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Fetal overnutrition and its role in obesity and diabetes.

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Avera 



Chronic disease in TODAY'S children



Chronic disease in TODAY'S children

13%
hypertension,
pre-hypertension



Chronic disease in TODAY'S children

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hypertension,
pre-hypertension

15%

diabetes or
pre-diabetes



Chronic disease in TODAY'S children

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33%
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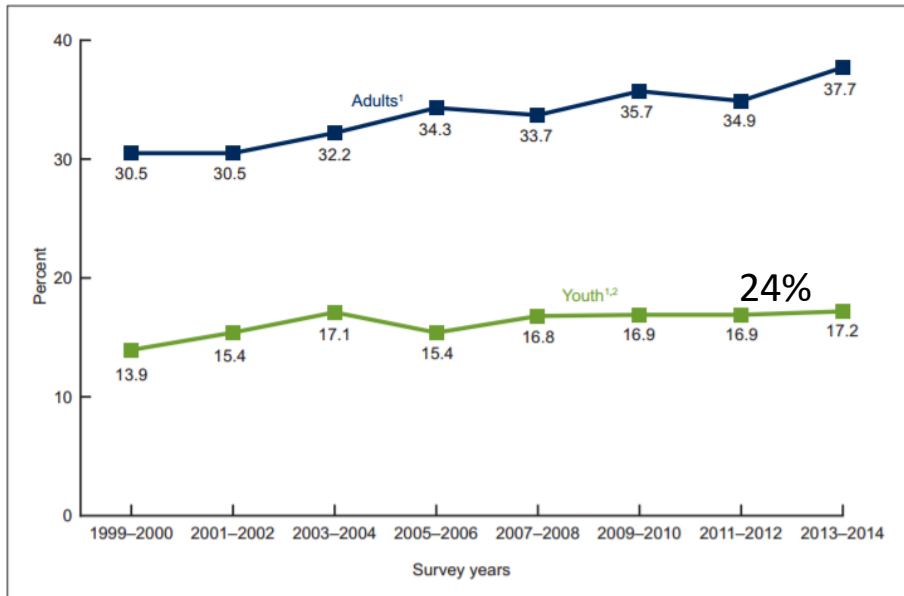
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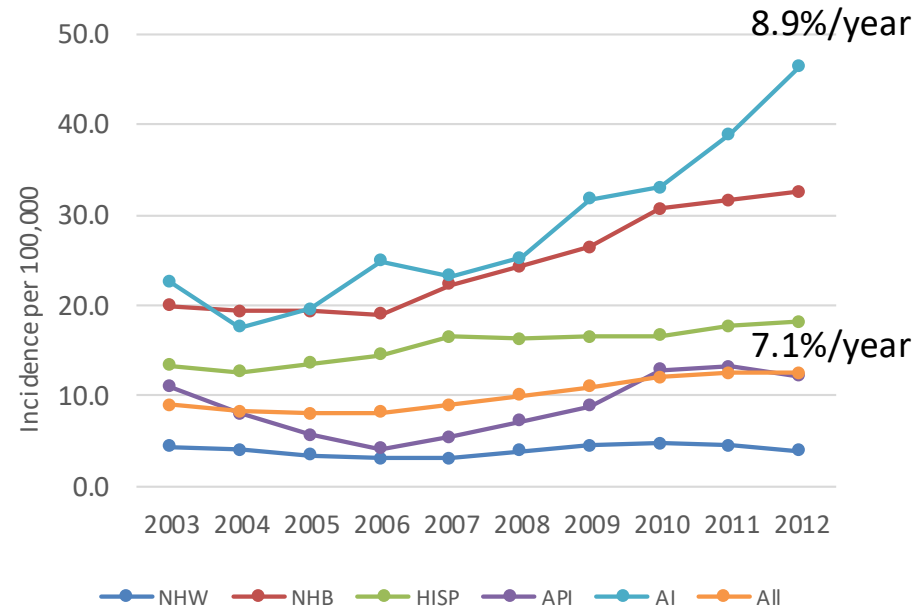
40%

