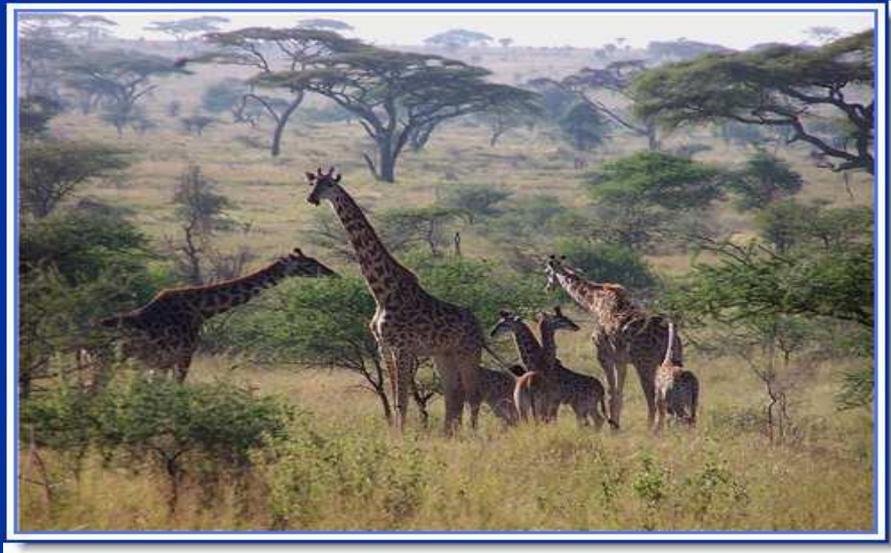


Getting to the Roots: How What Happens Early in Life Affects Adult Health and Mental Health



Ann Bullock, MD

IHS Division of Diabetes Treatment and Prevention

“Giving every child the best start in life is crucial to reducing health inequalities across the life course. The foundations for virtually every aspect of human development—physical, intellectual and emotional—are laid in early childhood. What happens during these early years (starting in the womb) has lifelong effects on many aspects of health and well-being—from obesity, heart disease and mental health, to educational achievement and economic status. To have an impact on health inequalities we need to address the social gradient in children’s access to positive early experiences.”

Fair Society, Healthy Lives: Strategic Review of Health Inequalities in England Post-2010

“Nothing records the effects of a sad life so graphically as the human body.”

Naguib Mahfouz

Our Current Path—

An all-too-common story: “Mary”

■ Pre-conception

- Mother’s grandparents went to boarding school, parents have had trouble with alcohol; most of them developed diabetes
- Family income below poverty line, buy food at reservation store

■ Pregnancy and Birth

- Single 15 year old, won’t say who FOB is
- Intermittent prenatal care
- WIC foods have to be shared with family
- Stopped using drugs when found out she was pregnant, cut down but continued smoking and got drunk “just a few times”
- Mostly kept going to high school thru pregnancy
- Mary born slightly SGA at 35 weeks gestation, spent 2 wks in hosp.

“Mary”

■ Early Life

- Grandmother already overwhelmed caring for other grandchildren, but agreed to watch Mary while mother tried to stay in school
 - Mary often sitting in front of TV most of day
- Then put into tribal child care
 - High staff turnover, minimal teacher-student ratio
- Family got by on commodities and WIC foods
- Mary gained weight rapidly in 1st yr, then stayed >95th % ile
- Mother’s boyfriend moved in
 - Intermittently employed, binged on alcohol and drugs, sometimes hit mother in front of Mary
- Mary held back to repeat 2nd grade as reading difficulties
- Mary left school after 10th grade

■ Now Mary becomes pregnant...

