

# Looking Ahead: Our Diabetes Model is Already Changing



**Ann Bullock, MD**

**Division of Diabetes Treatment and Prevention  
Indian Health Service**

# Childhood Trauma Predicts Adult Health

- Children born in Helsinki, Finland between 1934-44
- 320 were evacuated abroad during WW II—separated from their parents
  - Average age at evacuation: 4.8 years old
  - Average duration of evacuation: 1.7 years
- 60 years later, compared with children not evacuated, evacuees were much more likely to have:
  - Heart disease (OR 2.0) and hypertension
  - Type 2 Diabetes (OR 1.4)
  - Depressive symptoms (OR 1.7)
- “This study is among the first to show that early life trauma predicts higher prevalence of cardiovascular disease and type 2 diabetes in late adulthood...”

“...many adult diseases should be viewed as developmental disorders that begin early in life and that persistent health disparities associated with poverty, discrimination, or maltreatment could be reduced by the alleviation of toxic stress in childhood.”

“The Lifelong Effects of Early Childhood Adversity and Toxic Stress”

*Pediatrics* 2012;129:e232-e246

# International Diabetes Federation

## Conference on Type 2 Diabetes Etiologies

2002

1. Genetics
2. Fetal Origins
3. Lifestyle
4. Stress

# 1. Genes

## ■ Genes *Inherited*

- It does matter what genes we inherit
  - But proportion of predisposition explained for type 2 DM (5-10%) is *small*  
*NEJM 2010;363:2339-50*
  - And genes which are associated with ↑ diabetes risk are as common in non-minority as in minority people  
*Diabetes Care 2012;35:193-195*
- Only 15% of genes in cells “turned on” at any one time

## ■ Genes *Expressed*

- **“Epigenetics”**: the “on/off switches” for genes
  - Reaction to the environment
  - Not always reversible if at key developmental stage of life
  - Heritable—some may be passed to next generation
    - How the experiences of one generation help prepare the next
  - We know the body’s “on/off switches”: DNA methylation, histone acetylation, microRNA

*JAMA 2005;294:2221-4 and NEJM 2008;359:61-73*

# Epigenetics and Diabetes Predisposition

- Risk of dying from diabetes strongly related to *grandparents'* nutritional status

*Eur J Human Genetics* 2007;15:784-790 & 2002;10:682-8

- “...epigenetic changes occurring during gestation, possibly maternal nutrition-mediated, appear to influence adiposity and related metabolic phenotypes.”

*Diabetes* 2011;60:1859-60

- Genome-wide survey: clear-cut diabetes-predisposing DNA methylation signature in patients with vs. without diabetes

- Prospective study: different methylation patterns in young people who later developed diabetes vs. those who did not

*Hum Mol Genet* 2012;21:371-383

## 2. *In utero* Risks for Later Type 2 DM

- Fetuses of obese mothers develop insulin resistance *in utero*  
*Diabetes Care* 2009;32:1076-1080
- Maternal diet during pregnancy:
  - Epigenetically affects child's adiposity at age 9 yrs *Diabetes* 2011;60:1528-1534  
“Our findings suggest a substantial component of metabolic disease risk has a prenatal developmental basis.”
  - Affects adipose tissue development leading to insulin resistance  
*Cell Death Diff* 2012;doi:10.1038/cdd.2011.183
- Inverse relationship between birth weight and risk of diabetes  
*JAMA* 2008;300:2886-2897
- Rapid weight gain in first 3 months of life associated with ↑CVD and diabetes risk factors by early adulthood  
*JAMA* 2009;301:2234-2242
- Low birth weight is related to nephron number and future risk of kidney disease  
*Kidney Int* 2005;68:S68-S77

# “Fetal Programming of Type 2 Diabetes”

“It is important to understand that the story is not about birth weight but about fetal programming, and that intergenerational prevention of type 2 diabetes (primordial prevention) will need to target maternal nutrition and metabolism. ...Prevention of fetal programming of diabetes will need to concentrate on the health of young girls.”

*Diabetes Care* 2010;33:1146-8



# 3. Lifestyle

## Overeating as an *Adaptive* Response

### ■ Food Insecurity:

- Prevalence of overweight in women ↑'s as food insecurity ↑  
*Journal of Nutrition. 2001;131:1738-1745*
- Pregnancy: food insecurity assoc with pregravid obesity, ↑ gest wt gain, and gest diabetes  
*J Am Diet Assoc 2010;110:692-701*
- 42% of households below poverty level are food insecure, 21% of all households with children  
*NEJM 2010;363:6-9*
- Independent risk factor for poor glycemic control  
*Diabetes Care 2012;35:233-238*

### ■ Carbohydrates affect brain serotonin levels

*Obes Res 1995 Suppl 4:477S-480S*

### ■ “Comfort Foods” ↓ HPA axis stress response

*Proc Natl Acad Sci 2003;100:11696-11701*

## 4. Stress—in Early Life

- Chronic exposure to Intimate Partner Violence almost doubles (OR 1.8) risk of obesity at age 5 years

*Arch Pediatr Adolesc Med* 2010;164:540-546

- Young children who had objectively-measured poor quality maternal-child relationships had 2 ½ x ↑ prevalence of adolescent obesity c/w those who did not

*Pediatrics* 2012;129:132-40

- “...reducing toxic stress can target the common physiologic pathway implicated in an enormous array of health outcomes from asthma to cardiovascular disease.”

