Thinking About Pregnancy After A Preterm Birth

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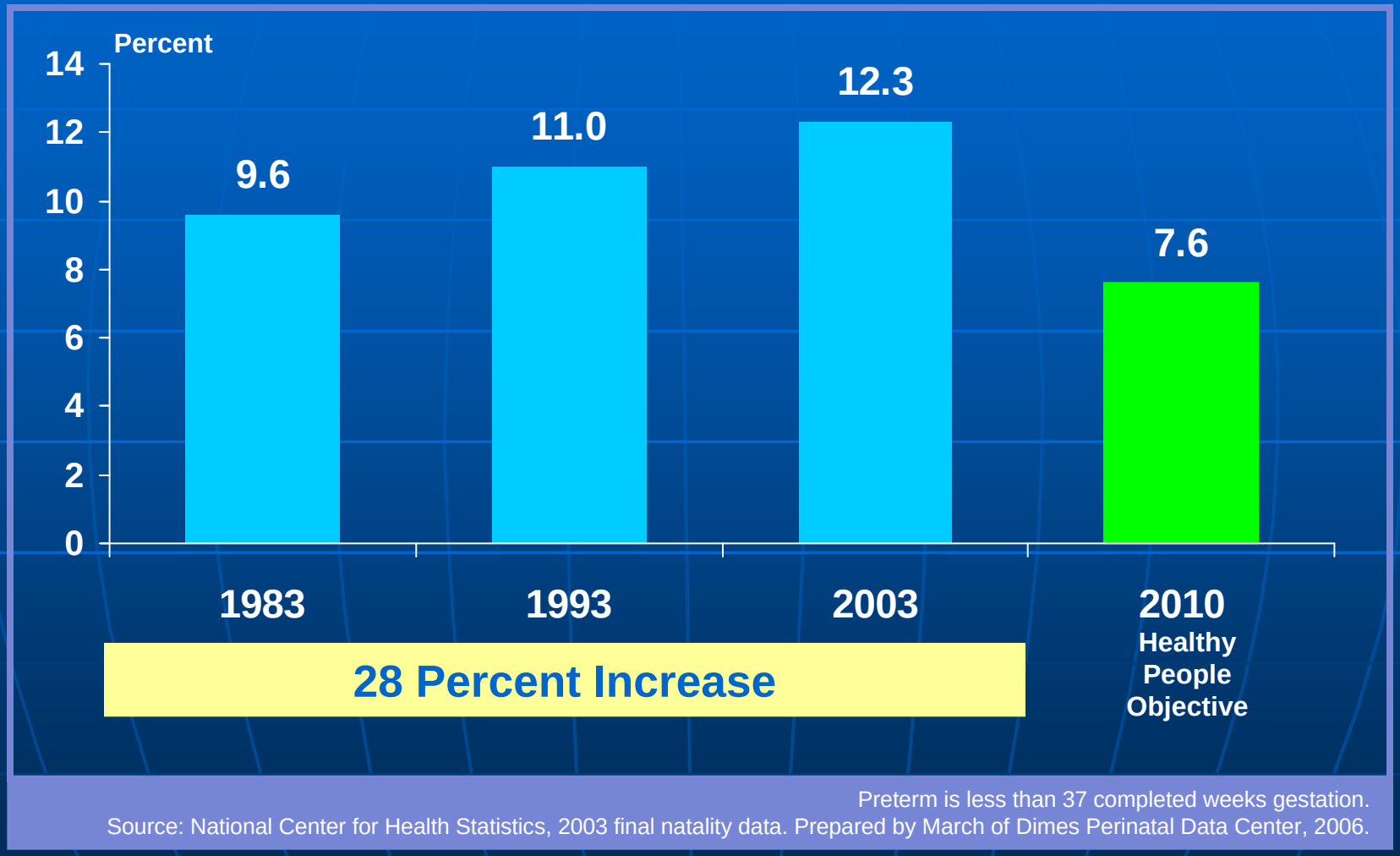
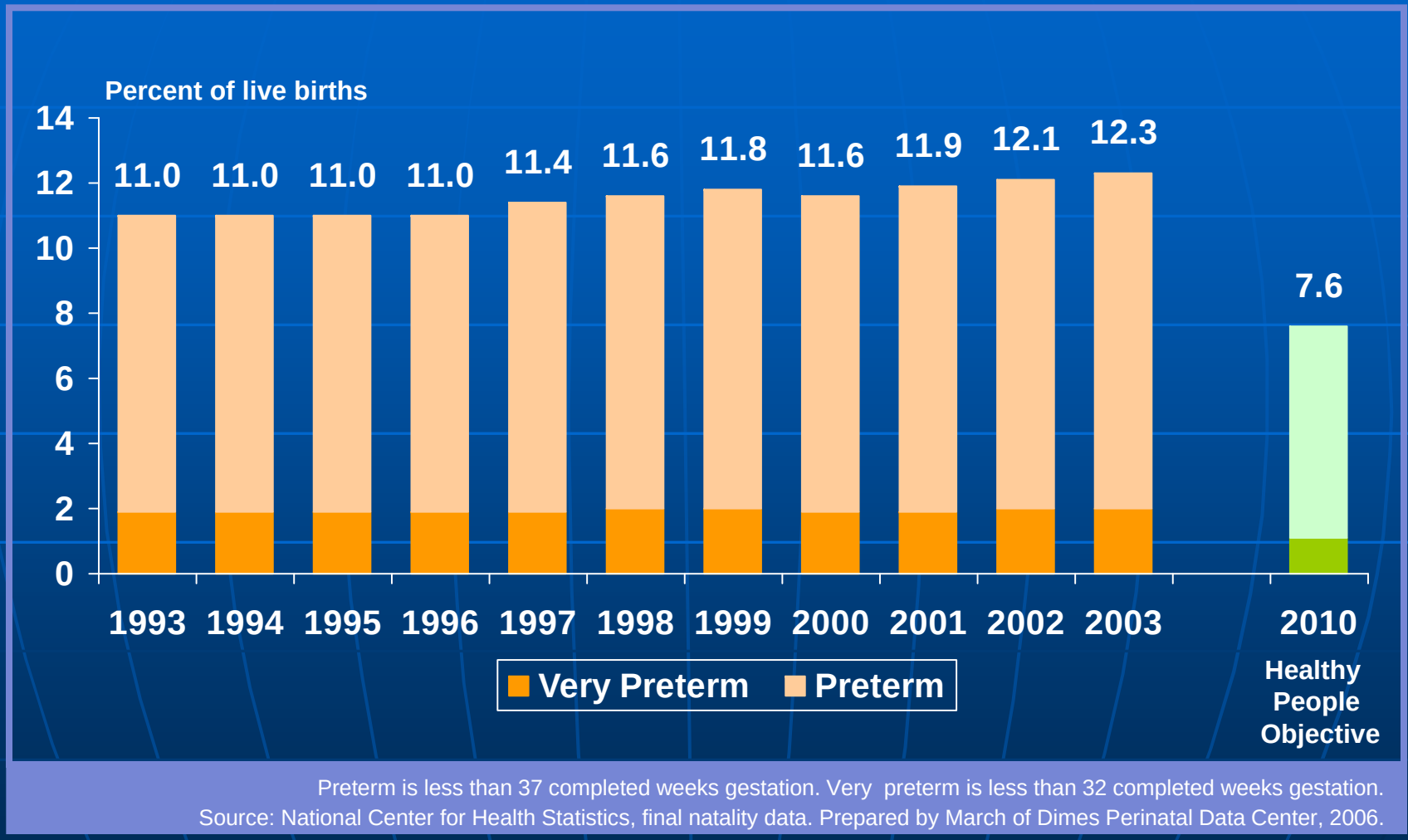
Preterm Births
United States, 1983-2003



