Fetal Origins of Obesity: The Role of Nutrition and The Environment

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Introduction

- I am an epidemiologist.
  - PhD in Environmental Health, Epidemiology
  - Postdoctoral trainee in Epidemiology
- My research examines how early-life exposures influence childhood growth and neurodevelopment.
  - Exposures: tobacco, cannabis, air pollution, and nutrition.

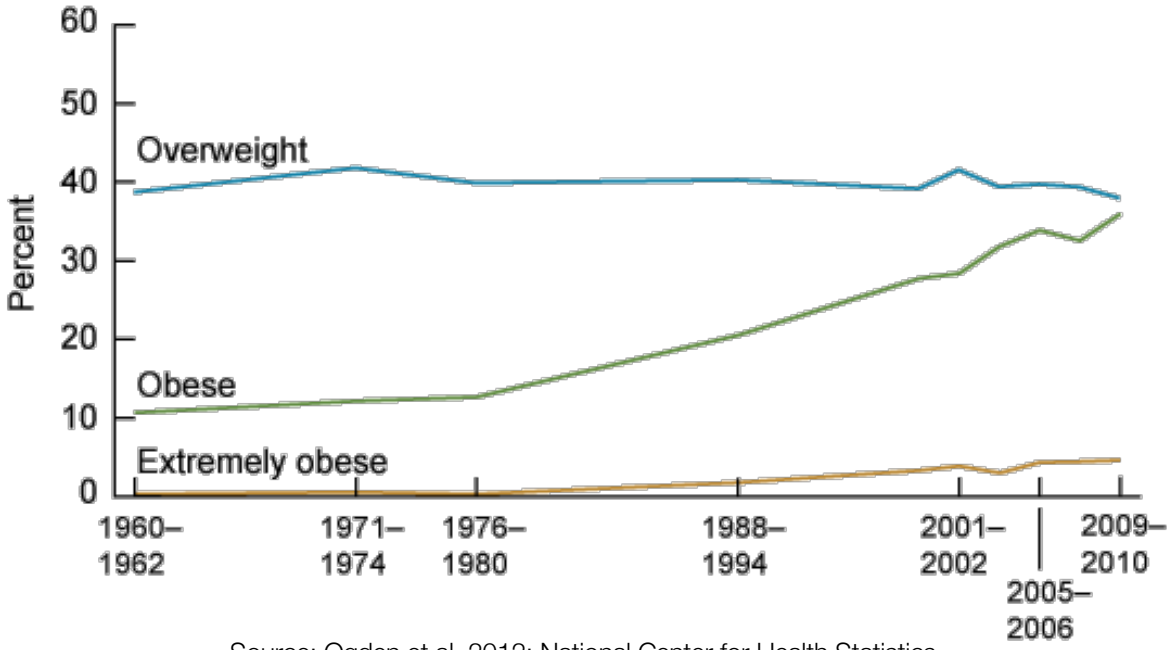
Outline

- Fetal origins hypothesis
- Fetal origins of obesity: The role of nutrition
- Fetal origins of obesity: The role of the environment
- Intersection of nutrition and the environment
- Translation of findings
- Future directions

Fetal origins hypothesis

Obesity is a growing public health concern

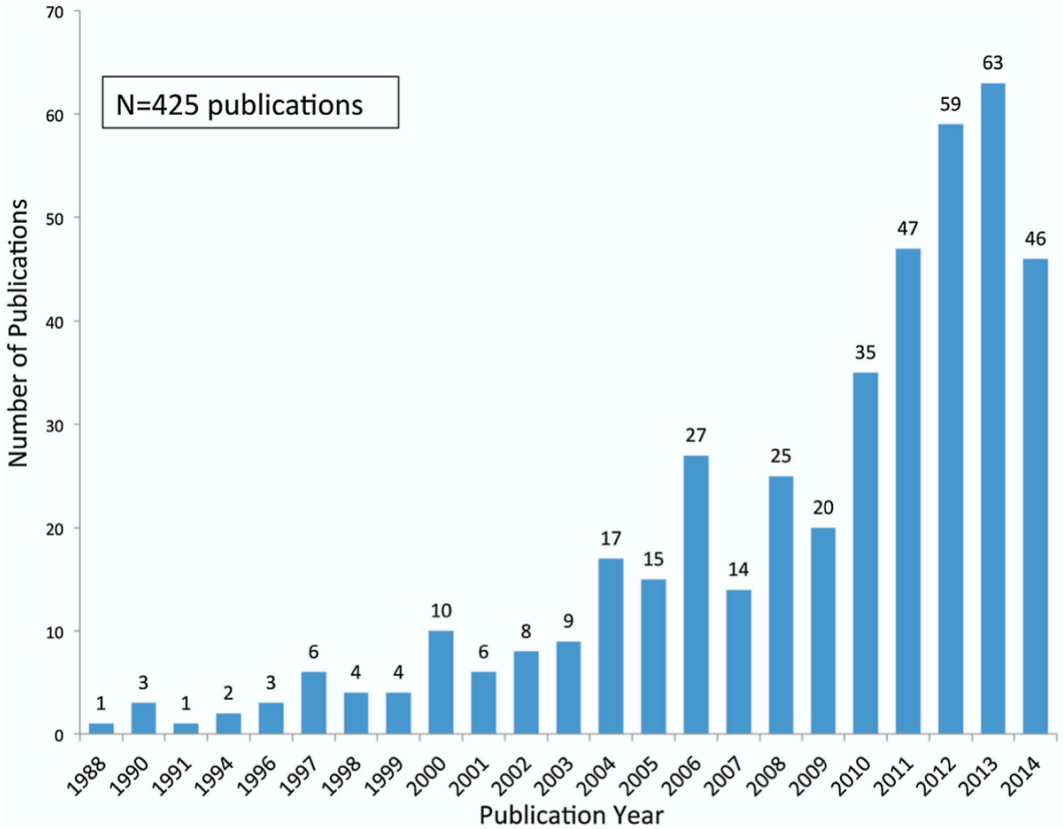
- Obesity has been increasingly steadily since the 1960's
- Diabetes, metabolic syndrome, and other cardiometabolic disturbances are also on the rise



Source: Ogden et al. 2012; National Center for Health Statistics

Fetal origins hypothesis

- Growing interest in Developmental Origins of Health and Disease (DOHaD) or the fetal origins hypothesis



Source: Heindel et al 2017; *Reproductive Toxicology*

Fetal origins hypothesis

- Sensitive windows in which environmental stressors can lead to increased susceptibility to adverse health outcomes.