*Pediatrics* 2013;131:319-327

# ACEs and Adult Health

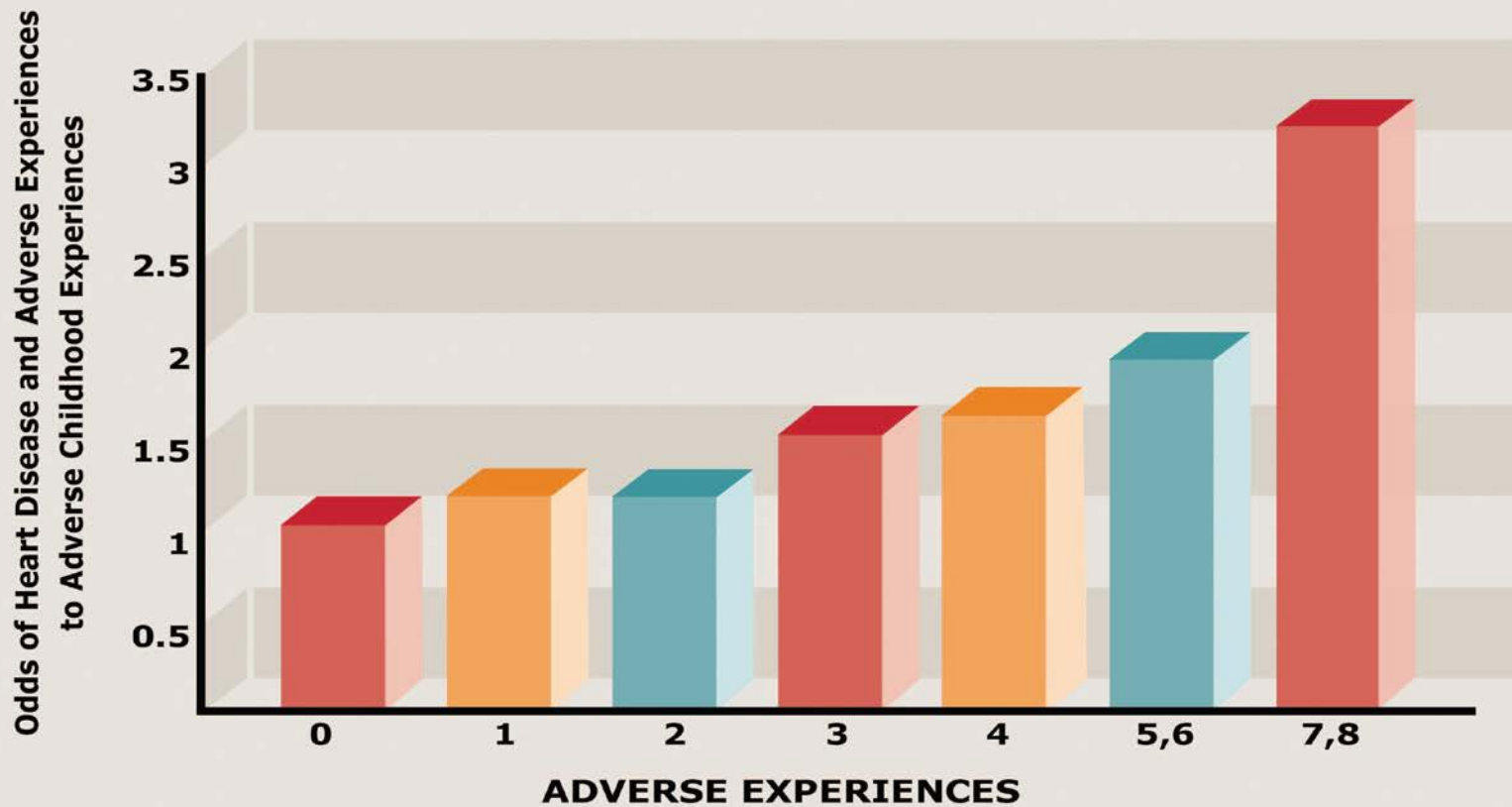
- ACE Score  $\geq 4$ 
  - 4-12 x risk for alcoholism, drug abuse, depression and suicide attempt
  - 2-4 x risk for smoking, teen pregnancy, STDs, multiple sexual partners
  - 1.4-1.6 x risk for severe obesity
  - Strong graded relationship at all levels of ACEs for almost all outcomes, including heart disease

*Am J Prev Med* 1998;14:245-258 and *Circulation* 2004;110:1761-6

- 10-county community surveys across multiple countries looked at assoc between childhood adversities and adult-onset chronic physical conditions
  - $\geq 3$  childhood adversities associated with hazard ratios:
    - Heart disease: 2.19
    - Diabetes: 1.59
    - Chronic pain: 1.63

