Testing DOHaD Hypotheses About Drivers of Childhood Growth Using Epidemiologic Study Designs

Challenges and Opportunities

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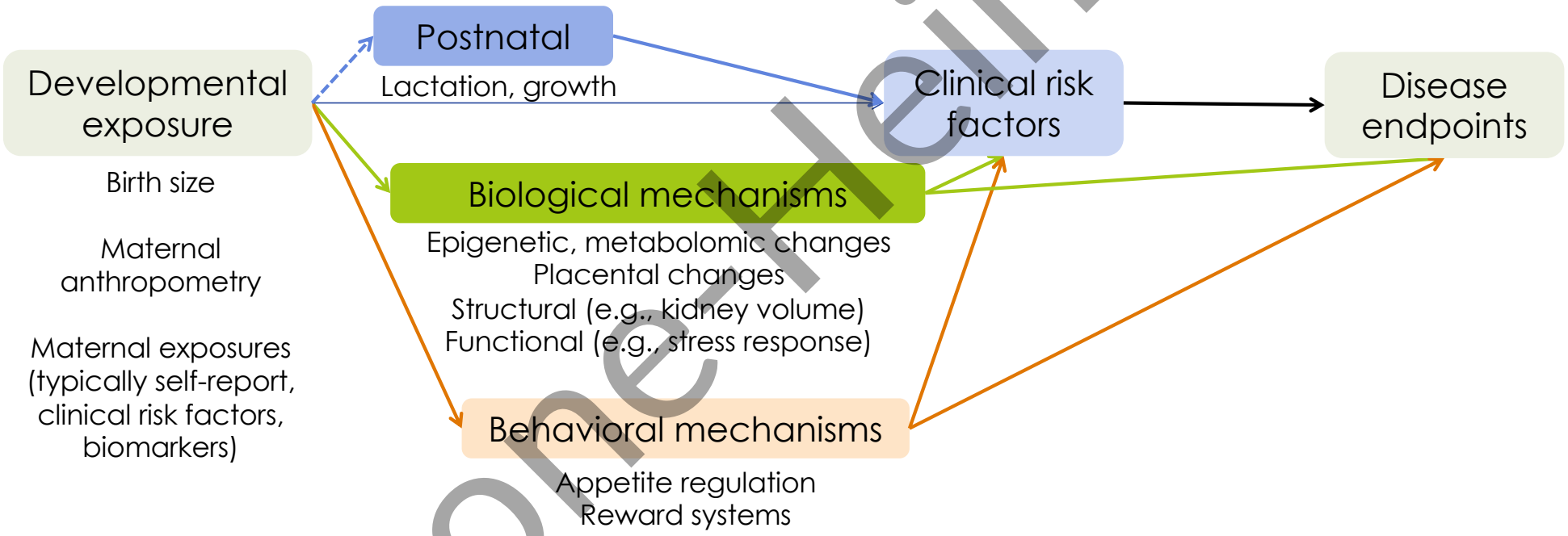
Objectives

- Share examples of **types of epidemiologic DOHaD research**: in the realm of childhood growth and cardiometabolic disease prevention
- Apply a **public health lens** to DOHaD research questions and implications

Types of processes and outcomes examined in epidemiologic DOHaD research



Study populations and data sources

Registry/vital records/linkage studies

Birth weight, Famine

Helsinki Birth Cohort

Disease, Mortality

Linked clinical records

Maternal BMI, conditions
Birth outcomes

Growth
BMI, BP, etc

Kaiser Permanente studies
PCORnet

Prospective studies

(linked birth record)
Maternal nutrition
Cord blood, Placenta

Growth
Bio/behavioral

Clinical outcomes

Project Viva
Pregnancy, Infection, and Nutrition (PIN) Study
Healthy Start I, II
Vellore Birth Cohort Study in South India
Cebu Longitudinal Health and Nutrition Survey

"Hybrid" studies (example)

Grandmaternal data from maternal birth record (F_0)