Brain Development

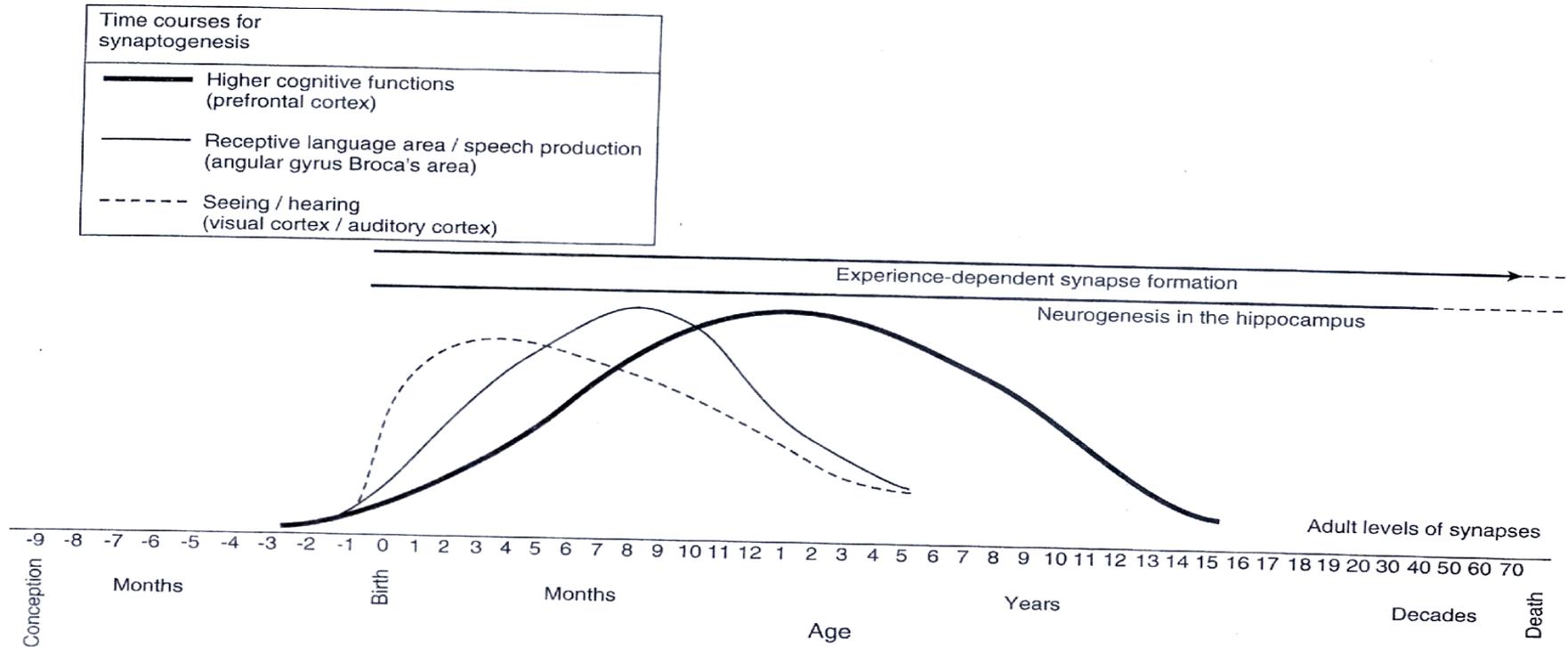


FIGURE 8-1 Human brain development. SOURCE: Charles A. Nelson, University of Minnesota. Reprinted with permission.

From Neurons to Neighborhoods: the Science of Early Child Development.

National Academy of Sciences, 2000, p. 188

International Diabetes Federation

Conference on Type 2 Diabetes Etiologies

2002

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

1. Genetics

■ 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

- Early Life Experiences: “programmed in”
 - Rat pups raised by nurturing mothers
 - Gene which codes for stress hormone receptors “turned on”
 - Grow up to be stress resilient
 - Rat pups raised by neglectful mothers
 - Gene which codes for stress hormone receptors “turned off”
 - Grow up to be very stress reactive
 - Same process now shown in humans

Nature Neuroscience 2009;12:342-348

Epigenetics and Diabetes

- Epigenetic mechanisms play important role in 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

- Gene imprinting comes from both parents

Diabetes Care 2010;33:1823-8

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

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

Hum Mol Genet 2011;21:371-383

2. Fetal Origins



- Alcohol/Drugs
- Nutrition
- Smoking
- Maternal Diabetes
- Toxic/Infectious Exposures
- Maternal Low Birth Weight
- Maternal Stress/Mental Health
 - Mother's own Childhood
 - Current/Prenatal

Low Birth Weight (SGA) and Preterm

- Babies can be either/both SGA and Preterm
 - they both are strongly associated with that baby's later risk for chronic disease