- Fetal life represents a critical period when an exposure may have lifelong effects.

- Investigated in both nutrition (David Barker) and environmental health fields, beginning in 1990's.

Field of Nutrition: David Barker

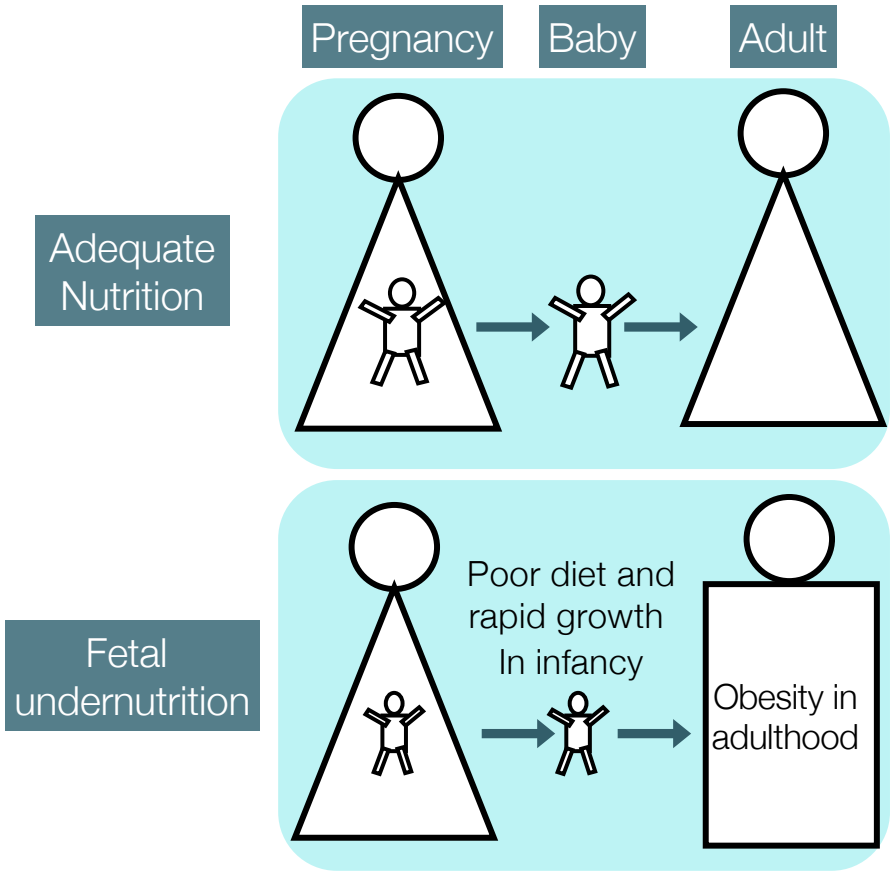


Figure adapted from Handbook of Famine, Starvation, and Nutrient Deprivation.

- Low birthweight is associated with coronary heart disease in adults.
- Why?
  - Undernutrition in utero permanently changes the body's structure, function and metabolism (example: Dutch famine).
  - Overnutrition (increased maternal fuels) also associated with increased risk of obesity.

Working in Parallel: Field of Environmental Health

- Early example:
  - Daughters of mothers who took diethylstilbestrol (DES, a synthetic form of estrogen) had a greater risk of clear cell adenocarcinoma (a rare vaginal cancer) (Herbst et al.; 1972).

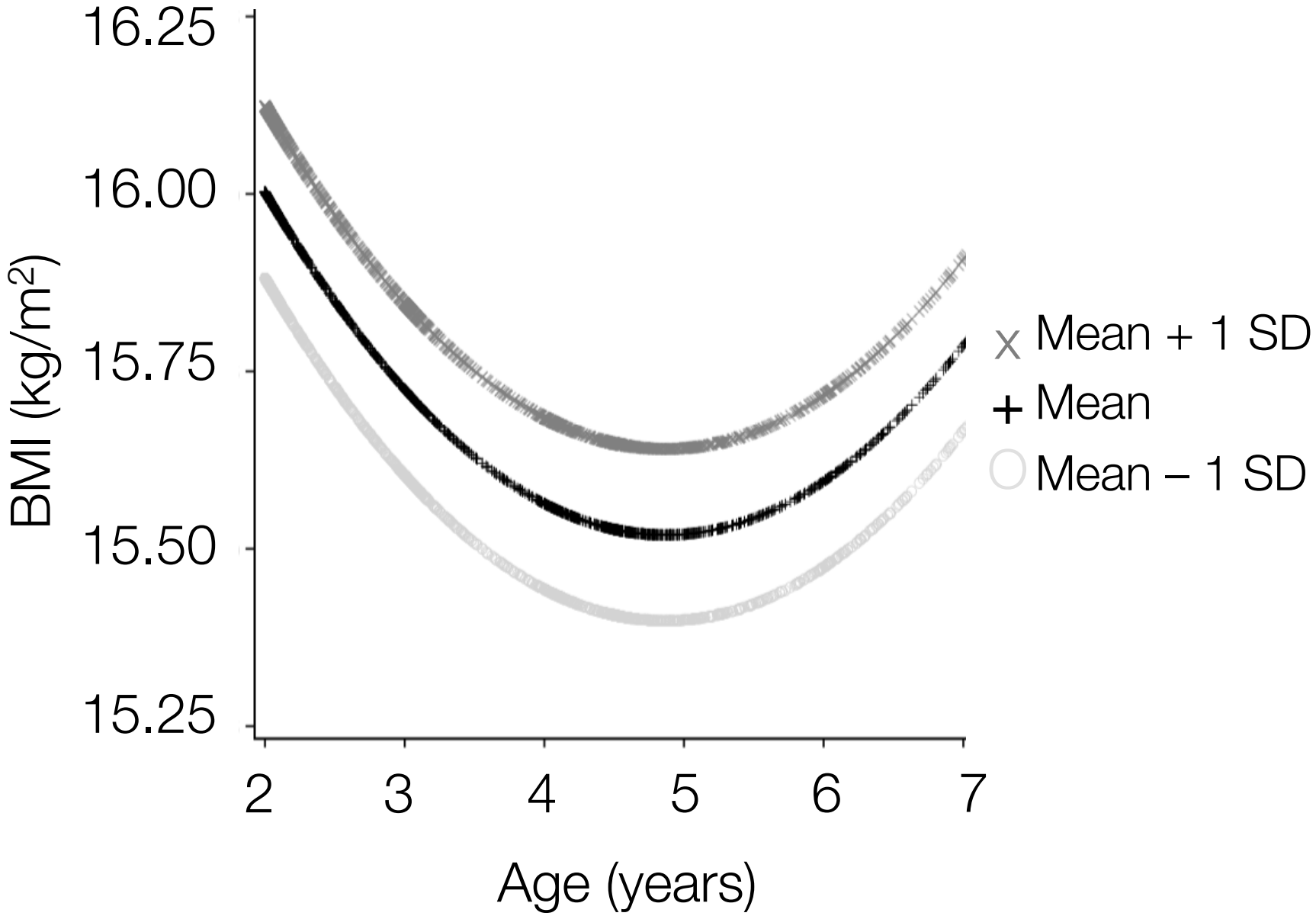
Programming of obesity may be evident at birth

