Maternal weight and gestational weight gain as predictors of long-term offspring growth and health

Emily Oken, MD, MPH
Department of Ambulatory Care and Prevention
Harvard Medical School and Harvard Pilgrim Health Care

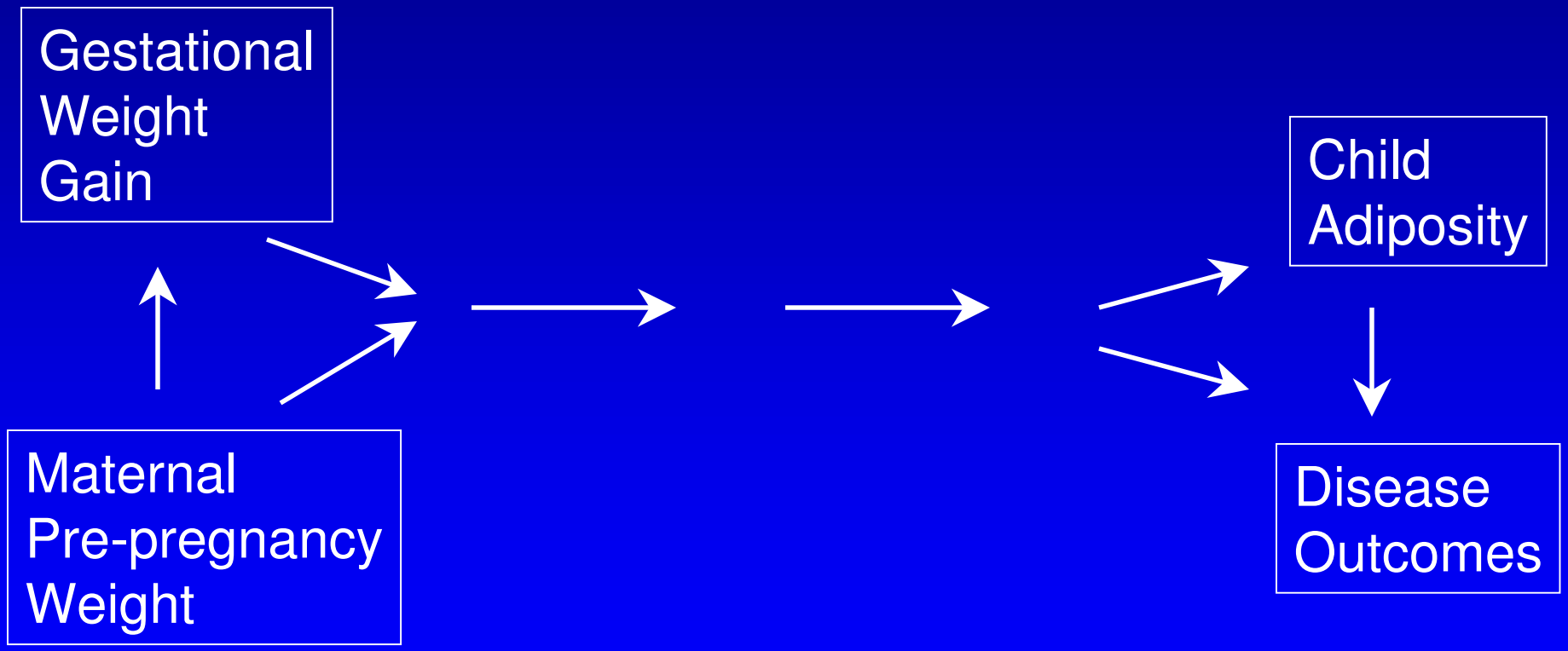
Outline

- Associations of maternal weight and gestational weight gain (GWG) with child outcomes
- Research gaps and challenges
- Mechanisms
- Areas for further study