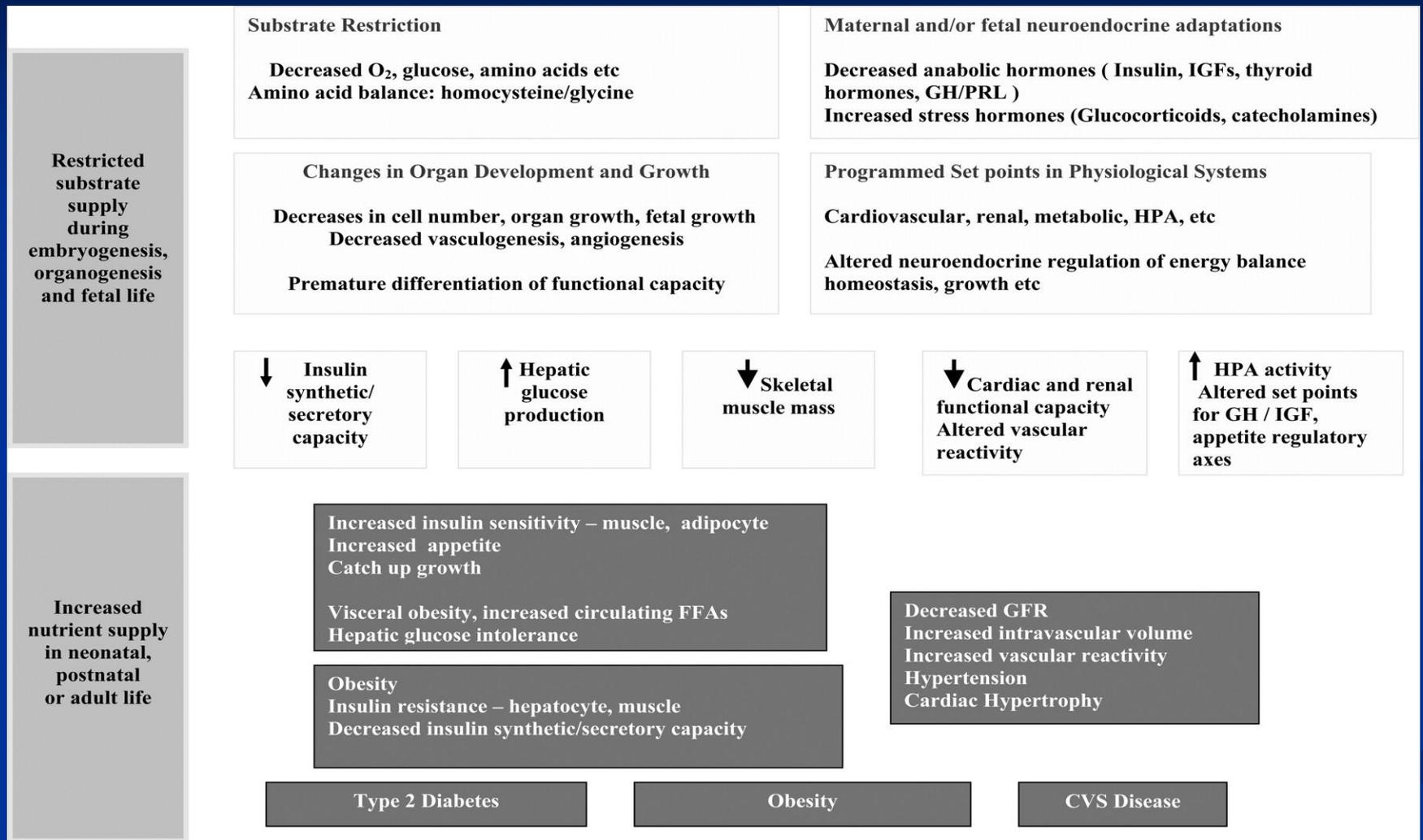
Diabetes 2009;58:523-526

- Maternal stressful life events during 1st trimester
↑ risk of preterm birth (OR 2.4) and SGA

Am J Obstet Gynecol 2010;203:34.e1-8



FIG. 7. The physiological mechanisms underlying the programming of the separate and combined elements of the metabolic syndrome



McMillen IC, et al. *Physiol. Rev.* 85: 571-633 2005;

In utero Risks for Later Type 2 Diabetes

- 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
 - 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”

- “...intrauterine environment may modify gene expression permanently. ...They might also be inherited transgenerationally, affecting the health of future generations. ...During intrauterine life, there are waves of epigenomic modification, intimately associated with growth and development, and opportunities galore for environmental factors to influence these processes. A fetus thus programmed travels a path of limited options.” *Diabetes Care* 2007;30:2754-5
- “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

- 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
- Childhood stressors including poverty, family dysfunction associated with obesity and later type 2 DM
Obesity Reviews 2011;12:e54-e63 and *BMC Public Health* 2010;10:525
- Toddlers who showed insecure attachment to their mothers at age 2 had a 30% increased risk of obesity by age 4 1/2
Arch Pediatr Adolesc Med 2011;165:235-242

Adverse Childhood Experiences (ACE)

- Physical, emotional, sexual abuse; mentally ill, substance abusing, incarcerated family member; seeing mother beaten; parents divorced/separated

--Overall Exposure: 86% (among 7 tribes)

| | <u>Non-Native</u> | <u>Native</u> |
|-------------------|-------------------|---------------|
| Physical Abuse-M | 30% | 40% |
| Physical Abuse-F | 27 | 42 |
| Sexual Abuse-M | 16 | 24 |
| Sexual Abuse-F | 25 | 31 |
| Emotional Abuse | 11 | 30 |
| Household alcohol | 27 | 65 |
| Four or More ACEs | 6 | 33 |

