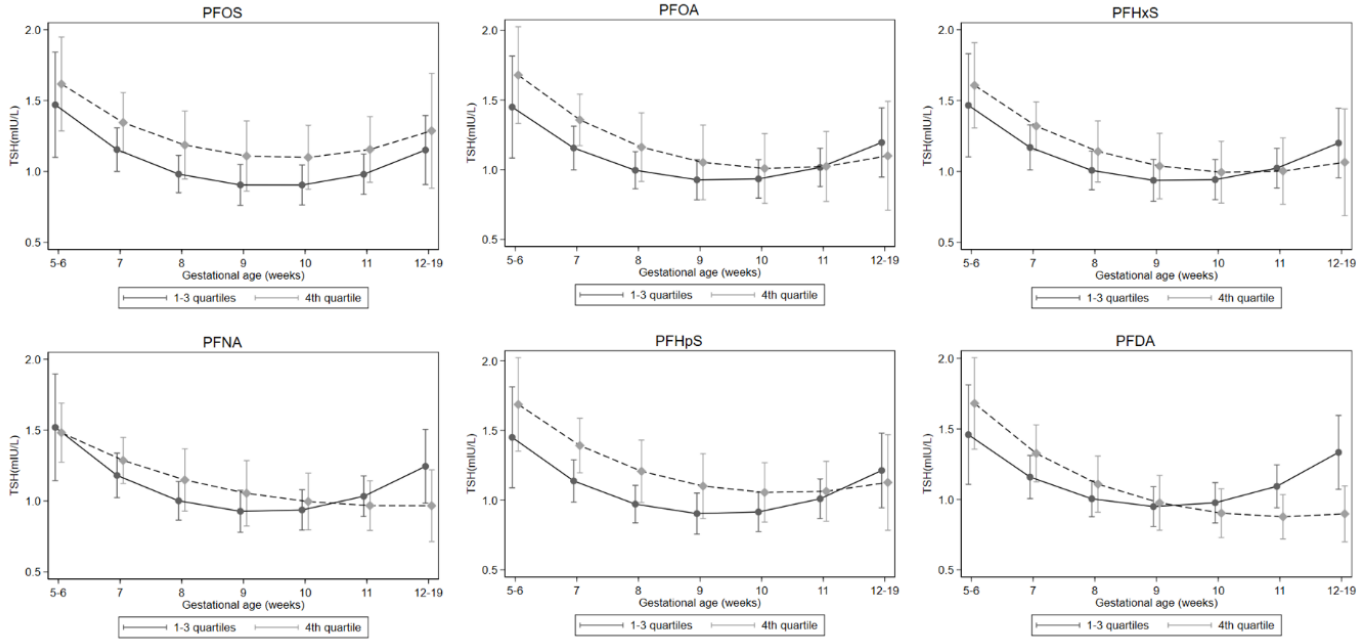
B) fT4



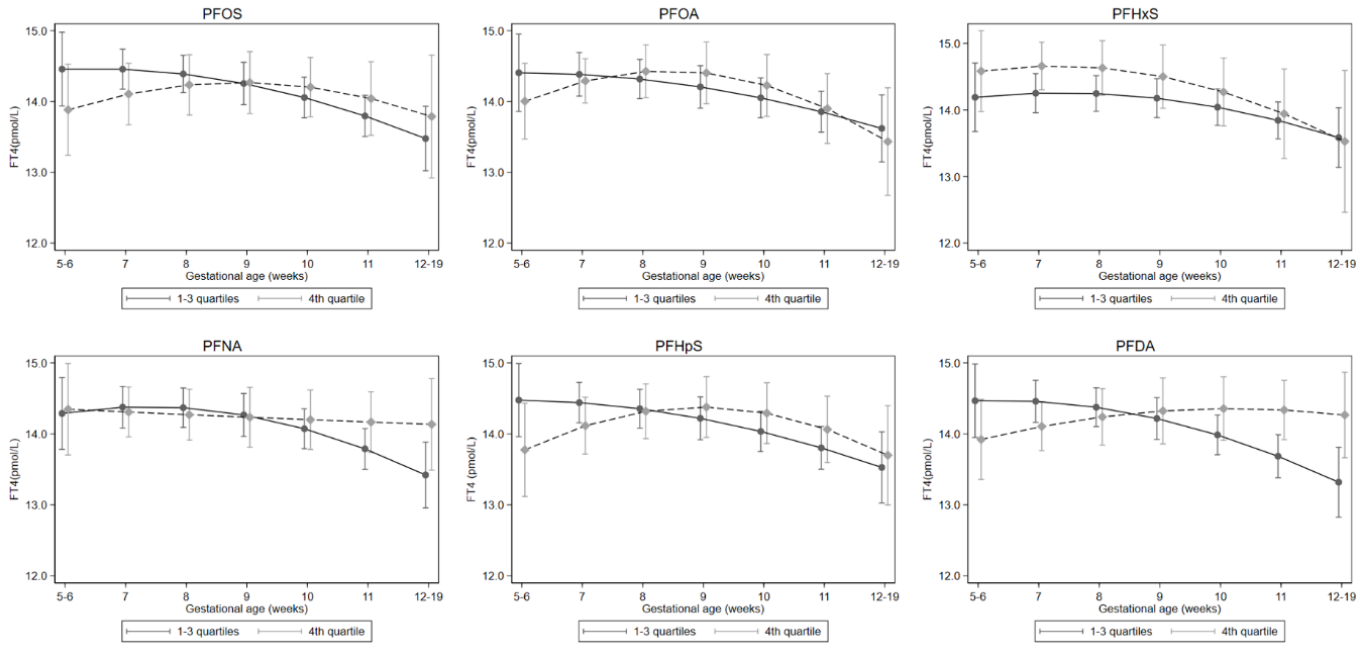
Legend: We estimated the expected TSH and fT4 value for each gestational week comparing the top PFAS quartile to the lowest quartile adjusting for maternal age, socio-occupational status, BMI, parity, smoke, and birth year. Study-specific distribution was used to define PFAS quartiles. The model also included the interaction terms between PFAS (binary) and gestational week (continuous value and a squared term). The bar shows 95% CI in each gestation week.

Figure S3. Adjusted TSH and fT4 levels in each gestational week according to binary PFAS exposure, mutual adjustment of all six PFAS in the same model.

A) TSH



B) fT4



Legend: We estimated the expected TSH and fT4 value for each gestational week comparing the top PFAS quartile to the lowest quartile adjusting for maternal age, socio-occupational status, BMI, parity, smoke, and birth year. All of the six PFAS levels were also included in the model. Study-specific distribution was used to define PFAS quartiles. The model also included the interaction terms between PFAS (binary) and gestational week (continuous value and a squared term). The bar shows 95% CI in each gestation week.