Organophosphate pesticides: Potential mechanisms & outcomes of prenatal exposure

Evidence from the New York University Children's Health and Environment Study (NYU CHES)

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Collaborative for Health & Environment (CHE) webinar | May 19, 2026

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Prenatal Organophosphate Pesticide Exposure and Targeted Maternal Pregnancy Metabolomic Profiles in the NYU CHES Cohort

Haleigh Cavalier, PhD, MPH

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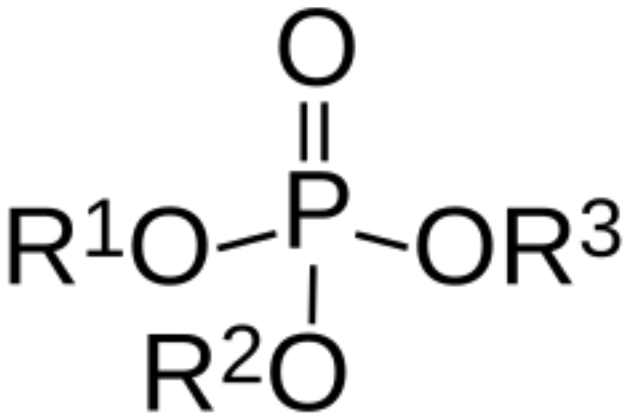
Research Goals

- Understand relationship between **prenatal organophosphate (OP) pesticide exposure and maternal/child health outcomes**
- **Probe biologically plausible mechanisms** proposed from animal and cell studies in humans using maternal metabolomics data

Why OP pesticides?

- Human exposure is **ubiquitous**
- OP pesticides are **known neurotoxicants**
- OP pesticides can induce **inflammation, oxidative stress, and hormone disruption,** while affecting **mitochondrial energy, lipid, and glucose metabolisms**
- Evidence in animals and humans that OP pesticides are associated with various adverse health outcomes
  - neurological deficits
  - reproductive health (reduced semen quality, hormone regulation)
  - chronic diseases (metabolic syndrome, certain cancers)

Organophosphate Pesticides



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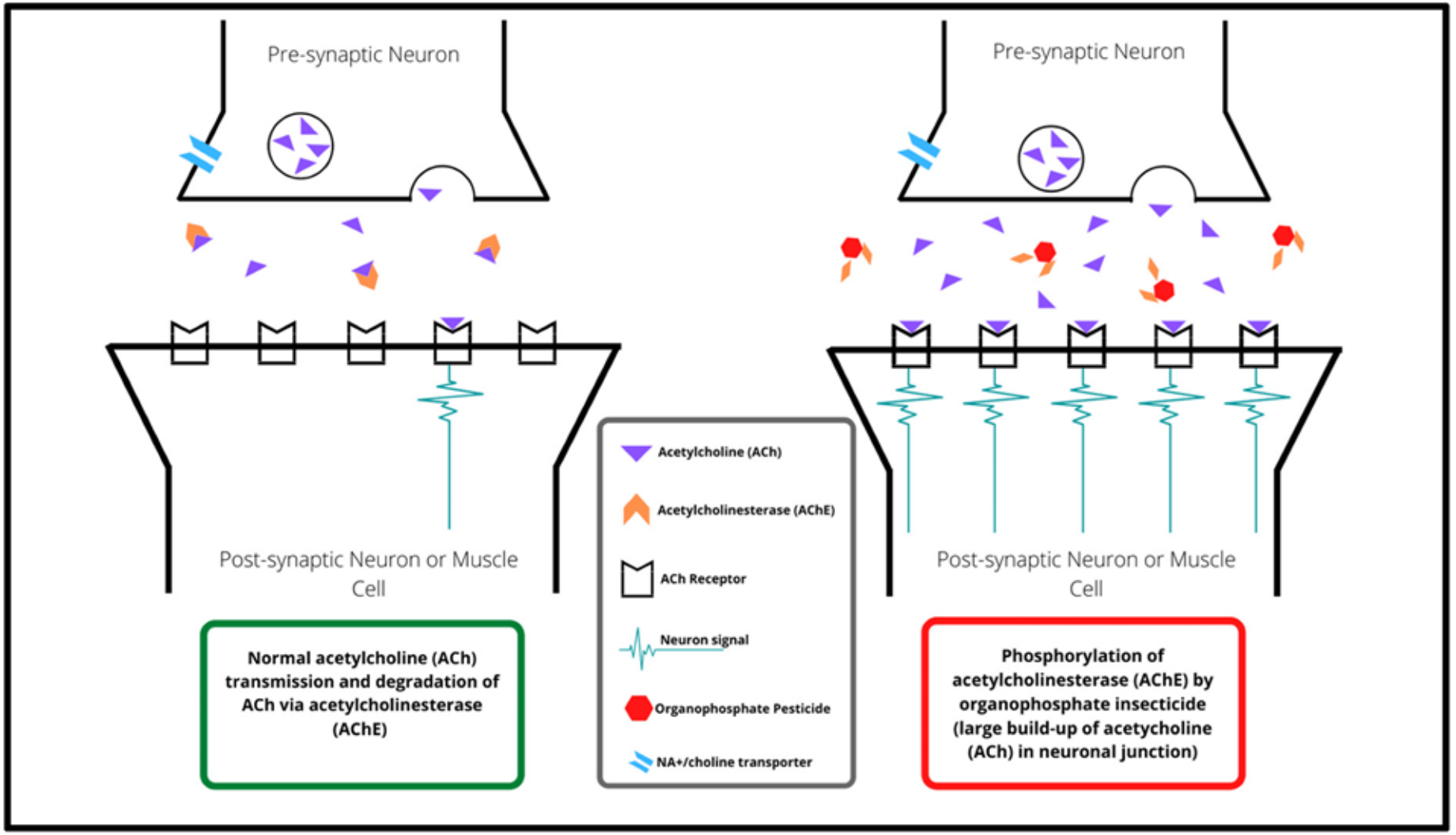

Neylon, 2022 doi: 10.3390/jdb10040049

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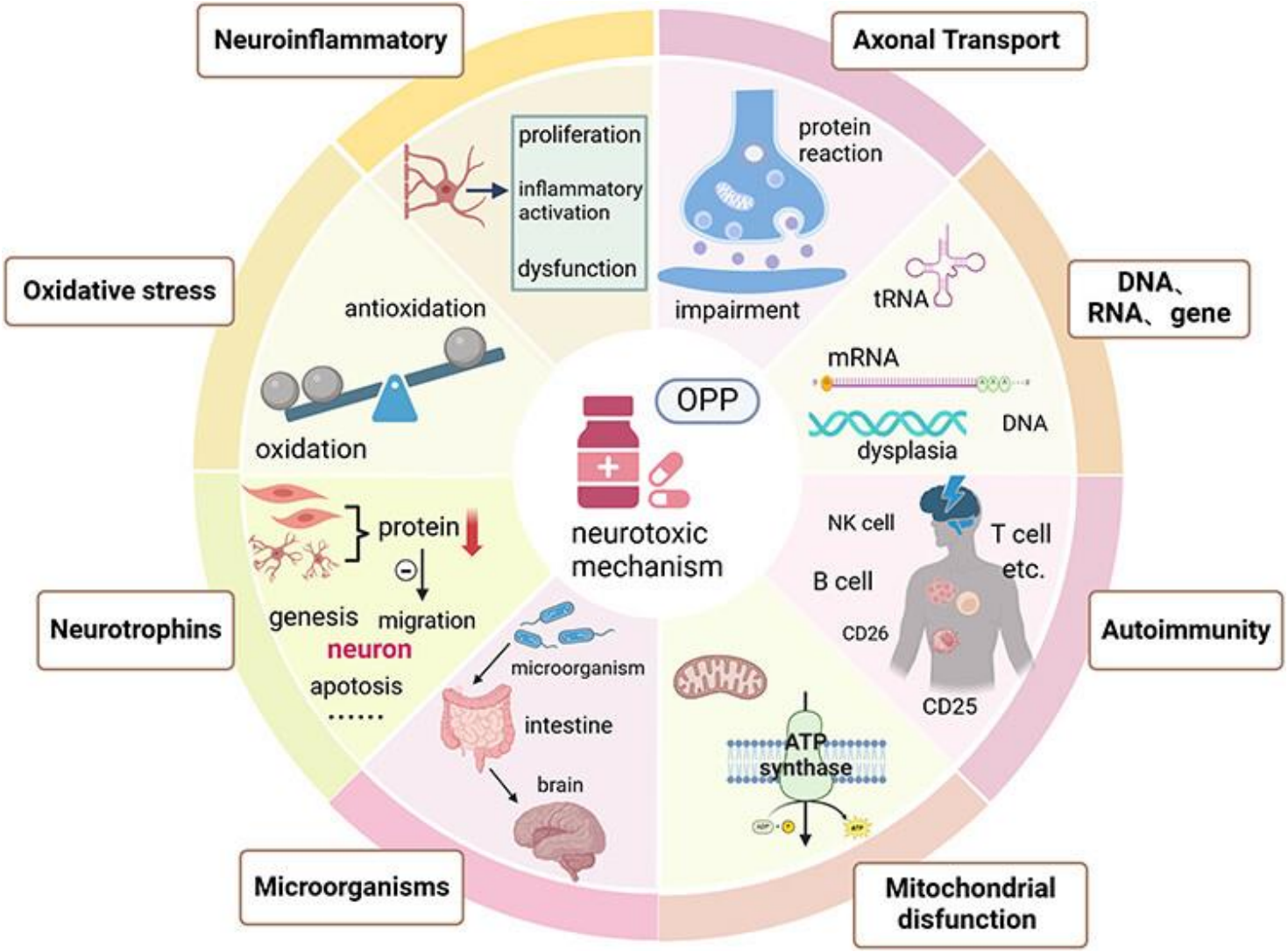

Chen Y, 2024 https://doi.org/10.2147/NDT.S479757

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Fetal Development

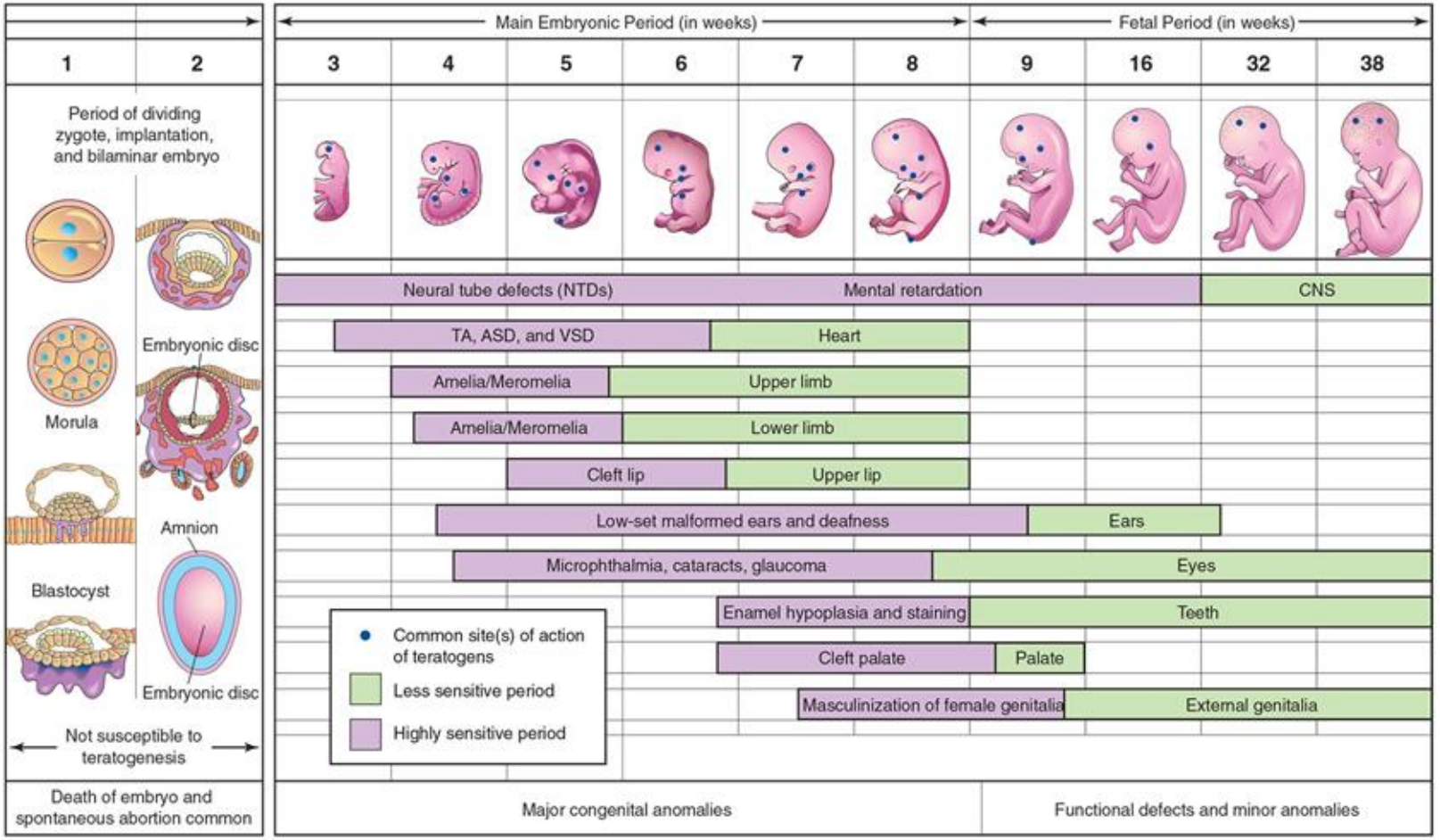

Image from: The Developing Human: Clinically Oriented Embryology (Revised) Clinically Oriented Embryology 10th Edition, Keith Moore, TVN Persaud, Mark Torchia Published by Saunders Copyright © 2016