- Birth weight has long been associated with childhood obesity.
- Pregnancy may be an ideal time for obesity prevention.
  - Some evidence that neonatal adiposity, but not birth weight, is influenced by mother's nutrition (Crume et al. 2016; *Am J Obstet Gynecol*)
- Does neonatal adiposity predict childhood BMI?

Neonatal adiposity and childhood obesity

- Air displacement plethysmography
- Neonatal adiposity is the proportion of fat mass divided by total mass (% fat mass)

Predicted BMI levels according to neonatal adiposity, girls



Moore et al. 2020; *Pediatrics*

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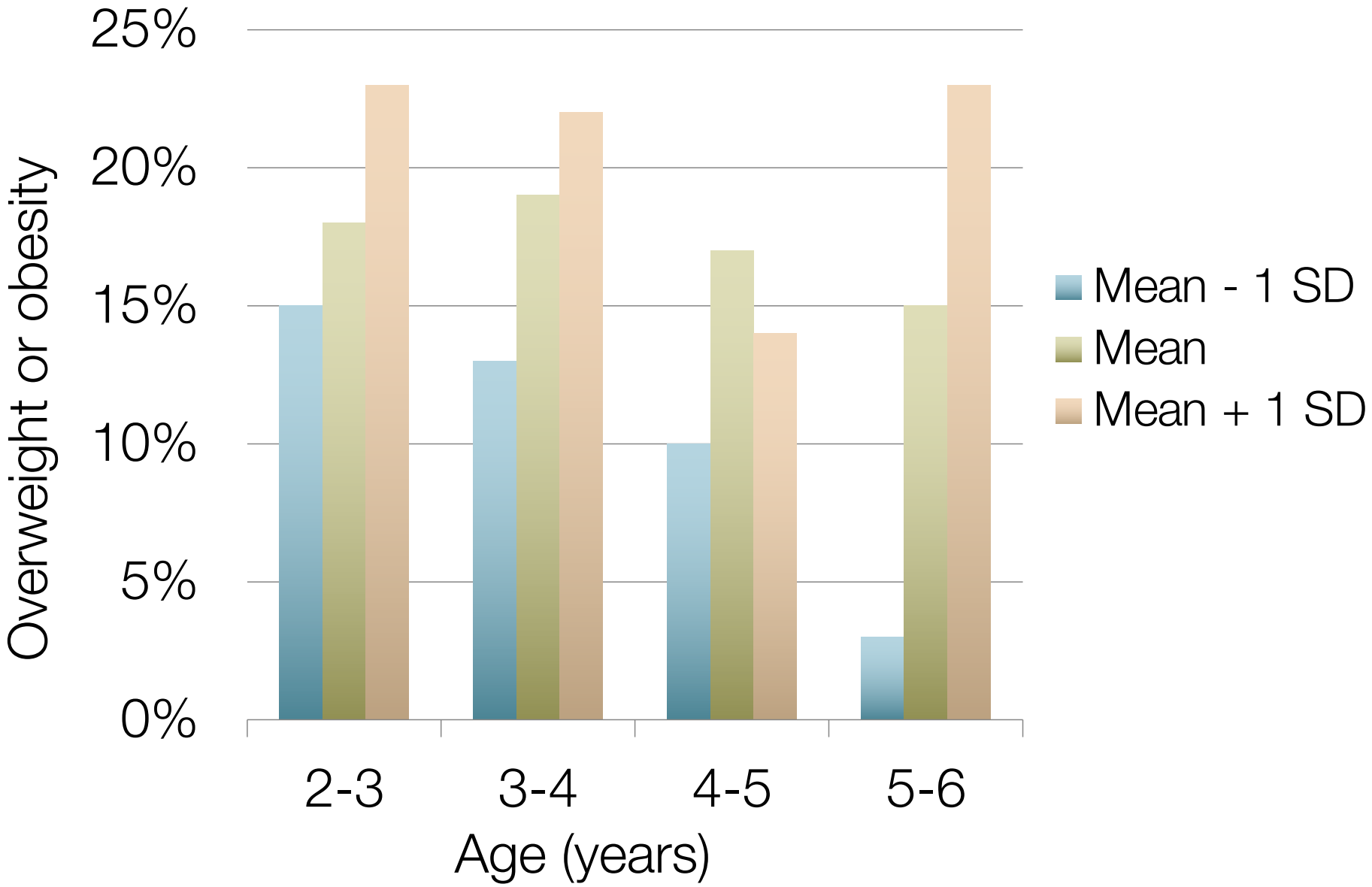