ACEs and Adult Health

■ ACE Score ≥ 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

■ Adult obesity risk \uparrow 20-50% if experienced in childhood:

- physical or verbal abuse, witnessed abuse, humiliation, neglect, strict upbringing, conflict/tension, low parental aspirations/+interactions

Pediatrics 2008;e1240-e1249, doi:10.1542/peds.2007-2403

■ Nurse's Health Study II: Childhood abuse

- dose-response association with risk of diabetes in adult women
- only *partly* explained by their \uparrow BMI

Am J Prev Med 2010;39:529-536

“Only in the presence of
compassion can people
allow themselves to see
the truth.”

Dr. Gabor Mate

Stress in Children

■ Positive

- Normal/necessary part of healthy development
 - First day with new caregiver; immunization
- Brief increases in heart rate and stress hormones

■ Tolerable

- More severe, longer lasting stressor
 - Loss of a loved one, natural disaster, injury
- If buffered by relationship with supportive adult(s), brain and body can recover

■ Toxic

- Strong, frequent, prolonged adversity
 - Abuse, neglect, caregiver mental illness, poverty
- If no adult support, can disrupt brain and organ development long-term

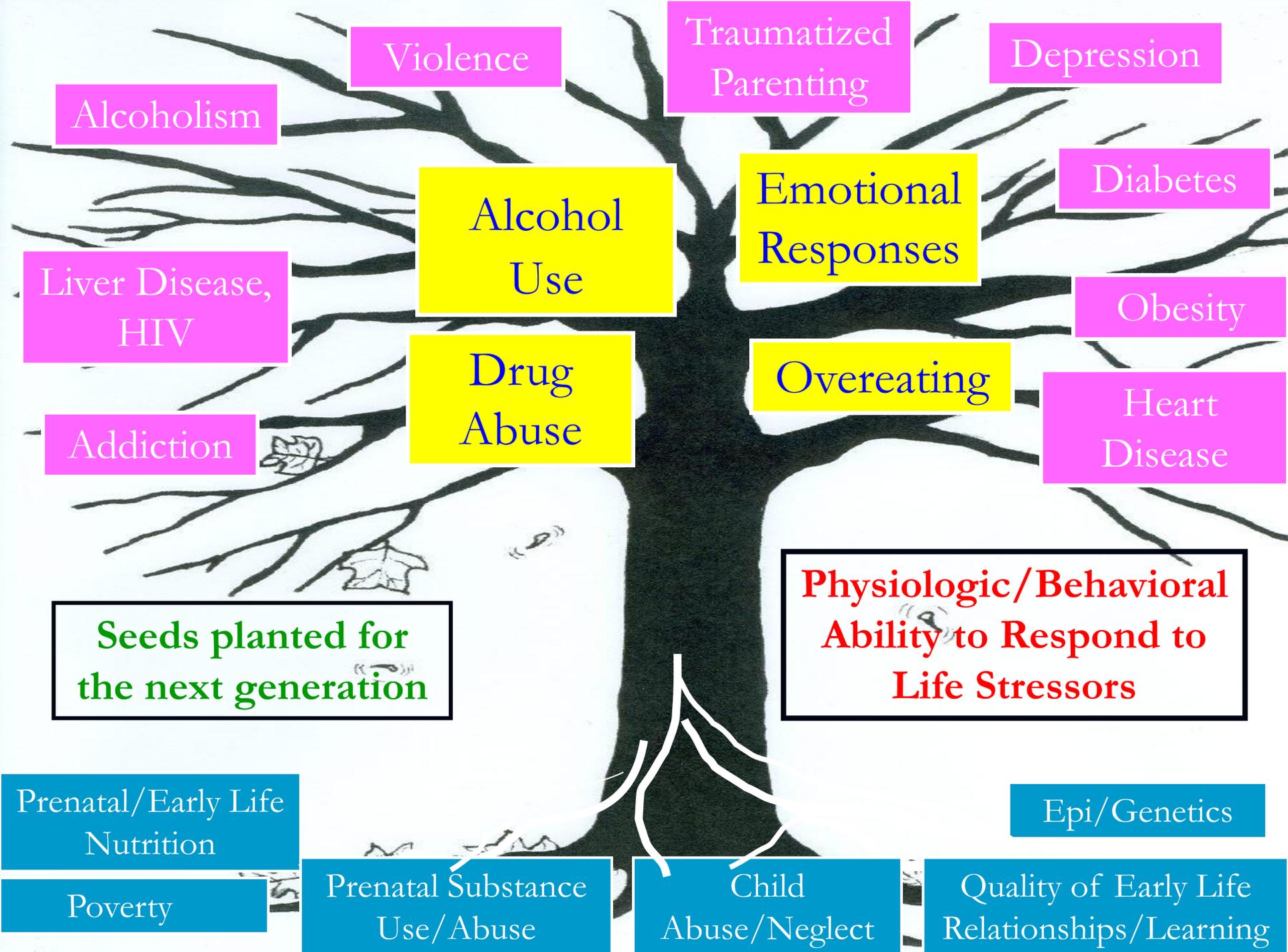
Domains of Impairment in Children Exposed to Complex Trauma