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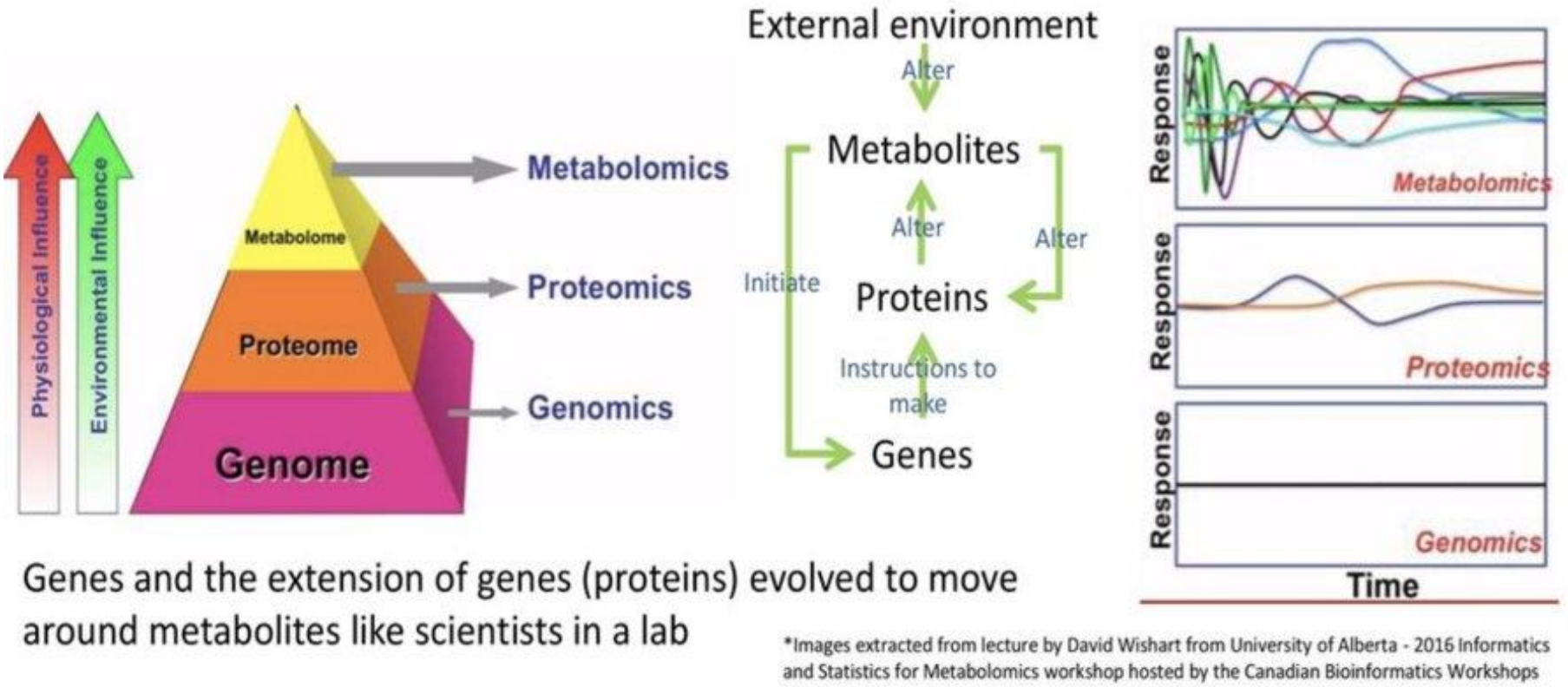
The metabolome in environmental epidemiology



Genes and the extension of genes (proteins) evolved to move around metabolites like scientists in a lab

*Images extracted from lecture by David Wishart from University of Alberta - 2016 Informatics and Statistics for Metabolomics workshop hosted by the Canadian Bioinformatics Workshops

National Academies of Sciences, Engineering, and Medicine. 2016. https://doi.org/10.17226/23414.

Kalia, V. Lecture: Biomarkers in Environmental Health; Metabolomics, 2019. Columbia University Mailman School of Public Health, Dept of Environmental Health Sciences

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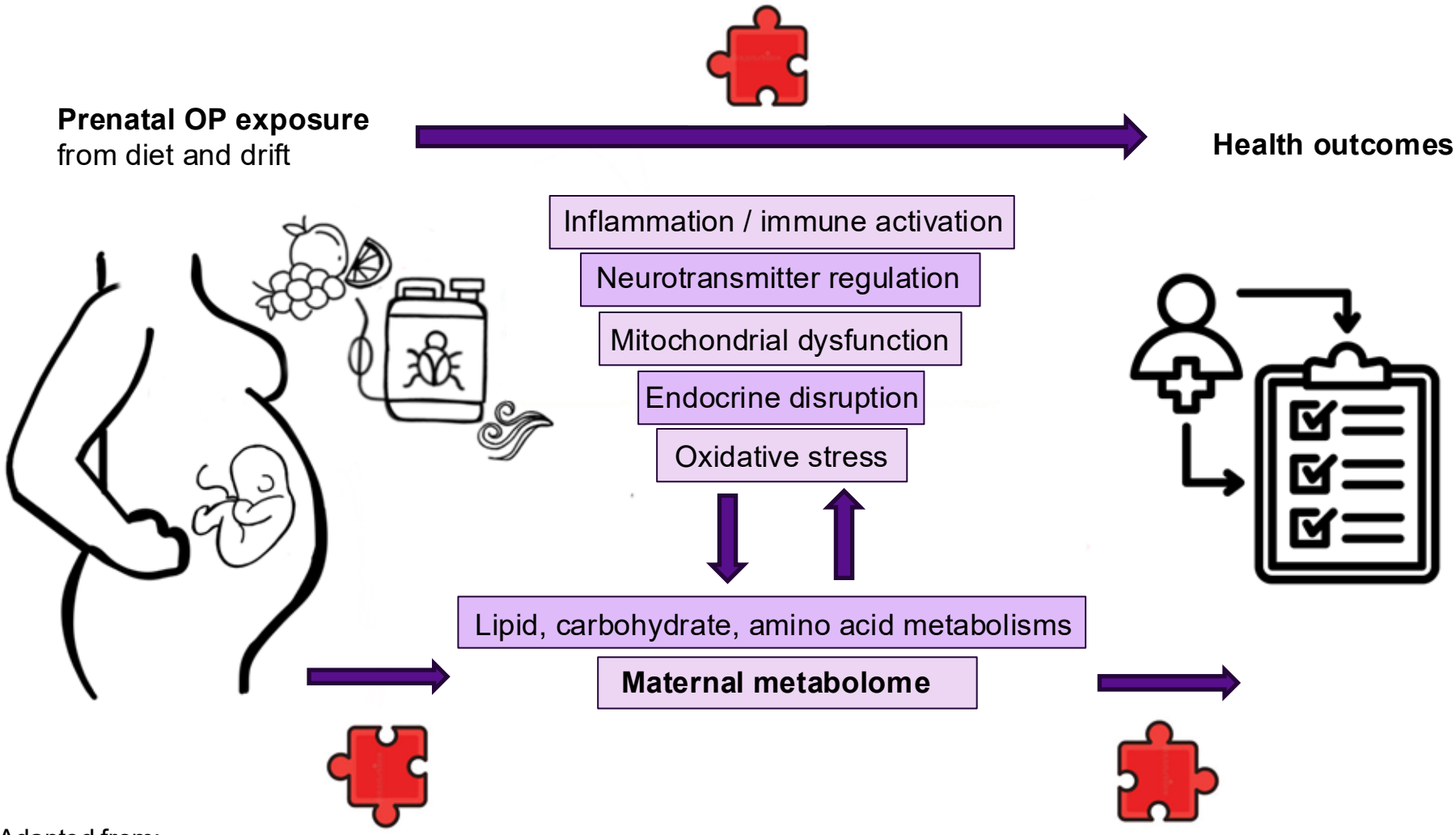
Research Conceptual Model



Adapted from:
Love, 2024, https:doi.org/10.1186/s12916-024-03617-3 and Hertz-Picciotto I, 2018, https://doi.org/10.1002/aur.1938

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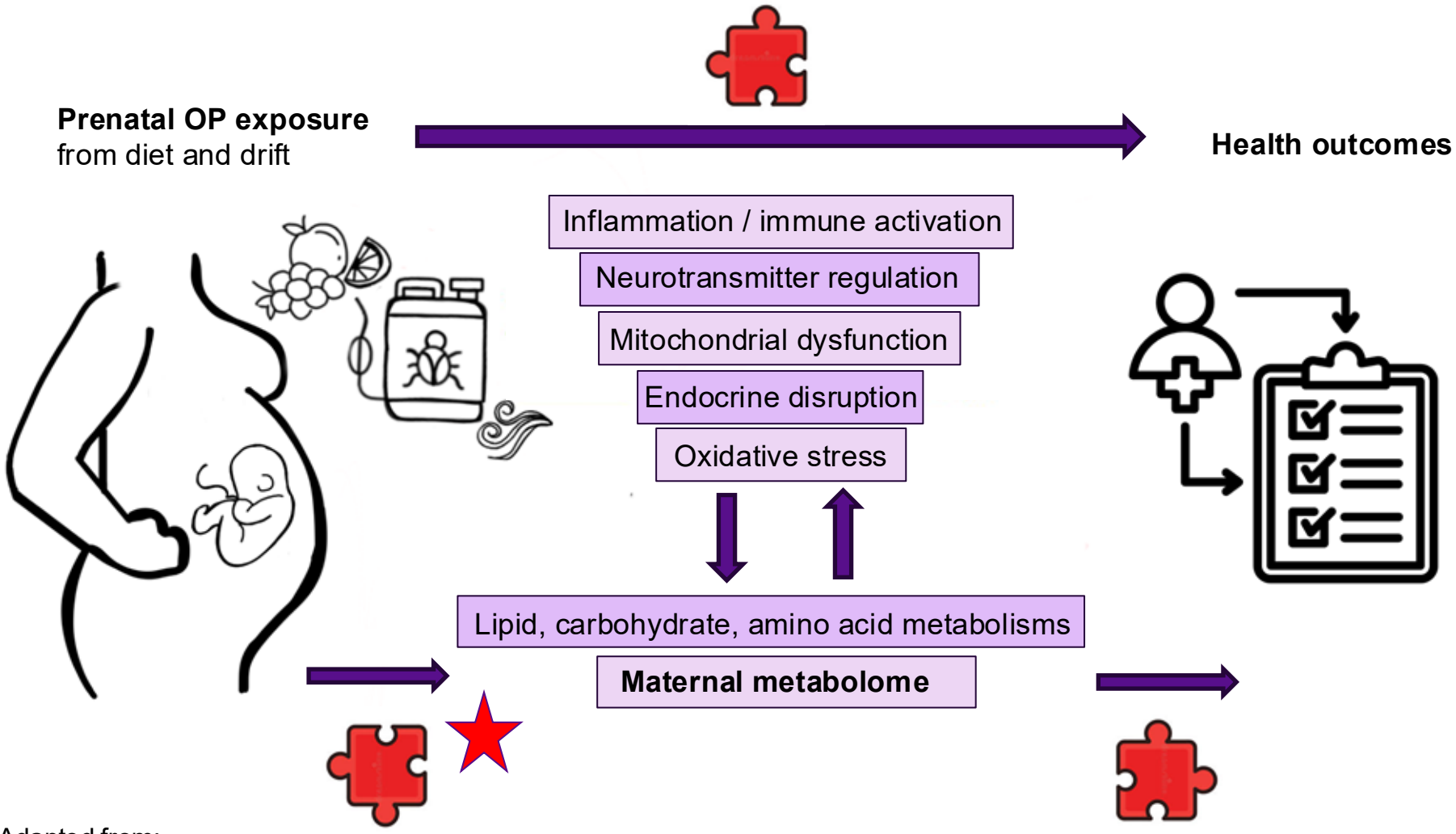