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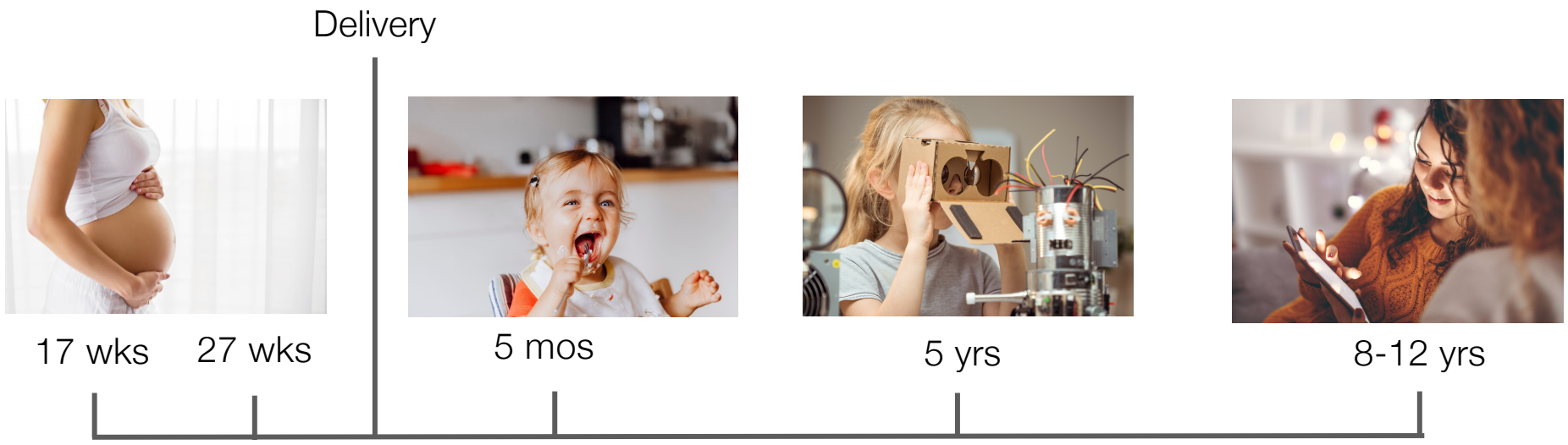
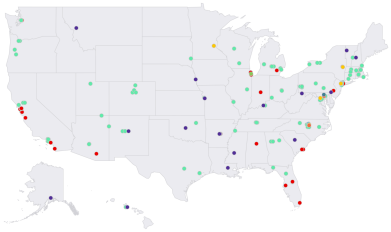
Leveraging a well-characterized cohort: The Healthy Start Study

The Healthy Start Study

- Pre-birth cohort of 1,410 ethnically diverse pregnant women and their offspring



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



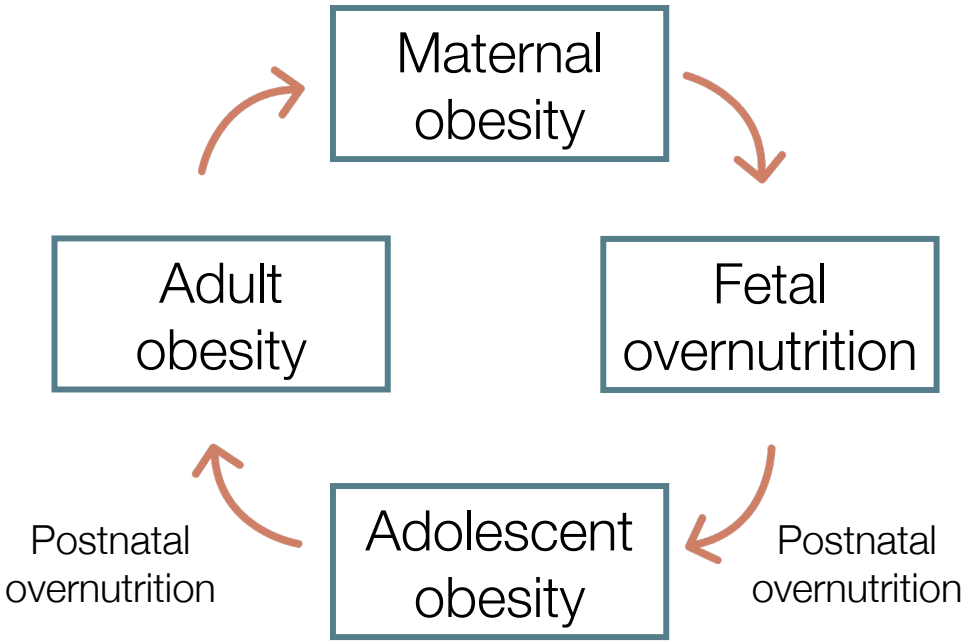
Examples of exposures and outcomes collected

- Pregnancy:
  - Maternal BMI, gestational weight gain, lipids, glucose, diet
  - Environmental exposures:
    - Perfluoroalkyl substances (PFAS), ambient air pollution, tobacco use/exposure (cotinine)
- Offspring
  - Body composition (PEA POD)
  - Heights/weights from medical records (trajectories)

Fetal origins of obesity: The role of nutrition

Overnutrition in pregnancy

- Fetal origins hypothesis suggests that obesity may be "transferred" from mother to offspring.
- Pre-pregnancy BMI and gestational weight gain increases neonatal adiposity (Starling et al. 2015; *Am J Clin Nutr*).
  - Effects may be trimester-specific.



