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Early Life PFAS Exposure and Child Health: Evidence from the NIH ECHO Cohort

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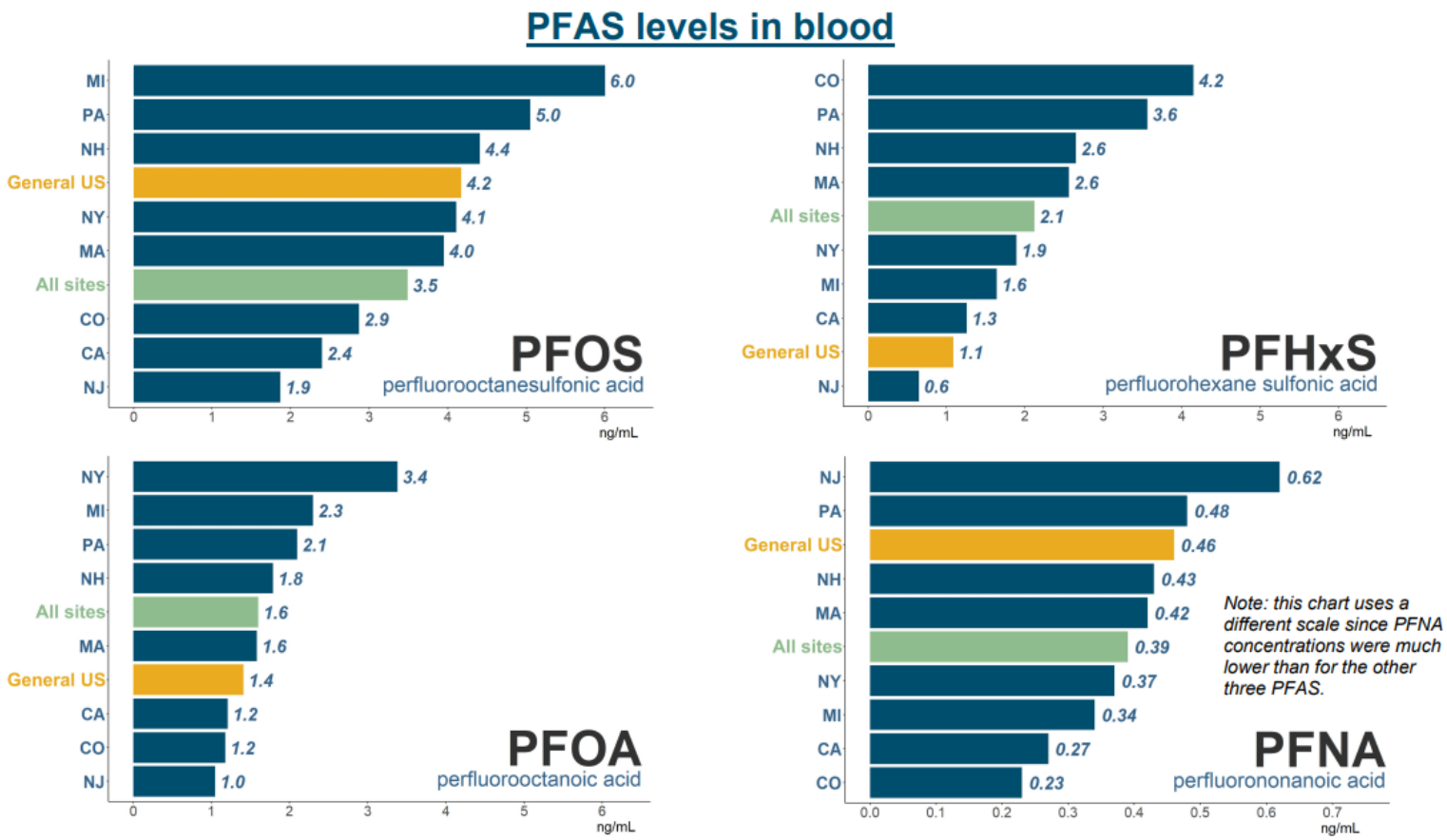
ECHO Discovery, March 11, 2026

PFAS Exposure and Child Health

- PFAS are synthetic chemicals used in industrial and consumer products
- Extremely persistent ("forever chemicals")
- Widespread human exposure (universally detected in adults and children)
- Increasing concern about impacts on **early life development**



Agency for Toxic Substances and Disease Registry
Pavuk et al. 2025 *Environment International*; PMID: 40570576

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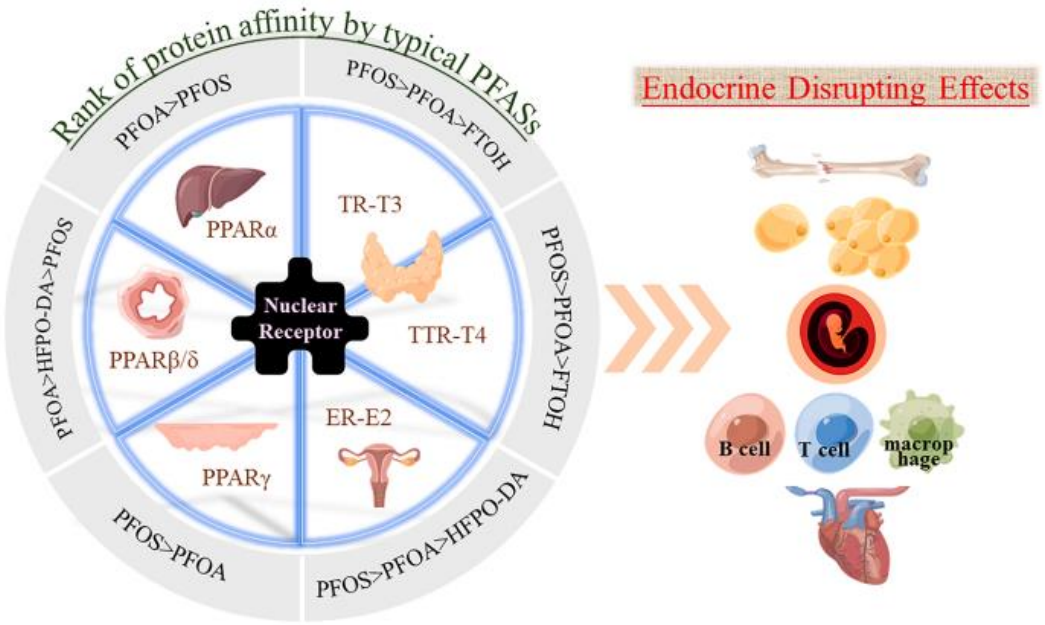
How Are Children Exposed?

- Prenatal exposure via placental transfer
- Postnatal exposure via breast milk and environment
- Contaminated drinking water
- Oil, water, and stain-resistant products
- Food packaging and diet
- Household products (carpets, textiles)

Despite some regulations on legacy PFAS, thousands of related compounds are still in widespread use and many newer PFAS remain poorly studied

PFAS as Endocrine Disrupting Chemicals (EDCs)

- PFAS can interfere with **normal hormone signaling**
- May activate PPAR receptors, which regulate lipid metabolism and development
- Evidence suggests interactions with:
  - Estrogen receptors (ER)
  - Androgen receptors (AR)
  - Thyroid hormone pathways
- PFAS may alter:
  - hormone production
  - hormone transport proteins
  - receptor signaling
- Endocrine disruption during development may affect:
  - growth
  - metabolism
  - pubertal timing