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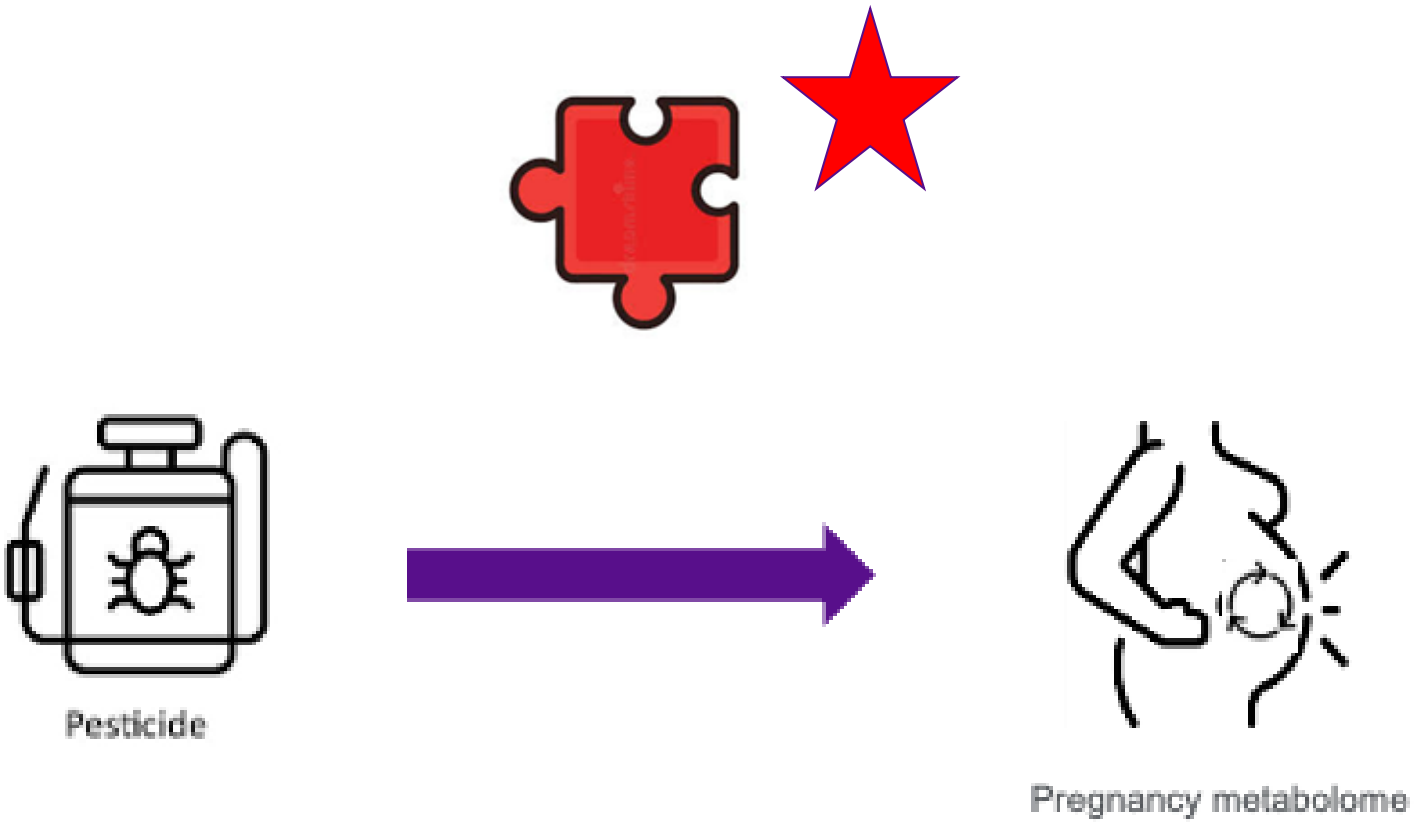

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ECHO
Environmental influences on Child Health Outcomes
A program supported by the NIH

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NYU CHES
Children's Health and Environment Study

- Ongoing, **prospective longitudinal cohort study**
- Recruits pregnant people from NYU Langone Hospital-Manhattan, Bellevue Hospital, and NYU Langone Hospital-Brooklyn
- Robust **biospecimen and questionnaire data** are collected during prenatal care visits at three timepoints during pregnancy
- **early pregnancy** (<18 gestational weeks, $T_{1,}$), **mid-pregnancy** (18–25 gestational weeks, T_2), **and late pregnancy** (>25 gestational weeks, T_3
- Follow up of children until age 7 (cycle I) or age 14 (cycle II)
- Part of the ECHO program

Methodology

Exposure: Organophosphate pesticides

- Sums of dialkyl (∑DAP) diethyl (∑DE), and dimethyl (∑DM) phosphate metabolites
- Measured at three timepoints

Outcome: Targeted metabolome

- 188 metabolites measured in urine
- Biocrates AbsoluteIDQ P180 kit
- Measured at three timepoints

Participants:

Overlap of CHES participants with DAP and metabolome measurements: (n = 890)

T_1 = 780

T_2 = 691

T_3 = 768

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Biocrates Absolute IDQ p180 kit
188 Metabolites and 44 Metabolic Indicators

Metabolite Class	#	Pathway indicator Examples
Amino Acids	21	**Neurotransmitter signaling**: (glutamate, tryptophan, serotonin) **Mitochondrial dysfunction** (serine)
Biogenic Amines	21	**Oxidative stress:** (methionine sulfoxide/methionine ratio, alpha-aminoadipic acid) **Neurotransmitter signaling:** (serotonin, dopamine)
Acylcarnitines	40	**Mitochondrial Dysfunction** (acylcarnitine panels, indicators of disturbed fatty acid oxidation)
Glycerophospholipids: Lysophosphatidylcholines (LPCs) Phosphatidylcholines (PCs)	90	**Inflammation** (LPC/PC ratio, LPC disruption) **Mitochondrial Dysfunction** (LPC)
Sphingolipids	15	**Inflammation** (disruption of sphingolipid homeostasis)
Hexoses (D-Glucose)	1	**Carbohydrate metabolism**

+ 44 Metabolic Indicators – sums or ratios of other metabolites with biological interpretation

Timepoint specific regression models based on detection percentages and data quality

188 metabolites and 44 metabolic indicators (MI) measured for all three timepoints

10 metabolites and 12 MI excluded in all timepoints due to high CVs

Detected in 80% of samples
T1 = 57, T2 = 58, T3 = 58
modeled as continuous variables

Detected in 10% - 79.9% of samples
T1 = 94, T2 = 91, T3 = 95 were modeled as binary variables **(detected/not detected)**

Detected in <10% of samples
T1 = 59, T2 = 61, T3 = 57
excluded

False Discovery Rate (FDR) correction of p-values to account for multiple comparisons

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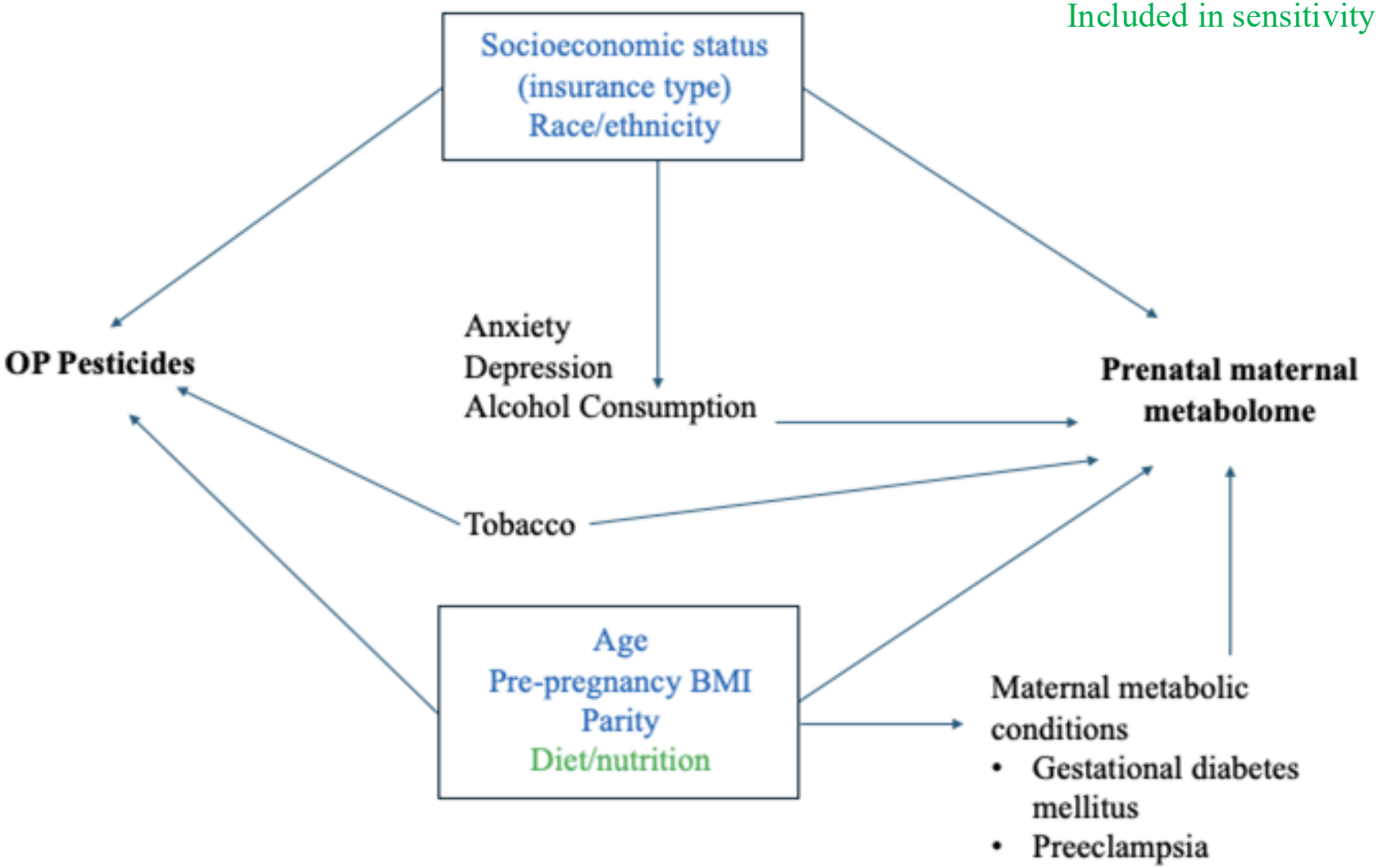
Covariates