*Arch Gen Psychiatry* 2011;68(8):838-844

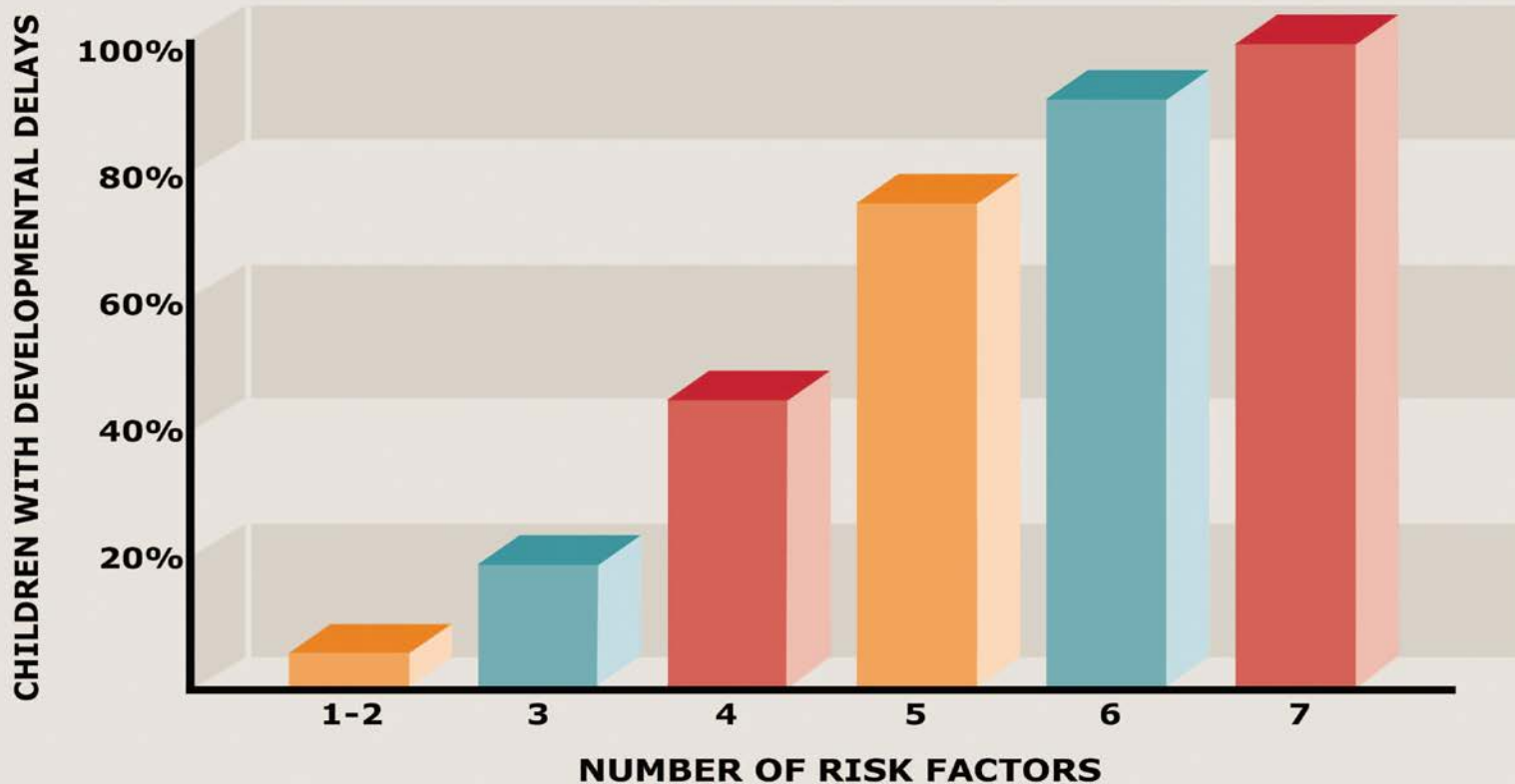
# 3:1 odds of adult heart disease after 7-8 adverse childhood experiences



Center on the Developing Child at Harvard website

Source: Dong et al. (2004)