Adapted from Dabelea and Crume 2011, *Diabetes*

Diet quality in pregnancy

- Healthy Eating Index (HEI-2010)
  - 13 dietary component
  - Scores range from 0-100
- Poor diet quality during pregnancy increases neonatal adiposity but not birth weight, independent of maternal BMI (Shapiro et al. 2017; *Int J Obes*).
  - Nutrition may be just as clinically important as BMI/gestational weight gain.

Mean difference for HEI-2010 score (≤57 vs. >57)	
Birth weight (g)	28g (-21g, 77g)
Neonatal adiposity (%)	0.6% (0.1%, 1.1%)*

Fetal origins of obesity: The role of the environment

Smoking

- Smoking consistently linked to low birth weight (Butler et al. 1972; *BMJ*).
- Smoking is also associated with rapid "catch up growth" and obesity.

Source: Alamy

Offspring born to active smoking mothers experience...

Lower birth weight (-341g; 95% CI: -472, -211) and neonatal fat mass (-79g; 95% CI: -131, -27).

- (Moore et al. 2018; *Int J Obes*)

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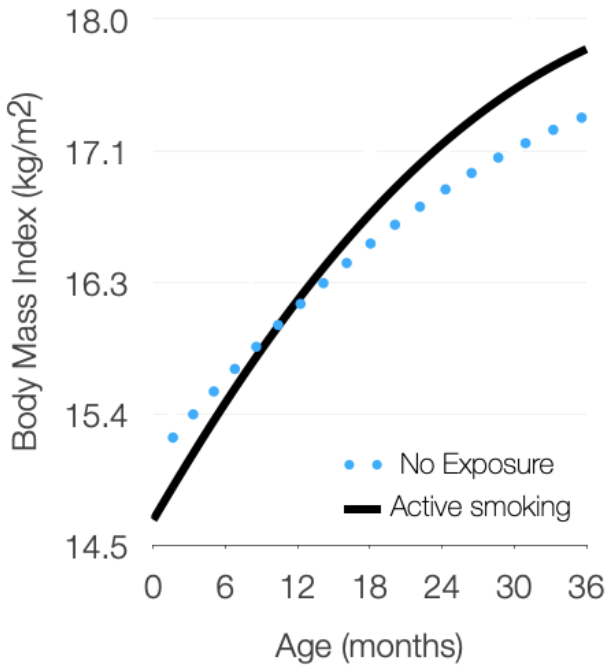

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Rapid "catch-up" growth that is similar to the offspring of secondhand smokers.

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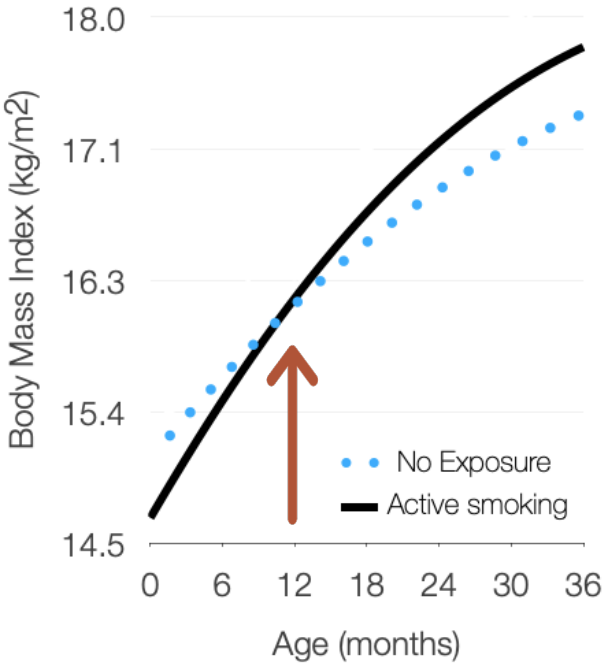

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Air pollution

- High levels of exposure to traffic-related and ambient air pollution ($PM_{2.5}$, ozone) have been linked to low birth weight.

Air pollution

- Limited evidence that ozone and $PM_{2.5}$ exposures in pregnancy were associated with birth weight or neonatal adiposity in Healthy Start (Starling et al. 2019; *Environmental Research*).
  - Inconsistent with previous studies.
  - Lower concentrations or low variability across Denver metro.
- Third factor may influence these associations.
  - Social factors (Martenies et al. 2019; *Environmental Epidemiology*)
  - Smoking (preliminary data)

Offspring of mothers with high exposure to $PM_{2.5}$ during the third trimester experience…

No difference in birth weight
or neonatal adiposity.

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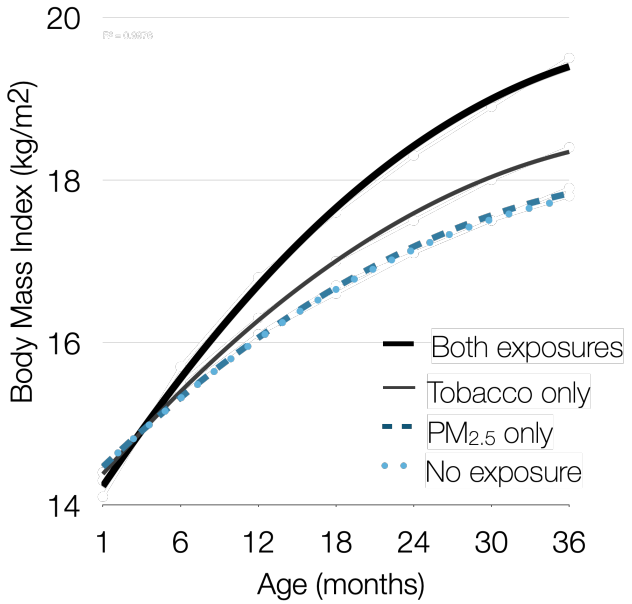


BMI growth that was more rapid than would be expected due to individual exposures