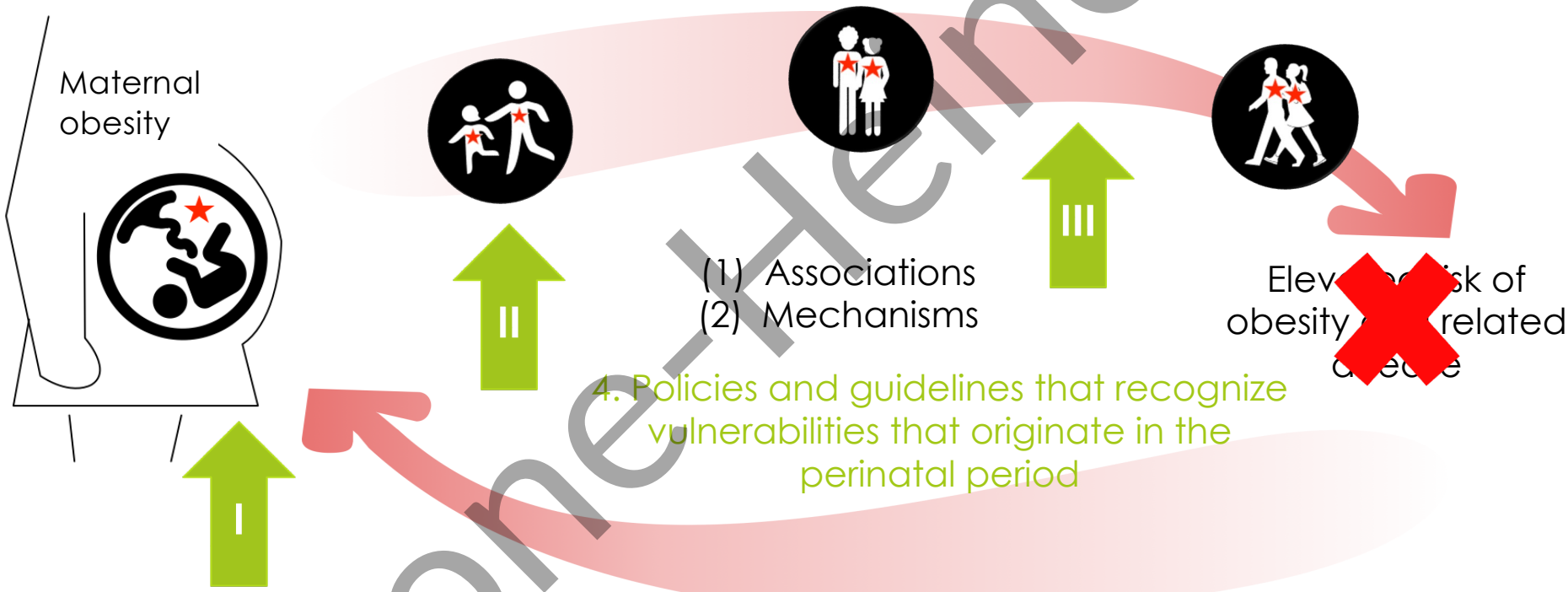
Prospective study (F_1)

Bogalusa Heart Study
Framingham Offspring
Add Health

Prospective offspring study (F_2)