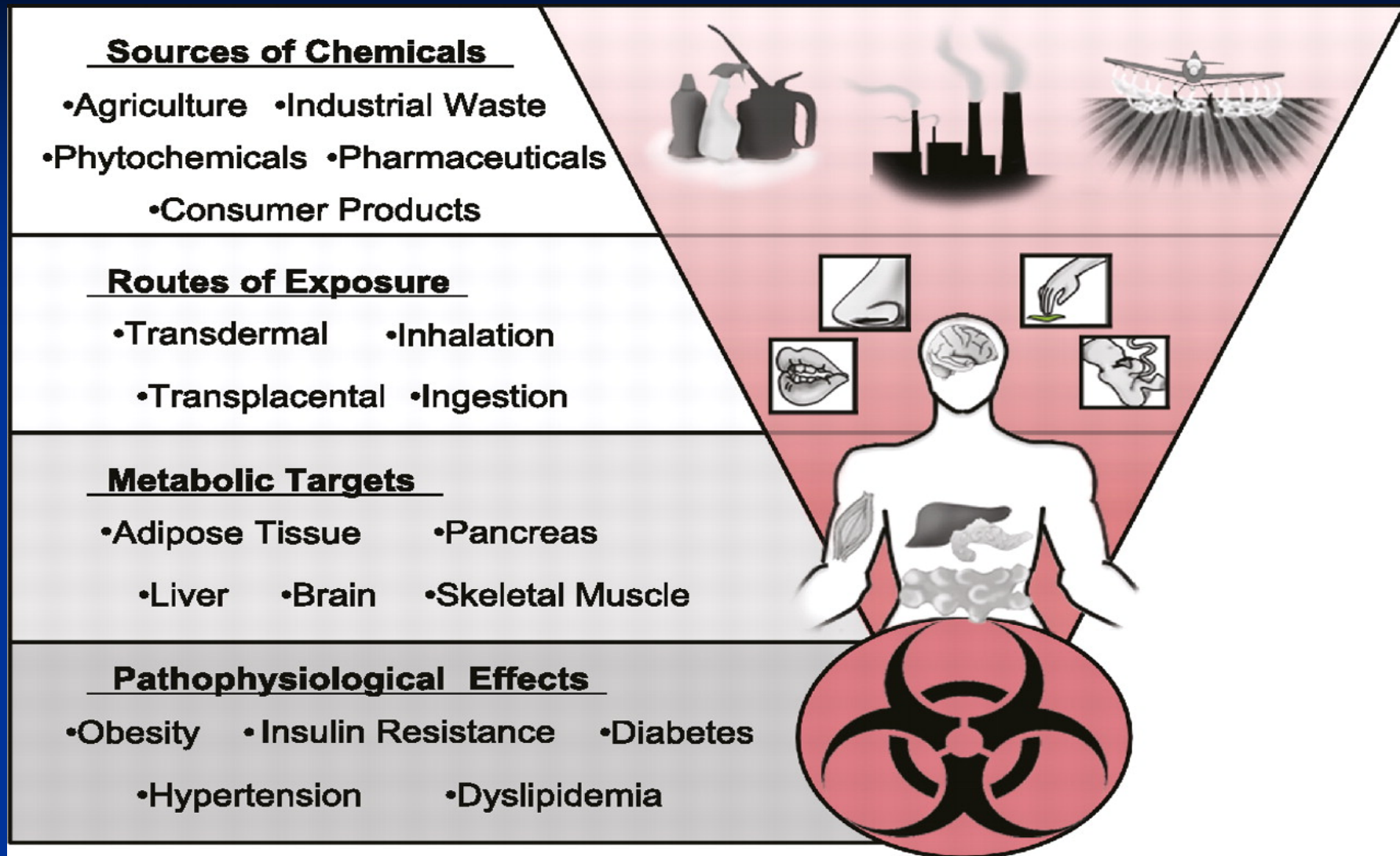
# 90-100% chance of developmental delays when children experience 6-7 risk factors



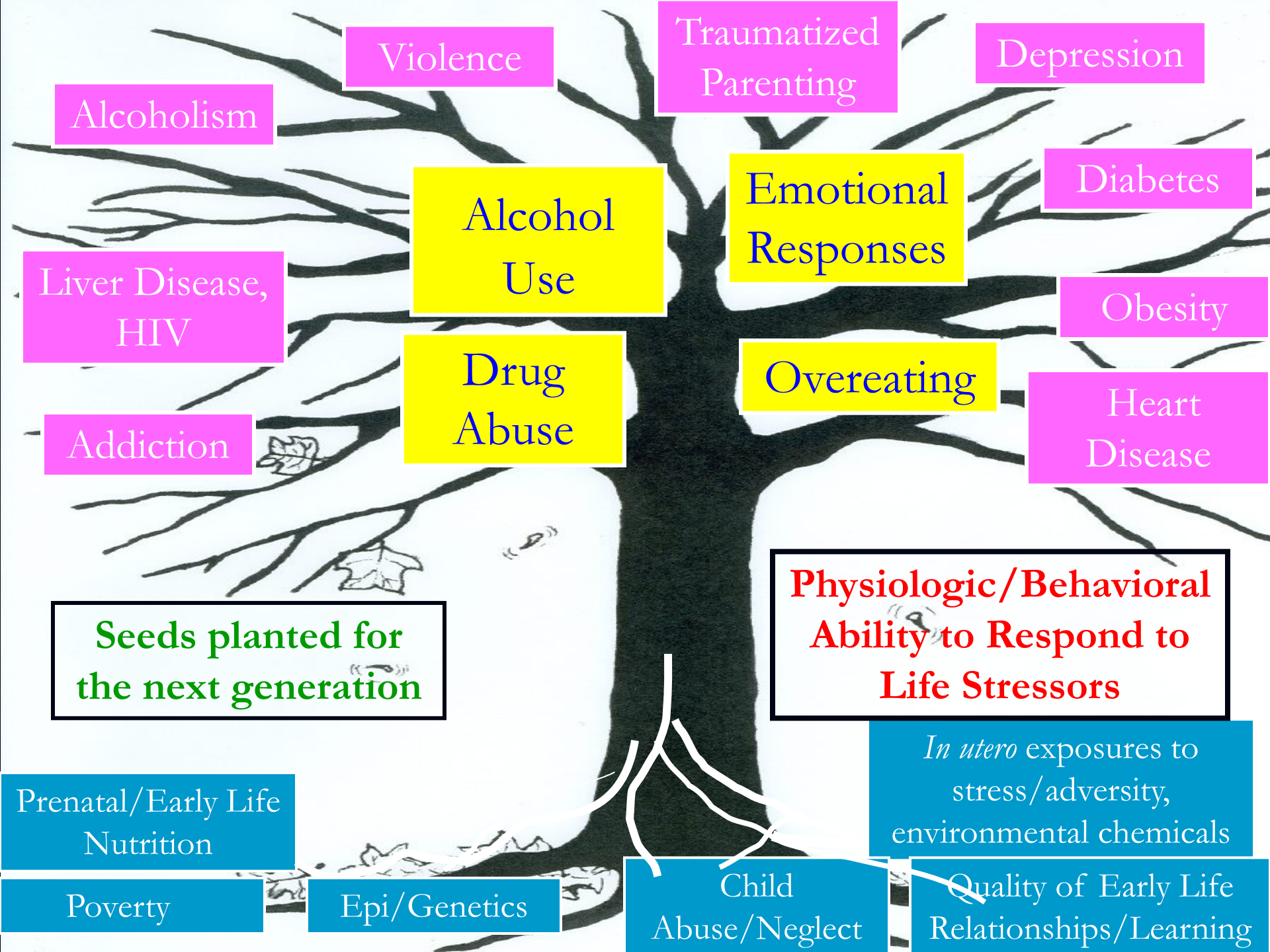
Center on the Developing Child at Harvard website