Preterm is less than 37 completed weeks gestation.

Source: National Center for Health Statistics, 2003 final natality data. Prepared by March of Dimes Perinatal Data Center, 2006.

Preterm & Very Preterm Births
United States, 1993-2003



Preterm is less than 37 completed weeks gestation. Very preterm is less than 32 completed weeks gestation.
Source: National Center for Health Statistics, final natality data. Prepared by March of Dimes Perinatal Data Center, 2006.

Who Must Be Concerned?

- Mother
- Family
- Providers
- Employer
- Society

Maternal Concerns

- The Future is Relevant
  - Social/Economic Possibilities
  - Age
- Control is Possible
- Risk Recognition

Family Concerns

- The Future is Relevant
- Young Women & Men of the Family Are the Future of the Family
- Family Life is Critical
- Risk Recognition

Provider Concerns

- Risk Recognition
- Biologic Risks Are Evaluated
- Sociologic Risks Are Evaluated
- Biologic & Sociologic Risks Are Addressed Vigorously
- Ownership of a Long View of Education, Societal Change & Prevention

Employer Concerns

- Vulnerability of the Work Force
- Work Force As a Valued Asset
- Corporate Citizenship
- Health Is Good For The Company
- Risk Recognition

Economic Consequences of Preterm Birth

- **Hospital charges for premature infants[1] totaled $18.1 billion in 2003.**
- **Premature infants accounted for half of the hospital charges for all infants ($36.7 billion).**
- **The average charge for the most severe stays[2] was $77,000 compared to $1,700 for an uncomplicated newborn stay.**

[1]Includes any diagnosis of prematurity/low birthweight
[2]Defined as having a principal diagnosis of prematurity
Source: Agency for Healthcare Research and Quality, 2003 Nationwide Inpatient Sample.
Prepared by March of Dimes Perinatal Data Center, 2006.

Costs to Employers

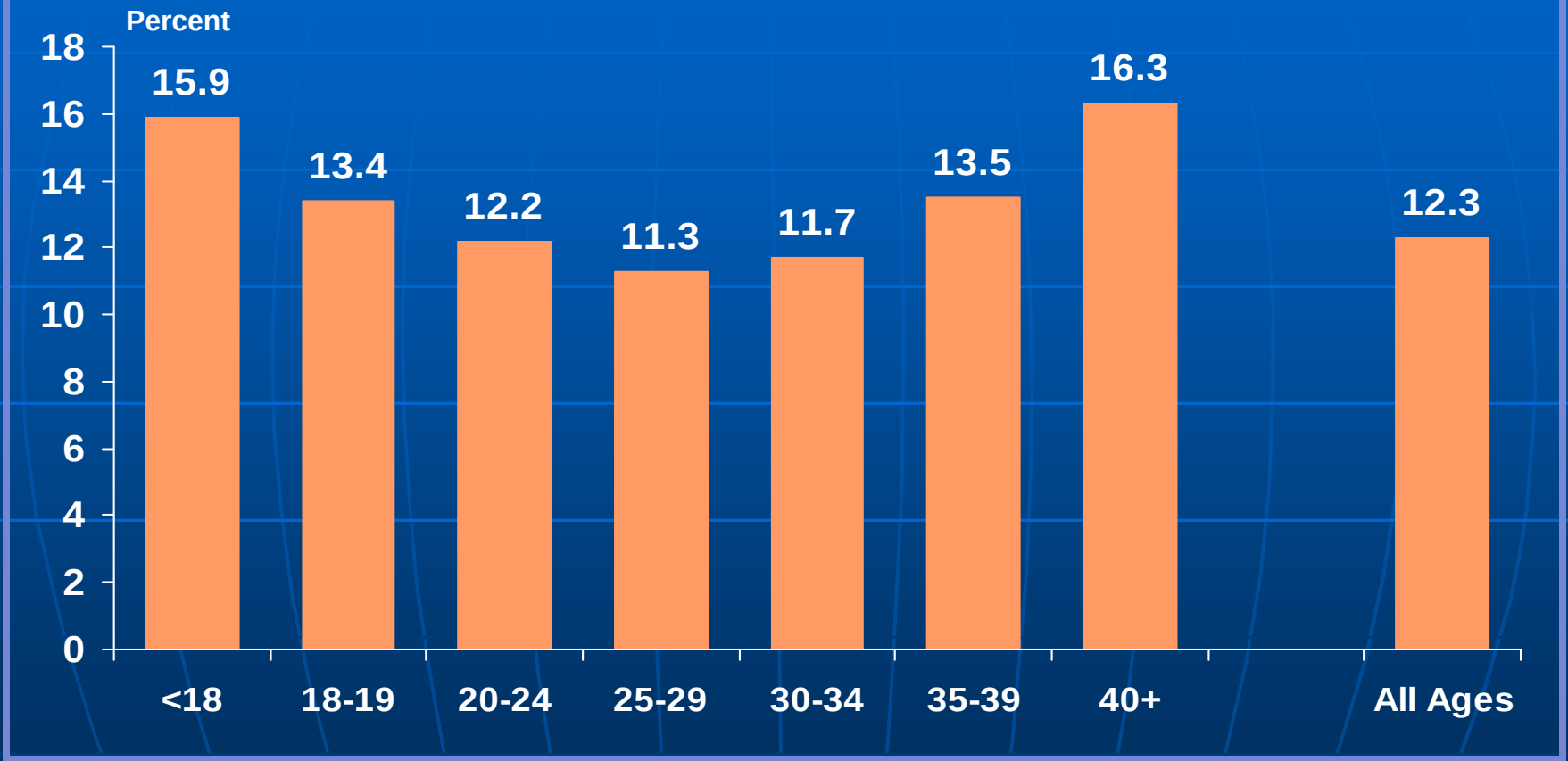
	Full-term Delivery	Preterm Delivery
Hospital Expenses	$1,210	$35,034
Physician Office Visits	$1,518	$ 6,079
Drug Expenses	$ 102	$ 497
Total	$2,830	$41,610