| I. Attachment | IV. Dissociation | VI. Cognition |
|--|---|---|
| <ul style="list-style-type: none"> Problems with boundaries Distrust and suspiciousness Social isolation Interpersonal difficulties Difficulty attuning to other people's emotional states Difficulty with perspective taking | <ul style="list-style-type: none"> Distinct alterations in states of consciousness Amnesia Depersonalization and derealization Two or more distinct states of consciousness Impaired memory for state-based events | <ul style="list-style-type: none"> Difficulties in attention regulation and executive functioning Lack of sustained curiosity Problems with processing novel information Problems focusing on and completing tasks Problems with object constancy Difficulty planning and anticipating Problems understanding responsibility Learning difficulties Problems with language development Problems with orientation in time and space |
| II. Biology | V. Behavioral control | VII. Self-concept |
| <ul style="list-style-type: none"> Sensorimotor developmental problems Analgesia Problems with coordination, balance, body tone Somatization Increased medical problems across a wide span (eg, pelvic pain, asthma, skin problems, autoimmune disorders, pseudoseizures) | <ul style="list-style-type: none"> Poor modulation of impulses Self-destructive behavior Aggression toward others Pathological self-soothing behaviors Sleep disturbances Eating disorders Substance abuse Excessive compliance Oppositional behavior Difficulty understanding and complying with rules Reenactment of trauma in behavior or play (eg, sexual, aggressive) | <ul style="list-style-type: none"> Lack of a continuous, predictable sense of self Poor sense of separateness Disturbances of body image Low self-esteem Shame and guilt |
| III. Affect regulation | | |
| <ul style="list-style-type: none"> Difficulty with emotional self-regulation Difficulty labeling and expressing feelings Problems knowing and describing internal states Difficulty communicating wishes and needs | | |

“...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



Violence

Traumatized Parenting

Depression

Alcoholism

Alcohol Use

Emotional Responses

Diabetes

Liver Disease, HIV

Obesity

Drug Abuse

Overeating

Heart Disease

Addiction

Seeds planted for the next generation

Physiologic/Behavioral Ability to Respond to Life Stressors

Prenatal/Early Life Nutrition

Epi/Genetics

Poverty

Prenatal Substance Use/Abuse

Child Abuse/Neglect

Quality of Early Life Relationships/Learning

“True compassion is more than
flinging a coin to a beggar...
It comes to see that an edifice
which produces beggars
needs restructuring.”

Dr. Martin Luther King, Jr.



“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
 - 19 tribes/T.O.'s now funded to provide home visiting
 - Tribal Research Center on MIECHV and Head Start/EHS

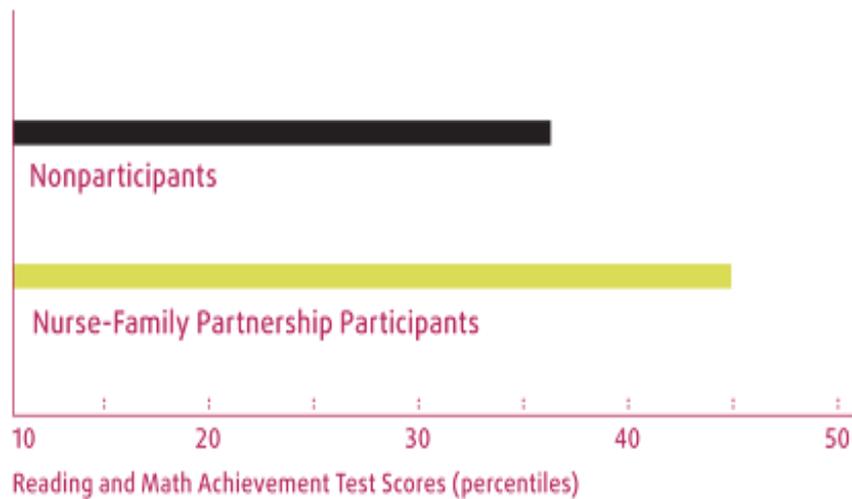


- Example of an evidence-based home visiting program
- Works with vulnerable first-time mothers living in poverty—starting early in pregnancy thru child's 2nd birthday
- Goals: Improve prenatal care, quality of parenting and life prospects for mothers by partnering them with a registered nurse.