cardiometabolic
risk factor

Chronic disease in TODAY'S children



Increasing prevalence of childhood obesity and younger age at onset



Rise in youth onset type 2 diabetes, novel pediatric condition

Chronic disease in TOMORROW'S adults

57%

will be obese at 35 years of age

45%

will have diabetes or pre-diabetes
by 2030

42%

will have hypertension by 2035

\$147 billion

In medical costs

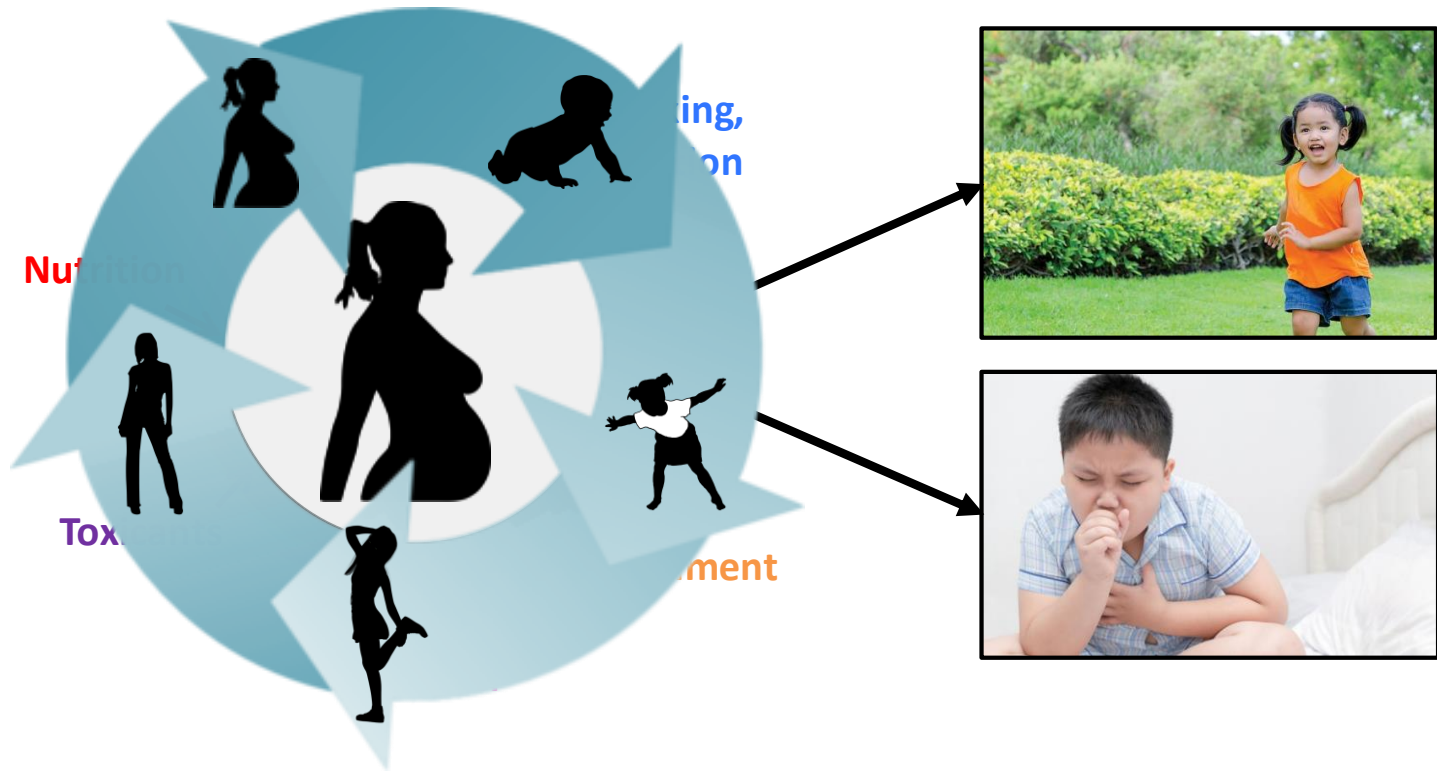


Chronic disease at YOUNGER ages

- Sharp increase in obesity among children aged 2-5 years
 - » 9.3% (NHANES 2013/14) vs. 13.7% (NHANES 2015/16)
- One quarter of pediatric diabetes cases today are type 2 diabetes