Based on analysis of births in 2001 followed for 12 months.
Expenditures have been adjusted to 2004 dollars using the medical component of the CPI.
Data largely from self-insured U.S. employers.
Research conducted and underwritten by Thomson Medstat.

Societal Concerns

- Future As A Shared Endeavor
- Risk Reduction = Health
- Policy Does Make A Difference
- Risk Recognition

Preterm Births
by Maternal Age, United States, 2003



Preterm is less than 37 completed weeks gestation

Source: National Center for Health Statistics, 2003 final natality data. Prepared by March of Dimes Perinatal Data Center, 2006.

Frame Work For Concern

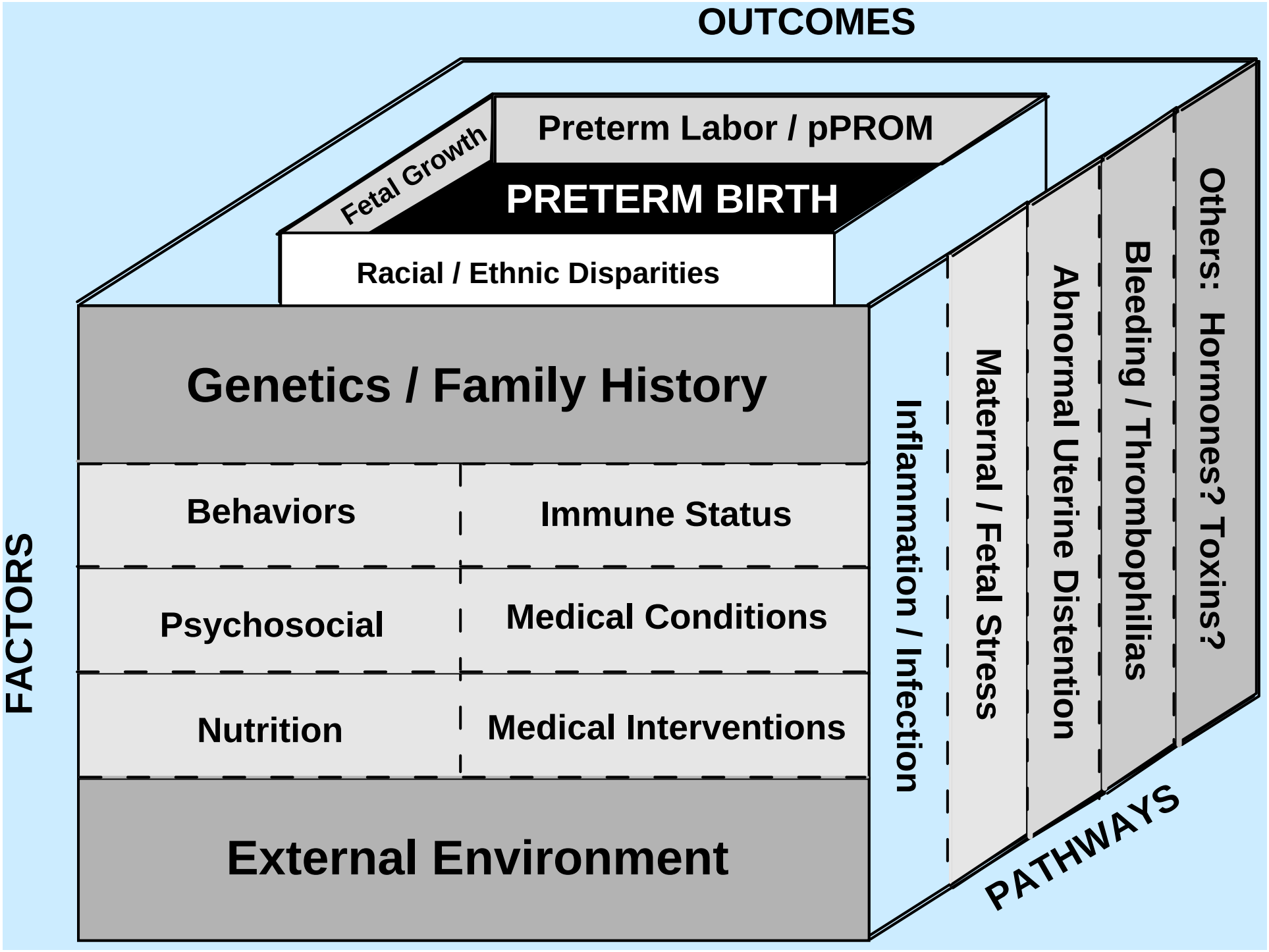
- Preterm Delivery – Emotional & Fiscal Cost
- Preterm Delivery – Demands Resources
- Preterm Delivery – Suboptimal Development
- Preterm Delivery – Long Term Societal Cost