Source: Barth, et al. (2008)

# Sources and targets of metabolic disruptors.



Neel B A , Sargis R M Diabetes 2011;60:1838-1848



Violence

Traumatized Parenting

Depression

Alcoholism

Alcohol Use

Emotional Responses

Diabetes

Liver Disease, HIV

Obesity

Addiction

Drug Abuse

Overeating

Heart Disease

Seeds planted for the next generation

Physiologic/Behavioral Ability to Respond to Life Stressors

*In utero* exposures to stress/adversity, environmental chemicals

Prenatal/Early Life Nutrition

Poverty

Epi/Genetics

Child Abuse/Neglect

Quality of Early Life Relationships/Learning





**“We ...know that sound maternal and fetal nutrition, combined with positive social-emotional support of children through their family and community environments, will reduce the likelihood of negative epigenetic modifications that increase the risk of later physical and mental health impairments.”**

Center on the Developing Child at Harvard University

Working Paper 10, 2010

# Prenatal/Early Life Home Visiting

- One of the key evidence-based interventions proven to improve the life trajectories of low income women and children
  - Positive effects now shown up to *age 19 yrs*  
*Arch Pediatr Adolesc Med 2010;164:9-15, 412-418, 419-424*
- If home visiting were a medication, it would be malpractice not to provide it
- Tribal Maternal, Infant & Early Childhood Home Visiting Program (MIECHV)
  - 25 tribes/T.O.'s now funded to provide home visiting
  - ACF: 9 home visiting models with “evidence of effectiveness”

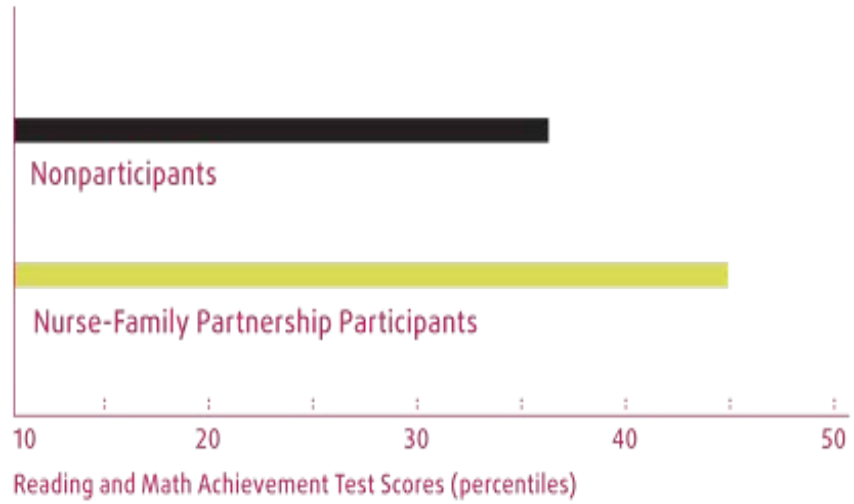


- Example of an evidence-based home visiting program
- Works with vulnerable first-time mothers living in poverty—starting early in pregnancy thru child's 2<sup>nd</sup> birthday
- Goals: Improve prenatal care, quality of parenting and life prospects for mothers by partnering them with a registered nurse.



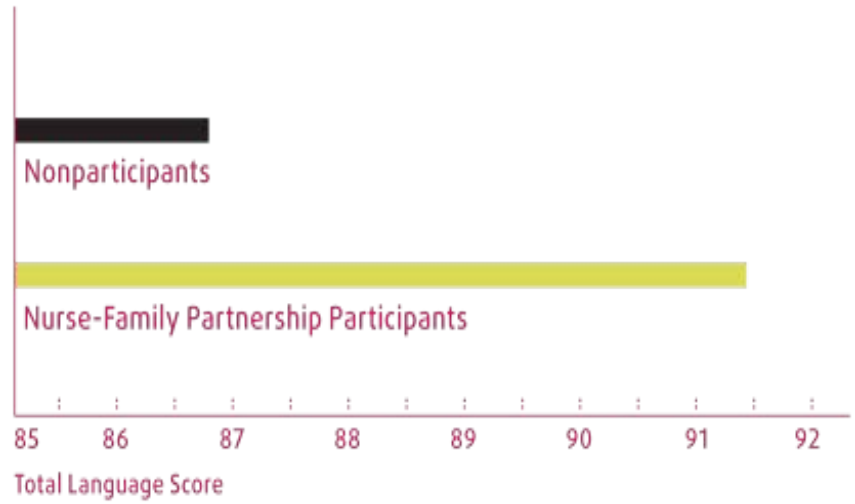
## Academic Achievement

Grades 1-3, Age 9—Memphis  
(Born to low-resource mothers)