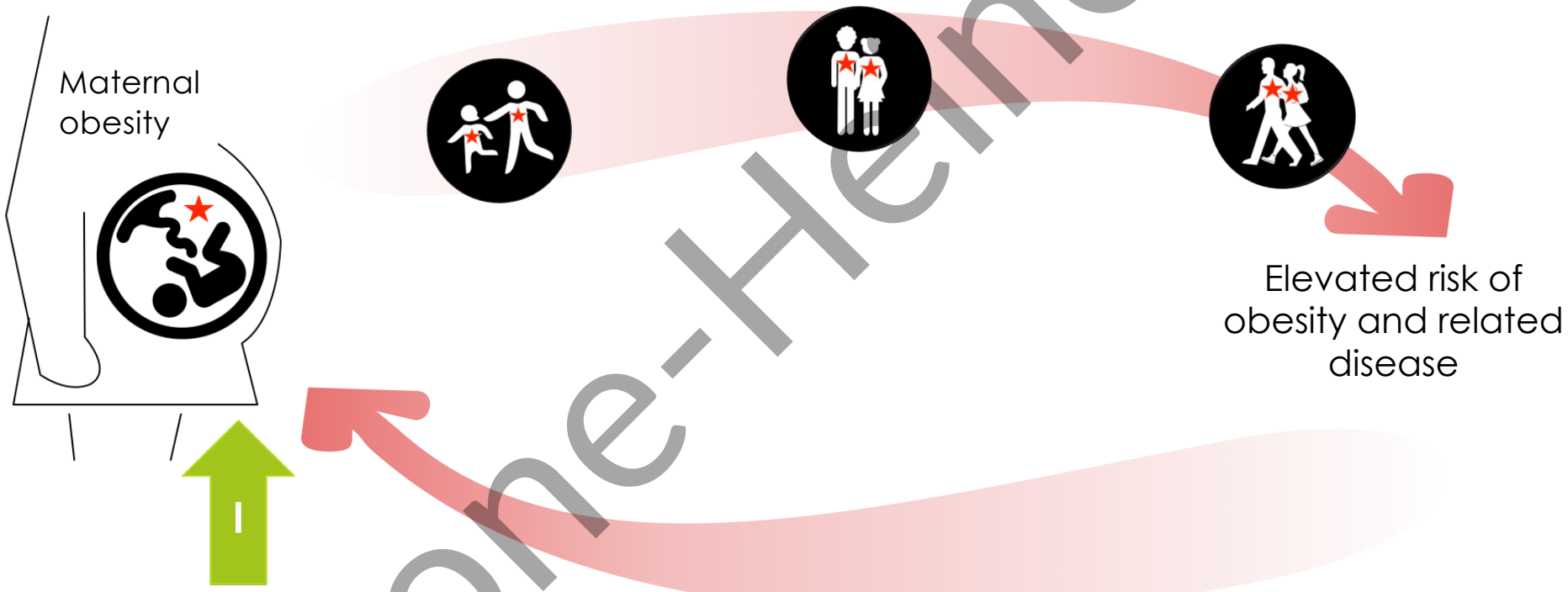
Noted *studies* are illustrative examples | General types of study designs shown

Public health lens: Mitigating the intergenerational cycle of cardiometabolic disease



Boone-Heinonen J, Messer LC, Fortmann SP, Wallack L, Thornburg KL (2015) Prev Med. 81:451-459

I. Pregnancy health



Primary focus of prevention efforts

a) Preconception weight loss, nutrition *(stay tuned: Kim Vesco's talk on Wed!)*
b) Healthy gestational weight gain, nutrition

1. What are optimal GWG patterns in pregnant people with Class II or III obesity?

GWG amount, timing

- Birth outcomes
- Longer-term child outcomes (to 5 years of age)

PROMISE: **PR**eventing **O**besity through healthy **M**aternal gestational weight gain **i**n the **S**afety N**e**t

- Pregnancies that started between 4/16/2004 and 7/6/2020 among OCHIN health network patients 15 years of age or older at pregnancy start (N>75,000)

ADVANCE Collaborative pcornet The National Patient-Centered Clinical Research Network