Frame Work For Concern

- Determinents of Risk
  - Maternal Health, IPI, Social Risk, Genetic Risk, Other Biologic Risks, Pathways to Prevention

Frame Work For Concern

Preterm Delivery → Death/Disability
→ Short Inter Pregnancy Interval
→ Preterm Delivery


OUTCOMES
Fetal Growth
Preterm Labor / pPROM
PRETERM BIRTH
Racial / Ethnic Disparities
Genetics / Family History
Behaviors
Immune Status
Psychosocial
Medical Conditions
Nutrition
Medical Interventions
External Environment
FACTORS
Inflammation / Infection
Maternal / Fetal Stress
Abnormal Uterine Distention
Bleeding / Thrombophilias
Others: Hormones? Toxins?
PATHWAYS

Summary of Mediators for Preterm Birth

- **Inflammation**
  - Interleukin-1
  - Tumor necrosis factor
- **Activation of the maternal / fetal hypothalamic– pituitary–adrenal (HPA) axis**
  - Corticotropin-releasing factor (CRH)
  - Estradiol
- **Decidual hemorrhage**
  - Thrombin activation
- **Uterine distension**
  - Myometrial stretch

Source: Lockwood CJ, Iams JD. In: Precis: Obstetrics, 3rd ed. ACOG, 2005.

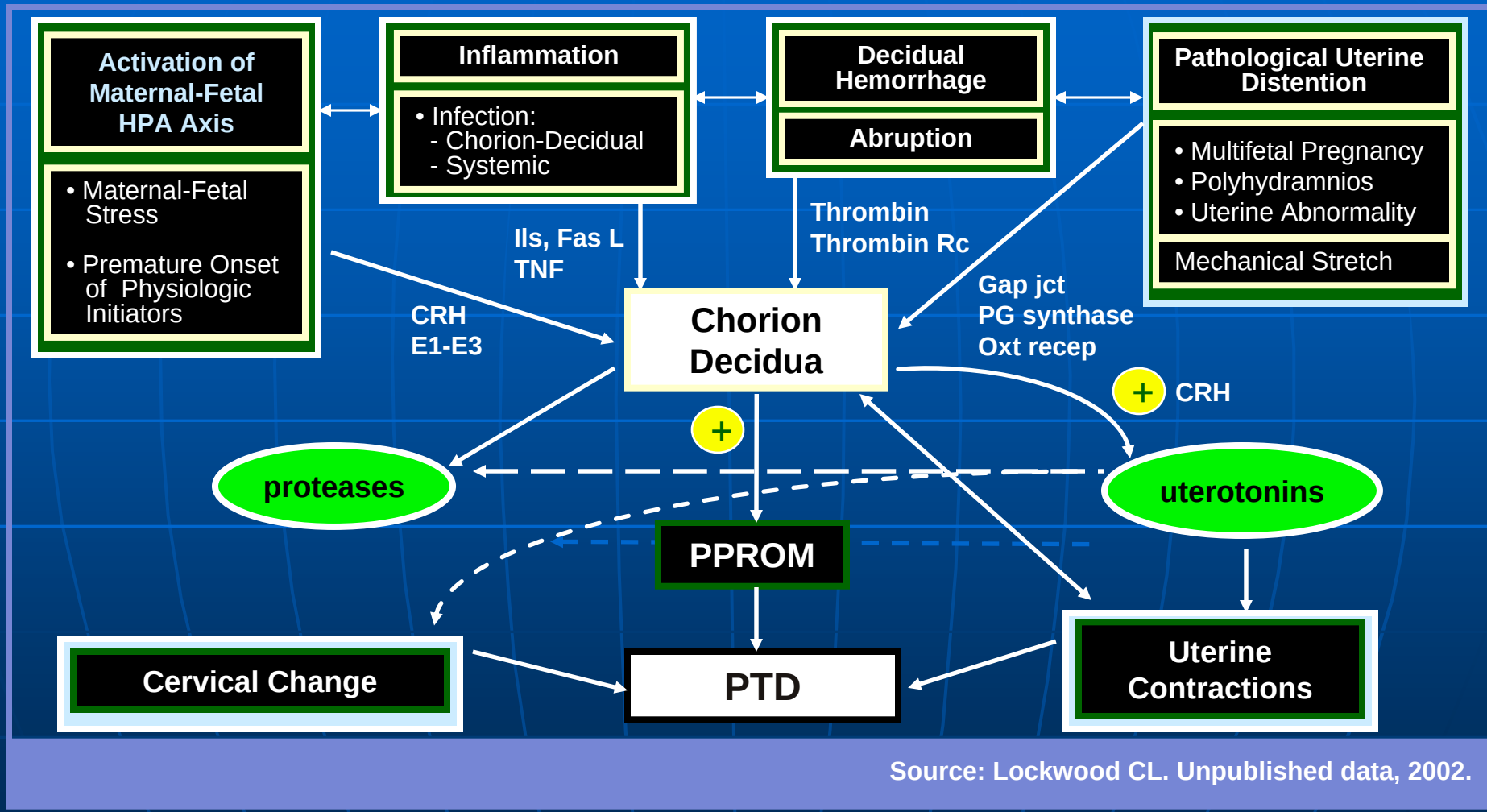
Risk Factors Associated With HPA Axis Activation