Zhao et al. *Environment International* 2023

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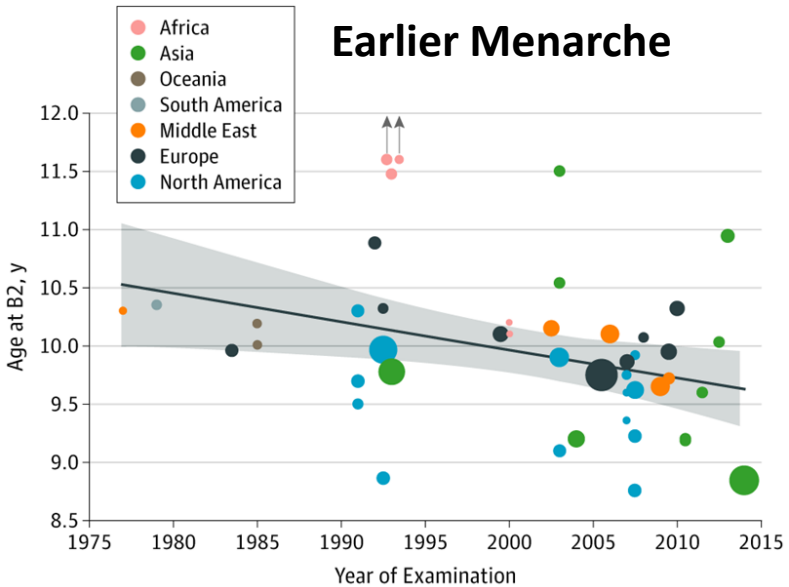
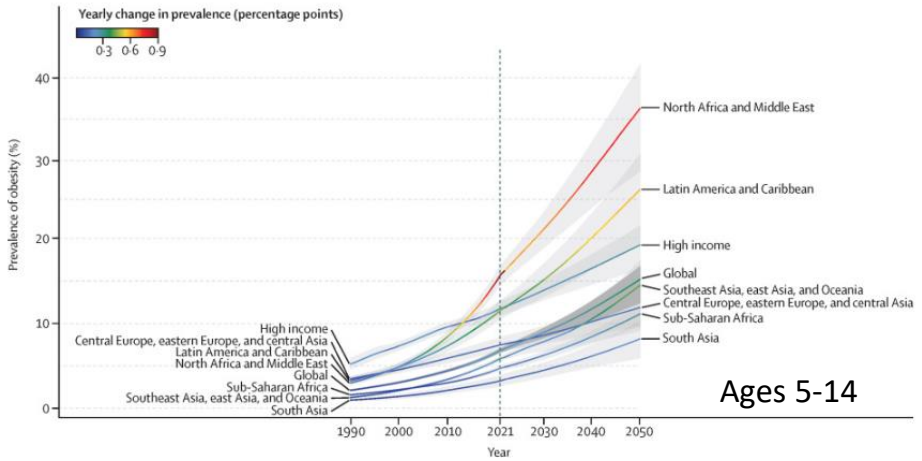
Possible population-level signals of endocrine disruption

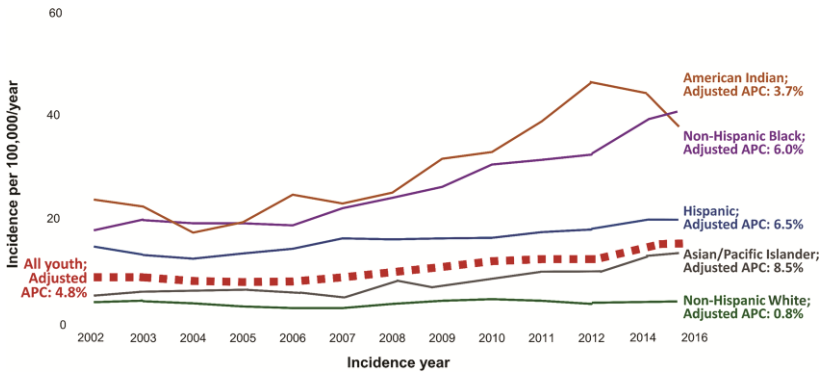
Earlier Menarche



Increased Prevalence of Childhood Obesity



Increased Youth T2D Incidence



Camilla Eckert-Lind et al. *JAMA Pediatrics*, 2020; GBD 2021 Adolescent BMI Collaborators, *The Lancet*, 2025; Perng et al. *Diabetes Care*, 2023

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Sensitive Windows of EDC Exposure May be Contributing to These Trends

- Pregnancy and early childhood are periods of heightened vulnerability to chemical exposures.
- EDCs can disrupt hormonal and metabolic pathways during these windows.
- Early-life exposures may have long-term consequences for maternal and child metabolic health.
  - DOHaD Hypothesis
- Targeting these windows offers opportunity for prevention.

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Why ECHO Is Valuable for PFAS Research

- Large sample size across many cohorts
- Geographic and demographic diversity
- Longitudinal follow-up
- Rich environmental and health data
- Ability to examine **multiple outcomes**