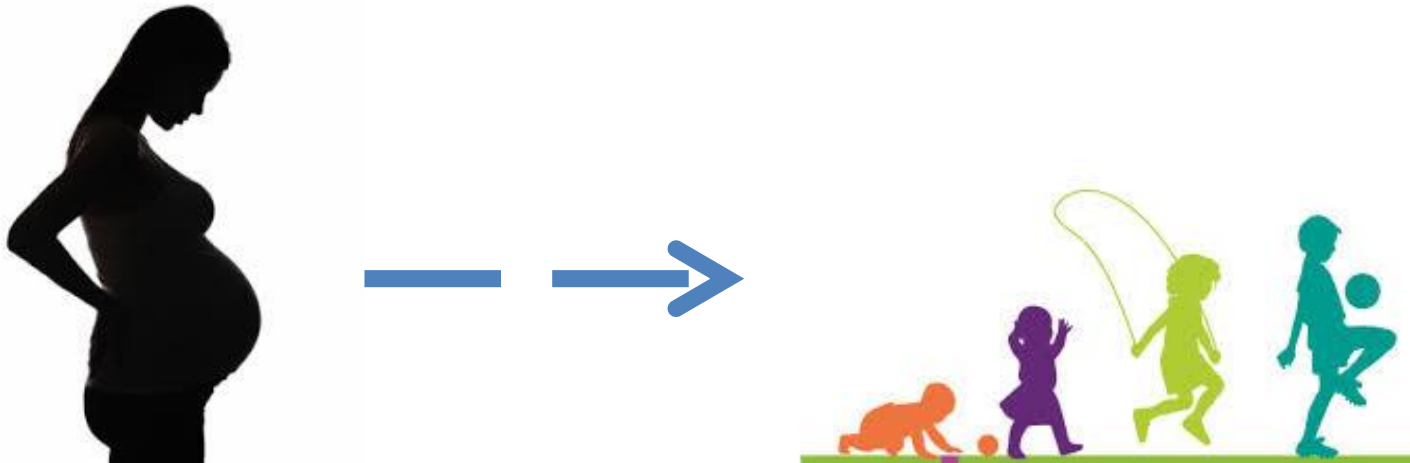


Developmental origins theory



Evidence for developmental origins

- Maternal factors in pregnancy
 - Undernutrition
 - Overnutrition
 - Physical activity
 - Substance use
 - Environmental exposures



Fetal UNDERnutrition



Fetal **UNDER**nutrition

- Dutch Hunger Famine, 1944-1945

Exposed to famine in 1 st trimester	Exposed to famine in 2 nd trimester	Exposed to famine in 3 rd trimester
↓ glucose tolerance ↑ atherogenic lipid profile		
Normal birth weight ↑ BMI, obesity as adults	↓ birth weight No increase in BMI, obesity as adults	
↑ coronary heart disease ↑ breast cancer ↓ selective attention	↑ obstructive airways disease ↑ microalbuminuria	

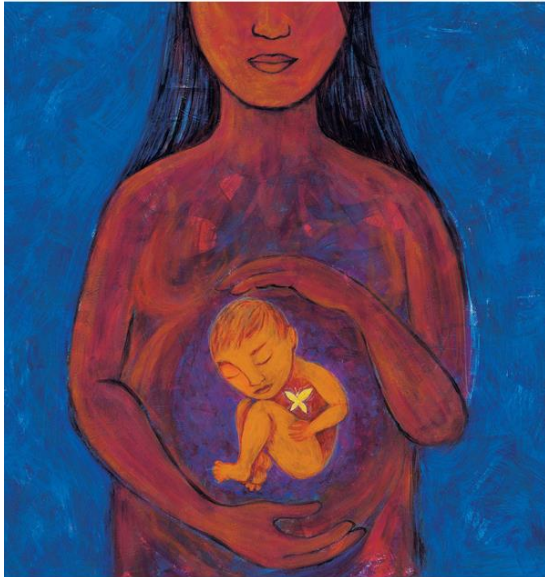
Fetal **OVER**nutrition

~50% of women
overweight/obese at conception

~50% of women
gain too much in pregnancy

~10% of women have
diabetes in pregnancy (T1, T2, GDM)

