Healthy Babies are Worth the Wait: High Risk Pregnancies Exempted

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March of Dimes
Birth Defects Foundation

Mission:

- **To improve infant health by preventing infant mortality, birth defects and PTB/LBW**

The Continuum of Reproductive Health

- Improving health of infants requires focusing on the entire spectrum of reproductive health from prior to conception through the first year of an infant's life and throughout the woman's childbearing years
- Preconception health is the cornerstone of healthy infants, children, families and communities

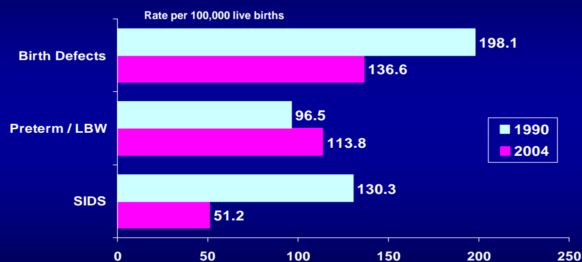
Objectives

- Briefly review the changing epidemiology of preterm birth
- Discuss the paradigm shift that most spontaneous preterm birth meets the criteria of other common complex disorders such as heart disease
- Summarize the impact of late preterm birth (34-36 weeks) on increasing rates of preterm birth

Preterm Birth

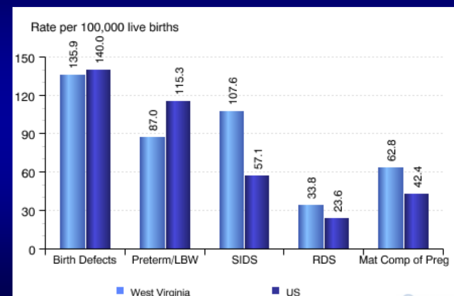
- **#1 obstetric challenge in the US**
- **Major cause of loss**
  - **majority of all perinatal mortality**
  - **leading cause of neonatal mortality (since 1999)**
  - **leading cause of black infant mortality and second leading cause of all infant mortality in US?**
- **Leading problem in pediatrics**
  - **leading cause of neonatal morbidity**
  - **half of all neurodevelopmental conditions**
- **Associated with higher rates of chronic illness in adults**
- **Serious, common, and costly**

Three Leading Causes of Infant Mortality
United States, 1990 and 2004*



Source: National Center for Health Statistics
*preliminary mortality data for 2004
Prepared by March of Dimes Perinatal Data Center, 2007

Cause Specific Infant Mortality
WV and US 2002



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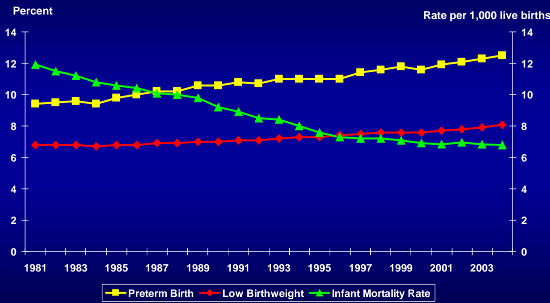
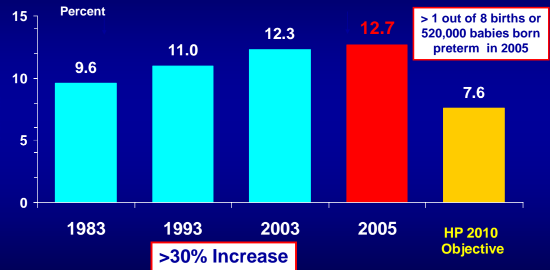
Preterm Births, Low Birthweight and Infant Mortality
United States, 1981 - 2004



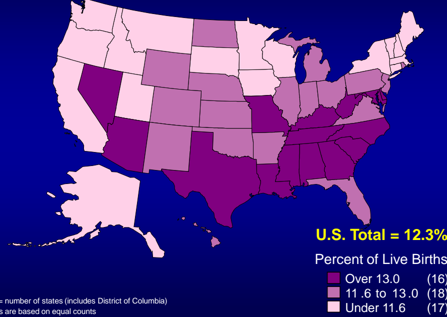
Source: National Center for Health Statistics, final natality and mortality data
Prepared by March of Dimes Perinatal Data Center, 2007

Preterm Birth Rates
United States, 1983, 1993, 2003, 2005*



Preterm is less than 37 completed weeks gestation.
Source: National Center for Health Statistics, final natality data
Prepared by March of Dimes Perinatal Data Center, 2005
*preliminary

Preterm Birth Rates by State
United States, 2003

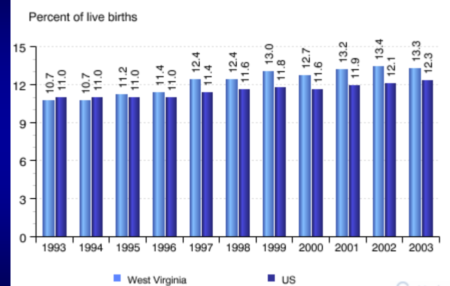


U.S. Total = 12.3%

Percent of Live Births
- Over 13.0 (16)
- 11.6 to 13.0 (18)
- Under 11.6 (17)

Note: Value in ( ) = number of states (includes District of Columbia)
Value ranges are based on equal counts
Source: National Center for Health Statistics, 2003 final natality data
Prepared by March of Dimes Perinatal Data Center, 2005

Preterm Birth (<37 wks)
WV and US, 1993-2003



WV PTB increase 24.3%
US PTB increase 11.8%

Preterm Birth as a Common Complex Disorder
(like other chronic conditions- heart disease, cancer)