Childhood PFAS Blood Samples

- 1,929 ECHO Families

Maternal Pregnancy PFAS Blood Samples

- 7,151 ECHO Families

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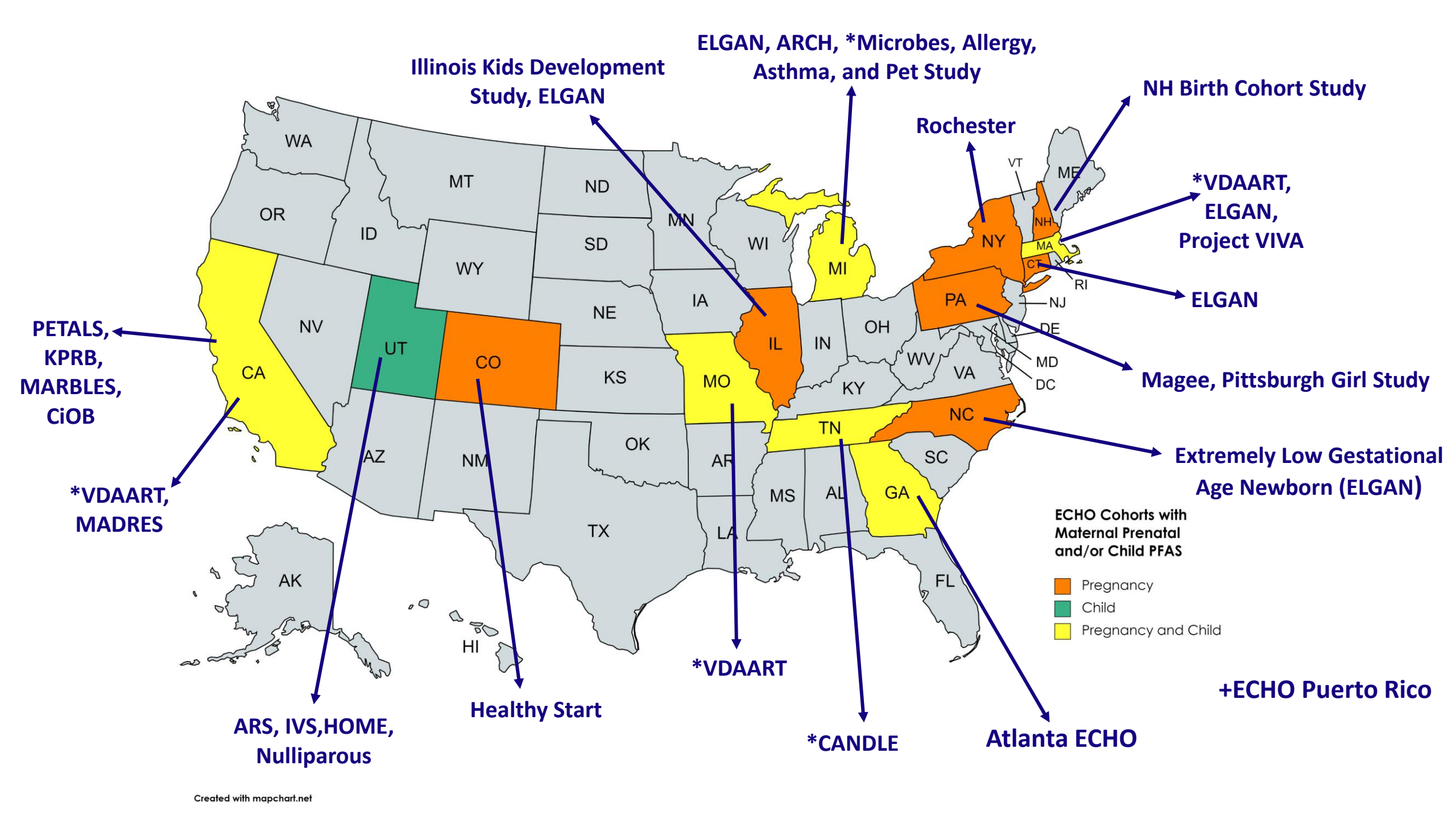
Illinois Kids Development Study, ELGAN
ELGAN, ARCH, *Microbes, Allergy, Asthma, and Pet Study
Rochester
NH Birth Cohort Study
*VDAART, ELGAN, Project VIVA
ELGAN
Magee, Pittsburgh Girl Study
Extremely Low Gestational Age Newborn (ELGAN)
+ECHO Puerto Rico
Atlanta ECHO
*CANDLE
*VDAART
Healthy Start
ARS, IVS,HOME, Nulliparous
*VDAART, MADRES
PETALS, KPRB, MARBLES, CiOB
ECHO Cohorts with Maternal Prenatal and/or Child PFAS
Pregnancy
Child
Pregnancy and Child
WA
OR
CA
ID
NV
MT
WY
UT
AZ
CO
NM
ND
SD
NE
KS
OK
TX
MN
IA
MO
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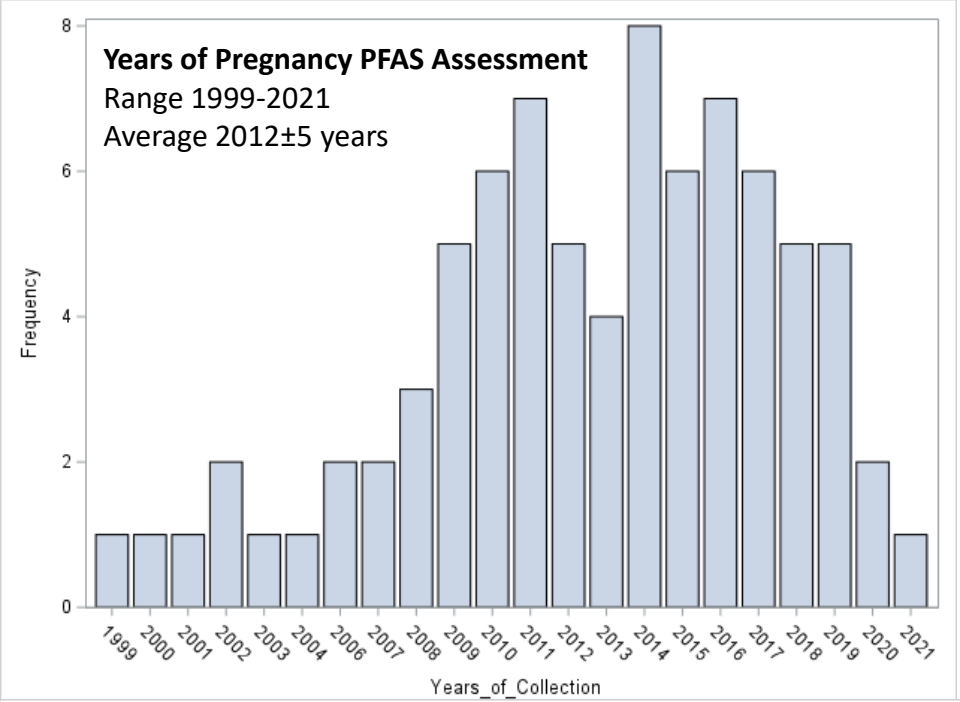
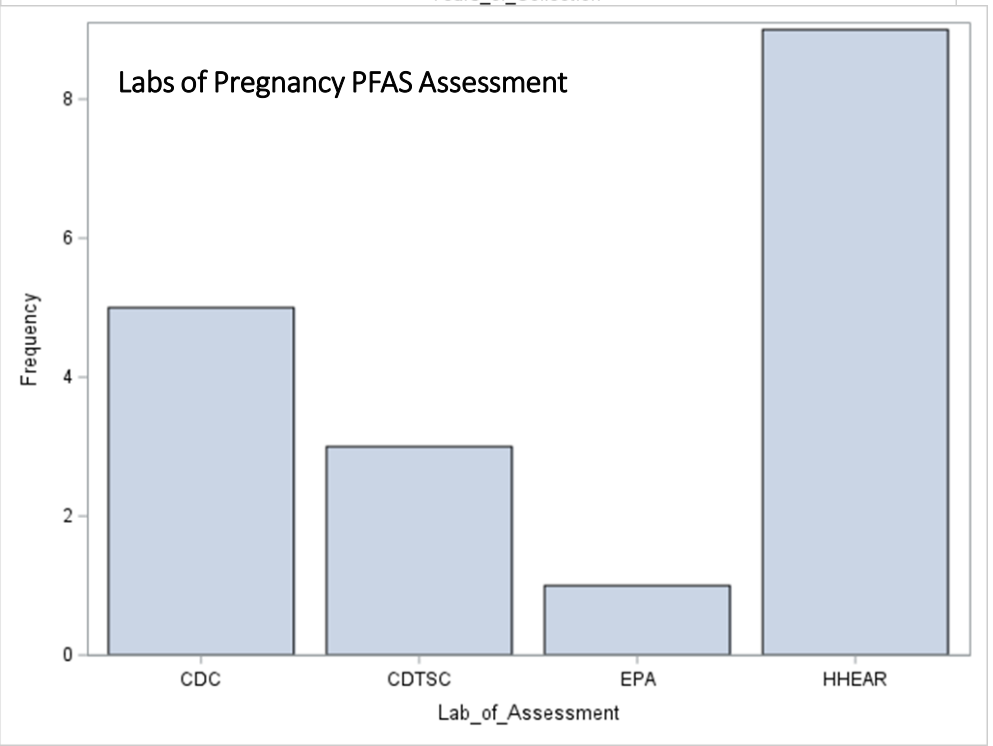
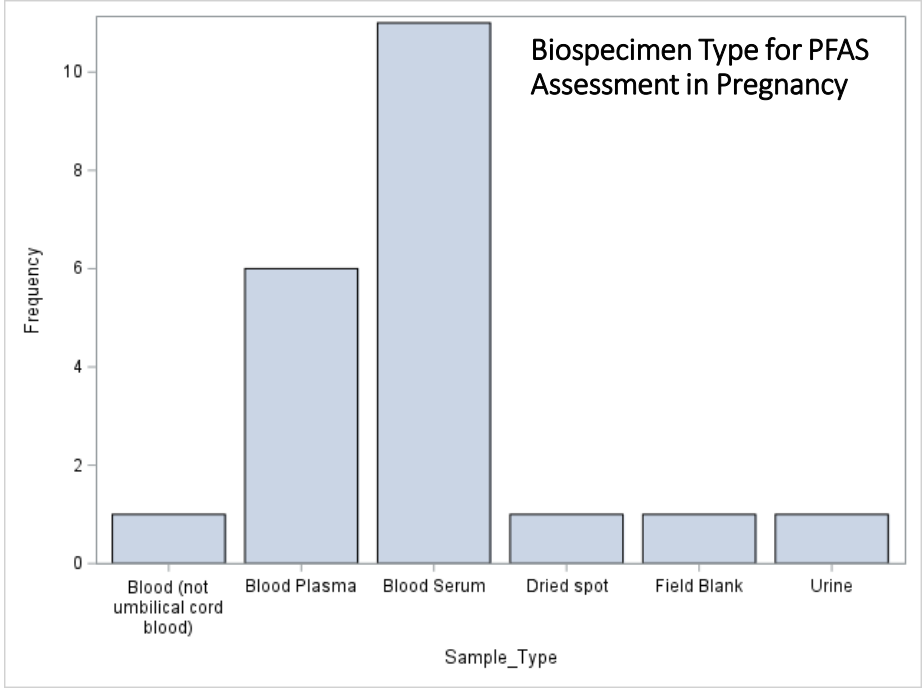
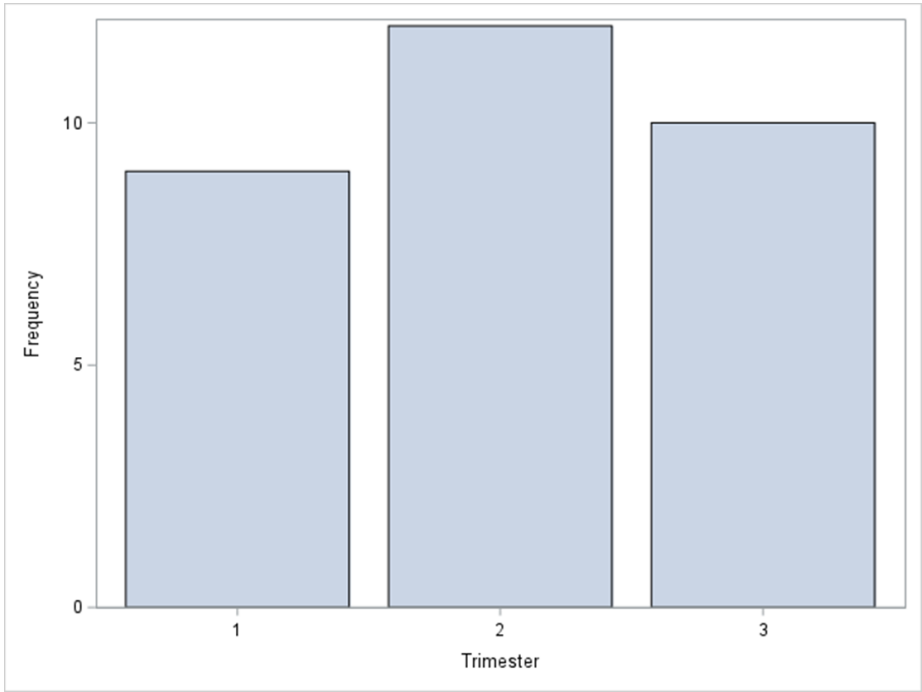