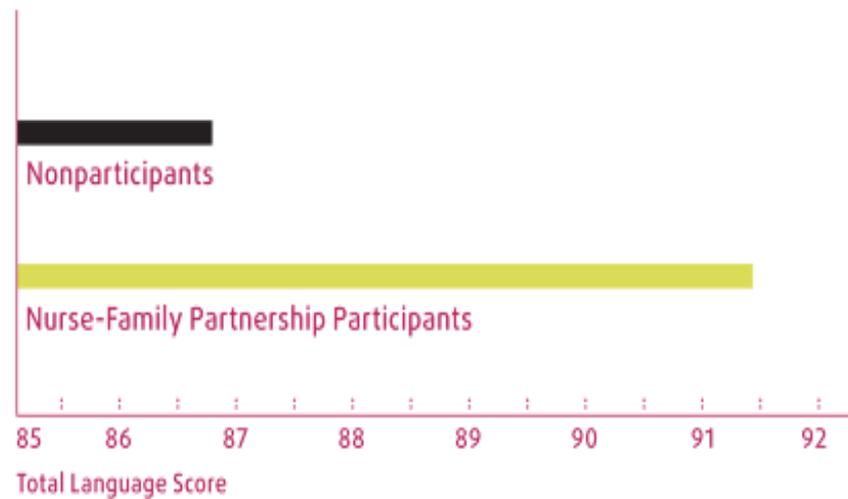
Academic Achievement

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



Preschool Language Scale

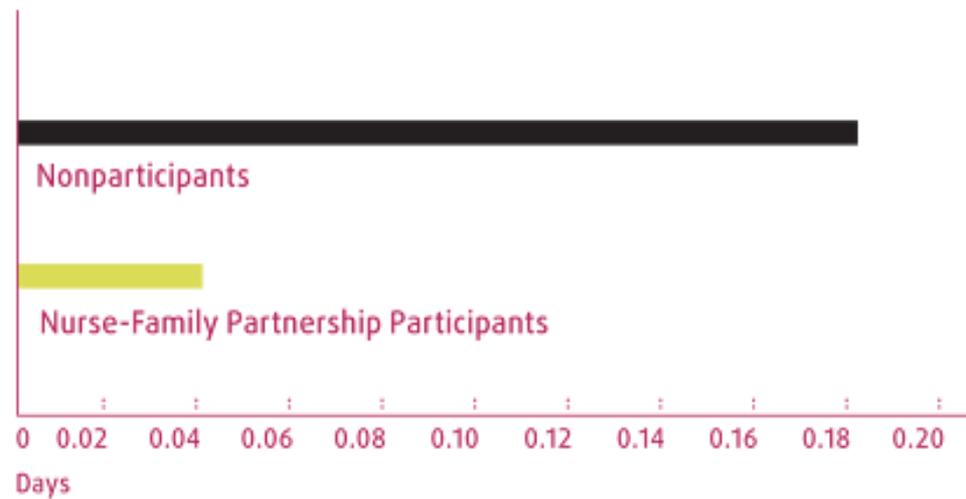
Age 4—Denver
(Born to low-resource mothers)