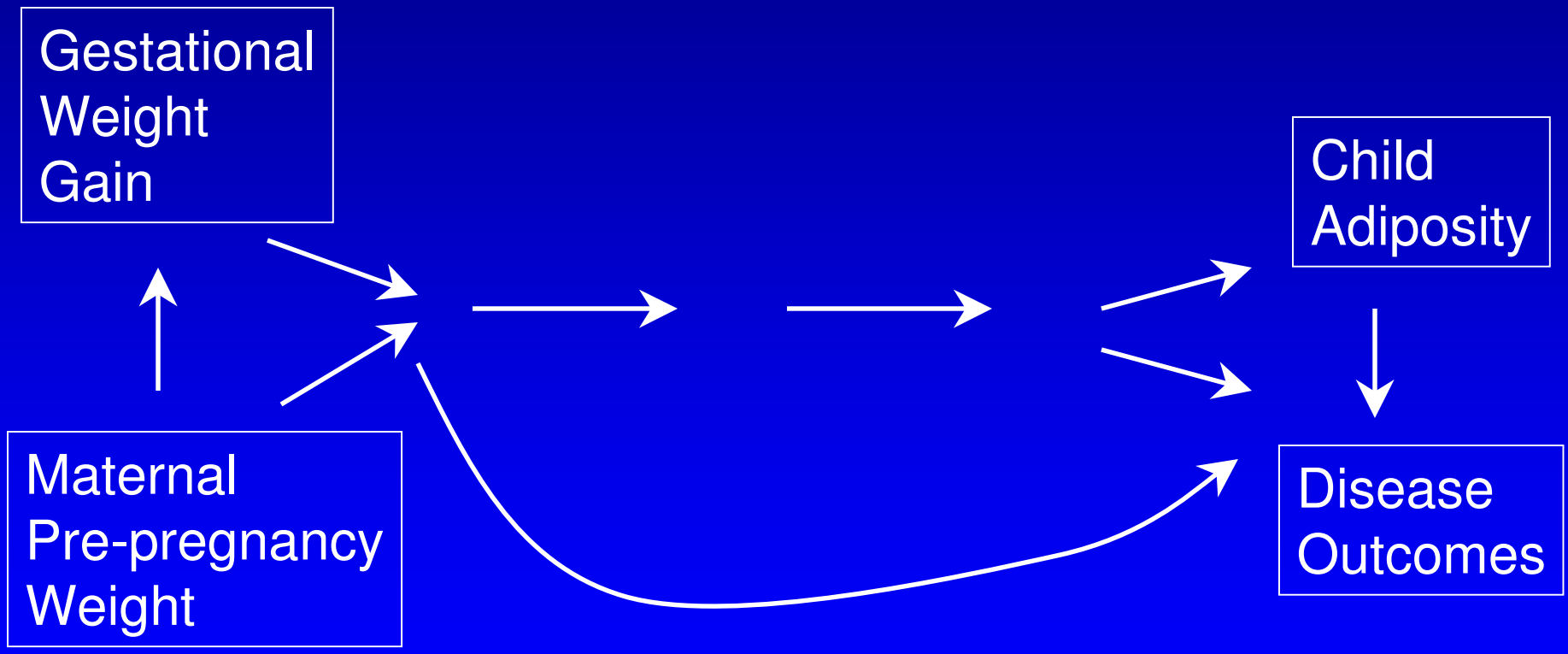
Longer-term child outcomes

- Overweight
- Adiposity and body proportions
  - Fat vs. lean body mass, central obesity
- Cardiovascular risk
  - Blood pressure, lipids, glucose intolerance, insulin resistance, type 2 DM, CVD
- Others
  - cancer, bone health, mental health