- **Maternal psychosocial stress**
  - Domestic violence
  - Racism
- **Fetal physiological stress**
  - Compromised uteroplacental blood flow
  - Placental pathology

Infections Associated with Preterm Birth

- **Sexually transmitted infections**
- **Bacterial vaginosis**
- **Genitourinary infections**
  - Asymptomatic bacteriuria
  - Pyelonephritis
- **Pneumonia**
- **Peritonitis**
- **Periodontal disease**

Pathways to Preterm Birth



Source: Lockwood CL. Unpublished data, 2002.

Pathways to Preterm Birth

- **Inflammation**
  - **Infection - ~40%**
- **Activation of the maternal-fetal hypothalamic– pituitary–adrenal (HPA) Axis**
  - **Stress - ~30%**
- **Decidual hemorrhage**
  - **Abruption - ~20%**
- **Uterine distension**
  - **Stretching - ~10%**

Sources: Lockwood CJ, Iams JD. Preterm labor and delivery. In: Precis: Obstetrics, 3rd ed. ACOG, 2005; Lockwood CJ, Kuczynski E. Paediatr Perinat Epidemiol 2001;15:78-89.

Preterm Birth
A Common, Complex Disorder

- Genetic contribution
- Environmental influences
- Gene-environment interactions

Classification of Preterm Birth

What are the conditions leading to preterm birth?

- **Spontaneous - 75%**
  - Preterm labor
  - Preterm premature rupture of membranes (PPROM)
  - Multiple gestation
  - Cervical insufficiency
  - Other related diagnoses
- **Clinically Indicated - 25%**
  - Mother or fetus at risk

Sources: Goldenberg RL et al. Am J Public Health 1998;88:233-8; Meis PJ et al. Am J Obstet Gynecol 1995;173:597-602; Meis PJ et al. Am J Obstet Gynecol 1998;178:562-7.

Known Risk Factors for Preterm Birth

Epidemiologic

- history of preterm birth
- unintended pregnancy
- previous fetal or neonatal death
- 3+ spontaneous losses
- assisted reproductive technology (ART)
- genetic predisposition
- folic acid deficiency
- environmental toxins
- low pre-pregnancy weight
- obesity
- anemia
- lack of social support
- tobacco use
- alcohol abuse
- illicit drug use

Source: Iams JD, Creasy RK. Preterm labor and delivery, Chapter 34. In: Maternal-Fetal Medicine: Principles and Practice, 5th ed., 2004.

Spontaneous Preterm Births

- **Clinical presentations**
  - Preterm labor - 50-60%
  - Preterm premature rupture of membranes (PPROM) - 40-50%
- **Risk factors similar**
  - PPROM
    - More often smokers, 2nd trimester bleeding, low socioeconomic status (SES)
- **50% have no risk factors**

Sources: Goldenberg RL et al. Am J Public Health 1998;88:233-8; Meis PJ et al. Am J Obstet Gynecol 1995;173:597-602; Meis PJ et al. Am J Obstet Gynecol 1998;178:562-7.