Days Hospitalized for Injuries

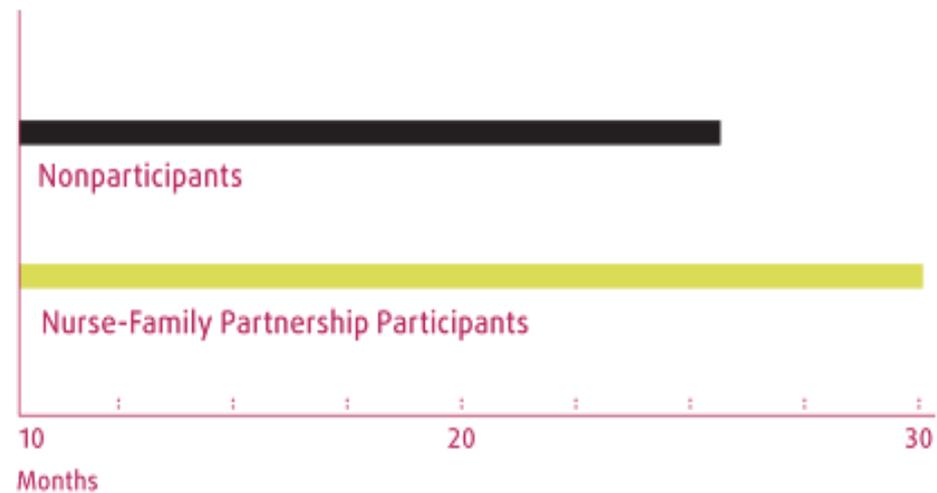
Birth to age 2—Memphis



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

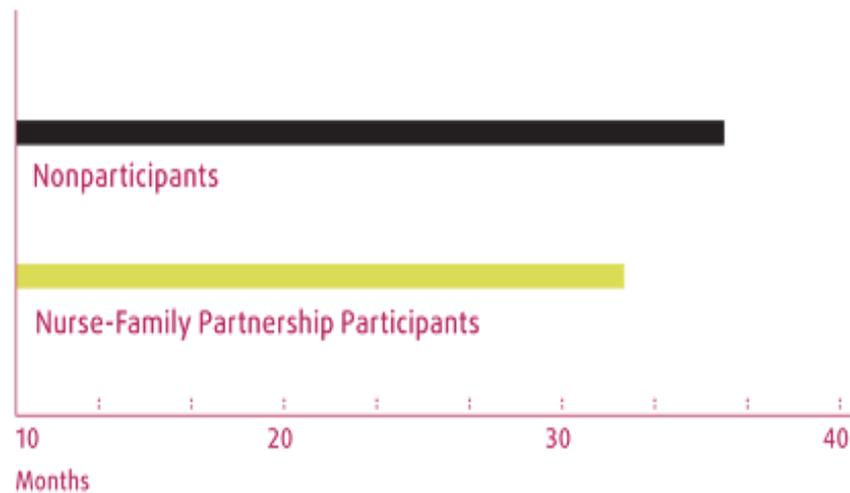


Source: *JAMA*, 2000, Vol. 283, 1987, Copyright © 2000, American Medical Association. All rights reserved.



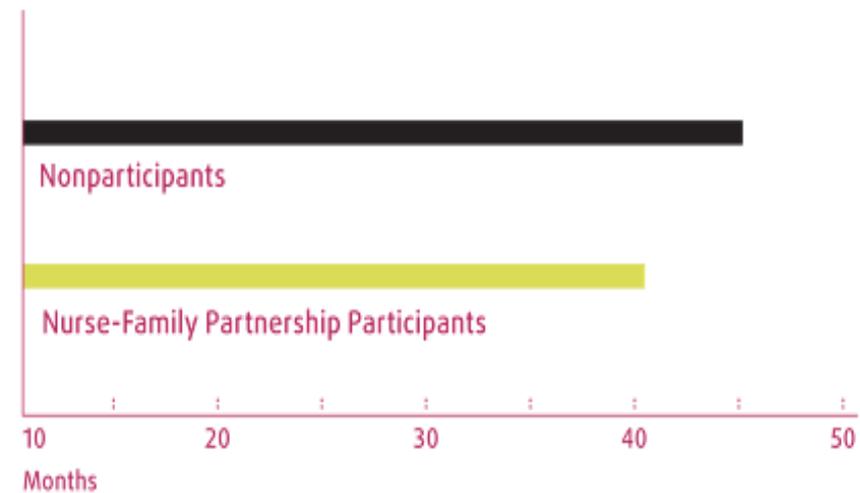
Months Receiving Welfare Assistance (AFDC)