NIDDK: R01-DK118484

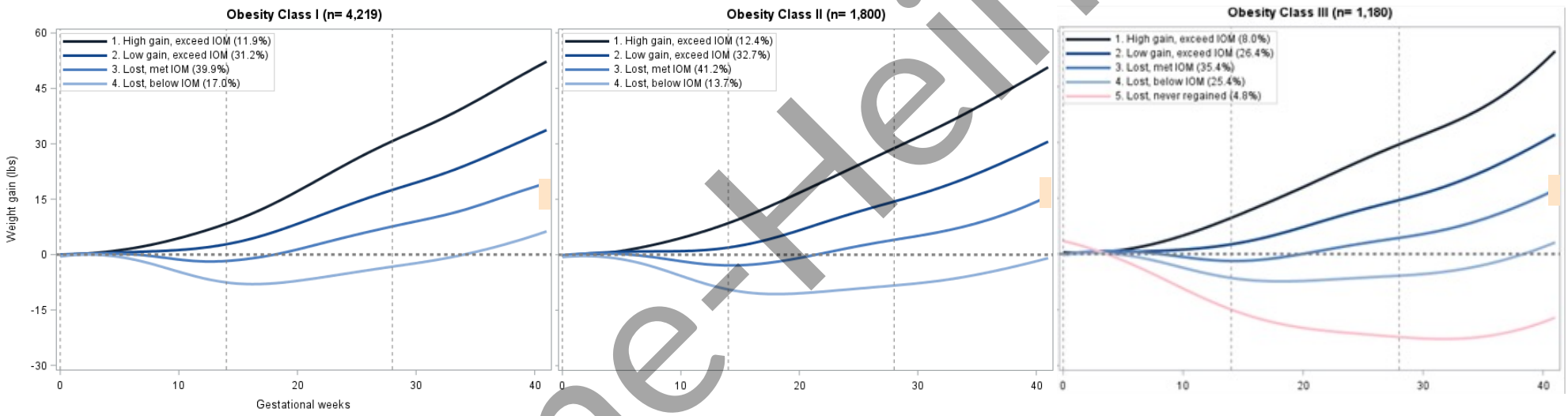
Existing GWG recommendations

- Not available for obesity sub-classes, largely due to scarcity of evidence
- Based on evidence in which women from racial and ethnic minority groups, and with lower income are under-represented

Characterizing GWG trajectories

PROMISE

Group-based latent trajectories



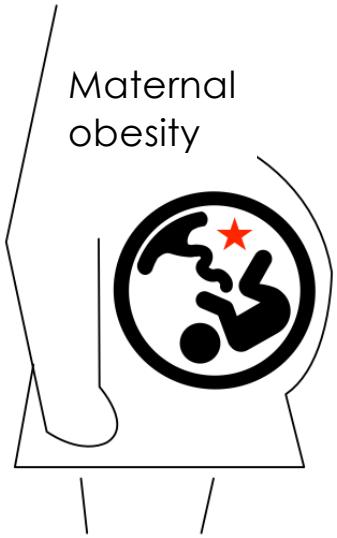
Key findings

- Over half of patients were classified in trajectory groups with first trimester weight loss
- The only trajectories that ended within IOM recommendations began with weight loss
- Weight loss is more extreme for women with Class III obesity

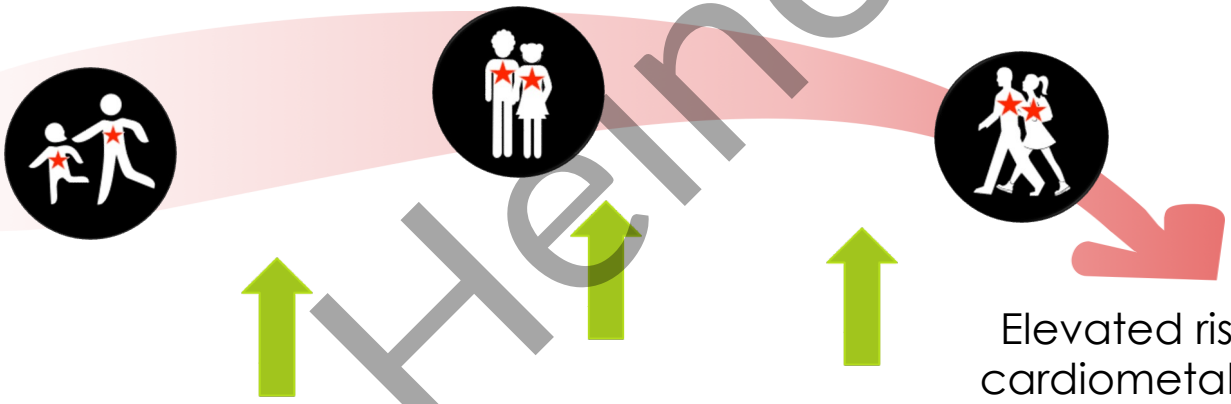
Tran ST et al. Oral presentation: SER Annual Research meeting, 2021. Manuscript drafted.

IOM recommendation for BMI ≥30:11-20 lbs total

II-III. **Mitigating** fetal programming effects



20% of children

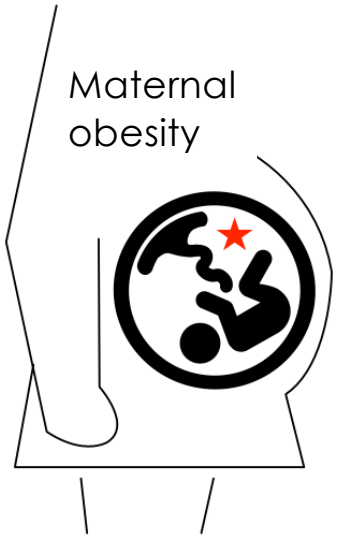


Elevated risk of cardiometabolic disease

- **What can be done to prevent cardiometabolic disease later in the child's life?**
- How and when can we prevent the manifestation of fetal programming effects?