Fetal **OVER**nutrition



Increased glucose and other nutrients in the maternal blood

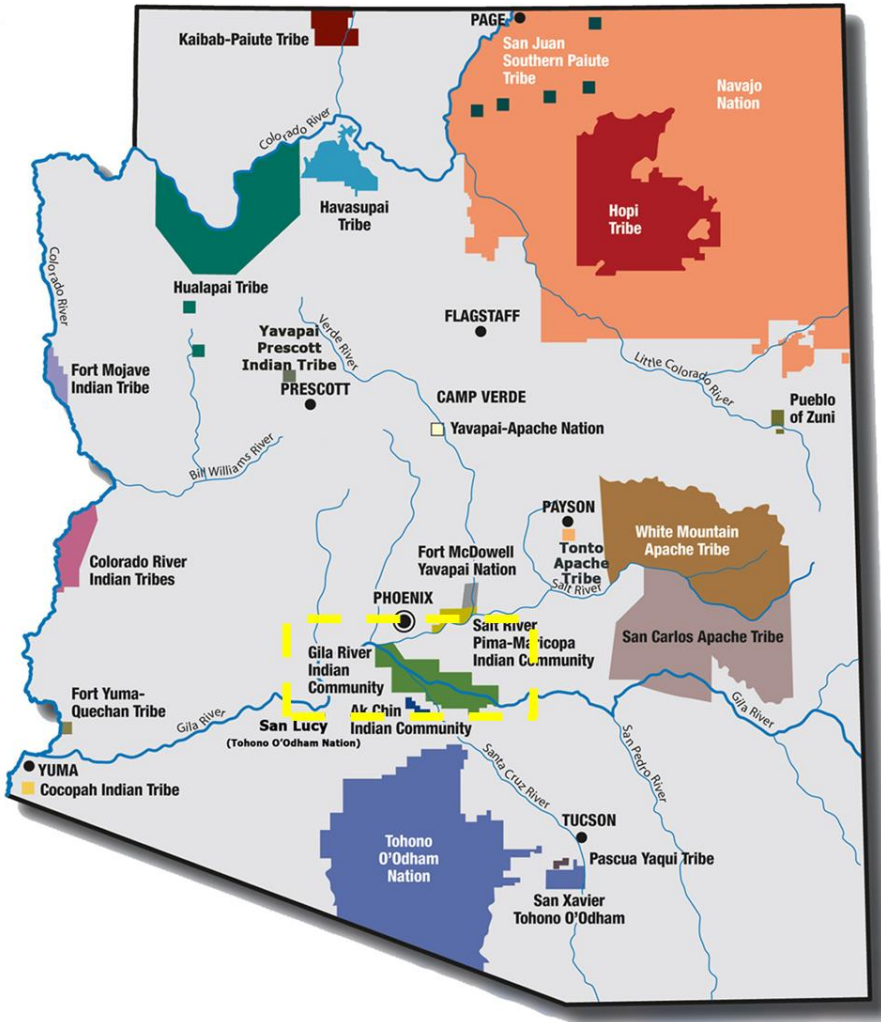
Maternal  Insulin



Increased anabolic hormones and growth factors promoting growth and adiposity in the fetus