Known Risk Factors for Preterm Birth **(continued)**

Inflammation

- systemic maternal disease
- infections
- PPROM

Overdistension/uterine problems

- multifetal pregnancy
- Overdistension
- Uterine Abnormalities

- cervical abnormalities

Decidual hemorrhage

- fetal / placental anomalies
- bleeding
- trauma

Activation of maternal hypothalamic pituitary adrenal (HPA) axis

- stress / violence

Source: Iams JD, Creasy RK. Preterm labor and delivery, Chapter 34. In: Maternal-Fetal Medicine: Principles and Practice, 5th ed., 2004.

Epidemiology of Spontaneous PTB

- **Multiple Gestation** — **OR 6**
  - compared to singleton births
- **Prior Preterm Delivery** — **OR 4**
  - compared to no history of preterm birth
- **2nd Trimester Bleeding** — **OR 2 or >**
  - compared to no early bleeding (before 28 weeks)
- **Genito-Urinary (GU) Tract Infection** — **OR 2**
  - compared to no GU infection
- **African-American** — **OR 2**
  - compared to non African-American ancestry
- **Body Mass Index <19.8 kg/m²** — **OR 2**
  - compared to body mass index ≥ 19.8 kg/m²

Source: Iams JD, Creasy RK. Preterm labor and delivery, Chapter 34. In: Maternal-Fetal Medicine: Principles and Practice, 5th ed., 2004.

Recurrent Preterm Delivery

Population-based cohort study — Georgia 1980 to 1995

- 122,722 white women and 56,174 black women
- *Of 1,023 white women w/ 1st delivery @ 20-31 weeks*
  - 8.2% delivered 2nd at 20-31 weeks
  - 20.1% delivered 2nd at 32-36 weeks
  - Total preterm deliveries = 28.3% < 36 wk
- *Of 1,084 black women w/ 1st delivery @ 20-31 weeks*
  - 13.4% delivered 2nd at 20-31 weeks
  - 23.4% delivered 2nd at 32-36 weeks
  - Total preterm deliveries = 36.8% < 36 wk

Source: Adams MM et al. JAMA 2000;283:1591-6.

Preterm Birth Following A Preterm Birth

- More Preterm Index Delivery – Higher Risk of Subsequent Preterm Delivery
- Late Second Trimester – Subsequent Pregnancy 60% Term
- Late Preterm – Subsequent Pregnancy 71% Term

Clin Ob Gyn 27:539, 1984

Preterm Delivery Following Miscarriage

- Second Trimester Loss – Subsequent Preterm Delivery 14%
- First Trimester Loss x3 – Subsequent Preterm Delivery 12%

Am J Perinatol 6:62, 1989

Recurrence Risk of Preterm Birth

- Rises with increased number of preterm deliveries (PTDs)
- Rises as gestational age of prior PTD declines
- Most recent birth is more predictive
- Risk greater in African-Americans

Source: Mercer BM et al. Am J Obstet Gynecol 1999;181:1216-21.

Intimate Partner Violence

- 16-23% of US Pregnant Women
- 40% of Pregnant Women Seeking Termination
- 4x LBW (Nigaragua)
- 7x NMR
- Most Significant Factor for Premature Birth (DC)

Clin OB Gyn 51:385, 2008

Preventive Preterm Birth

Unintended Pregnancies, Birth Spacing

Folic Acid, Smoking, Substance Abuse, Violence, Infection, Nutrition, Environment, Genetics/Familial Risks, Accurate Dating, Progesterone, Avoid Interventions with Risk of Preterm Delivery

Care Opin Ob Gyn 20:590, 2008

Periconception Surveillance
2006 – 26 Reporting Areas - US

Item	%
Tobacco Use	23.2
Alcohol Use	50.1
Dental Visit Ever	77.8
Pre-pregnancy Counseling	30.3
Physical Abuse	3.6
Four or More Stressors	18.5

Demographic Characteristics of Populations at Risk for Preterm Birth

- Maternal age (<18 and >35 years)
- Low socioeconomic status (SES)
- Unmarried
- African-American ancestry
- Violence

European Model
N=16,000

Universal Care, Risk ID, Focus on Home and Work, Early Leave – Shortened Cervix or Difficult Work