Boone-Heinonen J, Messer LC, Fortmann SP, Wallack L, Thornburg KL (2015) Prev Med. 81:451-459

What are the changes that need to be reversed or overcome?



Brain: appetite regulation

Skeletal muscle: low mass, glucose regulation

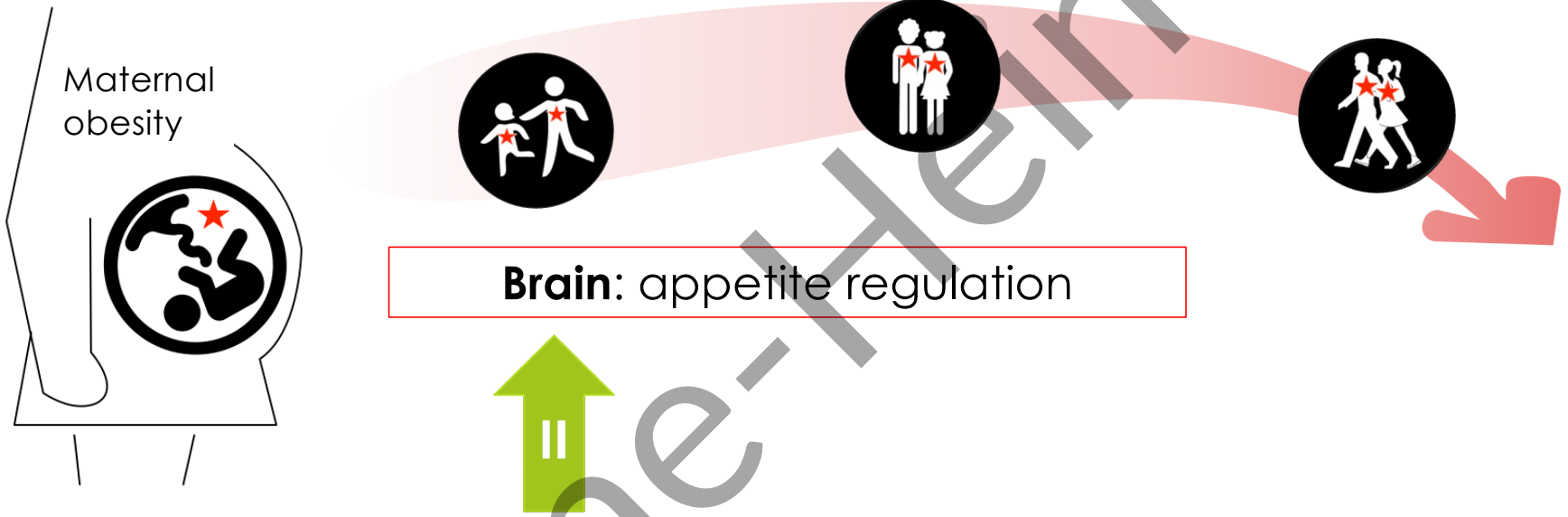
Liver: lipid metabolism

More adipose tissue
Insulin resistance

Obesity
Diabetes
Fatty liver
CVD

II. Behavioral mechanisms

Programming of early childhood eating behavior

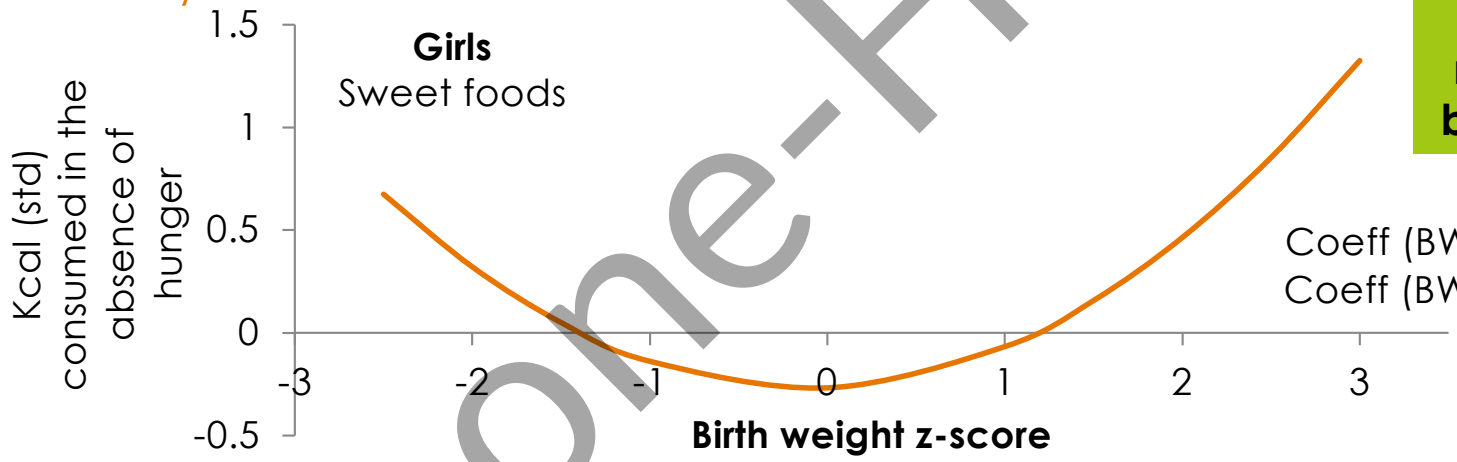


Programming of early childhood eating behavior

ABC Cohort (Appetite, Behavior, and Cortisol); low-income

- ABC Toddler (n=154; mean age 33 months)
- ABC Preschool (n=333; mean age 51 months)

Eating in the absence of hunger (EAH) protocol (gold standard measure of eating disinhibition)