Birth through age 5—Memphis

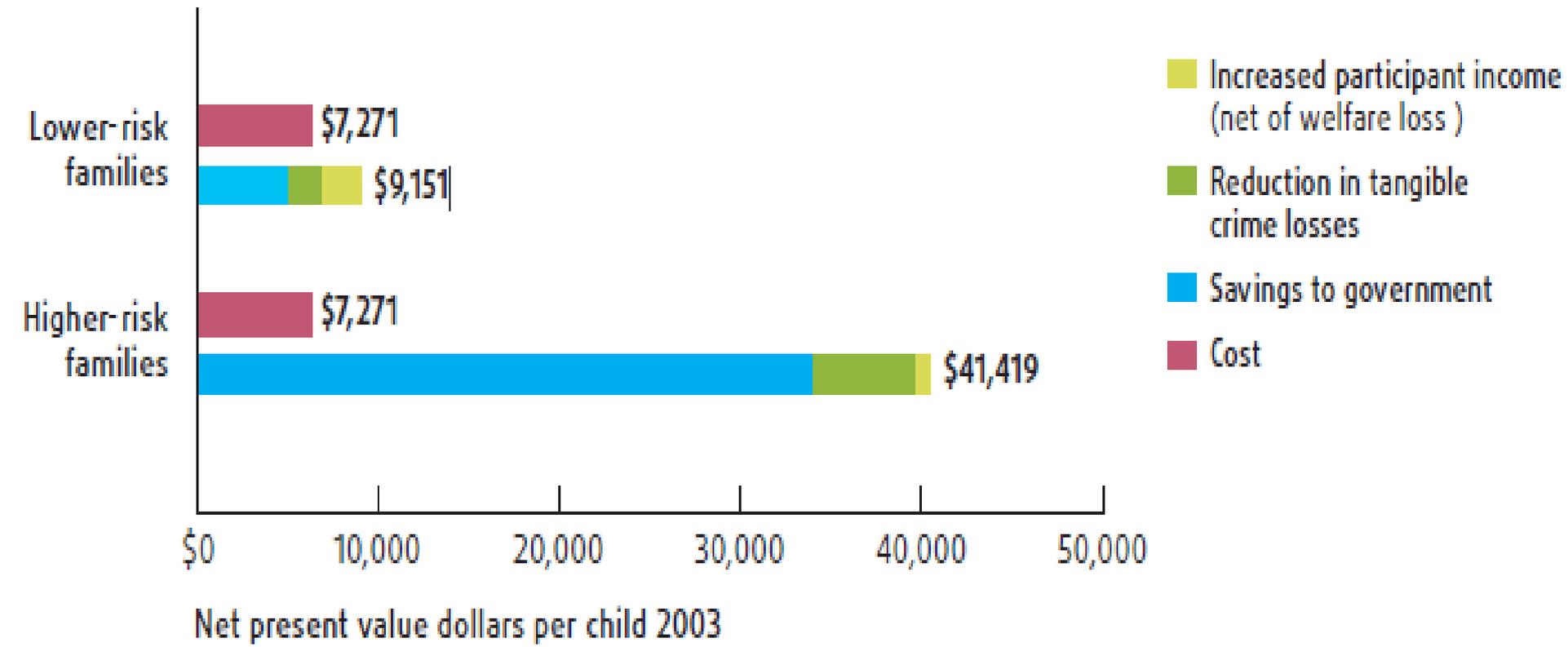


Months Receiving Food Stamps

Birth through age 5—Memphis



Monetary Benefits



Source: 2005 RAND Corporation Study

“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 what works

Create a Prenatal/Early Life intervention that will help heal the cycle of trauma in our communities

- We must have a common, unifying vision of healing in all life domains: health, mental health, education, ...
 - Intertwined and synergistic
 - metabolic, educational, mental health, etc.
 - more importantly, overall life experience: happiness, resilience, connections to others
- Cross the funding, administrative, “turf” divides
 - Tribal, federal, state/provincial, county, private
 - Social services, WIC, commodities, Head Start/child care, medical, mental health, schools, ...

What might this intervention look like?

- Cohesive, seamless, tailored intervention with one consistent staff person at the center for each family
 - *Not* a “stitched together” list of disjointed services
 - “Carrots” (not “sticks”) for participating in intervention
 - e.g.: Pay pregnant women for clean drug/cotinine screens, going to prenatal appointments and parenting classes, etc.
 - Strengths and relationship-based
 - Mirror back to young women (and men) that they have the ability to be a good parent
 - Pregnant women have to opt out, not opt in

Components

- *Prenatal/Early Life Case Management*--cornerstone
 - Home visiting--e.g. Nurse-Family Partnership, Nutaqsiivik
 - 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 tribal Head Start/Early Head Start, Child Care
 - Health & Development—prenatal, well child care integrated
 - Learning
 - Promise Neighborhoods, modeled on Harlem Children's Zone
 - Encourage parents to read to kids (e.g. Reach Out and Read)

The Path We *Could* Take

Rewind: “Mary’s” life

- As soon as mother’s pregnancy diagnosed:
 - Matched with a nurse home visitor/case manager
 - Weekly/biweekly visits focusing on developing a mentoring-type relationship, building on mother’s strengths, helping her to set goals, teaching her new skills
 - All services needed were offered and tailored to her needs
 - WIC foods supplemented so mother had enough good food even though shared with family
 - Mother rewarded for participation in each component
 - Mother went to 90% of her prenatal appointments
 - All but first urine drug screen negative and most cotinine screens
 - Mary born at 39 wks gest, normal weight for gestation

Rewind: “Mary”

- Visits from nurse home visitor continued until Mary was 2 yrs
- Mother set/achieved goals: became a CNA through health occupations class and graduated from high school
 - Mary cared for during day by excellent tribal child care program: bonding, learning, good food, social skills, active play, tribal language all emphasized
- Mother attended parenting classes
 - Praised and hugged Mary, appropriately disciplined her
 - Ate dinner together and read to Mary most evenings
 - Left her boyfriend when he wouldn't stop drinking
- Mary's weight stayed around the 90th % ile
- Mary graduated from high school, went to tribal college, got a good job, married a guy she met at college
- Now Mary becomes pregnant...



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