Years of Pregnancy PFAS Assessment
Range 1999-2021
Average 2012±5 years
Frequency
Years_of_Collection
1999
2000
2001
2002
2003
2004
2006
2007
2008
2009
2010
2011
2012
2013
2014
2015
2016
2017
2018
2019
2020
2021


Labs of Pregnancy PFAS Assessment
Frequency
CDC
CDTSC
EPA
HHEAR
Lab_of_Assessment


Biospecimen Type for PFAS Assessment in Pregnancy
Frequency
Blood (not umbilical cord blood)
Blood Plasma
Blood Serum
Dried spot
Field Blank
Urine
Sample_Type


Trimesters of Collection for PFAS Assessment
Frequency
Trimester

Published ECHO Wide Studies Using Prenatal PFAS Samples

Birthweight/Birth outcomes
Negative Associations
PMID: 36920051

Newborn DNA methylation
Associations Detected
PMID: 40401168

Early Childhood BMI/Obesity
Positive Associations
PMID: 37283528

Preeclampsia
Positive Associations in Subgroups
PMID: 41453703

Childhood autism-related outcomes
Modest positive associations
PMID: 36630444

Maternal pregnancy gut microbiome
Positive Associations
PMID: 40311903

Child Behavior
Primarily null associations
PMID: 40914105

Perinatal stress and depression
Mixed Associations
PMID: 41043503

Prenatal Bioactive Lipids
Positive Associations
PMID: 38691655

Childhood Language Development
Null Associations
PMID: 41015090

Ongoing Step 1s and Steps 2s Using PFAS Data

- 21 approved Step 2s ranging from pre-analysis planning to in press
- 3 Step 1s

ECHO PFAS Special Interest Group
Bimonthly meetings
Second Thursday of the month 12:15pm-1pm ET
Chairs: Drs. Ana Rosen Vollmar and Courtney Carignan
Next Meeting: 3/11/2026

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Prenatal PFAS Exposure and Pubertal Development: Insights from the ECHO Consortium

EC0791

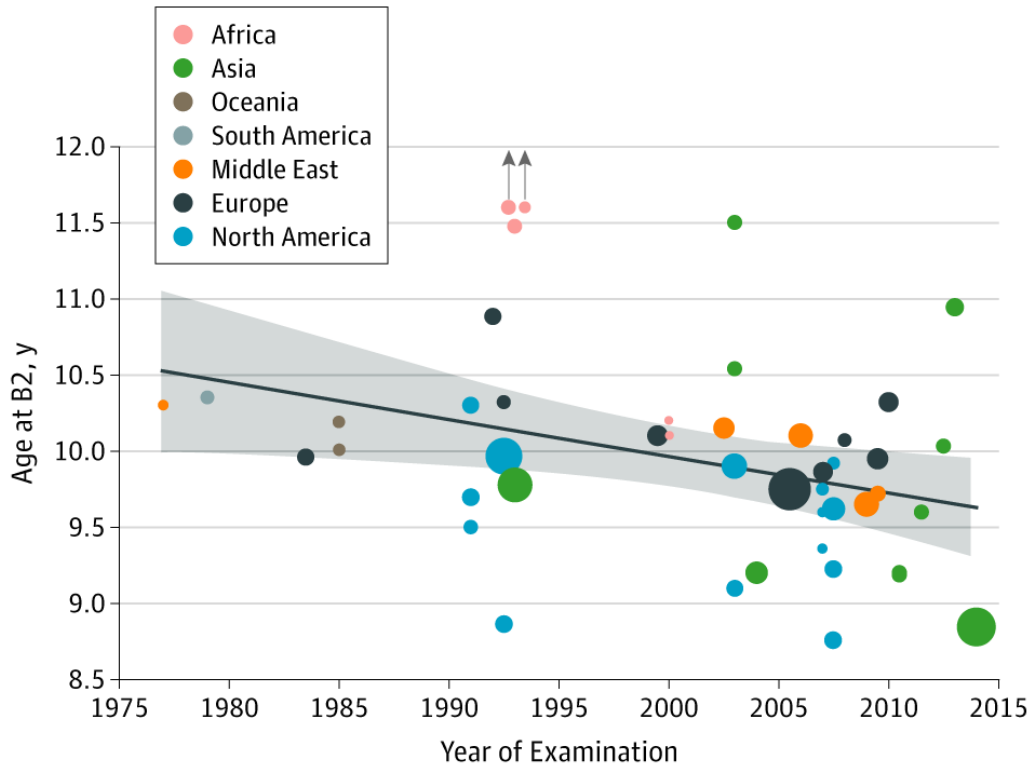
Puberty as a Sensitive Developmental Window

- Puberty is regulated by tightly coordinated endocrine signaling pathways
- Environmental chemicals may influence timing and progression of puberty
- Altered pubertal timing has been linked to:
  - metabolic disease
  - reproductive health outcomes
  - mental health and psychosocial impacts

Identifying environmental contributors is important for long-term population health

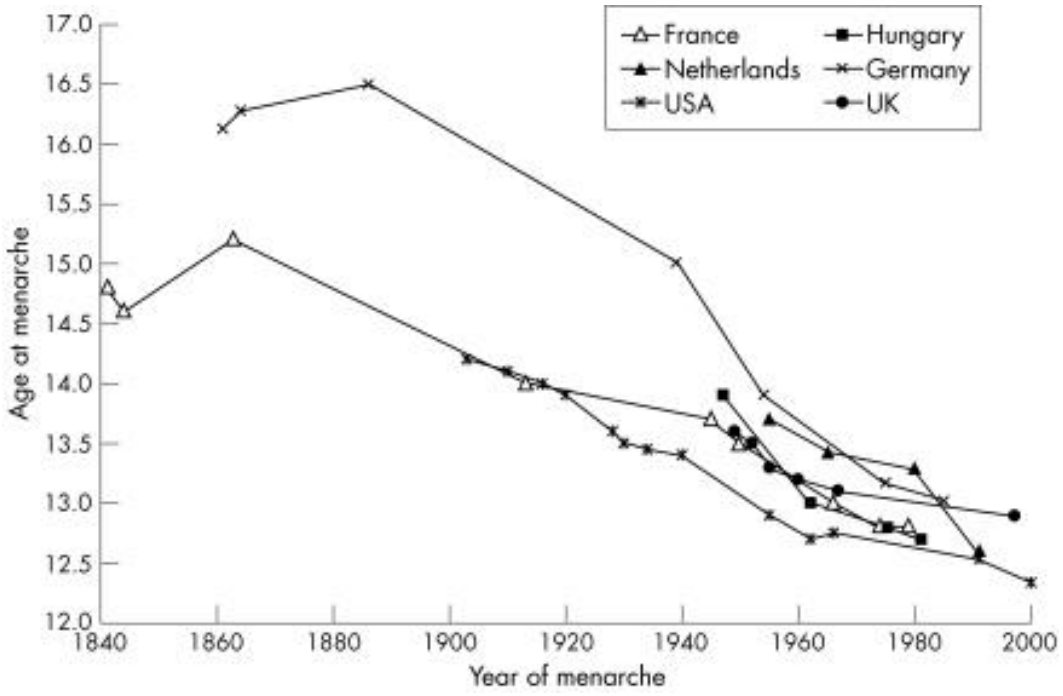
Pubertal Development Has Shifted Toward Younger Ages in Recent Decades

Secular decline in age at onset of breast development (thelarche)



Eckert-Lind et al. *JAMA Pediatrics*. 2020

Secular decline in age at menarche



Bellis et al. *J Epidemiol Community Health*. 2006

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Delayed Puberty Has Potential Health Impacts

1 Physical Growth & Development

- Short stature due to missed growth spurts
- Delayed bone maturation, increased fracture risk

2 Hormonal Imbalances

- Infertility risk from disrupted reproductive hormones
- Underdeveloped secondary sexual characteristics (e.g., breast development, body hair)