BW was NOT related to eating behaviors in BOYS

Coeff (BWz)=0.04 (-0.10, 0.17)
Coeff (BWz^2)=0.17 (0.05, 0.28)

Sex-stratified linear regression (n=195), adjusted for maternal age, race, child age.
Sweet kcal SD=62.

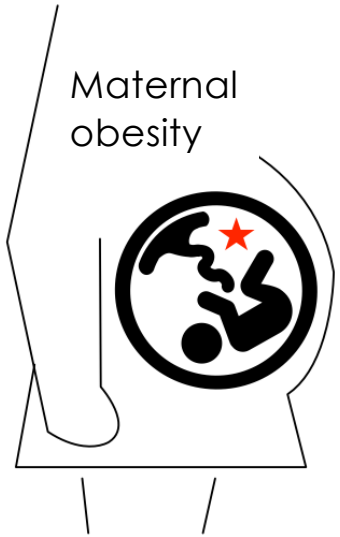
Boone-Heinonen J, Weeks H, Sturza J, Miller AL, Lumeng JC, Bauer KW (2019) Pediatr Obes. 14(11):e12554

Programming of early childhood eating behavior: **implications**

- Subgroups of children have difficulty regulating their intake
- Poor appetite regulation may be an important mechanism underlying prenatally-induced predispositions to obesity and cardiometabolic disease
  - Sex differences
- Food environment
  - Subgroups that may be hyper-responsive to food marketing, price, other manipulations
  - Opportunities to counteract poor appetite control