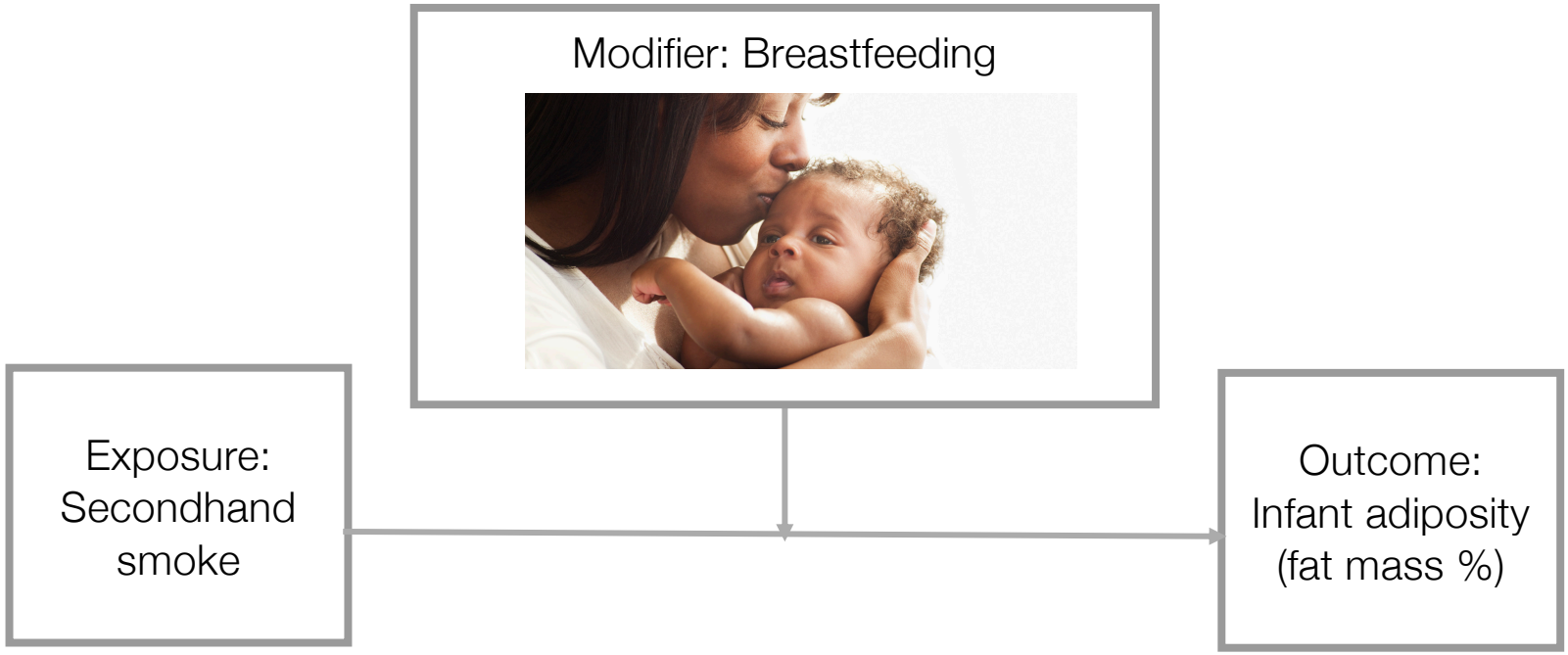
(0.6 kg/m^2 per year; 95% CI: 0.1, 2.3; p for interaction=0.03).

(preliminary data)

Intersection between nutrition and the environment

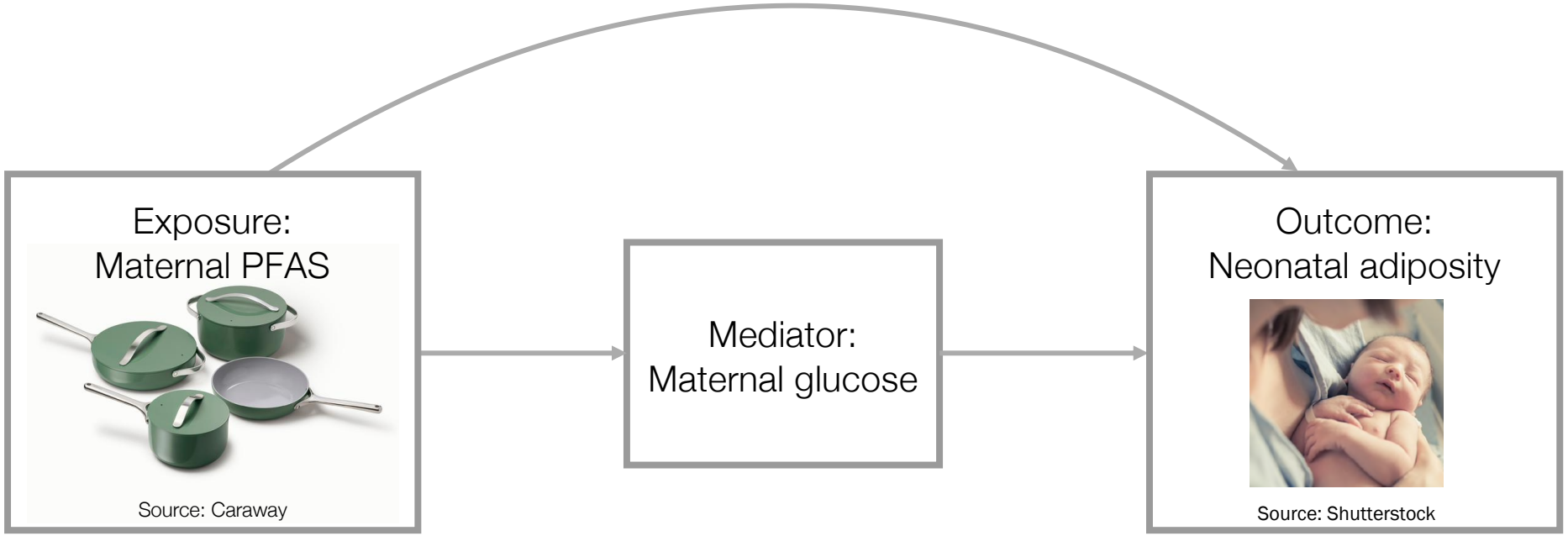
Do nutrition and the environment interact?