Included in adjusted models

Included in sensitivity analyses



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	High Exposure >13.78 ng/mL (n = 445)	Low Exposure < 13.78 ng/mL (n = 445)
Age Mean (SD)	32.0 (5.4)	31.2 (5.8)
BMI Mean (SD)	25.5 (5.5)	27.0 (5.8)
Race/ethnicity		
Hispanic	195 (43.9%)	270 (60.9%)
Non-Hispanic White	170 (38.3%)	106 (23.9%)
Non-Hispanic Black	18 (4.1%)	33 (7.4%)
Asian	42 (9.5%)	28 (6.3%)
Other/Multiple	19 (4.3%)	26 (1.4%)
Parity		
Nulliparous	230 (51.8%)	205 (46.3%)
Parous	214 (48.2%)	238 (53.7%)
Insurance Type		
Public	227 (51.0%)	264 (59.3%)
Private	218 (49.0%)	181 (40.7%)
Gestational Diabetes		
No	387 (87.0%)	378 (84.9%)
Yes	58 (13.0%)	67 (15.1%)
Education Status		
High school or less	144 (33.7%)	171 (39.3%)
Some college	62 (14.5%)	79 (18.1%)
Bachelor's degree	102 (23.9%)	98 (22.5%)
Post-graduate degree	119 (27.9%)	87 (20.0%)

Demographic characteristics by exposure level

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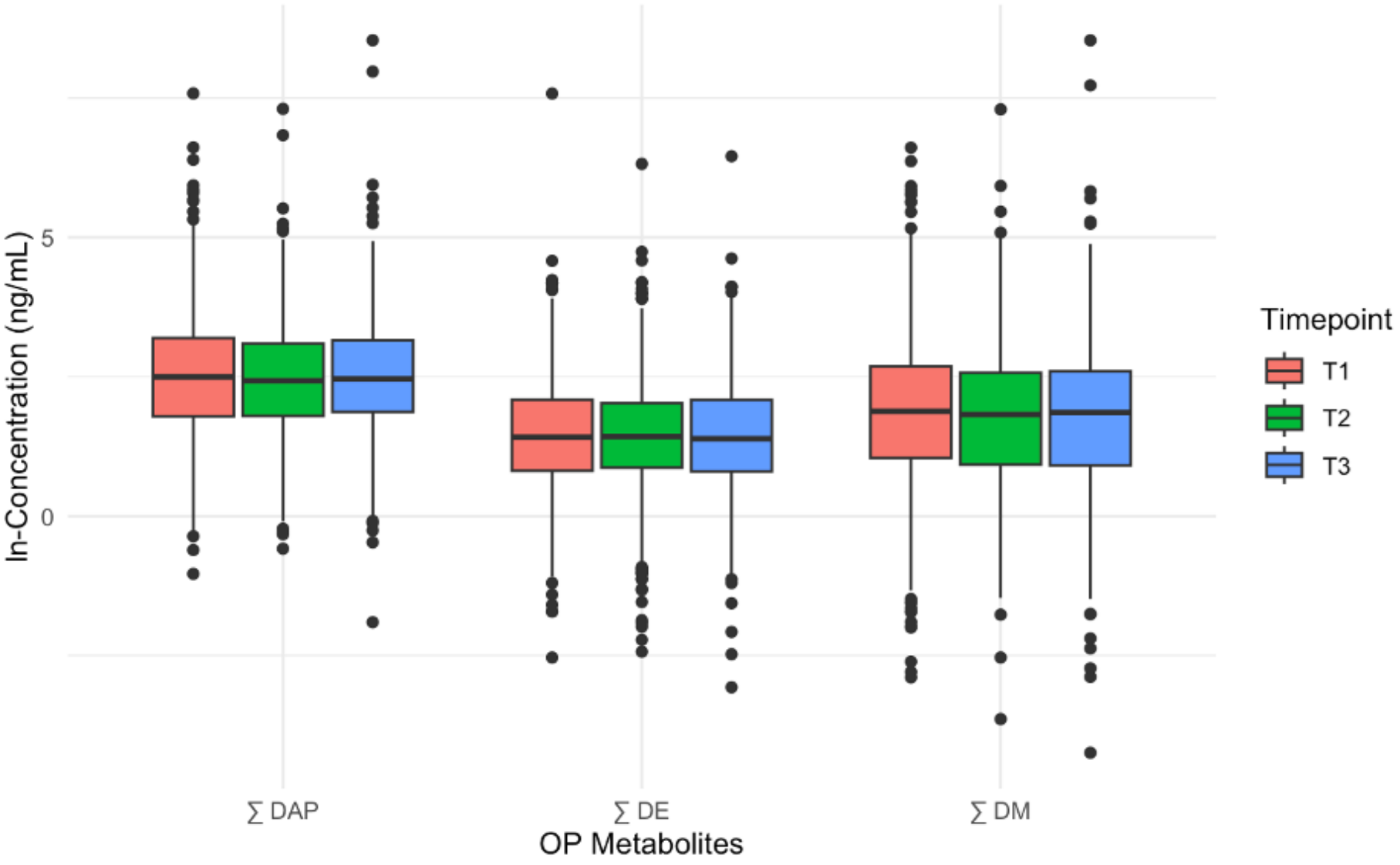
DAP concentrations in CHES participants



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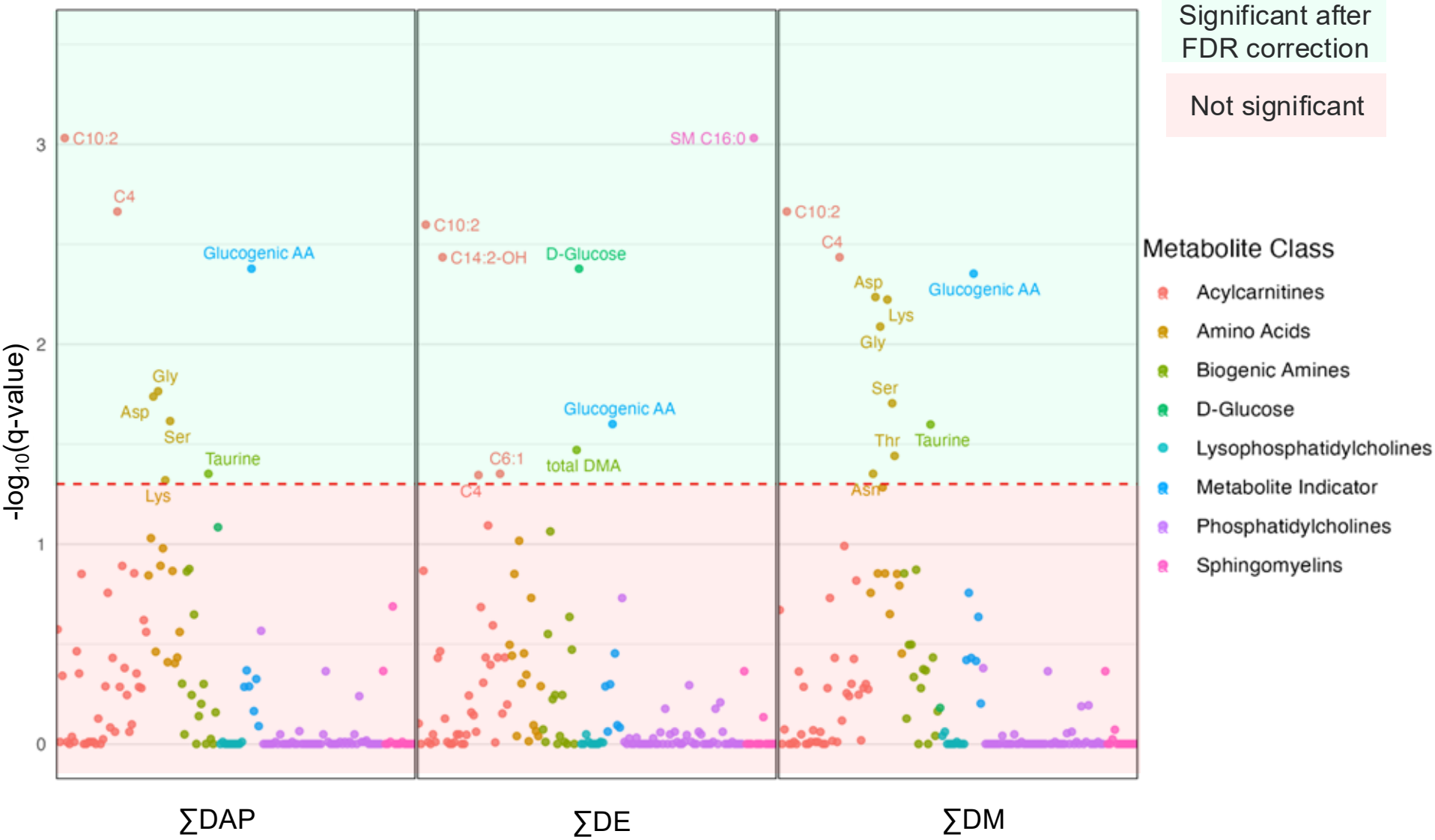
T1 Findings



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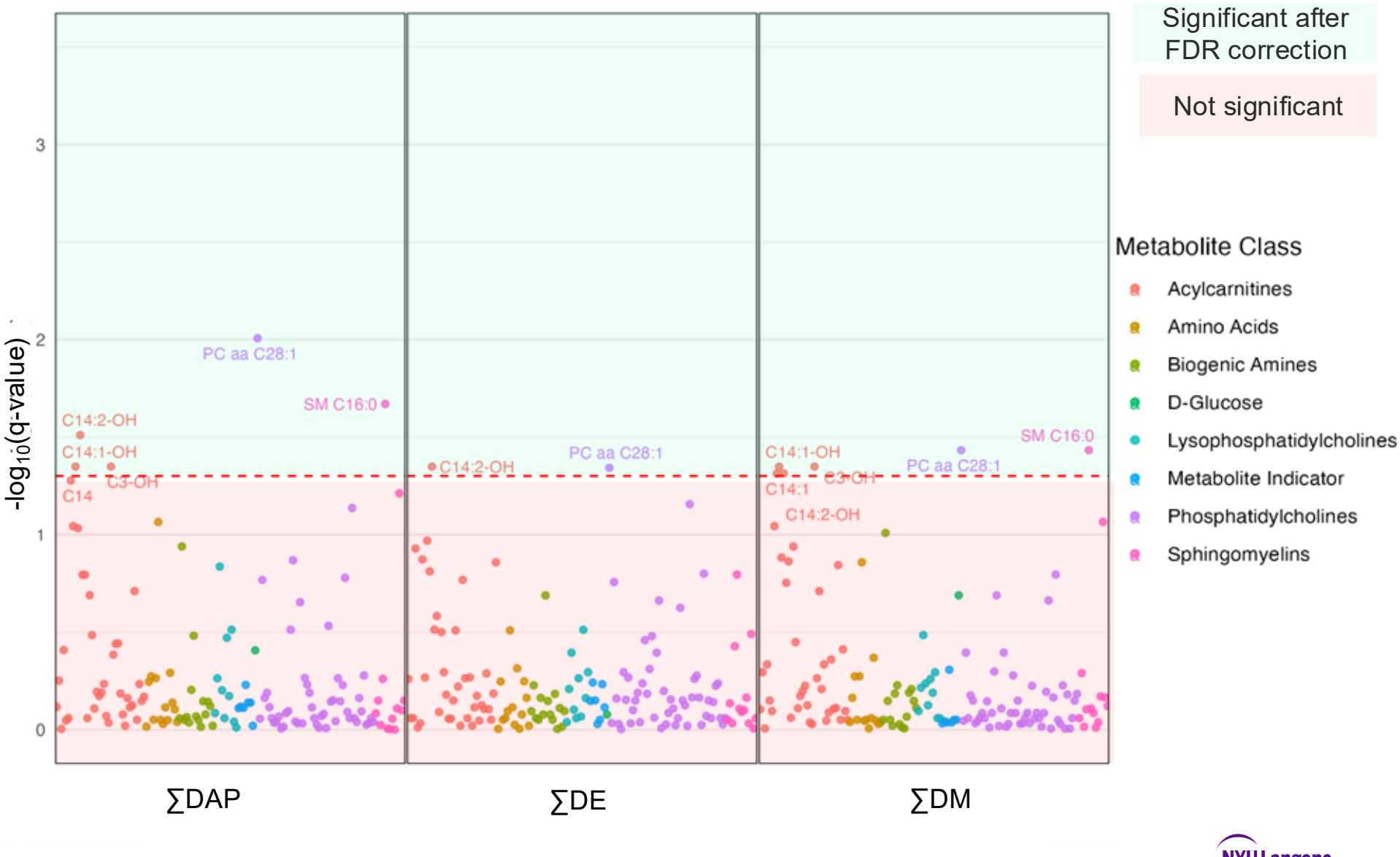
T2 Findings