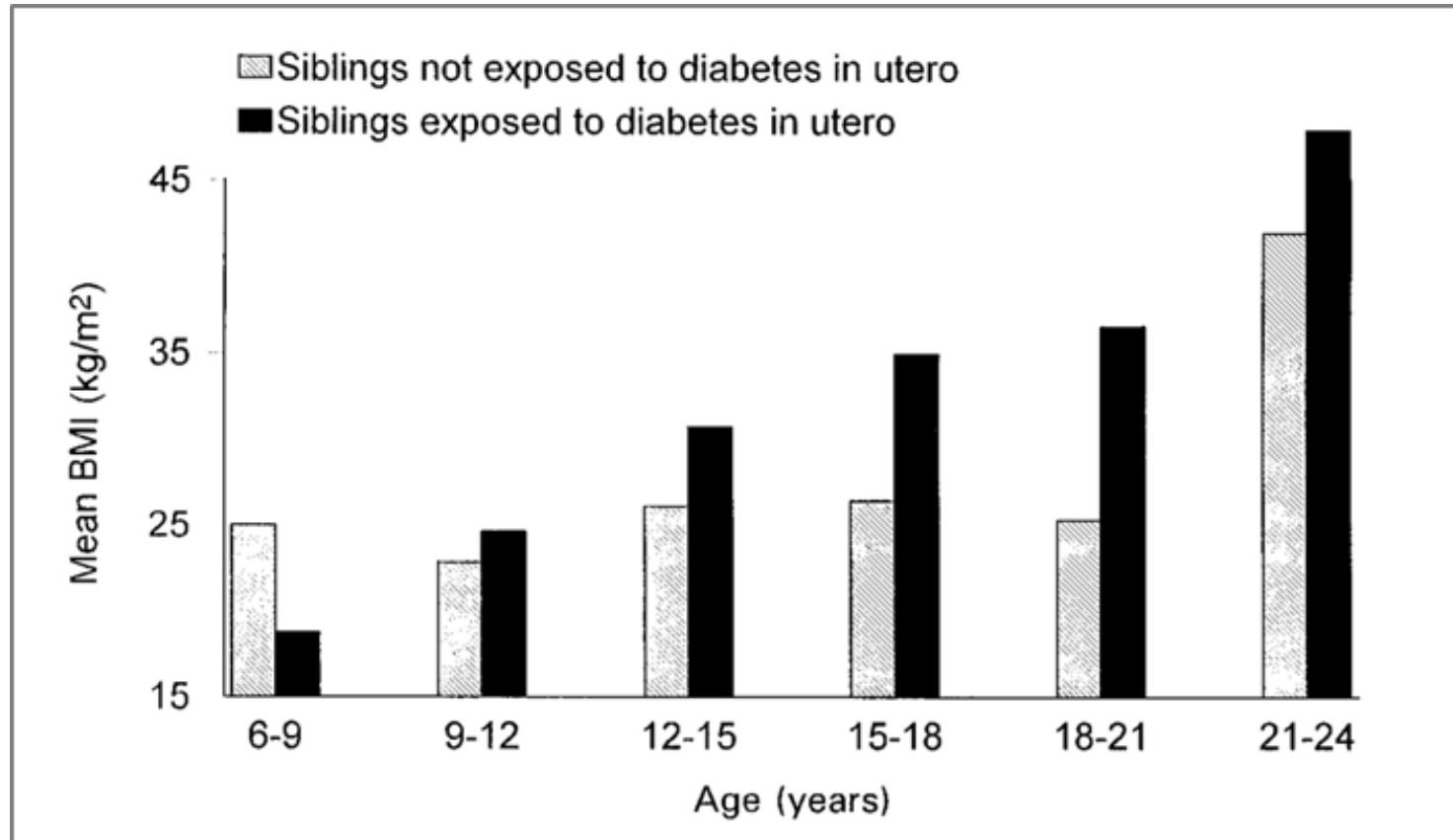
Fetal OVERnutrition – maternal diabetes



Fetal **OVER**nutrition – maternal diabetes

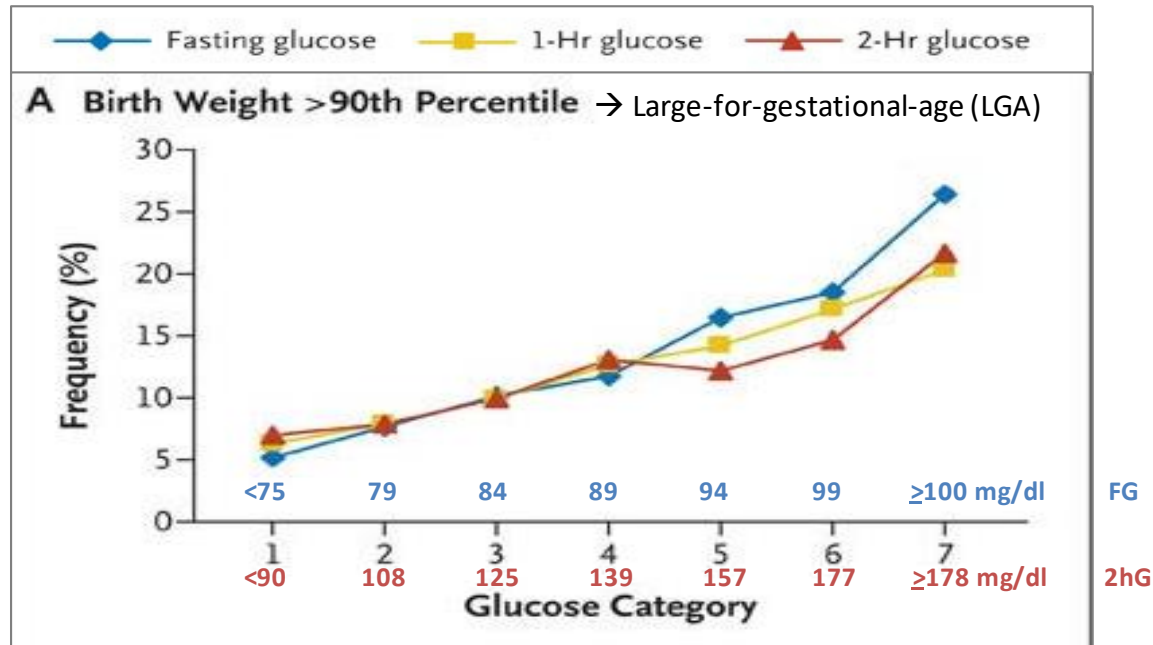
- Offspring exposed to maternal diabetes *in utero* had, on average,...
 - Higher prevalence of obesity
 - Higher 2-hour glucose levels
 - Higher prevalence of diabetes

Fetal **OVER**nutrition – maternal diabetes



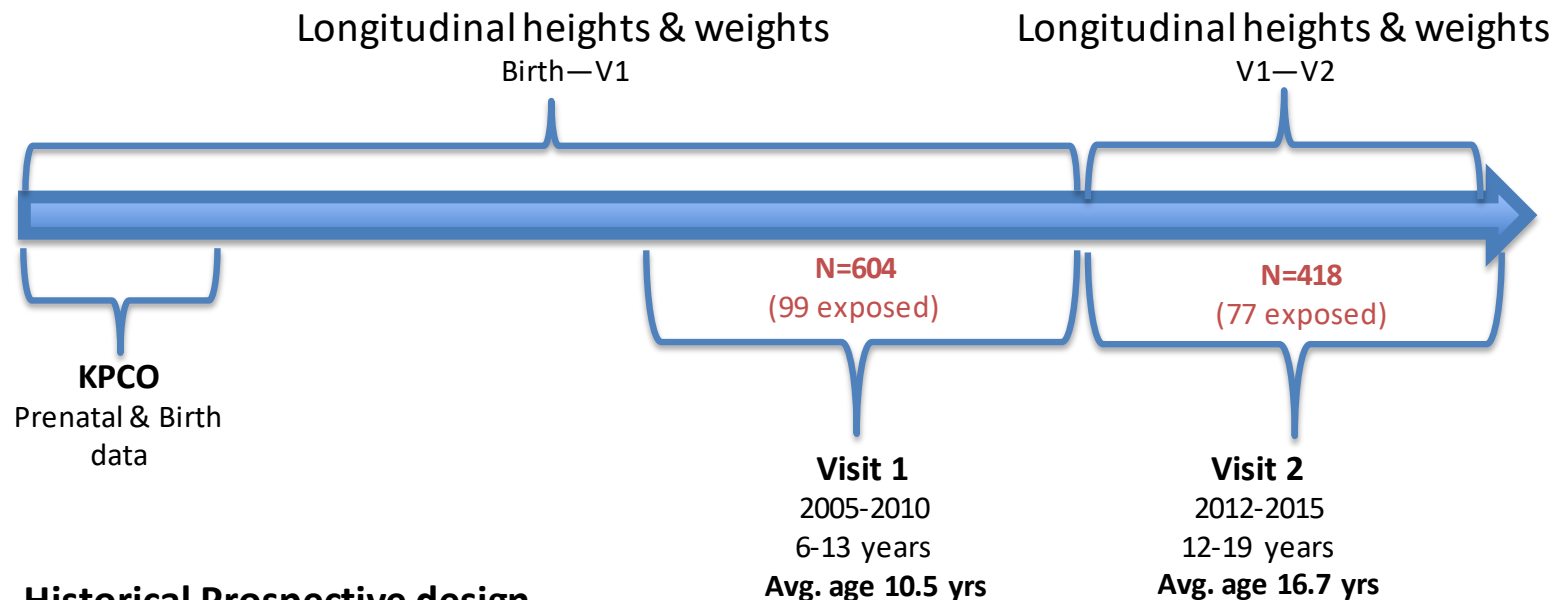
Specifically due to intrauterine exposure