Preterm	5.4 to 3.7%
<32 weeks	1.1 to 0.5%

MOD Series 25:1, 1989
Pediatr 75:154, 1985

Sweden – Maternal Protection Model

	LBW	Risk PTB
1920-1924	7.8%	OR – 2.50
1985	5.8%	OR – 1.22

Acta Pediatr 88:445, 1999

Strategic Directions

New Understanding

Apply Current Understanding

Use All Biologic Applications

Use All Sociologic Applications

Community Mobilization

- Families
- Providers
- NGOs
- Payers
- Public
- Media
- Policy Makers

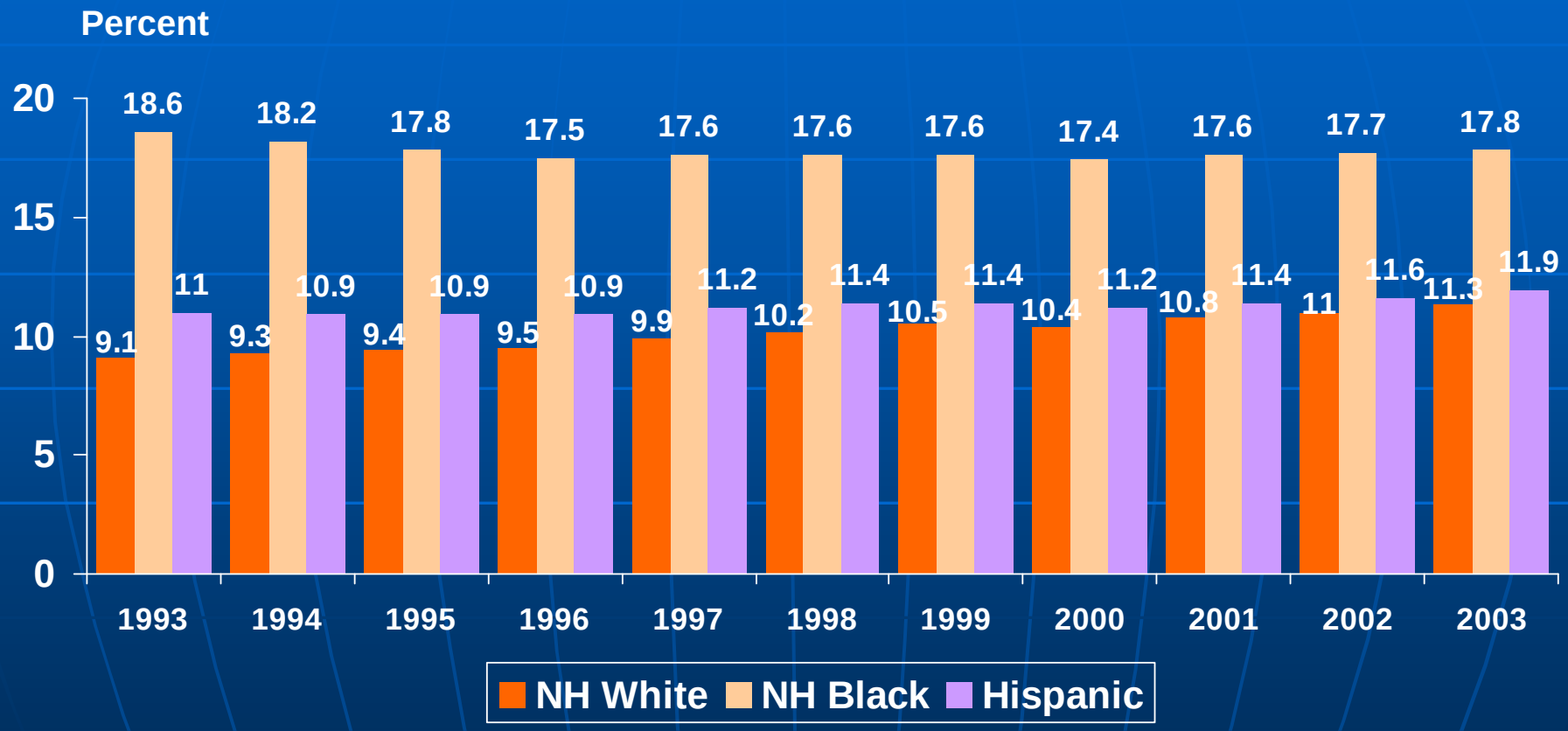
WHY?

We Care For Others

We Care For Our Community

We Can Be Effective

Preterm Births by Maternal Race/Ethnicity, U.S., 1993-2003



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