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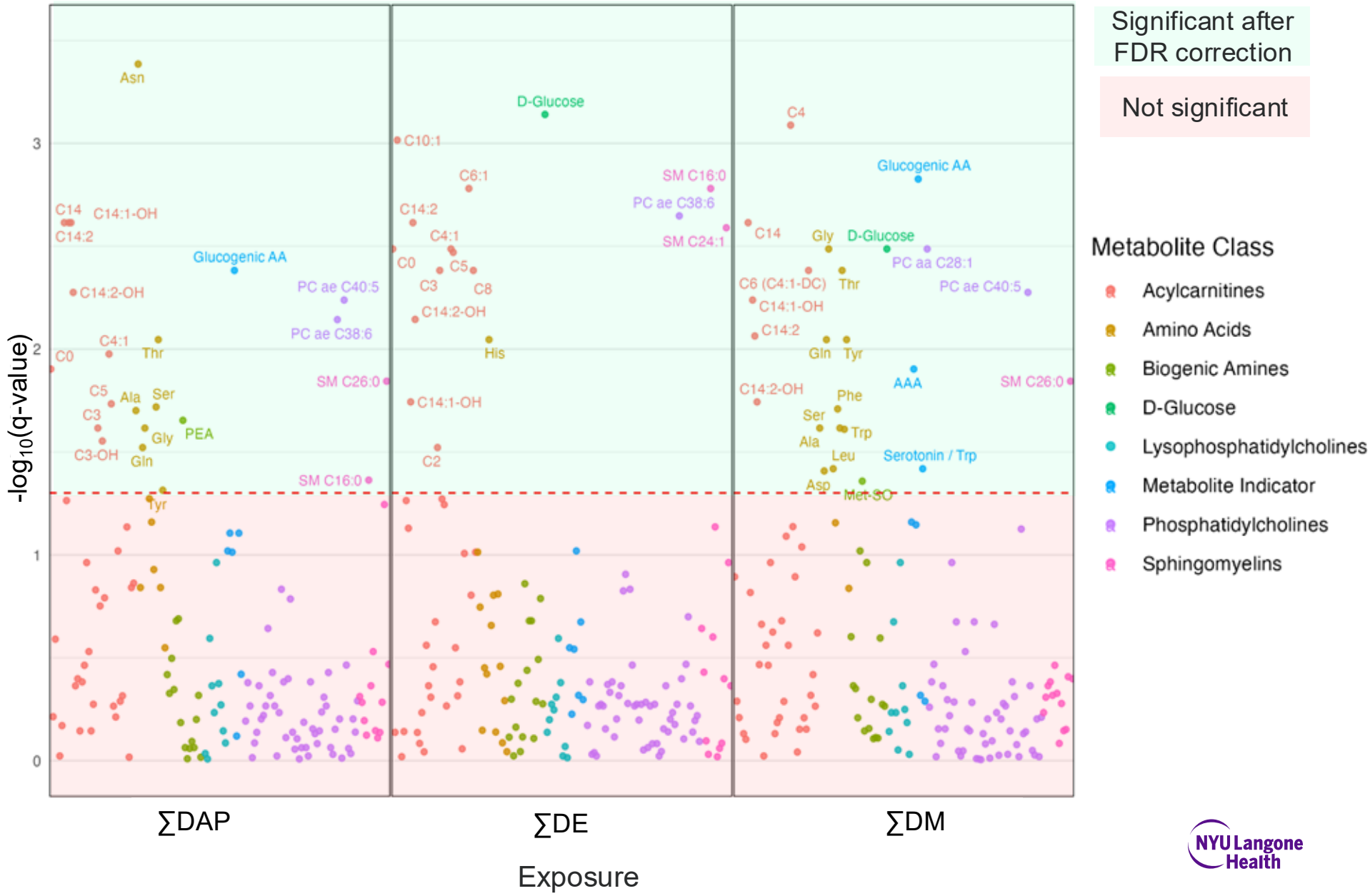
T3 Findings



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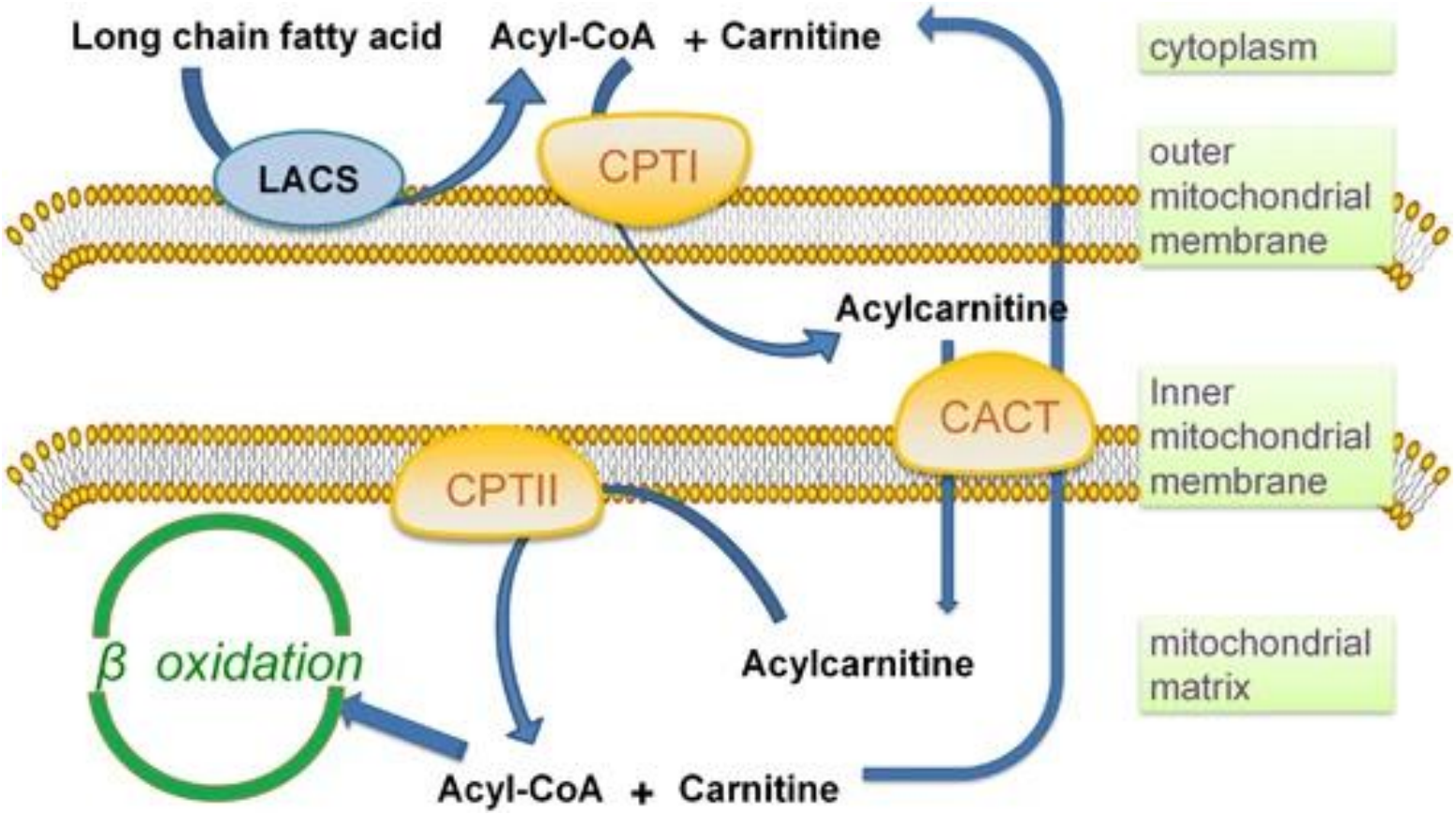
Summary of Results

- Notable **consistency across exposures and trimesters,** though also **trimester specific associations**
  - T3
- Mostly small positive effect estimates
- Consistent **altered acylcarnitine profiles**
  - **mitochondrial dysfunction** (IEM)
- Altered amino acid and related metabolism
  - including glutamine, tryptophan, serotonin
    - neurotransmitter pathways
- No LPCs significant

Acylcarnitines - fatty acid oxidation



Qu, Q 2016, https://doi.org/10.1038/cddis.2016.132

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Comparison to other studies

Yan 2021 (Central California):

- **Fatty acid β-oxidation** emerged as a common disrupted pathway across all three pesticide classes (OPs, OCs, PYRs)
- **disrupted acylcarnitine profiles**

Liang 2020 (Thailand)

- **Fatty acid oxidation** disruptions
- Tryptophan metabolism disruptions

Bonvollat 2013 (France)

- Lactate and citrate disruptions - suggest a shift toward anaerobic metabolism (potential **mitochondrial impairment/TCA cycle disruption)**

Strengths and Limitations

Strengths:

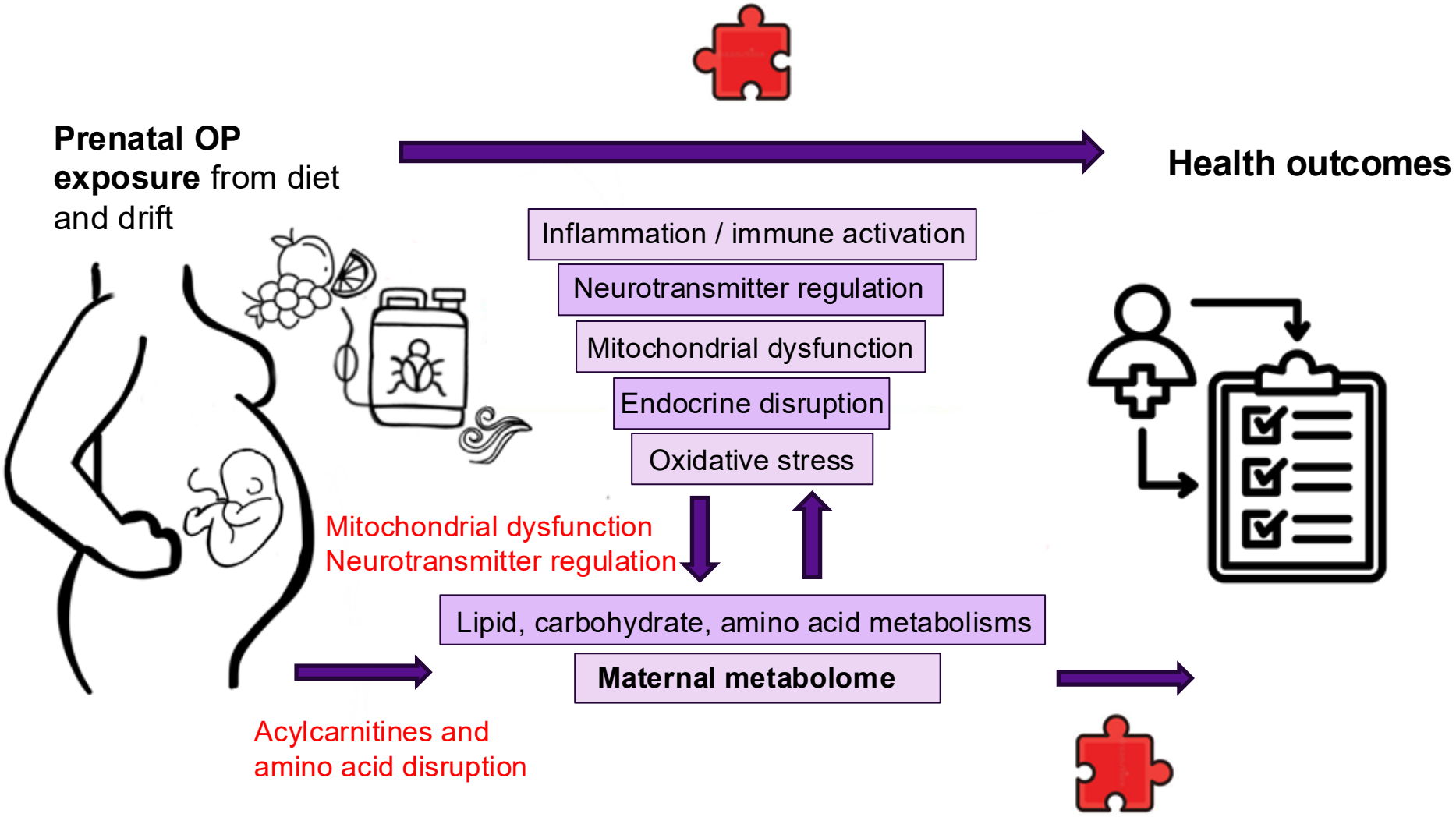
- Timepoint specific associations **– sensitive periods**
- Exposure levels relevant to general population– non occupational cohort
- Able to adjust for confounding variables and multiple comparisons– findings robust to this and additional sensitivity analyses