3 Psychosocial Impact

- Low self-esteem, anxiety, or depression from social/physical differences
- Peer relationship challenges due to delayed development

4 Metabolic Health Risks

- Possible increased risks of obesity and insulin resistance (evidence still emerging)

Liu et al. 2023; Pinney 2023, Fei et al. 2007; Carwile et al. 2021

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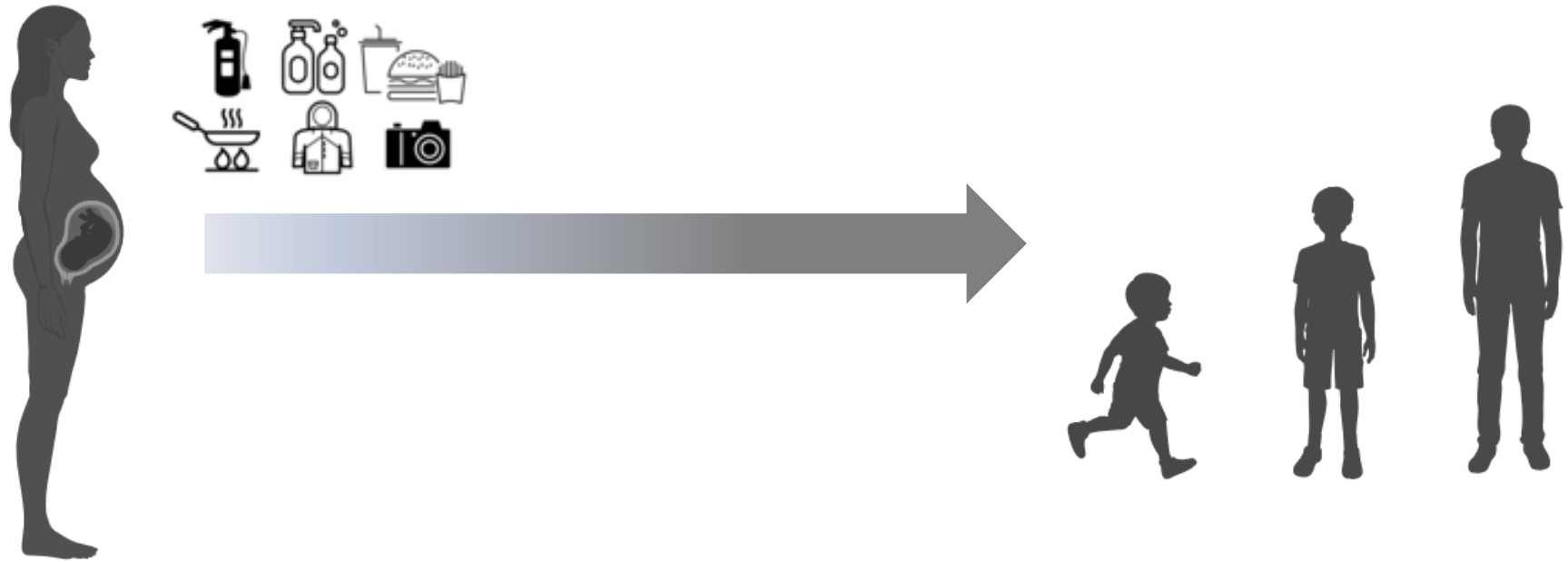
Objective

To evaluate the association between prenatal exposure to PFAS and pubertal onset in boys and girls, including age at menarche in girls, within a geographically and socially diverse cohort



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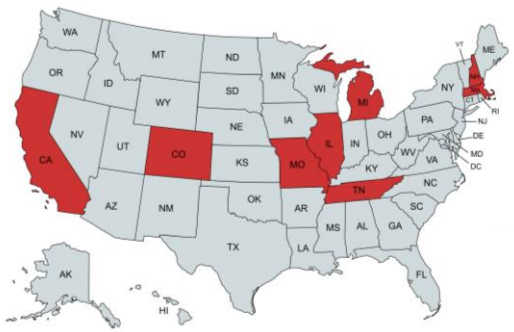
Methods



Adjusted Modified Poisson Regression with Robust Standard Errors and Linear Regression Models

Prenatal PFAS Exposure

- 1,646 mother-child pairs from 8 ECHO sites
- Maternal blood samples collected during pregnancy (20.7±9.6 weeks) 1999-2016
- 16 PFAS analytes measured by LC-MS
  - CDC, HHEAR, and EPA labs
  - Natural log transformed for modeling
  - Imputation: LOD/$\sqrt{2}$

Pubertal Development Scale (PDS)

Puberty Progression Stages:

- Height, Body Hair, Skin Changes
- Breast Growth, Menarche (Females)
- Facial Hair, Voice Deepening (Males)
- Continuous score dichotomized as pre-pubertal vs. pubertal using first available collection
- 857 girls, 789 boys

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Pubertal Development Scale (PDS) Definition and Interpretation

PDS

- Categorized as prepubertal vs. pubertal
- RR >1: higher likelihood of being pubertal at the time of assessment, suggesting potential earlier pubertal onset
- RR <1: higher likelihood of being prepubertal, suggesting potential delayed pubertal onset
- Sensitivity analysis ages 7–11 and ages 11+ years
- Models adjusted for age at assessment in years

Age at Menarche

- Measured in years
- Question from the PDS, only in girls

Pubertal Development Scale (PDS) At First Assessment	Overall N = 1,646
Child Age of Assessment Median (Q1, Q3)	11.6 (9.6, 17.1)
Total PDS Score Median (Q1, Q3)	2.2 (1.5, 3.5)
PDS at Assessment **Prepubertal (PDS=1)** **Pubertal (PDS>1)**	 **145 (9.3%)** **1,504 (90.7%)**
PDS Age At Assessment (categories) Ages 6.9-8.9 Ages 9.0-10.9 Ages 11.0-12.9 Ages 13 and above	 287 (17.4%) 332 (20.2%) 470 (28.6%) 557 (33.8%)
Age at menarche (N=159), years	**10.7 (1.1)**

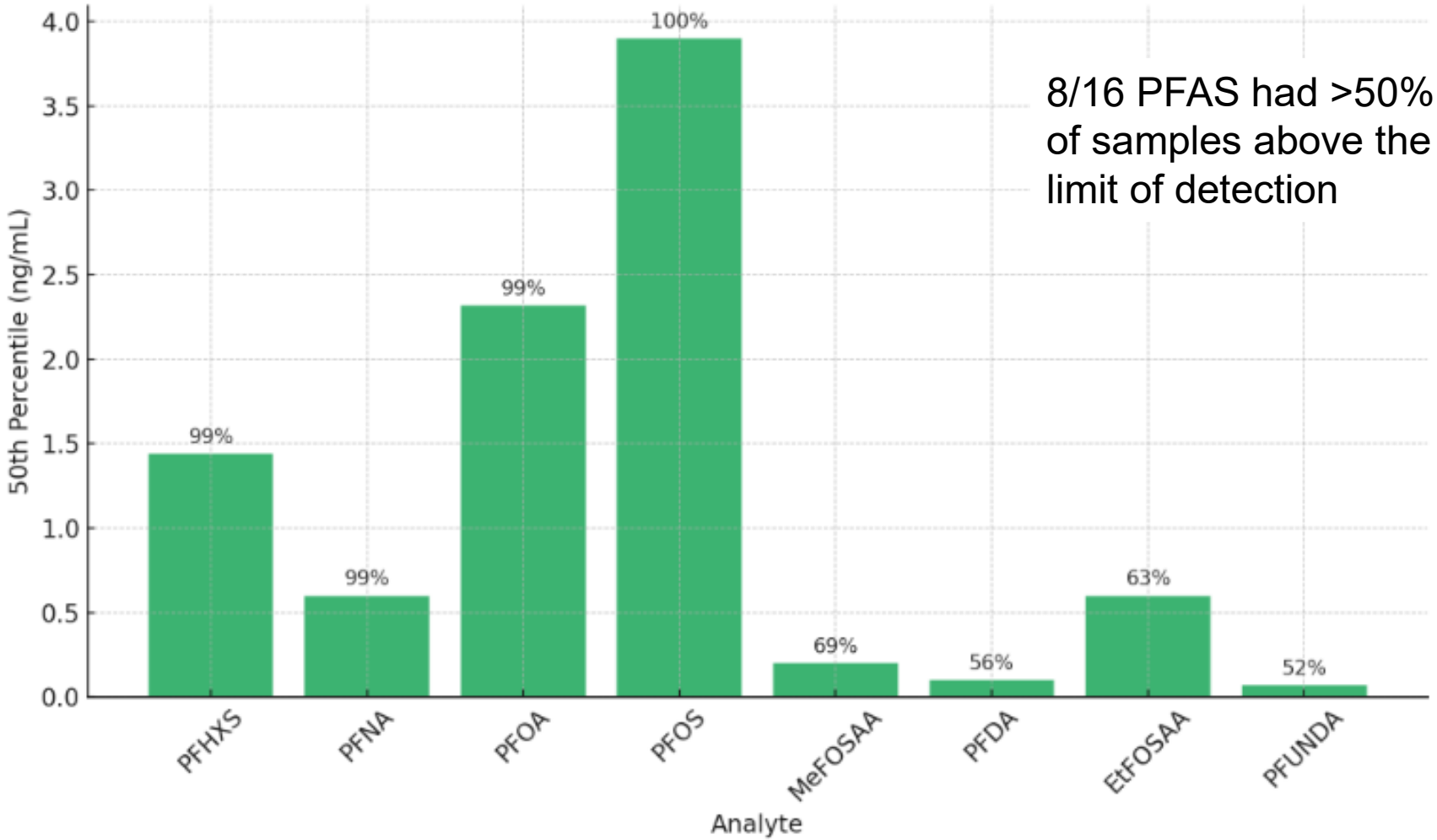
Note: *Characteristics were consistent with the full sample when stratified by sex.*