- The association between secondhand smoke and infant adiposity differed by the duration of exclusive breastfeeding (Moore et al. 2017; *Ped Obes*)
  - If infants who were breastfed, there was no change in adiposity.
  - If infants who were NOT breastfed, secondhand smoke was associated with increased adiposity.



Does overnutrition mediate environmental links?

- The association between perfluoroalkyl substances (PFAS) and neonatal adiposity mediated by maternal fasting glucose (Starling et al. 2017; *Environmental Health Perspectives*).



Translation of findings

Opportunities for intervention

- Nutrition:
  - Treatment or prevention of gestational diabetes (Ritchie et al. 2019 *Clinical Diabetes*; Gillman et al. 2010 Diabetes)
- Environmental Health:
  - Smoking cessation efforts
  - Community interventions:
    - Examples: Pest management, organically grown food, “natural” beauty/cleaning products (Brenner and Galvez, in *Endocrine Disrupting Chemicals*)

Opportunities for policy: Environmental health

- Air pollution:
  - EPA Air Quality Standards (Ozone, $PM_{2.5}$, NO_2, CO, Pb)
  - Reducing indoor exposures (cooking, carpeting, pets)
- Smoking:
  - Smoke-free policies
  - Tobacco taxes
  - Stronger warning labels

Opportunities for policy: Environmental health

- Perfluoroalkyl Substances (PFAS):
  - Voluntary phase out in 2006
  - Persistent in the environment (water) and human bodies
    - Half-life is 2-5 years (5 half-lives for complete removal)
  - “GenX” chemicals – less environmentally persistent

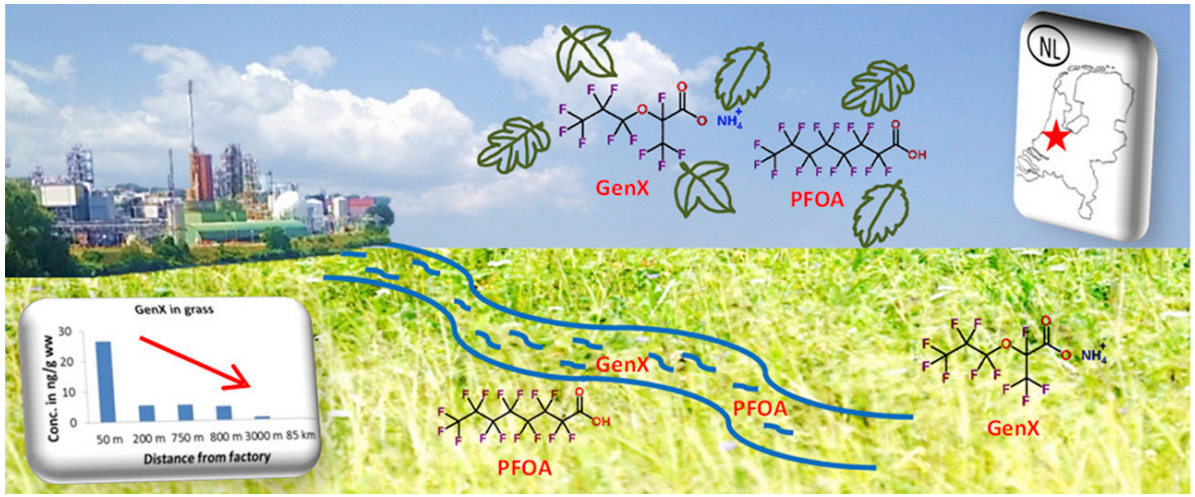


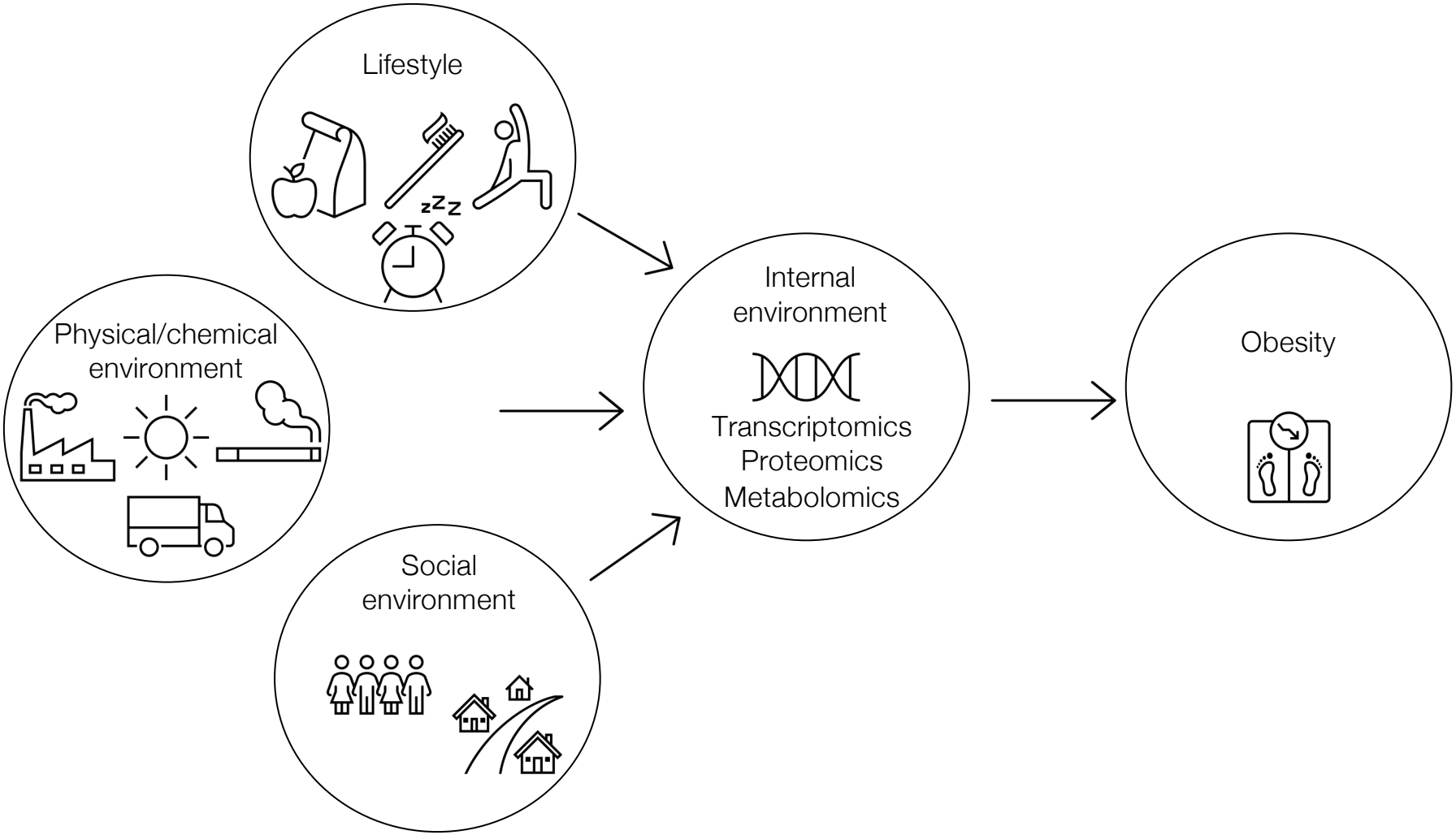
Image source: Brandsma et al., Chemosphere, 2019