Limitations:

- Cross sectional - differences in metabolism could affect exposure and outcome
- Spot urine samples
- DAPs - not specific exposures

Key Takeaways

- OP exposure related consistently to disruption of:
  - **acylcarnitine** profiles
    - Mitochondrial disruption
  - **amino acid** metabolism
    - **neurotransmitter pathways**
- Late pregnancy (T3) important period for exposure



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NYU CHES team

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Associations of prenatal organophosphate (OP) exposure with fetal growth

Eleanor Medley, MPH, PhD candidate in Epidemiology

Citations:

EA Medley et al. (2025) Prenatal organophosphate pesticide exposure and sex-specific estimated fetal size. *American Journal of Epidemiology* 194 (4)

Nguyen DQ et al. (2025) Maternal organophosphate pesticide exposure in relation to birthweight: Modification by placental transporter genotype. *Placenta* 172

In the US, OP pesticide use has decreased over time

1970s-80s:
OP pesticides replaced organochlorines (e.g. DDT), peak of use

Early 2000s:
Most OP pesticides banned for **indoor residential use**

2021 rule vacated by 8th circuit

2023

1996
Food quality & Protection Act

2021
EPA final rule banned use of **chlorpyrifos on food crops**

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Most OP pesticides banned for **indoor residential use**

2021 rule vacated by 8th circuit

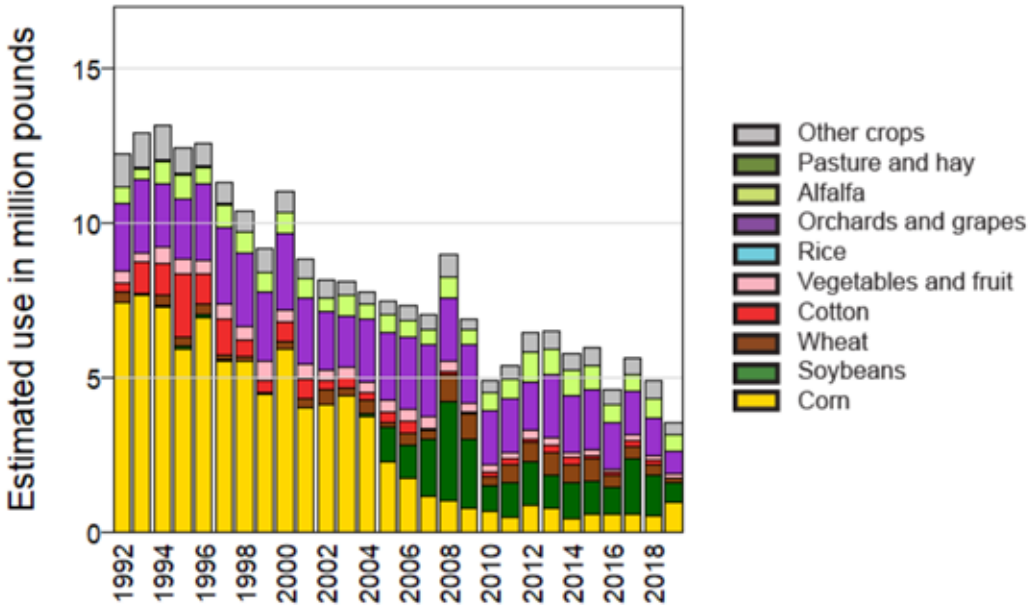
2023

1996
Food quality & Protection Act

2021
EPA final rule banned use of **chlorpyrifos on food crops**

Chlorpyrifos use by year and crop type:

(USGS, Pesticide National Synthesis Project)



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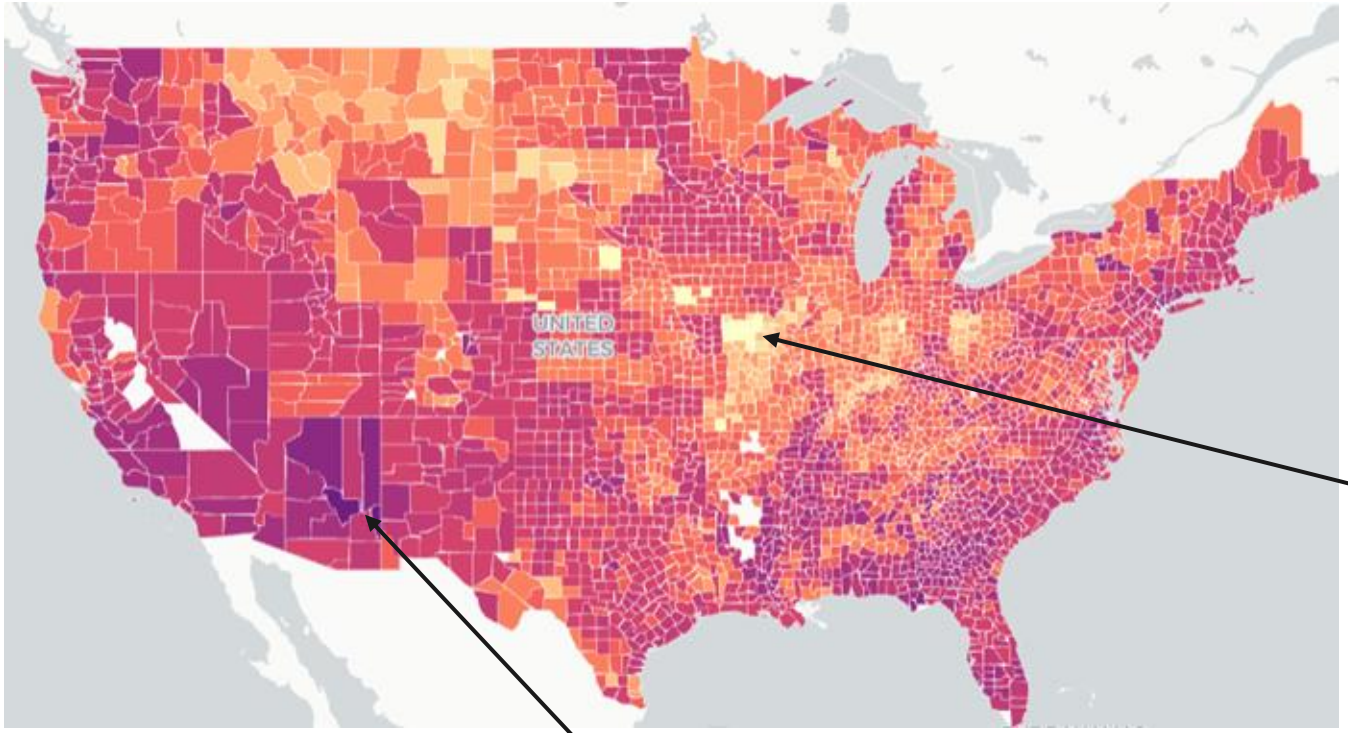
However, OP pesticides are still widely used in US agriculture

County-level concentrations for 14 OP pesticides (EPest-low)



Macon, MO: 0 lbs/sq mile harvested cropland

Earthjustice.org

Gila, AZ: 17,863 lbs/sq mile harvested cropland

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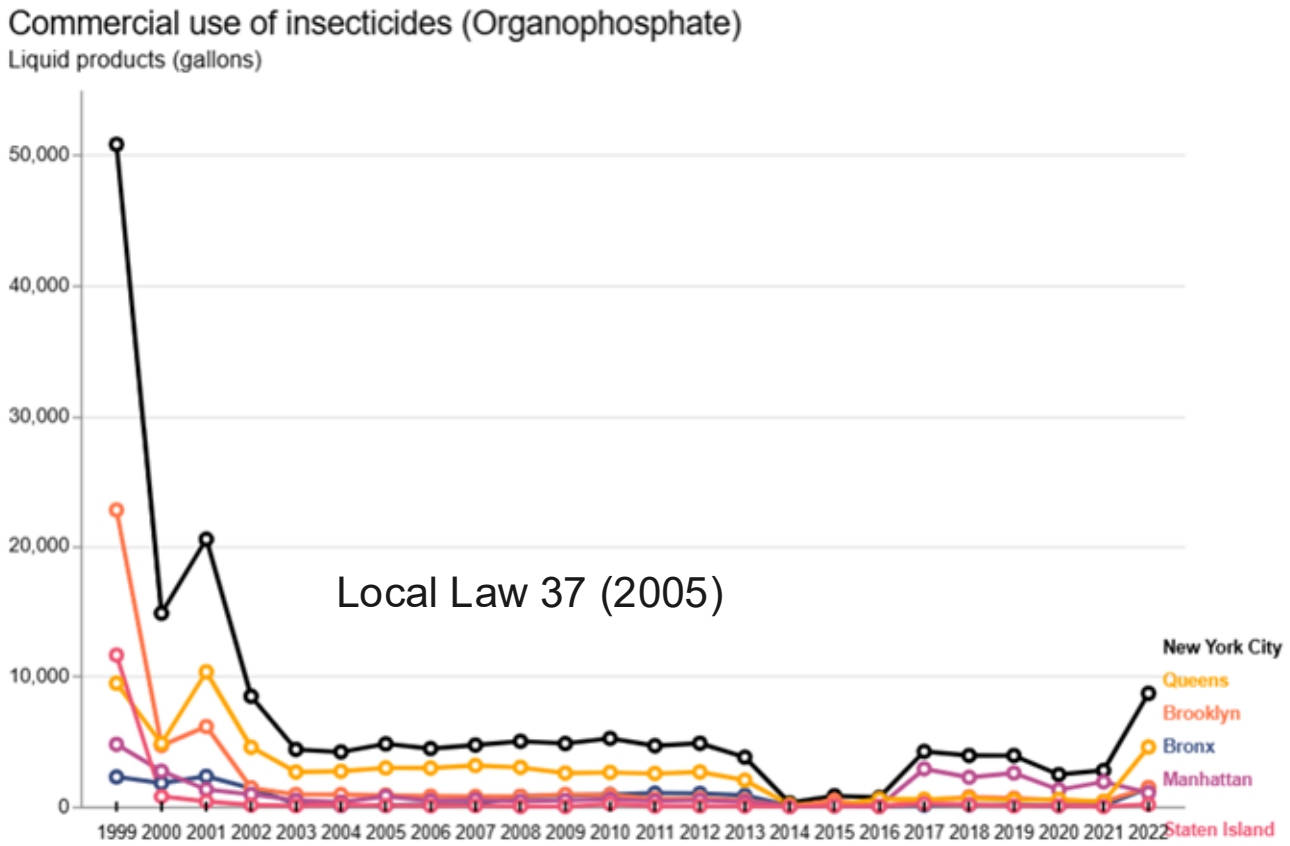
NYC heavily regulates OP pesticide use

General NYC populations likely primarily exposed through **diet**



NYC.gov Environmental Health & Data Portal

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Study population: NYU CHES (2016-)

NYC-based prospective pregnancy cohort

- Biospecimens
- Electronic medical record data
- Questionnaire data

Larger cohort is representative of all births in NYC in regards to maternal age, educational attainment, BMI, pregnancy length, delivery method, and birth weight

→ Study subsamples: fetal size (n=773), birth weight (n=240)

Trasande et al. (2020) Eur J Epidemiol.

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Why study OPs in relation to fetal growth?