Pathways linking maternal weight with child outcomes



Pathways linking maternal weight with child outcomes



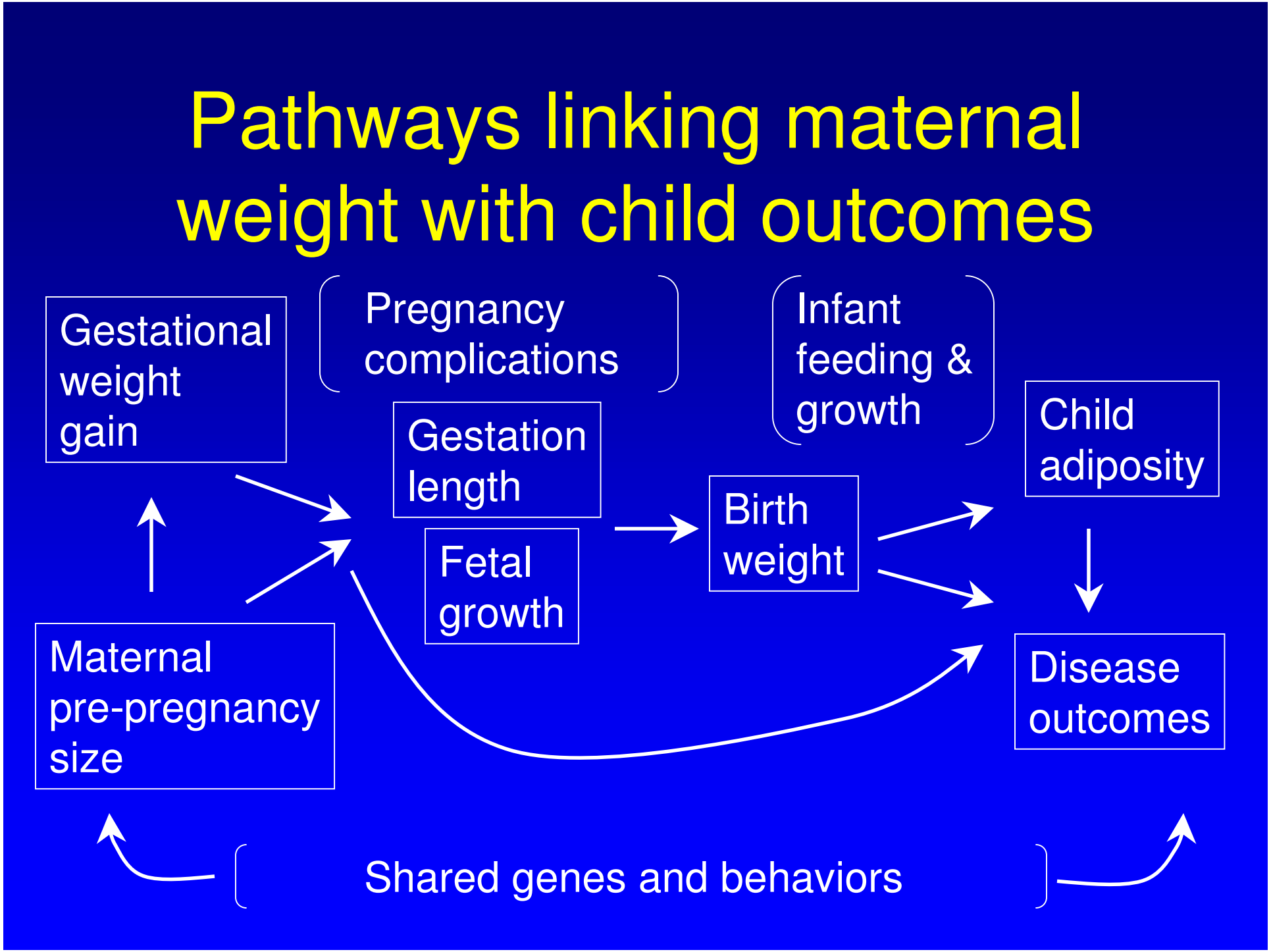
Early life factors
that may influence associations of maternal weight/GWG with offspring outcomes

- Glucose tolerance during pregnancy
- Birth weight (fetal growth)
  - Higher fetal growth more overweight
  - Lower fetal growth central obesity, glucose intolerance, CVD risk (after adjusting for BMI)
- Growth in early infancy

Other considerations

- Maternal and paternal BMI
  - a measure of shared genes and behaviors
- Smoking during pregnancy
- Infant feeding (breast vs. formula, timing of introduction of solids)
- Context
  - prevalence of maternal and offspring obesity
  - relevant for understanding associations and also for clinical and policy recommendations