Future directions

Lifecourse approach

- Exposures during pregnancy, infancy, childhood, etc.
  - Windows of susceptibility
  - Accumulation of risks over one's life
- Effect modification, mediation, and multi-pollutant/mixture models

The exposome



Adapted from Vrijheid 2014, *Thorax*

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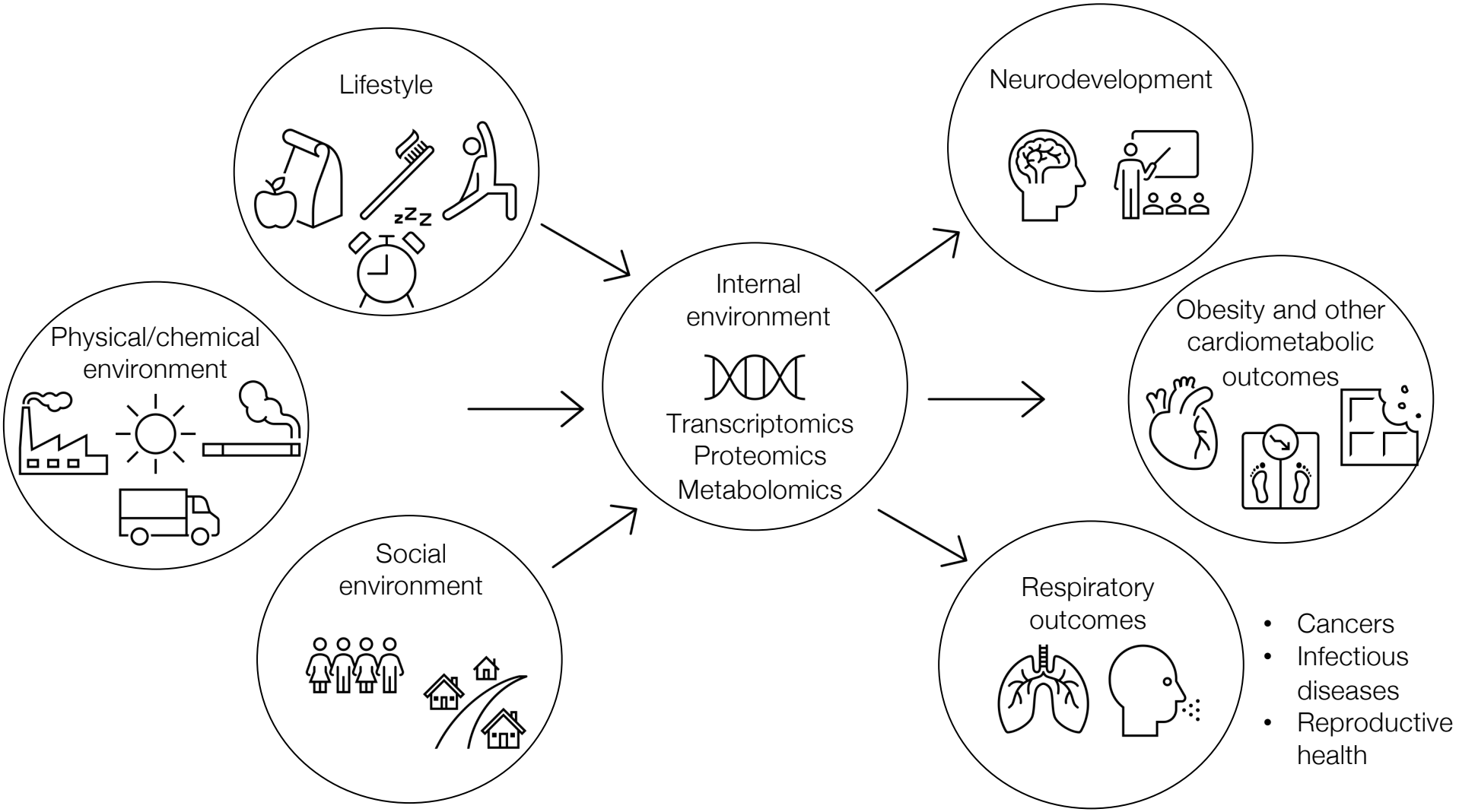

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ECHO

Environmental influences on Child Health Outcomes

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