Canonical mechanism of OP action:
cholinesterase inhibition → neurotoxicity

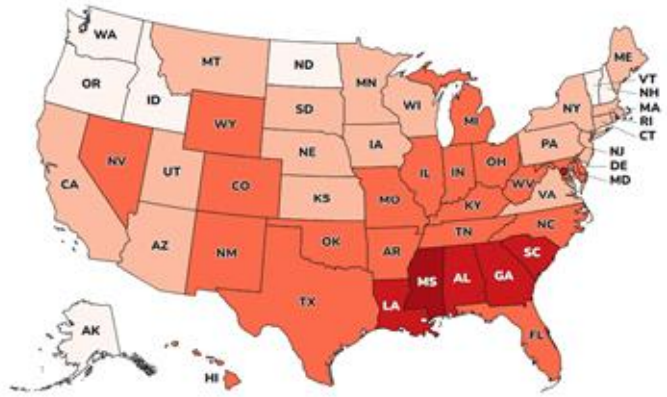
- OP exposure associated with altered neurodevelopment, even at relatively low levels of exposure
- Other non-cholinergic targets and potential multi-system effects?
  - e.g. metabolome
- OPs and their metabolites can cross the placental barrier
- Previous epidemiologic studies have reported associations of maternal OP exposure with reduced fetal growth, though results have been mixed
  - Evidence of modification by race/ethnicity and PON1 genotype (OP-metabolizing enzyme)

Why study OPs in relation to fetal growth?

Birth weight is a well-established life course health factor

- Low birth weight and fetal growth restriction associated with neonatal complications, neurodevelopmental outcomes, metabolic disorders later in life

8.6% U.S. babies born low birth weight



CDC LBW prevalences (2023) 5-13%

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Objectives

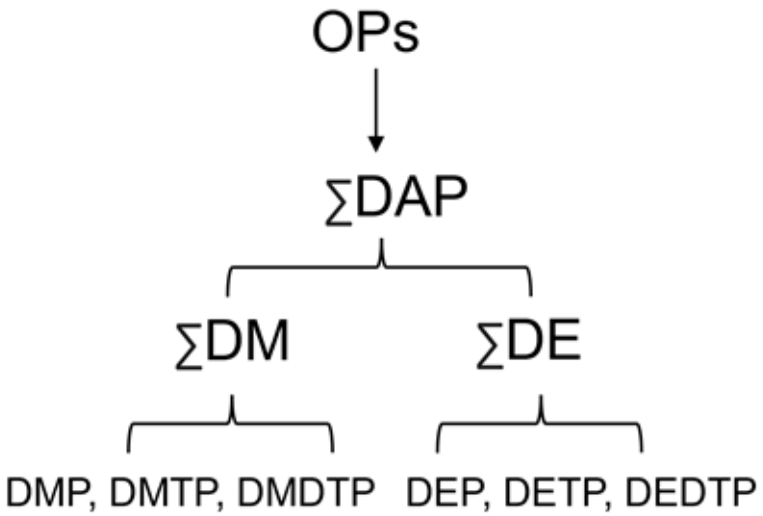
Evaluate associations of maternal OP exposure with…

1. **Estimated fetal size**
   - and investigate modification by fetal sex and gestational age

1. **Birth weight**
   - and investigate modification by placental transporter genotype

OP exposure measured through urinary dialkyl phosphate (DAP) metabolites

HPLC-MS/MS



Averaged 3 maternal spot urine samples collected across gestation:

Visit 1 (<18 weeks) → Visit 2 (18-25 weeks) → Visit 3 (>25 weeks)

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Birth weight and fetal biometry abstracted from electronic medical records

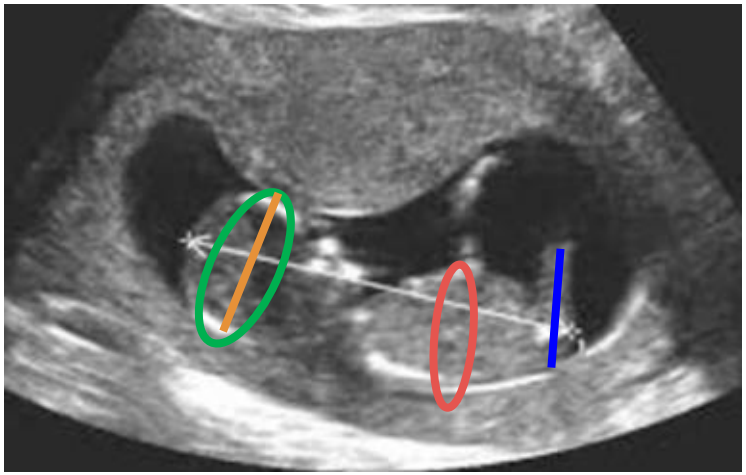
Fetal biometrics collected by ultrasound at 2 timepoints:

- Second trimester (18-22 weeks) *n*=773
- Third trimester (34-38 weeks) *n*=535

Z-scores for gestational age

- INTERGROWTH-21st global reference standards

Image adapted from Zaliunas et al. (2017)



Head circumference (HC)
Biparietal diameter (BPD)
Abdominal circumference (AC)
Femur length (FL)
Estimated fetal weight (EFW)

- Calculated from HC, AC, FL with Hadlock formula

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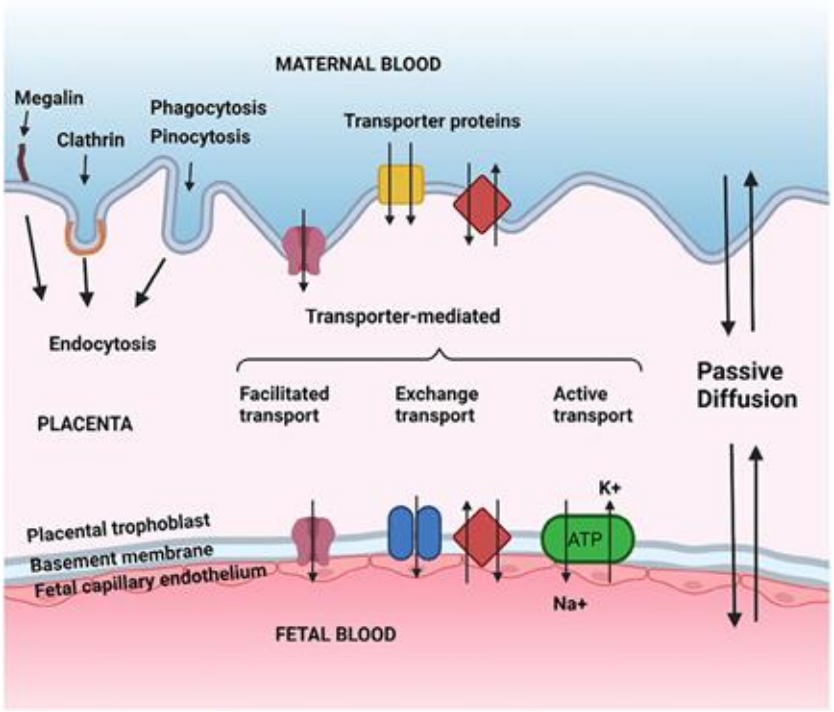
Placental transporters

- Placenta samples collected at delivery
- Candidate SNPs genotyped by real-time PCR
  - Key xenobiotic transporters



genotype	N (%)
All	240 (100%)
BCRP-rs2231142	
G/G*	160 (66.7%)
G/T	66 (27.5%)
OATP2B1-rs12422149	
G/G*	118 (49.2%)
A/G	78 (32.5%)
A/A	44 (18.3%)
OAT4-rs2078267	
C/C*	153 (63.7%)
C/T	70 (29.2%)
OAT4-rs17300741	
A/A*	136 (56.7%)
A/G	76 (31.7%)
G/G	28 (11.7%)

* denotes wildtype

Image from:
Chandrasekar et al. (2022)

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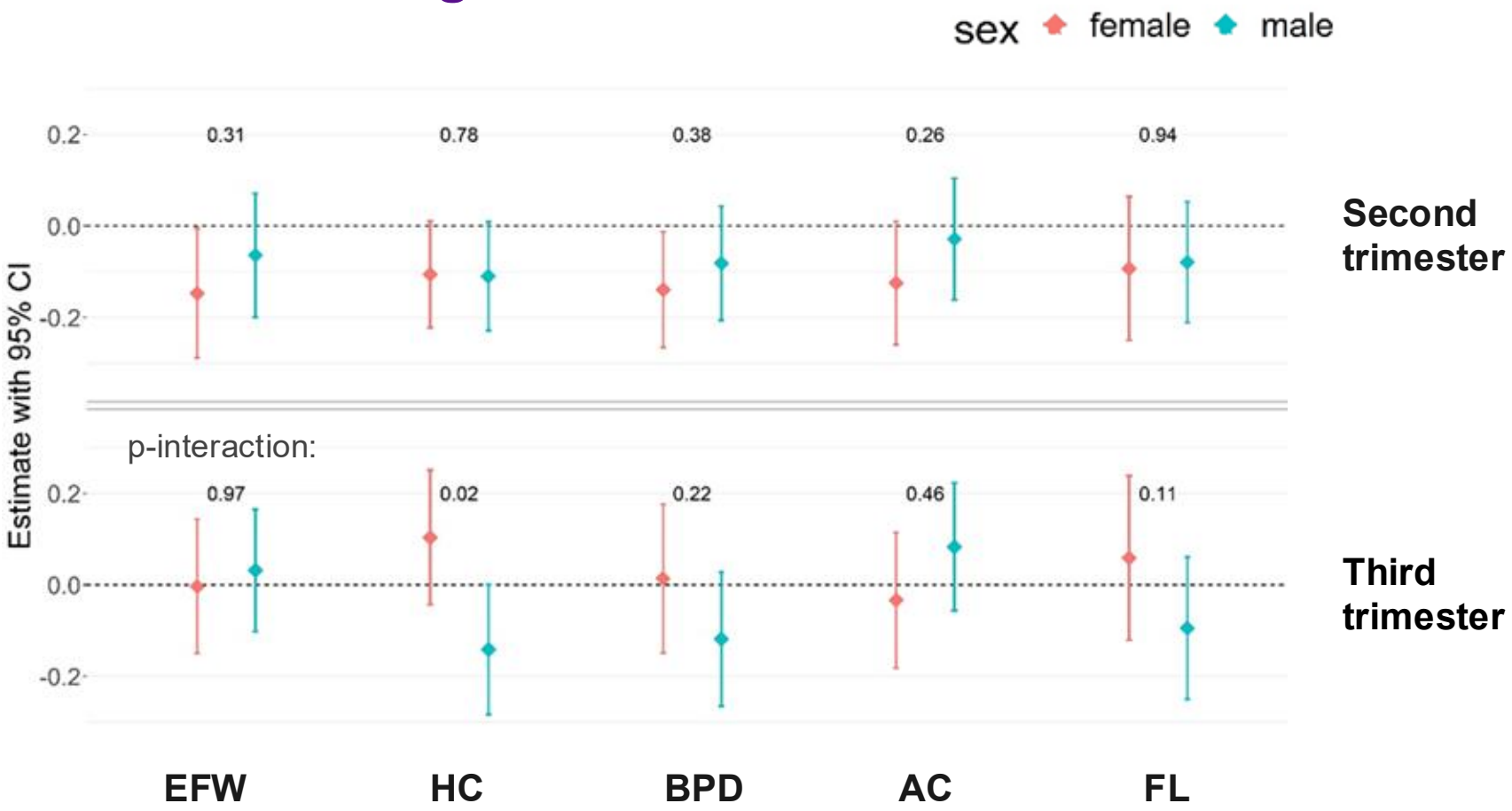
OP exposure

	Proportion detected in NYU CHES urine samples (*n*=801)	Median (IQR) of NYU CHES sample (ng/mL)	Median of NHANES 2017-2018 (ng/mL)
DMP	94.6%	2.24 (4.20)	1.30
DMTP	99.2%	1.74 (3.92)	0.64
DMDTP	79.8%	0.25 (0.84)	0.105
DEP	97.1%	2.73 (4.07)	2.28
DETP	79.6%	0.34 (0.75)	0.120
DEDTP	8.1%	0.04 (0)	<LOD

Moderate positive correlations, $\rho = 0.2 - 0.7$

Maternal urinary DAPs associated with lower fetal biometrics, particularly among females in mid-gestation and males in late-gestation