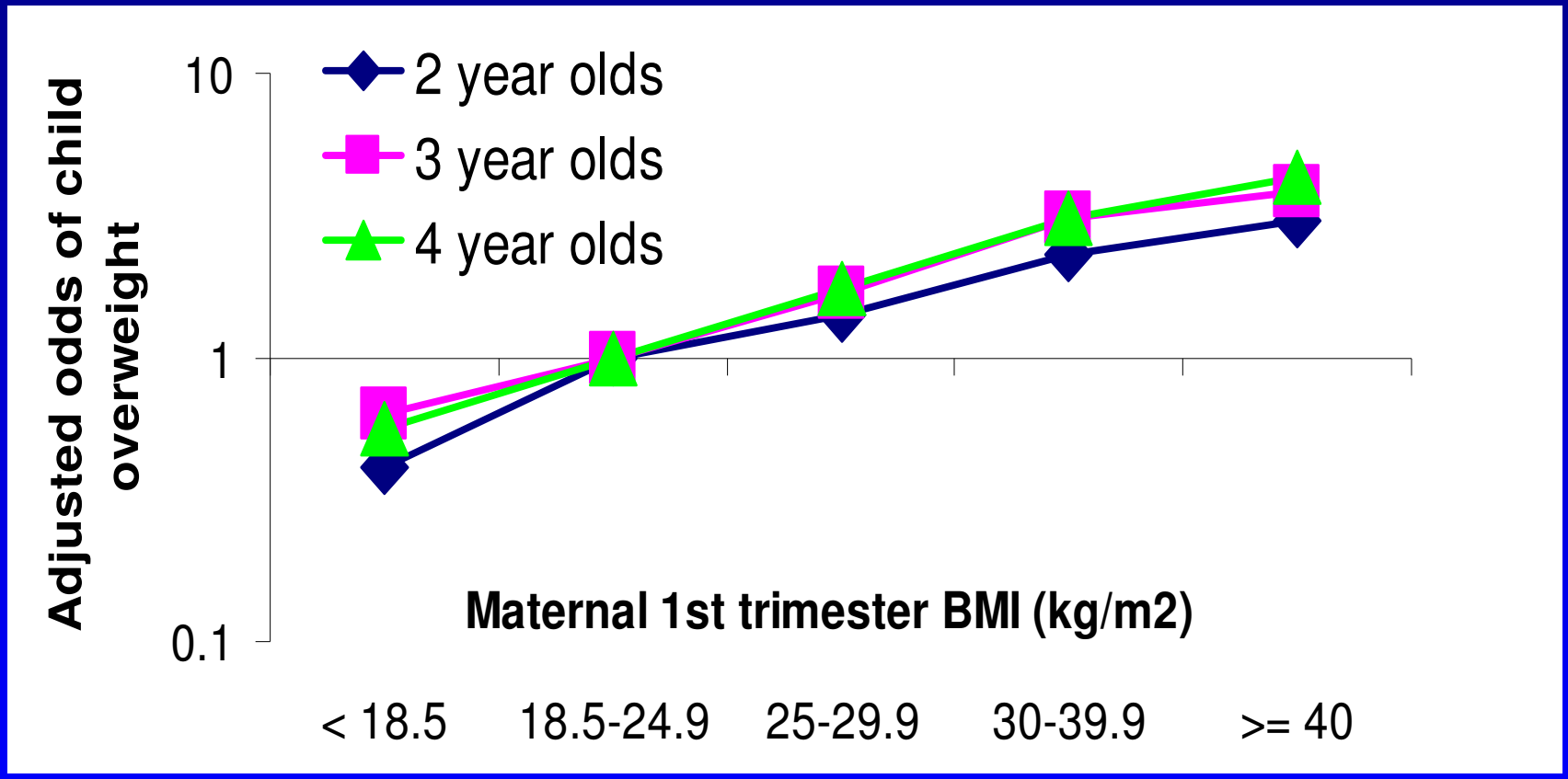
Pathways linking maternal weight with child outcomes



Maternal weight and offspring weight

- Fairly extensive literature linking maternal weight with
  - fetal growth
  - later offspring weight and risk for overweight (independent of effect on fetal growth)
- When paternal weight available, generally not as strongly associated with child weight
- Limited information available on outcomes other than weight

Maternal BMI and child obesity



8494 children in WIC Ohio. Adjusted for maternal, race/ethnicity, parity, smoking, education, marital status, age; gestational weight gain, and child sex, fetal growth and birth year

Whitaker, Pediatrics 2004;114(1):e29

Maternal BMI and offspring BMI

	BMI (kg/m^2)	GWG (kg)
Age	Beta (95% CI) for child BMI	
1	0.05 (0.03, 0.07)	
3	0.06 (0.03, 0.08)	
6	0.07 (0.05, 0.10)	
8	0.08 (0.06, 0.10)	
14	0.10 (0.08, 0.13)	
42-44	0.12 (0.10, 0.14)	

3426 births in Copenhagen 1959-61. 9% of moms and 43% of offspring with BMI > 25 kg/m2. Adjusted for sex, bw z-score, mom age, SES, smoking

Shack-Nielsen et al. Ped Research 2005 (abs)