Fetal OVERnutrition – maternal diabetes



- Even with glucose levels below GDM criteria, there was a dose-response in the prevalence of LGA
 - Similar results for offspring adiposity at birth.

Exploring Perinatal Outcomes In Children (EPOCH)



Historical Prospective design

- Cohort identified based on exposure status
- Recruited all exposed offspring and random sample of unexposed, age 6-13, from Kaiser Permanente of Colorado Health Plan (KPCO)
- Retention ~75% from Visit 1 to Visit 2

Measures collected at visit

- Demographic
- Adiposity (BMI, waist, abdominal fat by MRI)
- CVD risk factors (BP, lipids, OGTTs)
- Diet (FFQ) and Physical Activity (3D-PAR)

EPOCH Results

- Offspring exposed to maternal diabetes *in utero* had, on average,...



Higher BMI, waist/height ratio, VAT and SAT

Hockett et al, Diabetologia 2019



Females had higher total cholesterol and LDL

Perng et al, Ped Obesity 2020



Males had higher systolic blood pressure

Perng et al, Ped Obesity 2020

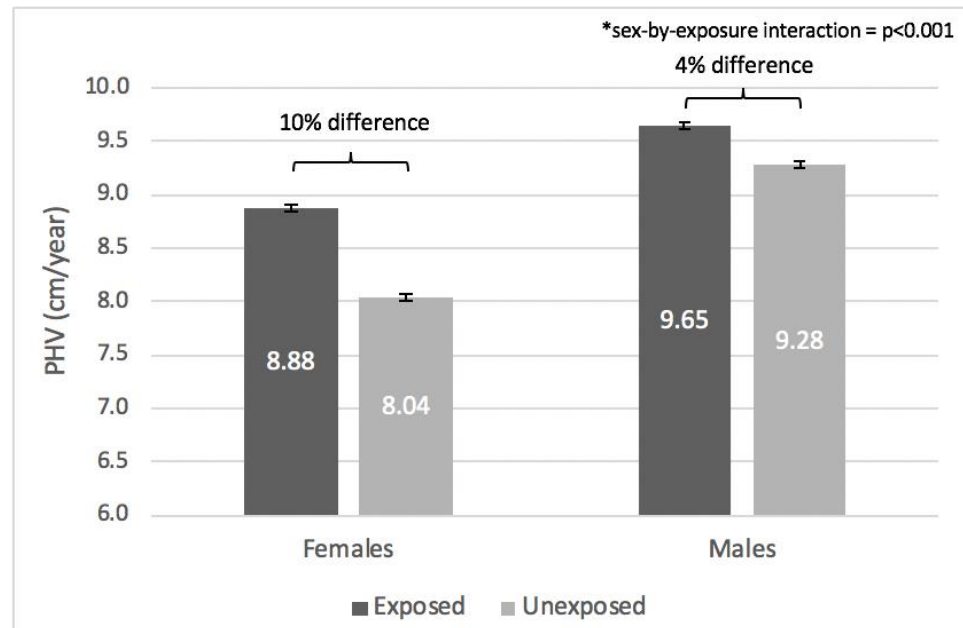


Increased insulin resistance (HOMA2-IR), lower Matsuda index, and decreased β -cell function (HOMA2- β)

Sauder et al, Diabet Med 2017

EPOCH Results

- The median age of pubertal timing was 2% younger, or ~3 month age difference, in exposed youth compared with unexposed youth.
- Exposed females had a 10% greater PHV than unexposed females, and exposed males had a 4% greater PHV compared with unexposed male.