III. Overcoming programmed susceptibility

Prenatal-postnatal interaction

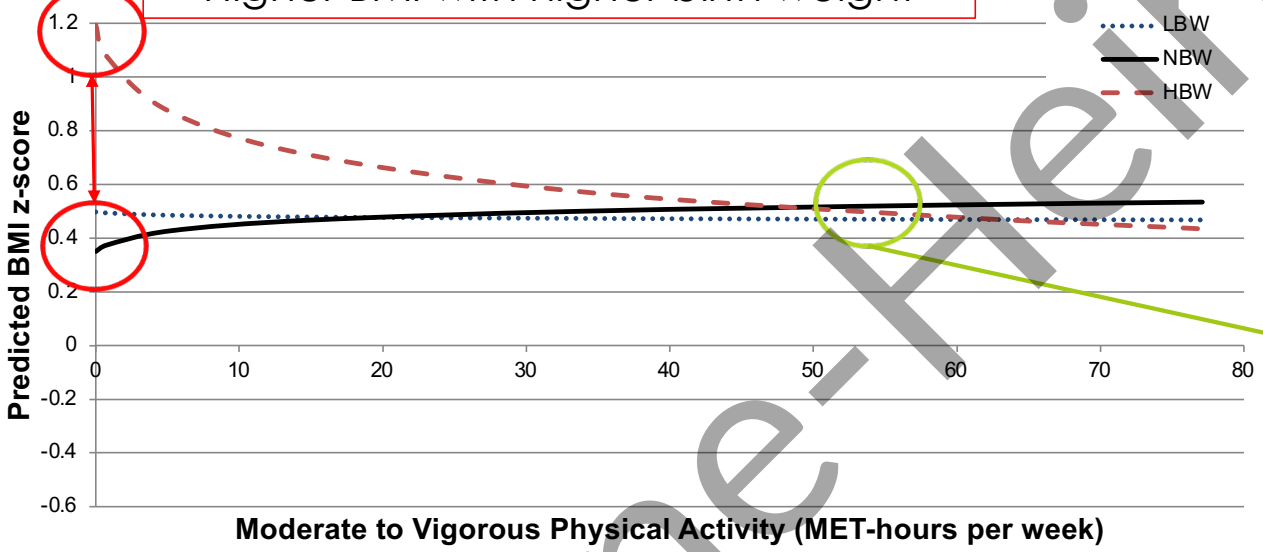


Skeletal muscle: lower mass, glucose regulation

Prenatal-postnatal interaction

Overcoming birth weight: can physical activity mitigate birth weight related differences in adiposity?

Higher BMI with higher birth weight



PA-BMI associations differ by BW (p interaction=0.05)

Weaker BW-BMI association among those with higher MVPA

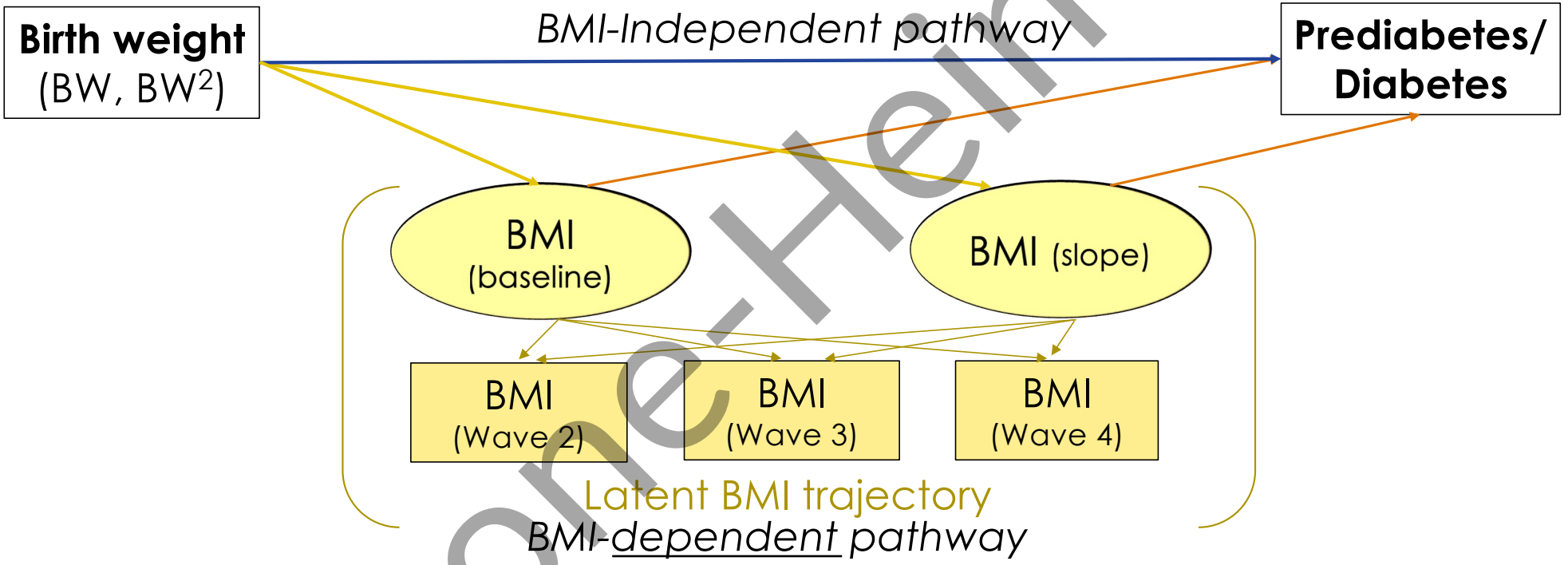
National Health and Nutrition Examination Survey 1999-2006