Maternal BMI and metabolic syndrome

Outcome	Maternal BMI at 15 weeks gestation				
Age 41-47yrs	<= 19.2	19.3-20.5	20.6-22.3	>22.3	P trend
2hr glucose	133	126	128	101	0.008
Fasting insulin	49	50	41	40	0.07
2 hr insulin	399	299	252	181	0.02
LDL chol	122	104	108	107	0.01

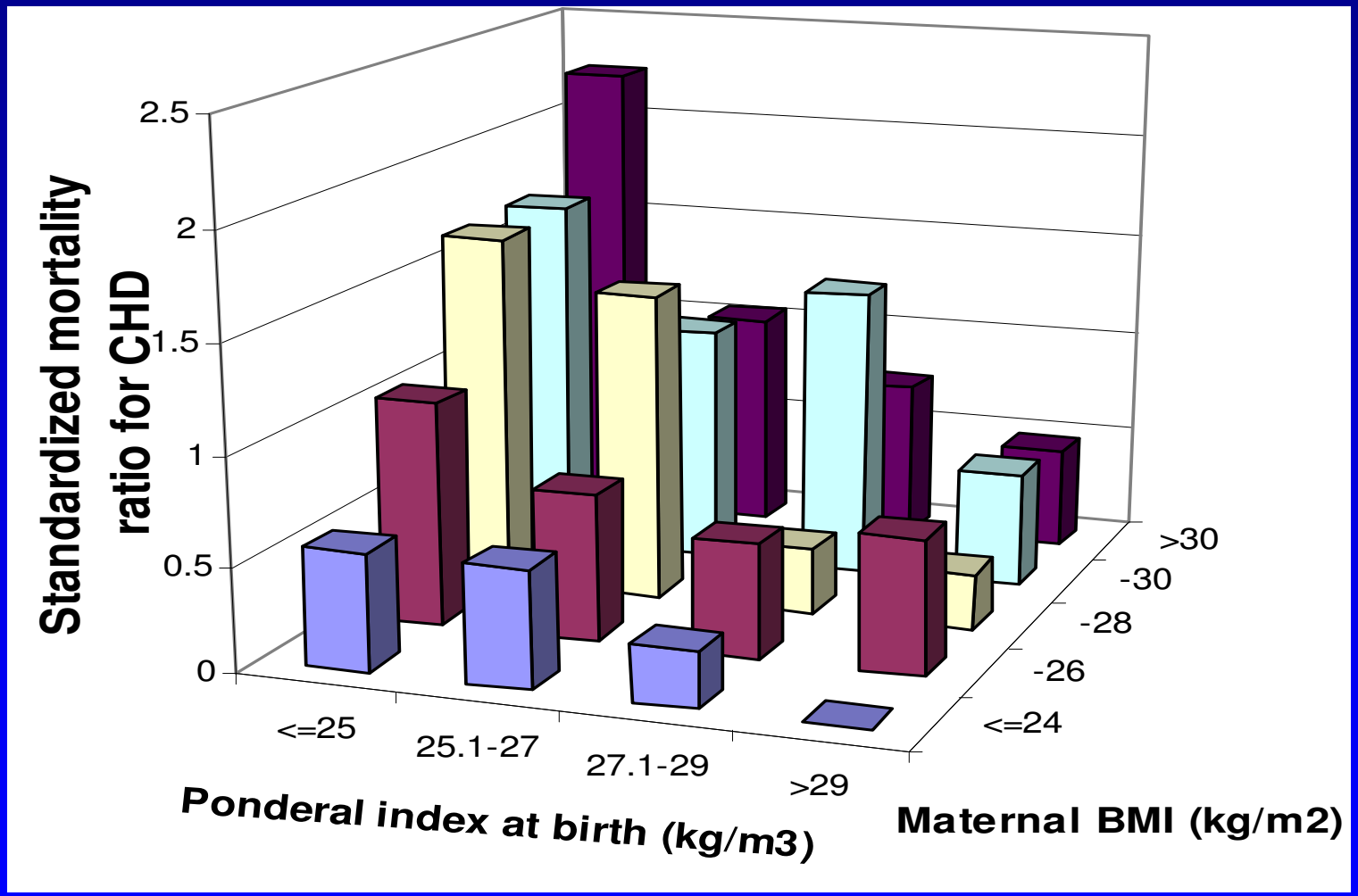
627 Chinese men and women aged 41-47yrs with available obstetric records. Estimates adjusted for offspring sex and BMI.