## Preschool Language Scale

Age 4—Denver  
(Born to low-resource mothers)



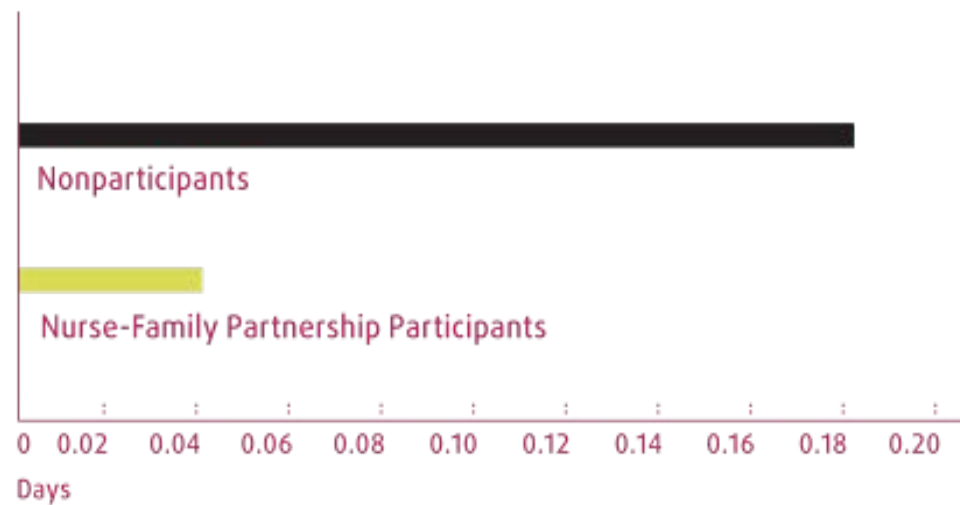
Source: Reproduced with permission from *Pediatrics*, Vol. 120, e838, Copyright © 2007 by the AAP.

Source: Reproduced with permission from *Pediatrics*, Vol. 114, 1565, Copyright © 2004 by the AAP.



## Days Hospitalized for Injuries

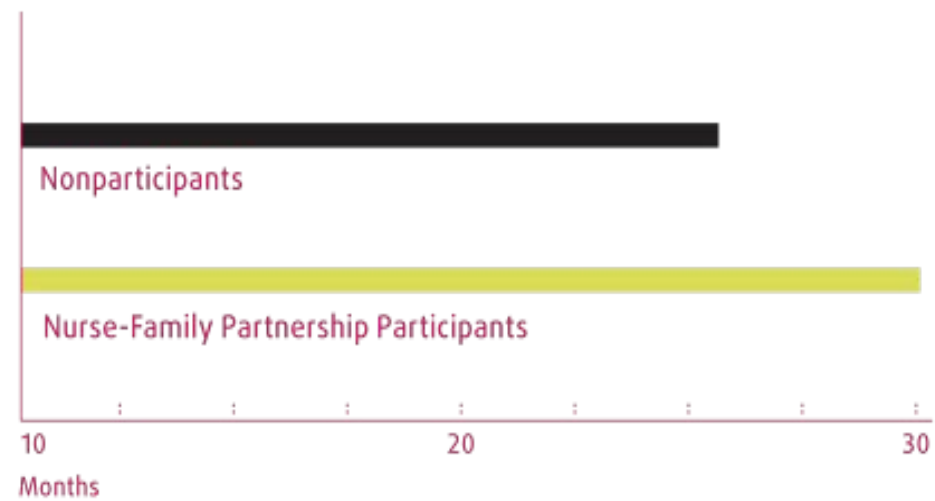
Birth to age 2—Memphis



Source: *JAMA*, 1997, Vol. 278, 650, Copyright © 1997, American Medical Association. All rights reserved.

## Months Between Births

Between first and second child  
(by first child's fifth birthday)—Memphis

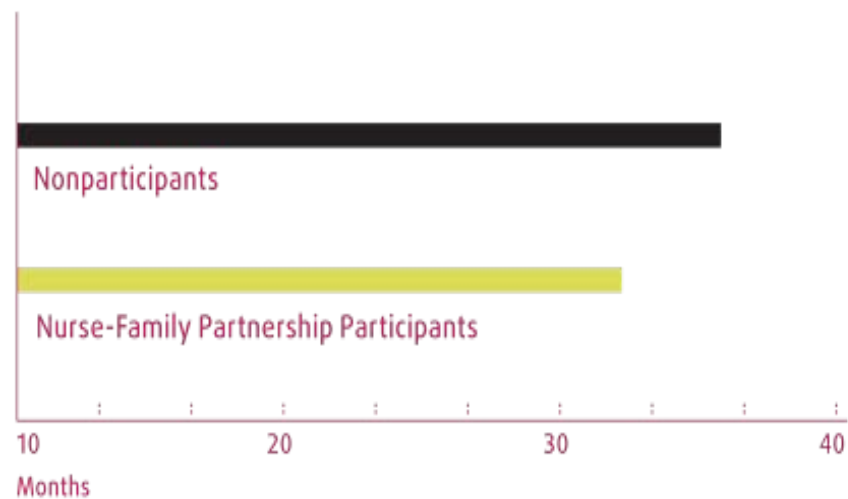


Source: *JAMA*, 2000, Vol. 283, 1987, Copyright © 2000, American Medical Association. All rights reserved.