Maternal Demographics

Characteristics	Overall N = 1,646
Maternal Age, years	30.0 ± 5.8
Maternal race-ethnicity	
Hispanic	184 (11.2%)
non-Hispanic Asian	58 (3.5%)
non-Hispanic Black	355 (21.6%)
non-Hispanic other	67 (4.1%)
non-Hispanic White	979 (59.6%)
Maternal Education	
Highschool diploma or below	362 (22.5%)
Some college, Bachelor's	788 (48.9%)
Master's degree or above	461 (28.6%)
Pre-pregnancy BMI, kg/m^2	25.8 ± 6.7
Smoking during pregnancy	
Yes	87 (5.6%)

Note: *Demographics were consistent with the full sample when stratified by sex (boys and girls).*

Median PFAS Concentrations and Detection Frequencies

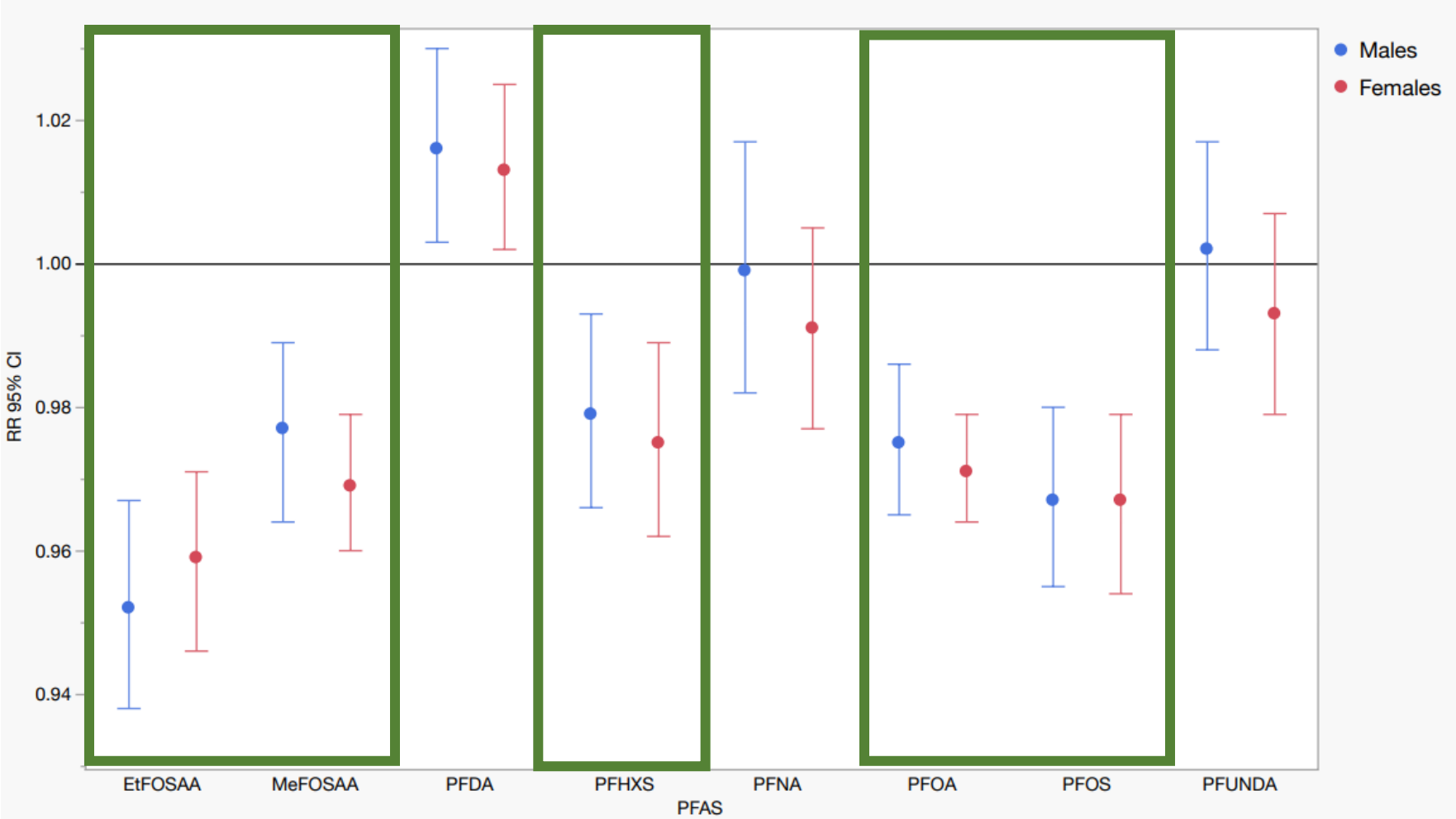


8/16 PFAS had >50% of samples above the limit of detection

Prenatal PFAS Exposure and Pubertal Development at Time of Assessment

RR >1: Greater likelihood of being pubertal at assessment → potential earlier onset

RR <1: Greater likelihood of being prepubertal at assessment → potential delayed onset



Models adjusted for maternal age at delivery, maternal education level, pre-pregnancy BMI, smoking during pregnancy, parity, child's age at PDS assessment, SVI score, ECHO site.

Note: per log unit increase of PFAS exposure

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Prenatal PFAS Exposure and Pubertal Development at Time of Assessment