"no association of GWG with elements of the insulin resistance syndrome"

Mi et al, Ann Int Med 2000;132:253-260.

Maternal BMI and CHD risk

*among moms with height < mean



Not adjusted for attained BMI

Forsen et al, BMJ 1997;315:837-40.

Maternal weight and offspring outcomes - summary

- Linear relationship of maternal with child weight
  - Independent of fetal growth
  - Perhaps stronger with increasing child age
  - Reflects shared genes and behaviors
  - ? Also suggests fetal programming
- Limited information about offspring outcomes other than weight
  - Available data suggestive of a link with CVD risk
  - Historical data make it difficult to generalize
- May be difficult to modify especially in the short-term

Gestational weight gain and offspring weight

- Potentially more readily modifiable
- Minimal & limited published data
  - GWG not included in many studies of early life determinants of weight
  - When considered, often a covariate but not the primary exposure of interest
  - Mostly abstracts, few full-length studies, though some in progress

GWG and offspring weight

	Wt/ht > 95th %ile	Wt/ht < 5th %ile
Age	Mean GWG (kg)	
Birth	14.2	10.1
4	12.3	11.2
7	12.2	11.0

Unadjusted

Minnesota CPP, 1786 children born 1960's. Mean mat weight 68 kg for large babies and 54.8 kg for small babies

Fisch et al, Pediatrics 1975;56(4):521-8.

GWG and offspring weight

- Philadelphia CPP
- 447 African Americans born 1959-1965 followed to age 18.0-22.9 years
- 13.9% increased adiposity (SS+TR>85th %ile)
- Median maternal GWG 9.5 kg (10th %ile 3.6 kg, 90th %ile 16.8 kg)
- Pre-pregnancy BMI 22.5 kg/m^2 (10th %ile 19.1, 90th %ile 29.1)
- “null”

Stettler et al, Am J Clin Nutr 2000;72:378-83

Maternal weight and offspring BMI

	BMI (kg/m^2)	GWG (kg)
Age	Beta (95% CI) for child BMI	
1	0.05 (0.03, 0.07)	0.03 (0.02, 0.05)
3	0.06 (0.03, 0.08)	0.02 (0.00, 0.04)
6	0.07 (0.05, 0.10)	0.02 (0.00, 0.04)
8	0.08 (0.06, 0.10)	0.03 (0.02, 0.05)
14	0.10 (0.08, 0.13)	0.03 (0.01, 0.05)
42-44	0.12 (0.10, 0.14)	0.03 (0.01, 0.04)

3426 births in Copenhagen 1959-61. 9% of moms and 43% of offspring with BMI > 25 kg/m2. Adjusted for sex, bw z-score, mom age, SES, smoking No interaction.

Shack-Nielsen et al. Ped Research 2005 (abs)

GWG and offspring weight

- 11,428 children born 1974-6 in Jerusalem followed to age 17 years
- Effect of GWG > 16 kg (90th %ile) vs. less:

	Odds ratio (95% CI) for obesity (child BMI > 90th %ile)
Boys	1.70 (1.31, 2.20)
Girls	1.74 (1.28, 2.36)

Adjusted for maternal prepreg BMI, SES, ethnicity, education, occupation; Infant birth order, birth weight, gestational age

Seidman et al, Pediatr Res 1996;39:112A (abs).

GWG and offspring weight

- 1363 Caucasian children in Italy aged 4-12 years in 1988
- Recalled total GWG (mean 12 kg)

	Odds ratio (95% CI) for obesity (child BMI > 95th %ile)
Boys	1.01 (0.96, 1.05)
Girls	1.01 (0.96, 1.05)

Adjusted for birth weight, breastfeeding, age at weaning; father's and mother's age, BMI, education, and occupation. Mean maternal BMI 23.5 kg/m2. Obesity in 19% of boys and 21% of girls.