Breaking the cycle



Breaking the cycle - Childhood



- School-based prevention
 - Alter environment and improve education for many
- Family-based prevention
 - Adopt and maintain healthy lifestyle
 - Leverage family unit in family-based interventions



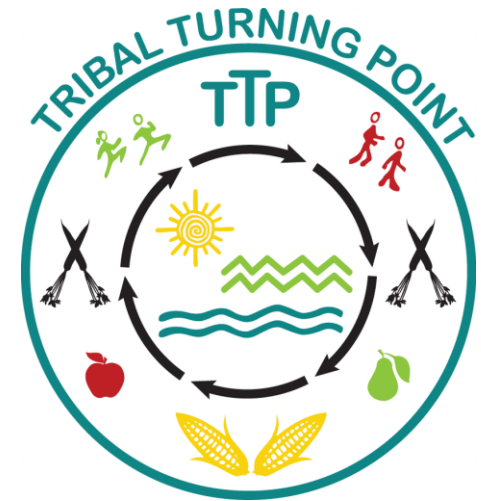
Tribal Turning Point (TTP)



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Using Community-based Participatory Research (CBPR), our goal was to develop a culturally-appropriate, multi-component intervention to reduce type 2 diabetes risk in AI youth

Tribal Turning Point (TTP)

- Delivered by trained health coach
- Active Learning group classes
 - Physical activity, interactive learning, culture, group meal
 - Goals: 5-2-1-0 (stop light diet for food)
 - Kids “Work-Out”



RED= lichí'

Whoa foods - high in fat and calories. Eat rarely. STOP and THINK before we eat these foods.

YELLOW= litso

Slow foods - have nutrients but have a little more fat and calories than go foods. Eat sometimes and/or in a smaller amount.

GREEN= doot'izh

Go foods - low in fat and calories and packed full of vitamins, minerals & fiber. Eat every day.

Tribal Turning Point – PILOT study results (n=60)

Changes between Intervention and Control

- BMI z-score decreased in the intervention group, no change in control group
- Waist circumference remained the same in the intervention group, but significantly increased in the control group

NO changes between Intervention and Control

- Glucose, HbA1c, HOMA-IR, or blood pressure no changes.
- No behavioral changes

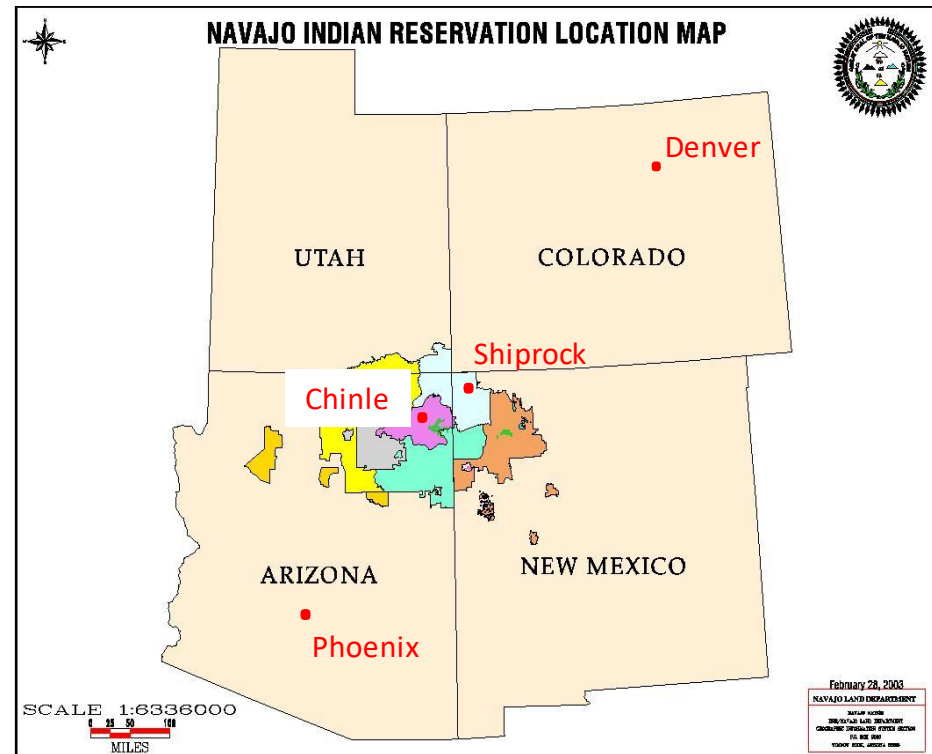
High program acceptability

Tribal Turning Point – Next steps

- Pilot study was promising, but program needs more work
 - Change in obesity measures was small, clinical or long-term significance unknown
 - Pilot study done on rural reservation, unknown if program will work in urban settings
 - Need to understand best practices for implementation before disseminating the program
- Ultimate goal: program that is effective and feasible to deliver in different Native settings