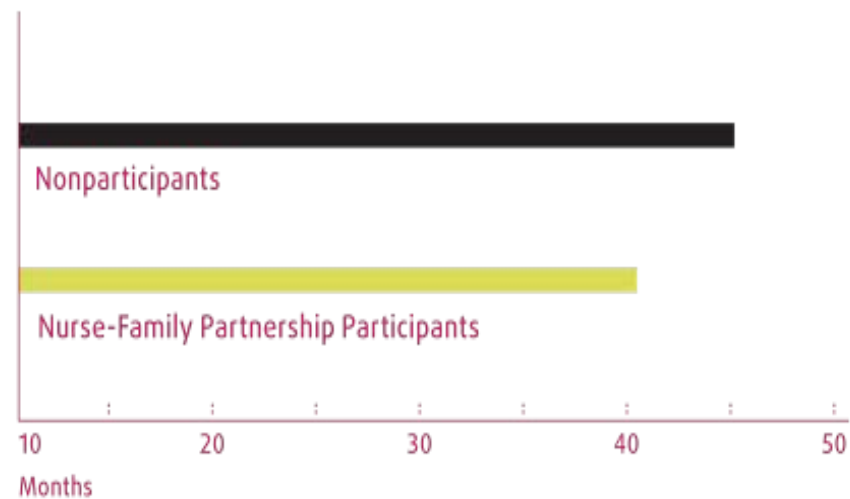
## Months Receiving Welfare Assistance (AFDC)