Maffeis et al, IJO 1994;18:304-8

GWG and offspring weight

Child outcome age 9 years	Beta	95% CI
BMI	-0.25	(-0.47, -0.03)
TR skinfold	-0.01	(-0.19, 0.17)
SS skinfold	0.10	(-0.14, 0.34)
% body fat (bio-impedance)	-0.27	(-0.61, -0.01)

Retrospective study of 110 Italian 4th graders; not adjusted for maternal BMI or other characteristics

Antonella et al., IJO 1994;18:596-601

GWG and offspring weight

	Quartile of net GWG			
	1	2	3	4
Age (y)	Odds Ratio (95% CI) for overweight			
2	1.0 (ref)	0.79 (0.62,1.00)	1.00 (0.79, 1.26)	0.92 (0.72, 1.16)
3	1.0 (ref)	0.84 (0.67, 1.05)	0.95 (0.75, 1.20)	1.07 (0.86, 1.34)
4	1.0 (ref)	0.95 (0.76, 1.20)	1.12 (0.89, 1.42)	1.09 (0.87, 1.37)

Net GWG = (GWG – birth weight) /gestation length

Odds ratios adjusted for maternal 1st trimester BMI, race/ethnicity, parity, smoking in pregnancy, education, marital status, age; and child sex, fetal growth and birth year

Whitaker, Pediatrics 2004;114(1):e29

Probability of Childhood Overweight by Maternal PWG & pre-pregnant BMI

Model adjusted for child's age, sex, race/ethnicity, state and mother's age, height, education, pregnancy smoking status

AJ Sharma, et al, (2006) Maternal and Child Nutrition, Division of Nutrition and Physical Activity, CDC

GWG and offspring weight-
Project Viva

- Pregnancy and child cohort including over 2000 births 1999-2002
- Recruitment: initial OB visit at multi-specialty group in eastern MA
- Follow-up of over 1000 children to age 3 years

GWG and offspring weight-
Project Viva

- Maternal pre-pregnancy BMI
  - Mean 24.6 kg/m2 (SD 5.0)
  - 13% BMI 26.1-29.0, 16% BMI > 29.0
- Gestational weight gain
  - Mean 15.6 kg (SD 5.4)
  - 14% inadequate, 35% adequate, 51% excessive per IOM guidelines
- Child weight (age 3 years)
  - Mean BMI z score 0.46 units
  - 9% overweight

GWG and offspring weight-
Project Viva. Effect per 5kg of GWG

Additionally adjusted for maternal prepregnancy BMI, smoking, race/ethnicity, household income, marital status, glucose tolerance tolerance in pregnancy; paternal BMI; and infant sex, gestation length, and breastfeeding duration. No interaction between BMI and GWG