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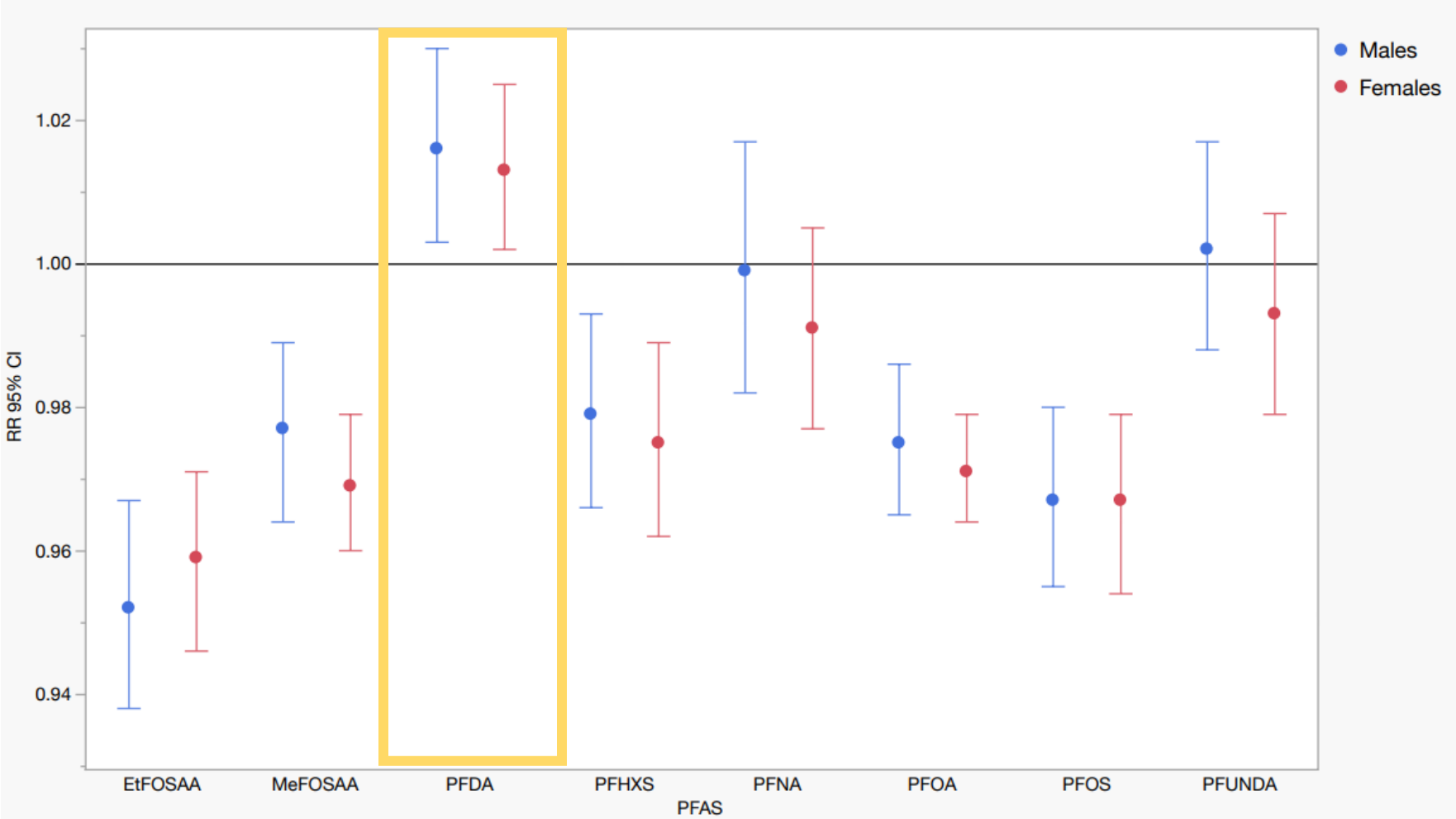

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Note: per log unit increase of PFAS exposure

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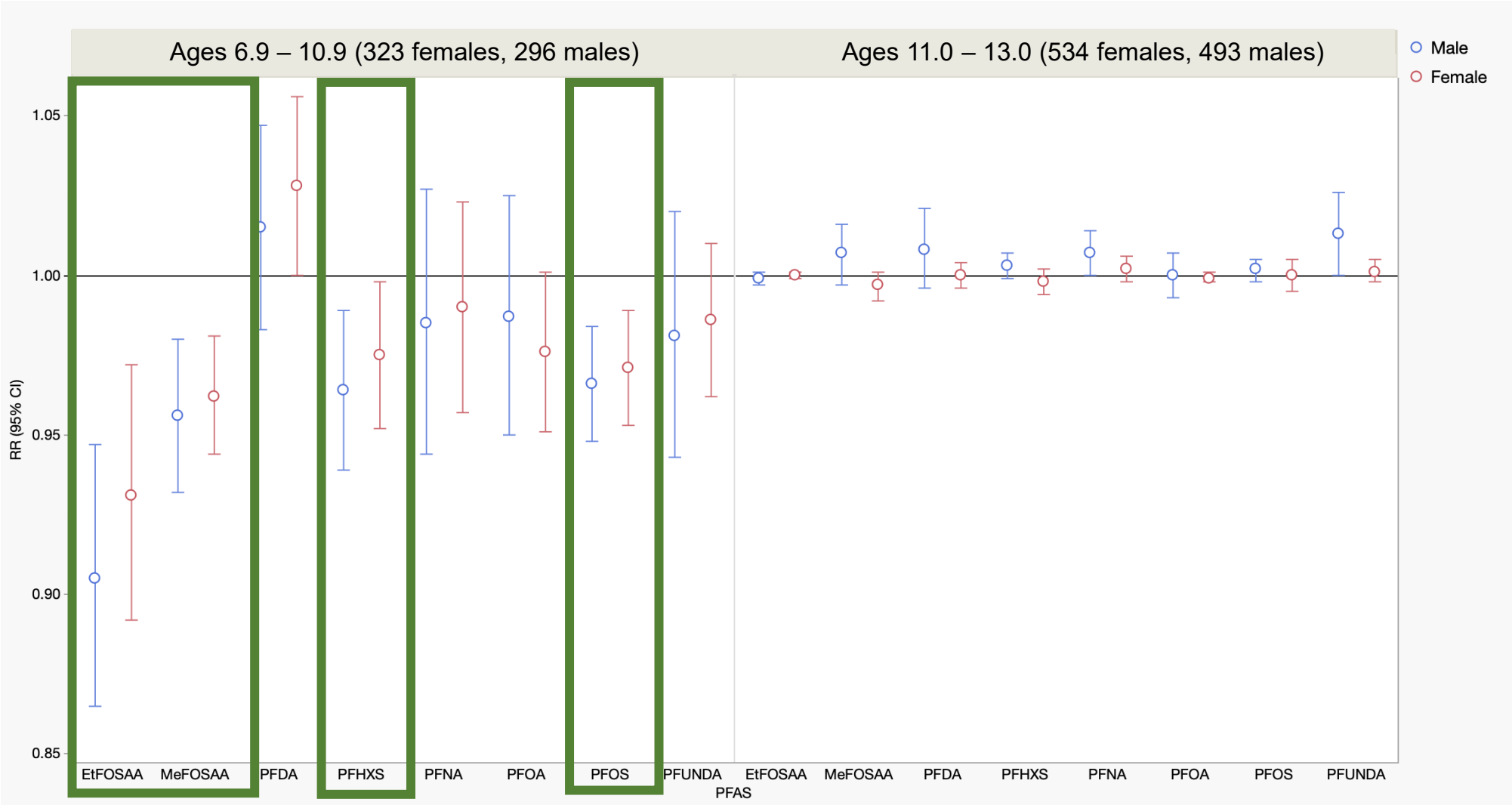
Results Stratified by Age at PDS Assessment (<11 vs. ≥11)

RR >1: Greater likelihood of being pubertal at assessment → potential earlier onset

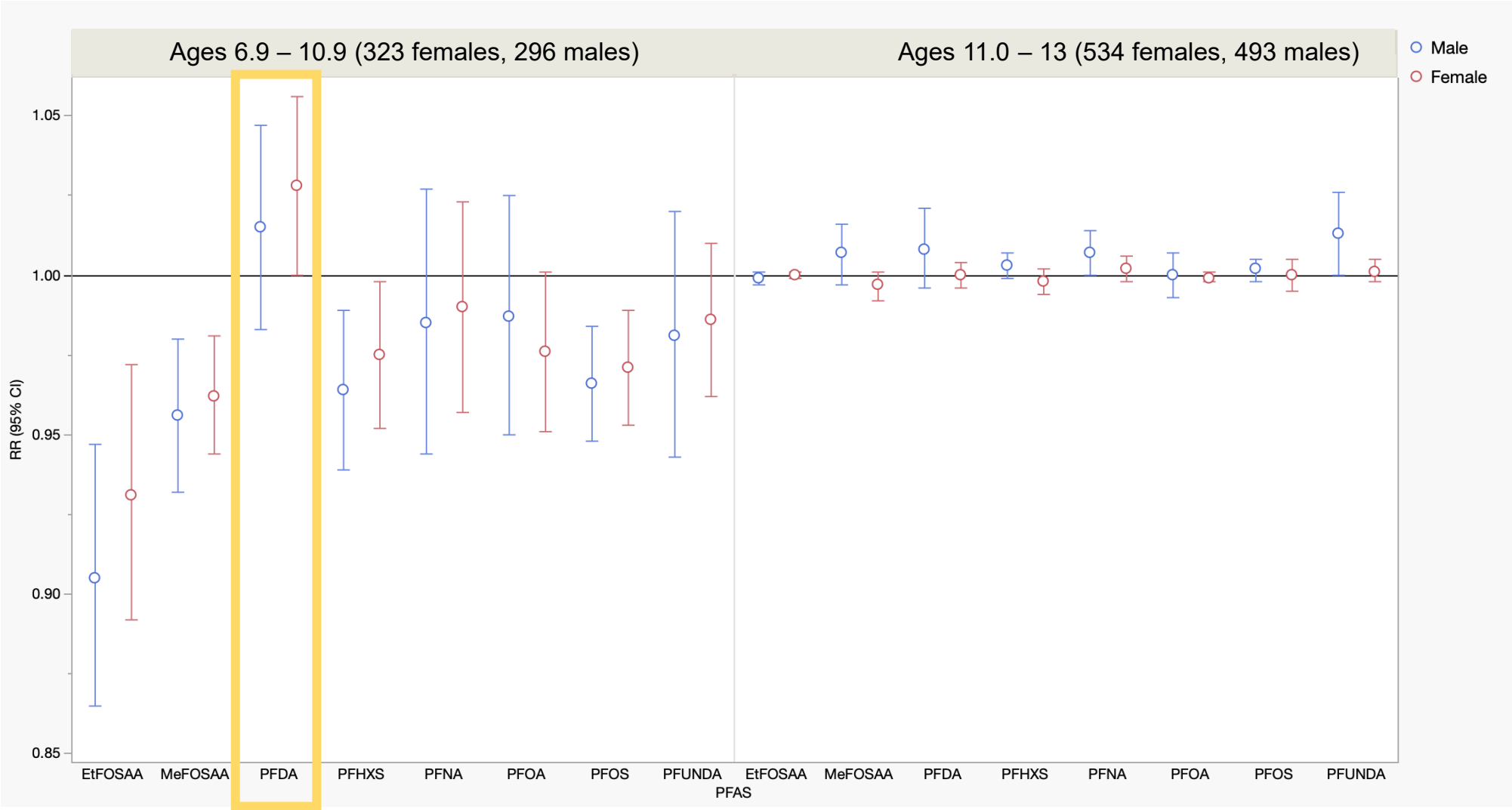
RR <1: Greater likelihood of being prepubertal at assessment → potential delayed onset