Girls 12-15 years of age

Sex-stratified linear regression, BMIz as a function of HBW, LBW, MVPA, HBW*MVPA, LBW*MVPA, adjusted for age, race/ethnicity, parent education, household income

Boone-Heinonen J, Markwardt S, Fortmann SP, Thornburg KT. Pediatr Obes. 11(3):166-73

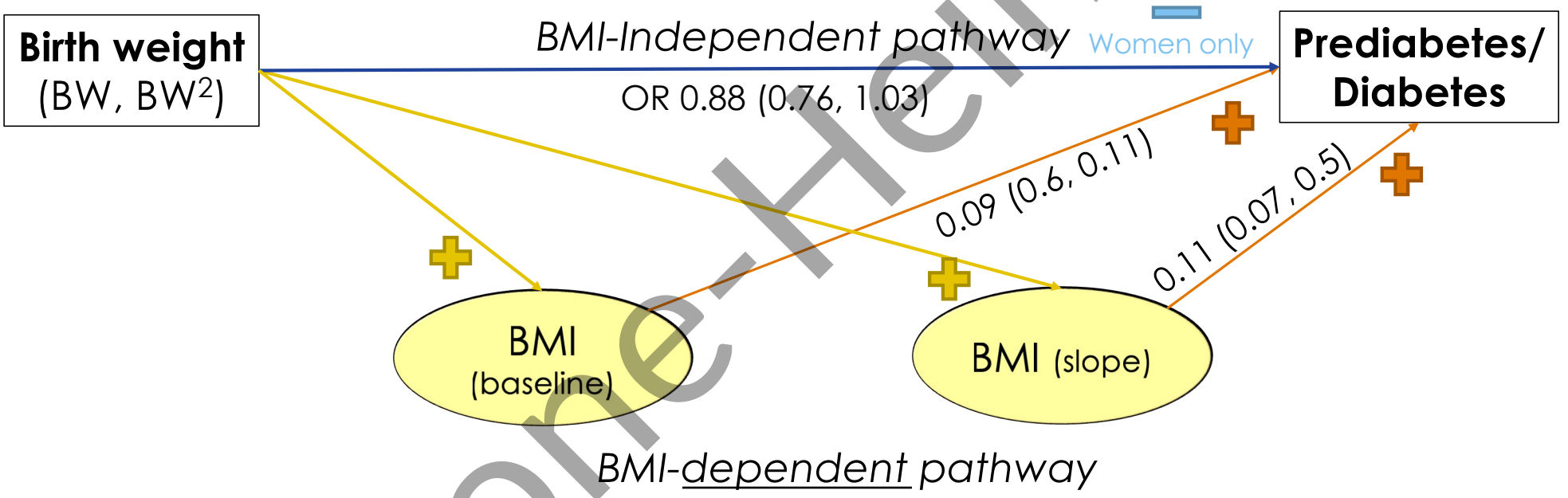
Prenatal development and adolescent obesity: two distinct pathways to diabetes in adulthood



National Longitudinal Study of Adolescent to Adult Health (AddHealth); n=13,413

Boone-Heinonen J, Sacks RM, Takemoto E, Hooker E, Harrod C, Dieckmann N, Thornburg KL. (2018) *Childhood Obesity*. 14(3):173-181.

Prenatal development and adolescent obesity: two distinct pathways to diabetes in adulthood



Suggests that mitigation of BW-associated diabetes risk requires intervention on factors other than obesity

Boone-Heinonen J, Sacks RM, Takemoto E, Hooker E, Harrod C, Dieckmann N, Thornburg KL. (2018) *Childhood Obesity*. 14(3):173-181.

Challenges and opportunities

- Challenges
  - Measurement of developmental exposures and intermediate outcomes: Need…
    - Rigorous measures (specific nutrition, chemical, etc exposures; placental or epigenetic metrics)
    - In large study populations
- Opportunities
  - Methods to combine data/evidence from many types of study designs: systems science, data sharing and collaboration
  - Getting closer to biologic signatures for exposures and disease processes (?)
    - Epigenetic
    - Metabolomic
    - Microbiome
    - Placenta

Acknowledgements

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Thank You!!!

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