Birth through age 5—Memphis

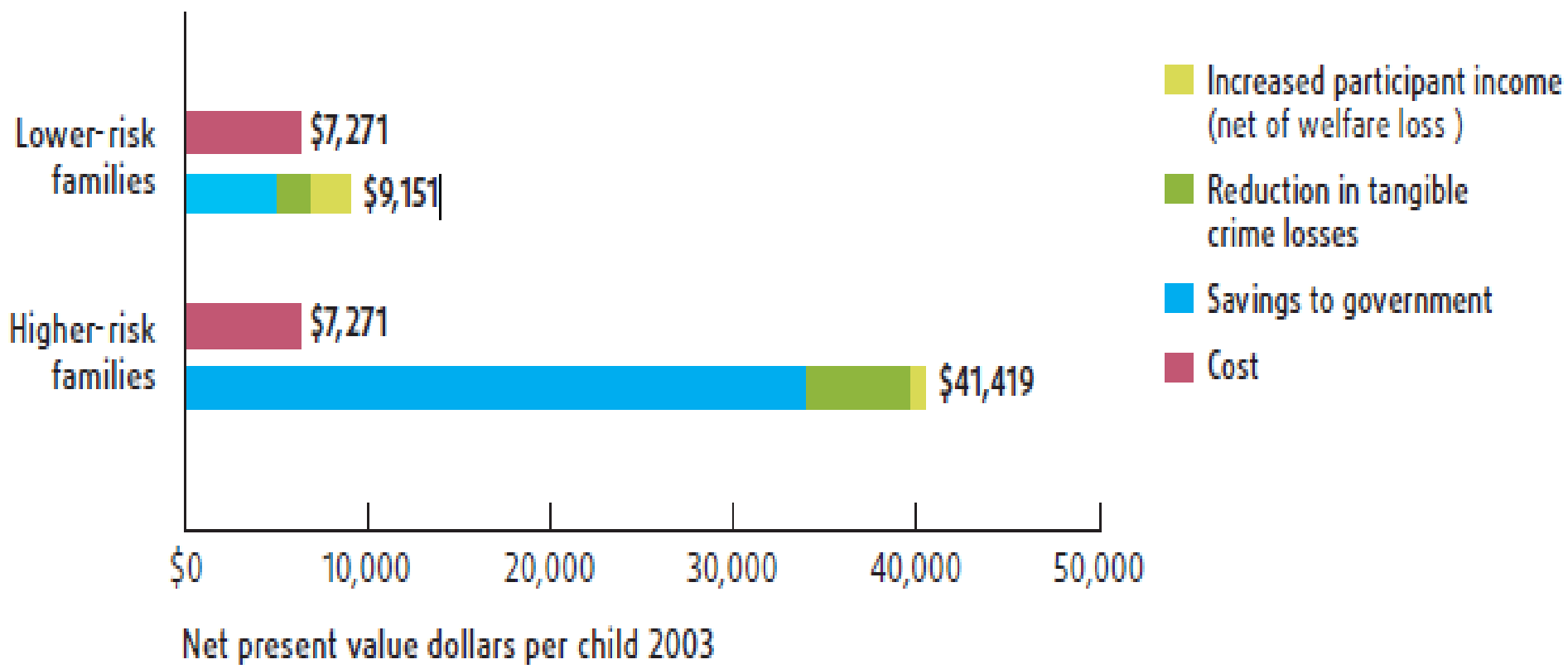


## Months Receiving Food Stamps

Birth through age 5—Memphis

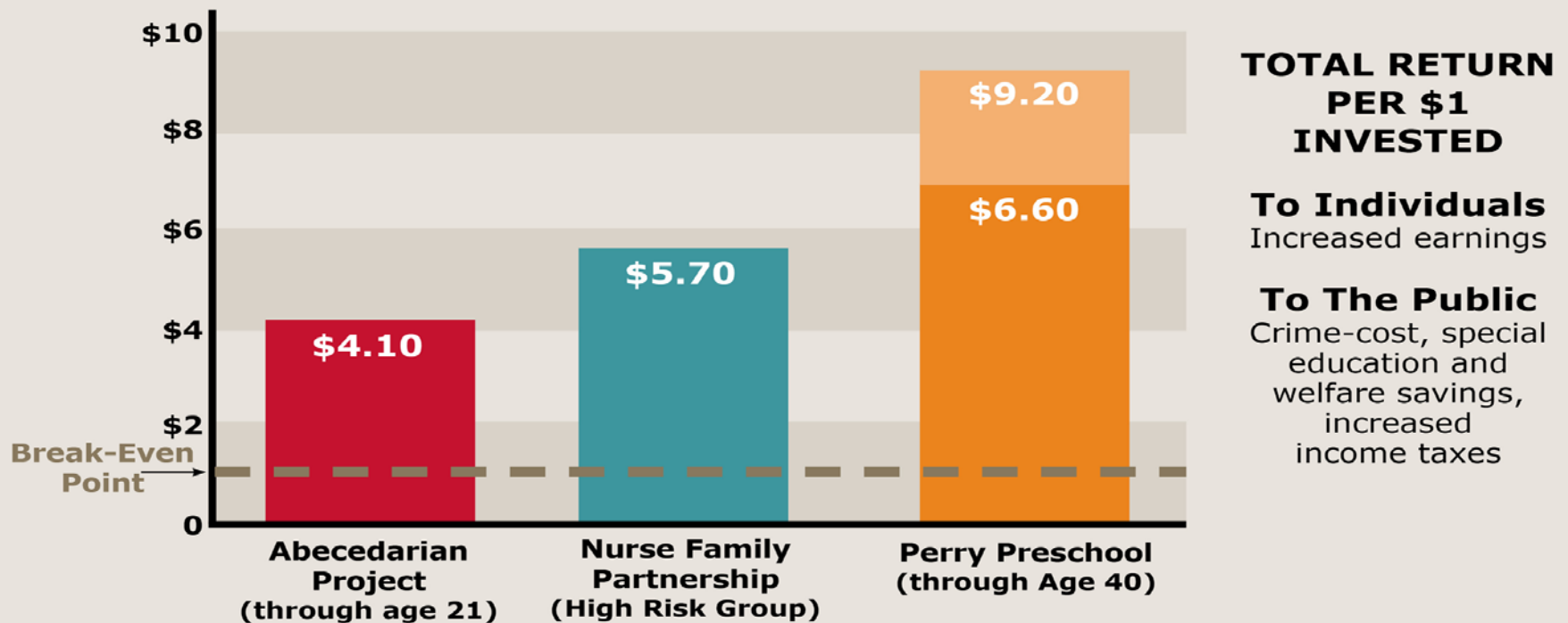


# Monetary Benefits



Source: 2005 RAND Corporation Study

# \$4-\$9 in returns for every dollar invested in early childhood programs



[Center on the Developing Child at Harvard website](#)

Sources: Masse, L. and Barnett, W.S., A Benefit Cost Analysis of the Abecedarian Early Childhood Intervention (2002); Karoly et al., Early Childhood Interventions: Proven Results, Future Promise (2005); Heckman et al., The Effect of the Perry Preschool Program on the Cognitive and Non-Cognitive Skills of its Participants (2009)



# Daphne Colacion

## Program Coordinator

Gouk-Gumu Xolpelema

Tribal Home Visiting Program

Lake County Tribal Health Consortium



“You did then what  
you knew how to do,  
and when you knew  
better, you did better”

*Maya Angelou*

The time has come to develop,  
fund and disseminate  
comprehensive, intensive  
interventions for pregnant  
women and young  
children/families—  
*we know where to start*

# Components

- Prenatal/Early Life Case Management--cornerstone
  - Home visiting
  - Provide *good* nutrition in sufficient quantities
    - WIC, food stamps, commodities don't go far enough
  - Parenting
    - Bonding, breastfeeding starting at delivery (e.g. BFHI)
    - Parenting and coping skills training
    - Screen for/treat depression, trauma symptoms, substance abuse
    - Screen for/intervene *early* in adverse childhood experiences
      - Court Referral Program (e.g. Zero to Three)
    - Strengthen, renew tribal pregnancy/childrearing practices
      - Traditional midwifery, doulas, support of young parents by elders, relatives
    - Strong Head Start/Early Head Start, Child Care
  - Reduce exposure to endocrine disrupting chemicals
  - Learning
    - e.g. Promise Neighborhoods, modeled on Harlem Children's Zone
    - Encourage parents to read to kids (e.g. Reach Out and Read)

# What Can Diabetes Programs Do ...Now?

- Nutrition
  - Food Insecurity/Quality
  - Advocate for food programs in schools, community
- Case Management
  - Mental Health, Substance Abuse
  - Housing, transportation, child/elder care, etc.
- Contraception, Preconception counseling
- Form new partnerships
  - Prenatal clinic, WIC, Head Start/Early Head Start
- Compassion, relationships most important

**How will we address  
early life risk factors for  
diabetes and other  
adverse life outcomes  
...soon?**

**Let's imagine it together!**



# The Time of the Seventh Generation Has Come

Is this work not something AI/AN  
people should be a leader in?

“The medicine is already within the pain and suffering.  
You just have to look deeply and quietly. Then you realize  
it has been there the whole time.” Duran, 2006