Results Stratified by Age at PDS Assessment (<11 vs. ≥11)

RR >1: Greater likelihood of being pubertal at assessment → potential earlier onset

RR <1: Greater likelihood of being prepubertal at assessment → potential delayed onset



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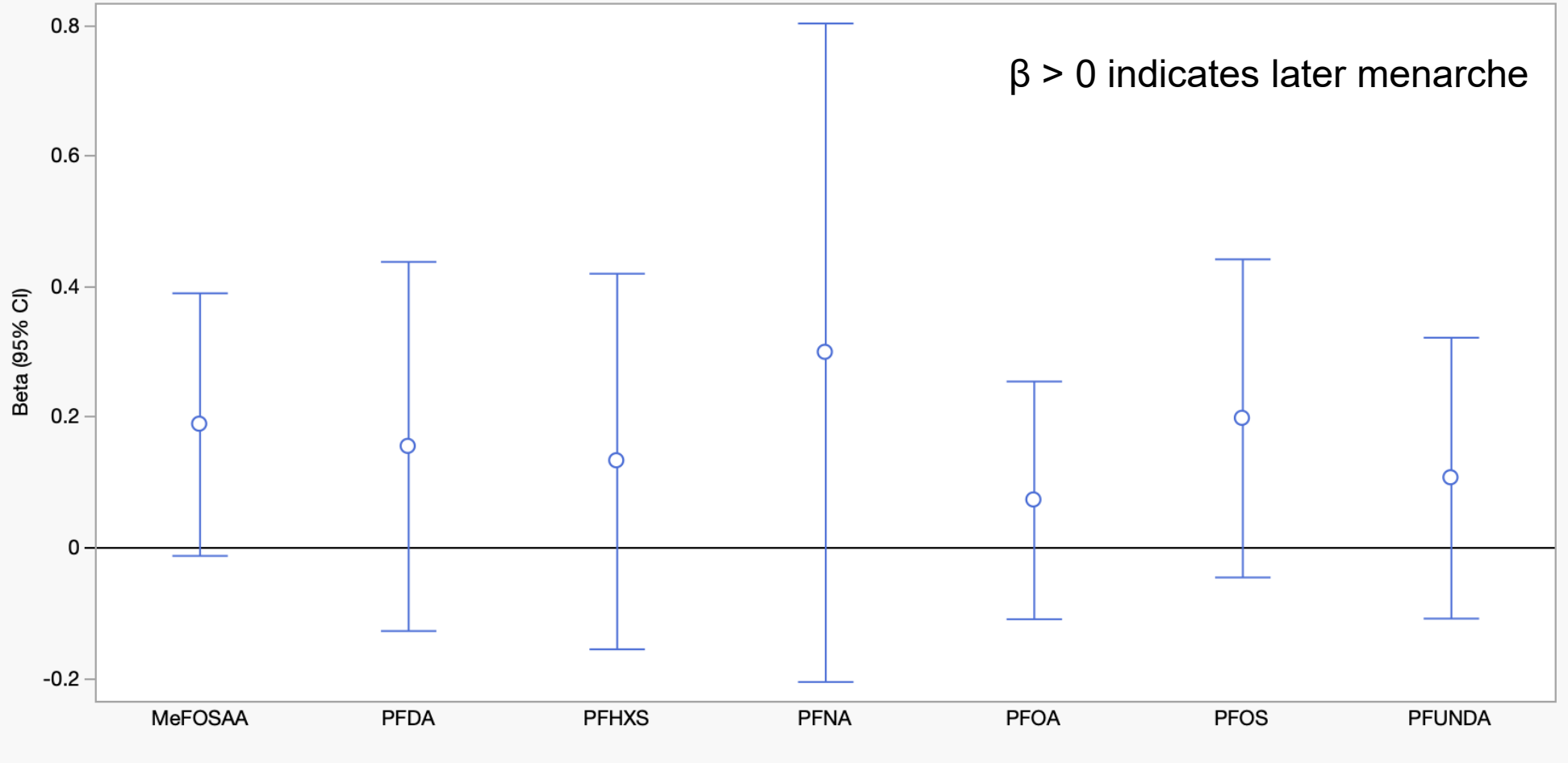
Prenatal PFAS Exposure and Age at Menarche in Girls (N=159)



Models adjusted for: maternal age, maternal education level (college vs non-college), smoking during pregnancy (Yes vs no), parity (0 vs >=1), SVI score, ECHO site.

Note: per log unit increase in PFAS exposure.

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Conclusions

- **Delayed Puberty:** Prenatal exposure to EtFOSAA, MeFOSAA, PFHxS, PFOA, and PFOS was associated with a lower likelihood of being pubertal at assessment.
- **Earlier Puberty:** PFDA exposure was associated with a higher likelihood of being pubertal at assessment, but the association was attenuated when restricting to those <11 years of age.
- **Menarche Timing:** No significant associations with age at menarche were observed, likely due to limited sample size, but trends suggested a later age.
- **Biological Plausibility:** Prenatal PFAS exposure may disrupt the hypothalamic-pituitary-gonadal (HPG) axis and sex hormone production by interfering with endocrine signaling and hormone receptor activity, leading to delayed puberty.
  - Consistent direction observed in girls from other studies Pinney et al. 2023; Liu et al. 2023, Carwile et al. 2021.

Strengths and Limitations

Strengths:

- Large, geographically and socially diverse cohort (ECHO)
- Harmonized pubertal outcomes across multiple cohorts
- Evaluation of multiple individual PFAS compounds
- Sensitivity analysis stratified by age groups (7–11 vs. ≥11 years)

Limitations:

- Lack of longitudinal and time-to-event data limits causal inference

Next Steps:

- Conduct PFAS mixture analysis
- Explore mediation by child BMI prior to PDS assessment
- Extend analysis to include childhood PFAS levels

Remaining Challenges in PFAS Research

- Thousands of PFAS compounds exist
- Most PFAS remain **poorly studied**
- Exposure often occurs as **mixtures**
- Limited data on **newer replacement PFAS**

Methodologic Challenges:

- Exposure mixtures are difficult to analyze
- Variability in exposure measurement across studies
- Limited long-term follow-up in many cohorts
- Mechanistic pathways are still not fully understood

Opportunities for PFAS Research in ECHO

- Utilizing childhood samples, all currently published work in ECHO uses prenatal samples
- Expanding PFAS biomonitoring
- Studying mixture effects
- Evaluating trends over time and by U.S. region
- Integrating biological mechanisms
- Evaluating long-term child health outcomes

BATF will solve many of the previous challenges for PFAS

- Propose to measure PFAS in the earliest available blood sample from pregnancy. These will be calculated in Population 1, approximately 6500 pregnant people in the subcohort, and an additional 525 pregnant people for the autism cases/neurodevelopment concerns and controls
- Will measure **57 PFAS Compounds**
- Same study protocol (ECHO SOP), biospecimen matrix, and lab of assessment

Acknowledgments

Writing Team

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