Tribal Turning Point – RCT

- Sites
 - Two rural reservation
 - Shiprock
 - Chinle
 - One urban
 - Phoenix
- Participants
 - 100 per site (300 total)
 - 7-10 years, BMI \geq 85th percentile
 - Participating parent/caregiver



Breaking the cycle – Opportunities

- Develop a perinatal research database to investigate child health outcomes and inform practice and policy in South Dakota.
 - already identified a potential funding source
- A 5-2-1-0 program for Avera children and families
 - already identified priority for Pediatric Service Line

Breaking the cycle – Opportunities



ECHO

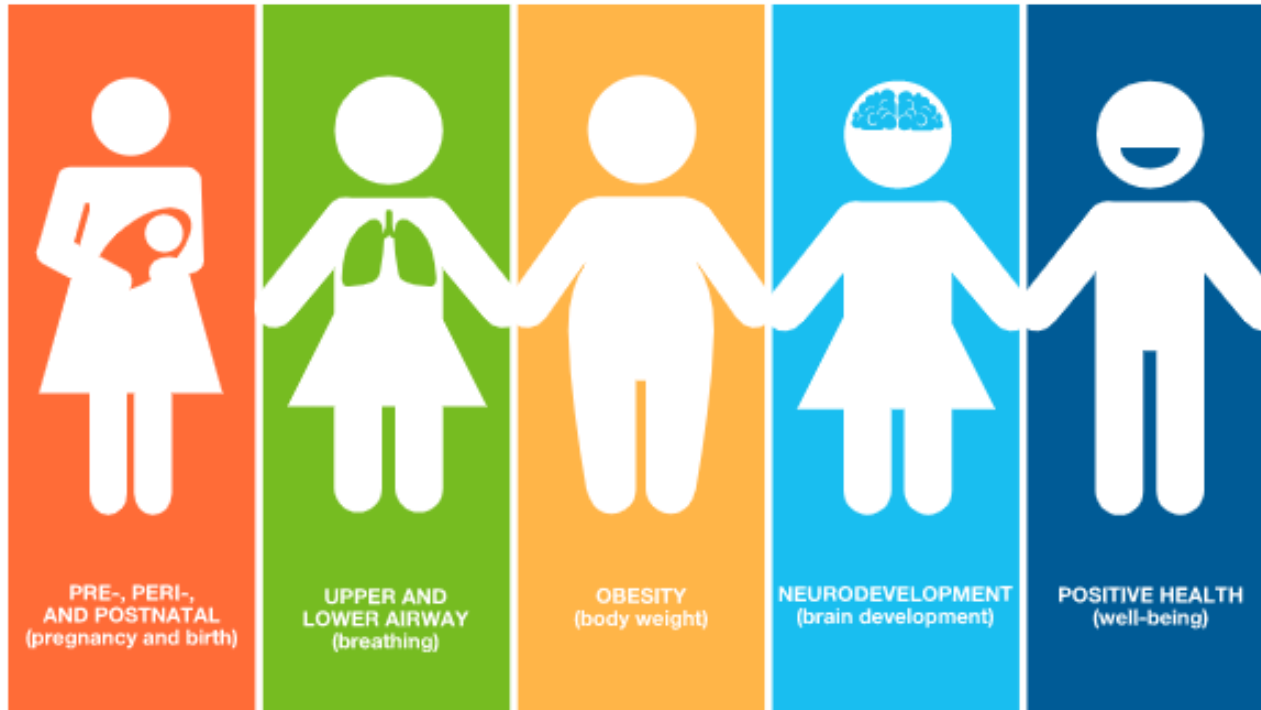
Environmental influences
on Child Health Outcomes

A program supported by the NIH



IDEA States Pediatric Network

ECHO ▶ A program supported by the NIH



Breaking the cycle – Opportunities

OBSERVATION:

Understand what influences children's health as they grow and develop.



ECHO

Environmental influences
on Child Health Outcomes

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INTERVENTION:

Test whether making changes
in children's lives will enhance
their health.

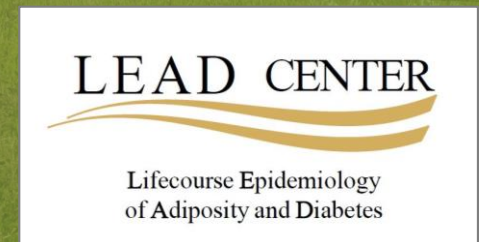
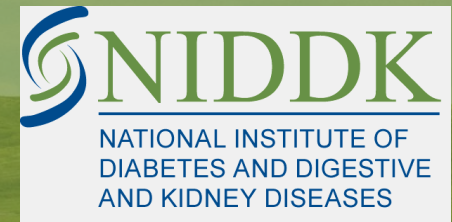


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THANK YOU

to the study participants, investigators,
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