Linear regression models of fetal biometry z-scores as functions of average ∑DAP, adjusted for maternal age, education, race/ethnicity, parity, BMI, urinary cotinine

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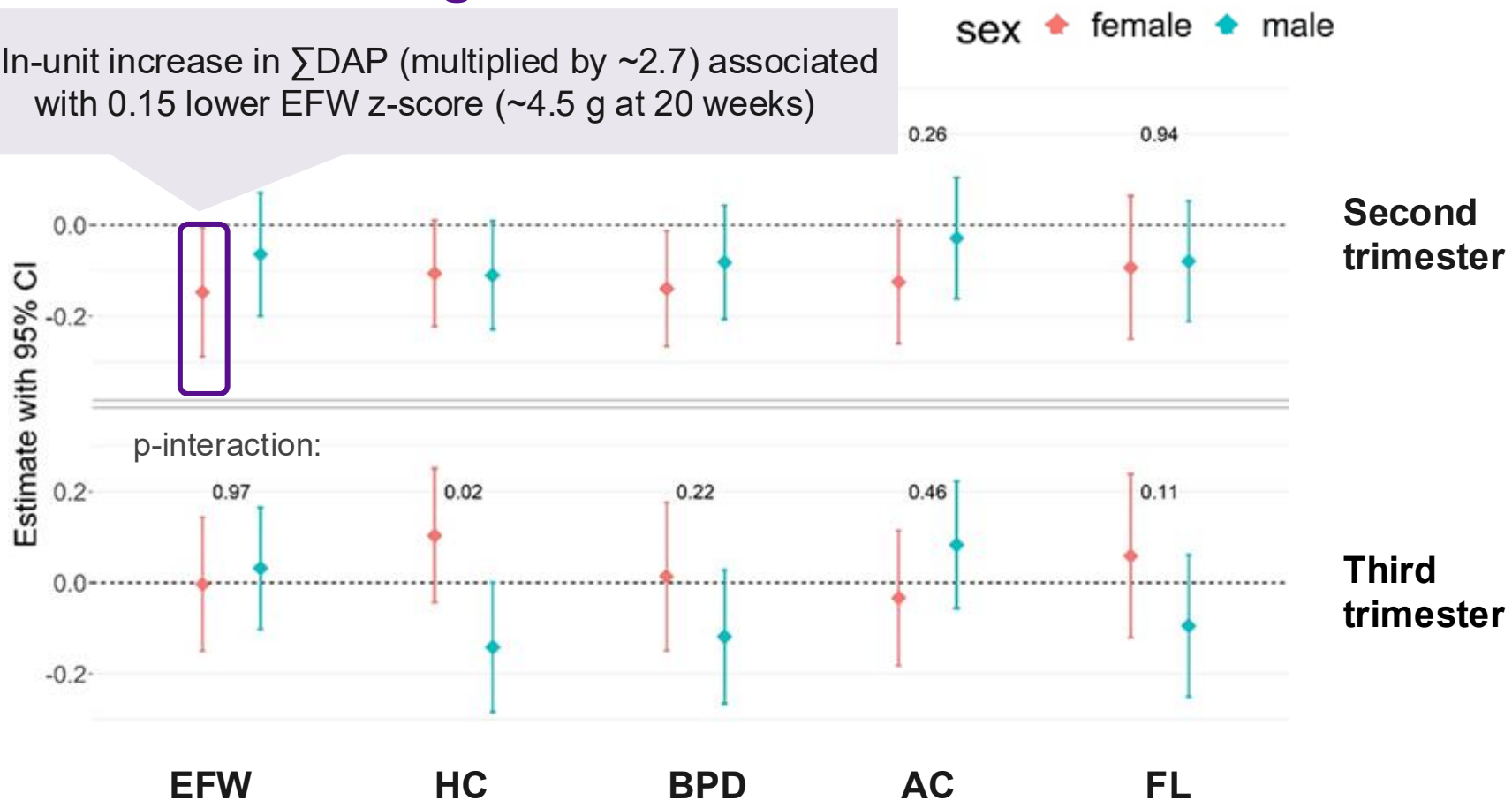
Maternal urinary DAPs associated with lower fetal biometrics, particularly among females in mid-gestation and males in late-gestation

1 ln-unit increase in ∑DAP (multiplied by ~2.7) associated with 0.15 lower EFW z-score (~4.5 g at 20 weeks)



Linear regression models of fetal biometry z-scores as functions of average ∑DAP, adjusted for maternal age, education, race/ethnicity, parity, BMI, urinary cotinine

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OPs & fetal biometry

Sex-specific fetal growth patterns:

Male fetuses tend to grow faster

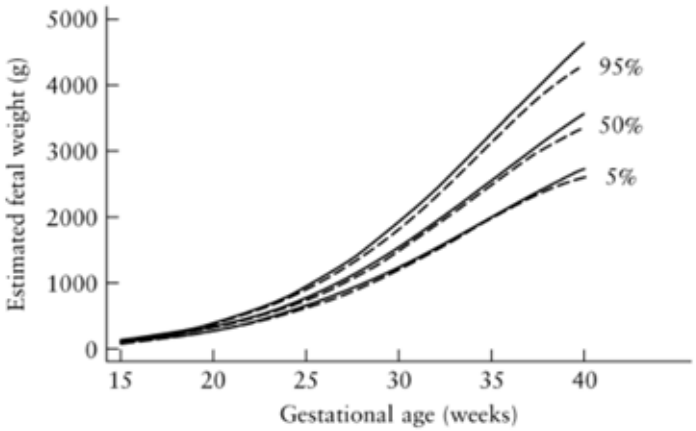
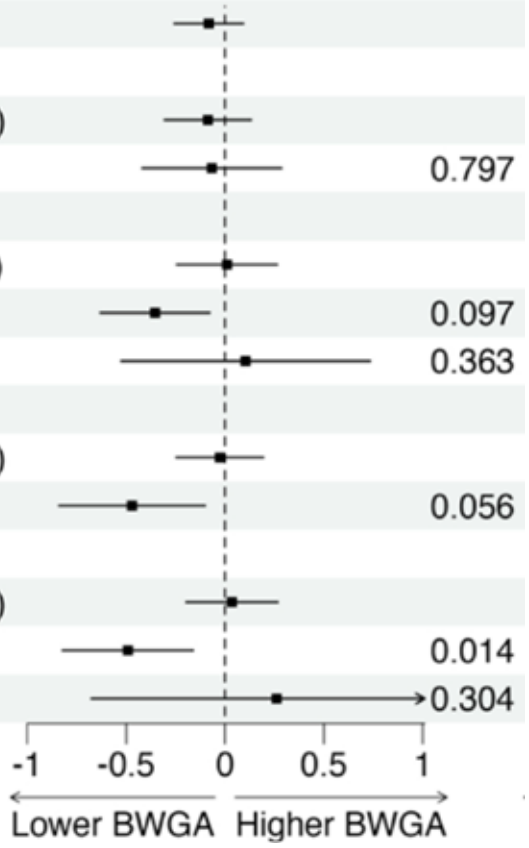


Figure from Schwarzler et al. (2004)

- Reduced head size in males consistent with male susceptibility to neurotoxicity of OPs throughout the life course
  - Though relation between prenatal head size and neurodevelopment is not clear
- Females only affected in second trimester
  - Unclear clinical implications, but may reflect perturbation in early prenatal growth and subsequent “catch up”

Maternal urinary DAPs associated with lower birth weight in specific placental transporter genotypes

genotype	N (%)	ΣDAP	p-int
All	240 (100%)		
BCRP-rs2231142			
G/G*	160 (66.7%)		
G/T	66 (27.5%)		0.797
OATP2B1-rs12422149			
G/G*	118 (49.2%)		
A/G	78 (32.5%)		0.097
A/A	44 (18.3%)		0.363
OAT4-rs2078267			
C/C*	153 (63.7%)		
C/T	70 (29.2%)		0.056
OAT4-rs17300741			
A/A*	136 (56.7%)		
A/G	76 (31.7%)		0.014
G/G	28 (11.7%)		0.304



* denotes wildtype

Linear regression models of BWGA z-score as a function of average ∑DAP, adjusted for maternal age, education level, race/ethnicity, insurance status, BMI, alcohol consumption during pregnancy, delivery method, and infant sex.

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Maternal urinary DAPs associated with lower birth weight in specific placental transporter genotypes

genotype	N (%)	ΣDAP	p-int
All	240 (100%)		
BCRP-rs2231142			
G/G*	160 (66.7%)		
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OATP2B1-rs12422149			
G/G*	118 (49.2%)		
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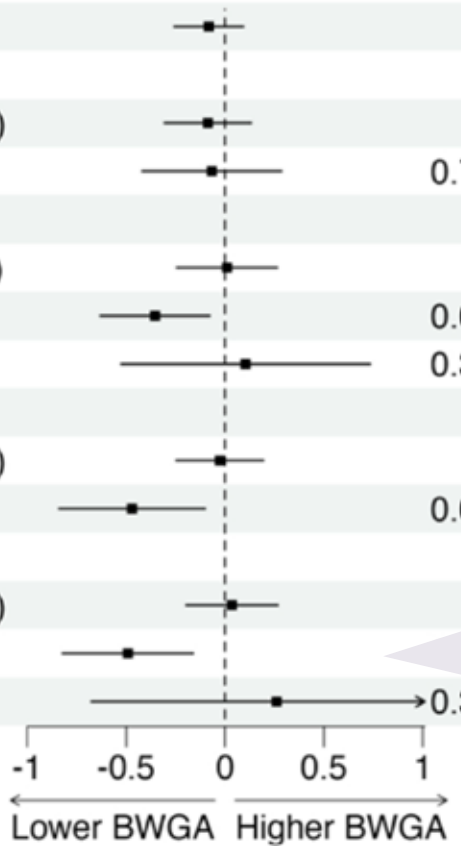
A/G	76 (31.7%)		
G/G	28 (11.7%)		0.304



* denotes wildtype

1 ln-unit increase in ∑DAP (multiplied by ~2.7) associated with 0.5 lower BW z-score (~180 g at 40 weeks)

Linear regression models of BWGA z-score as a function of average ∑DAP, adjusted for maternal age, education level, race/ethnicity, insurance status, BMI, alcohol consumption during pregnancy, delivery method, and infant sex.

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OPs & birth weight

- Genotype of specific placenta transporters may modulate fetal exposure to OPs, thereby affecting birth weight

- Heterozygotes with 1 variant allele associated with reduced birth weight
  - Low number of homozygotes with 2 variant alleles → reduced statistical power
- Need more in vitro studies of OP placental transport

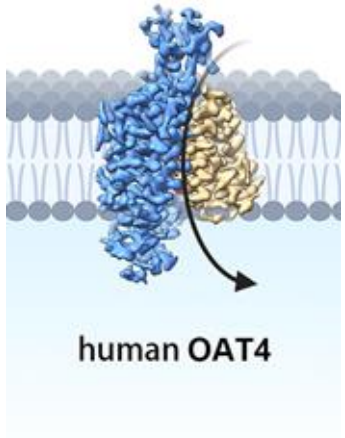

Image from Zhang et al. (2025)

In summary:

In NYU CHES, concentrations of maternal urinary DAP metabolites (indicating OP pesticide exposure) was associated with reduced fetal size and reduced birth weight **in specific subgroups:**

- Gestational age- and sex-specific associations with fetal biometry
- Placental transporter genotype-specific associations with birth weight

Strengths / What these studies add

- Study population with chronic, relatively low-dose exposure levels primarily from diet
  - After significant OP regulation
- Repeated measurements of OP exposure and fetal growth outcomes
- Investigation of fetal size, which may be obscured when only using birth weight outcomes
- Exploration of Gene x Environment interactions

Limitations and future directions

- Results from this study population may not be generalizable to other populations*
  - Different exposure levels, routes
- Potential mismeasurement of OP exposure
  - Non-specific metabolites
  - Direct exposure to pre-formed DAP metabolites
  - Spot urine samples (and rapid metabolism of OPs)

Future studies should collect multiple exposure indices
e.g. Blood concentrations of parent compounds, dietary information, geospatial data, metabolizing enzymes (PON1)

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