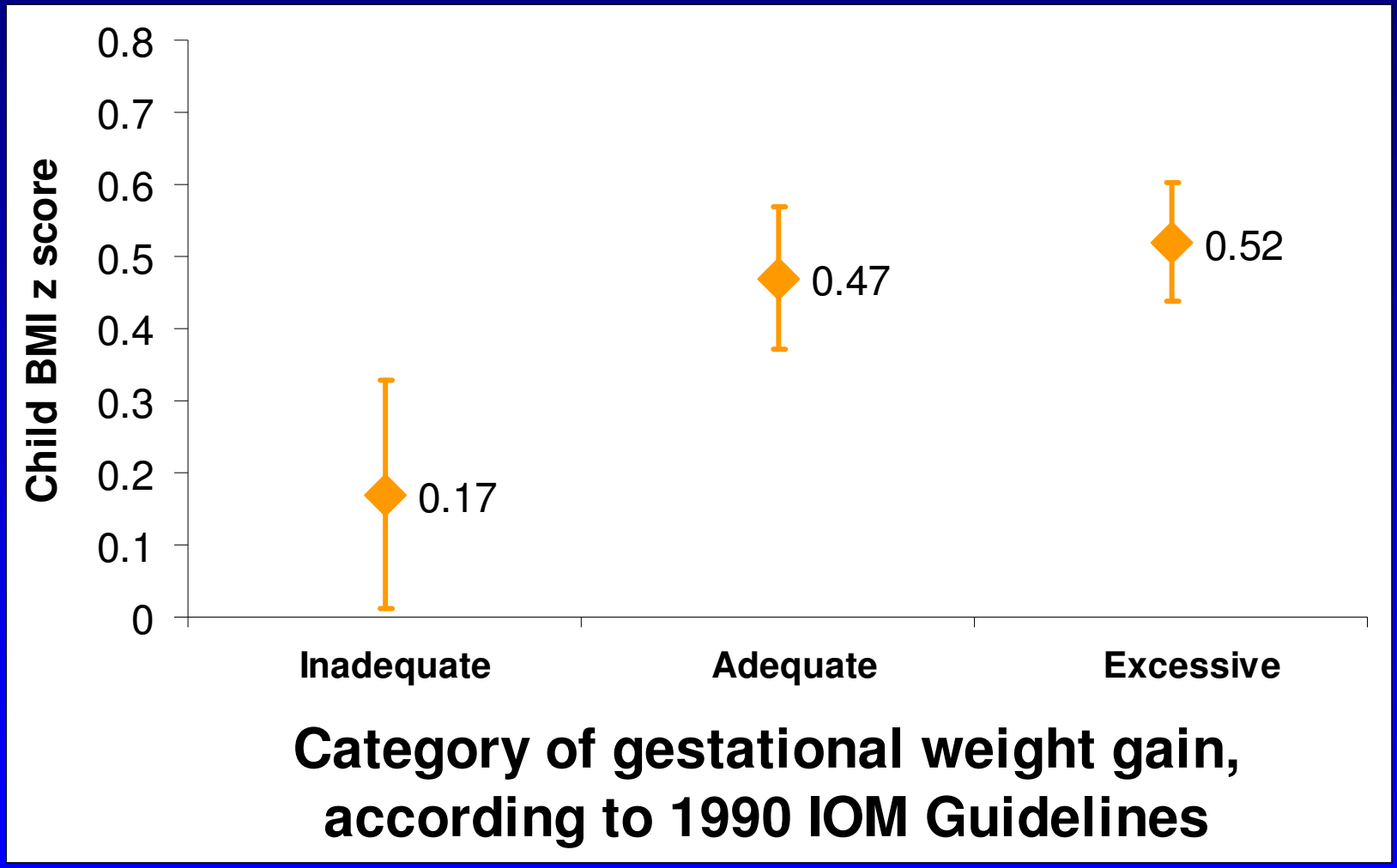
Oken et al., in progress

GWG and infant growth - Viva

Adjusted for maternal pre-pregnancy BMI, smoking, race/ethnicity, household income, marital status, glucose tolerance tolerance in pregnancy; paternal BMI; and infant sex, gestation length, and breastfeeding duration

Oken et al., in progress

GWG and offspring weight



Adjusted for maternal prepregnancy BMI, smoking, race/ethnicity, household income, marital status, glucose tolerance tolerance in pregnancy; paternal BMI; and infant sex, gestation length, and breastfeeding duration

Oken et al., Ped Res 2005 (abs)

GWG and offspring weight - summary

- Preponderance of evidence suggests a direct association of GWG with offspring overweight
  - But some exceptions
- Independent of fetal growth
- Shape of association not yet clear
  - ? higher risk of overweight with low GWG, especially in underweight mothers
- Interaction between maternal BMI and GWG not consistent across studies

GWG and offspring weight – limitations of the literature

- Most data from a previous generation with different obesity and weight gain prevalence
- Many studies not adjusted for important covariates
  - Incl. SES, smoking during pregnancy, paternal weight, breast feeding, weight gain in infancy
- All from observational studies
- Limited information on adiposity, fat distribution, and sequelae of overweight

GWG and offspring weight - areas for future research

- Studies using IOM weight gain categories
- Measures of body fat distribution and disease risk
- Longer f/u of children born post-1990
- Child f/u of trials targeting GWG
- Vulnerable populations
  - "nutrition transition"

Mechanisms

- Lessons learned from
  - Intrauterine exposure to diabetes mellitus
  - Animal studies

Lessons from animal studies

- Animal models (mainly rats)
  - Experimental induction of GDM
  - Injection of insulin or glucocorticoids into pregnant mother
  - Neonatal overfeeding
- Physiologic responses include:
  - More sedentary behavior, increased appetite
  - Increased body fat
  - Alterations in hypothalamic nuclei responsible for appetite regulation
  - Hormonal changes – higher leptin, insulin

Diabetes during pregnancy

- Offspring of mothers with DM in pregnancy:
  - Higher risk of obesity
  - More glucose intolerance, insulin resistance, diabetes
  - More hyperglycemic, hyperinsulinemic
  - Persistent changes in pancreatic function
  - Increased appetite, decreased activity

Summary

- Available data suggest that maternal weight and gestational weight gain are independently associated with risk for offspring overweight and perhaps cardiovascular disease risk

- Current weight gain recommendations should be re-evaluated, considering longer-term offspring outcomes