- Complex
  - Genetic contribution
    - Familial aggregation
    - Recurrence of preterm birth
    - Racial disparity
  - Environmental influences
  - Gene-environment interactions
- Many of the risk factors are the same

PTB Risk Factors

- The strongest risk factors for PTB suggest a maternal or fetal genetic predisposition
- Women born preterm are more likely to deliver preterm
- ~20% of women who deliver preterm have recurrence with the same partner
  - changing partners reduces the risk by one third
- The heritability of PTB is estimated to be 17%-36%
- 18 studies reviewed on genetic polymorphisms showed that polymorphisms in TNF alpha showed the most consistent increase in PTB
- Environmental factors such as infection, stress, and obesity suggest that environmental and genetic RF might operate and interact through related pathways.

Crider, et al. Genetic variation associated with preterm birth: a HuGE Review. Genetics in Med 7(9) 593-604, 2005.

Risk Factors for Preterm Labor/Delivery

- The best predictors of having a preterm birth are:
  - ✓current multifetal pregnancy
  - ✓a history of preterm labor/delivery or prior low birthweight
  - ✓mid trimester bleeding (repeat)
  - ✓some uterine, cervical and placental abnormalities
- *Other risk factors:*
  - –unintended pregnancy
  - –maternal age (<17 and >35 yrs)
  - –black race
  - –low SES
  - –unmarried
  - –previous fetal or neonatal death
  - –3+ spontaneous terminations
  - –uterine abnormalities
  - –incompetent cervix
  - –cervical procedures
  - –genetic predispositions
  - –low pre-pregnant weight
  - –obesity
  - –infections
  - –anemia
  - –major stress
  - –lack of social supports
  - –tobacco use
  - –illicit drug use
  - –alcohol abuse
  - –folic acid deficiency

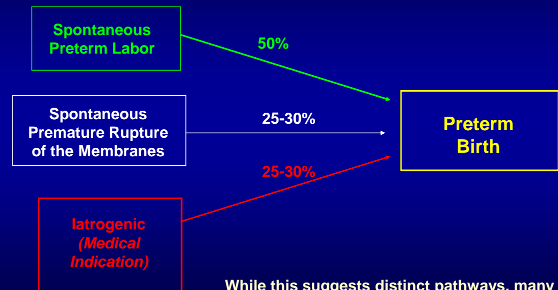
Can Preterm Labor be Prevented?

- Primary prevention is the goal
  - – especially risk reduction in the preconceptional period and early in pregnancy
- Preterm prevention programs have focused on risk assessment or prediction of preterm labor
  - – risk assessment identifies only half of preterm births
  - – during pregnancy most biomarkers, even in combination with risk factors, do not have good positive predictive values
- Causation is the great unknown

Major Pathways to Preterm Labor

- Inflammation/infection (ascending), 40%
  - – cytokines
- Stress (maternal/fetal), 25%
  - – CRH
- Bleeding (decidual hemorrhage, abruption), 25%
  - – thrombin
- Stretching (uterine distention), 10%

TYPE of Preterm Birth

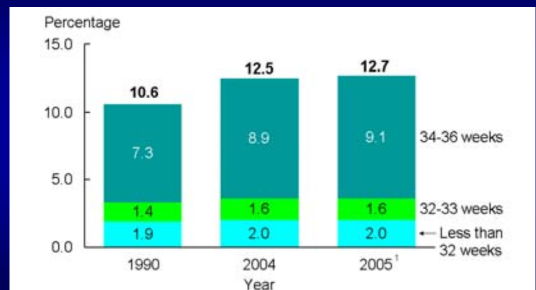


While this suggests distinct pathways, many of the risk factors for all 3 are similar

Definitions

- Preterm birth:
  - < 37 completed weeks gestation
- Late preterm (or Near-Term):
  - 34-36 completed weeks
- Very preterm:
  - <32 completed weeks

Percent of Preterm Births by Gestational Age Category, US, 1990, 2004, 2005

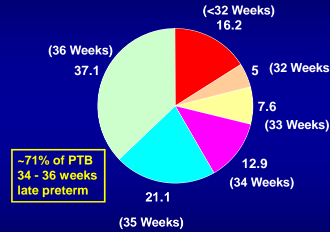


[1] Based on preliminary data.
SOURCE: CDC/NCHS, National Vital Statistics System

Why are Late Preterm Rates Rising?

- Changing culture of childbearing
  - more high risk pregnancies (AMA, chronic/developing problems, multiples, infertility management, obesity, GDM)
  - public preference/autonomy (induction and cesarean on maternal request)
  - changes in clinical management (more interventions)
    - litigious environment, fear of suit, defensive medicine
      - 2006 ACOG liability survey 89.2% (79.1% in 2003) named in a claim, avg 2.6/career
    - reimbursement system changes
    - window to administer antenatal steroids 24-34 weeks
    - increase in survival to almost 100% at 34 weeks
    - increasing rates of elective inductions and section before 39 weeks despite ACOG guidelines

Distribution of Preterm Births by Gestational Age, US, 2002



"Near term infants had significantly more medical problems and increased hospital costs compared with contemporaneous full term infants

Near term infants may represent an unrecognized at-risk neonatal population."

Wang, et al. Clinical Outcomes of Near-Term Infants, Pediatrics (114) 372-6, 2004.

Source: National Center for Health Statistics, 2002 natality file
Prepared by the March of Dimes Perinatal Data Center, 2004

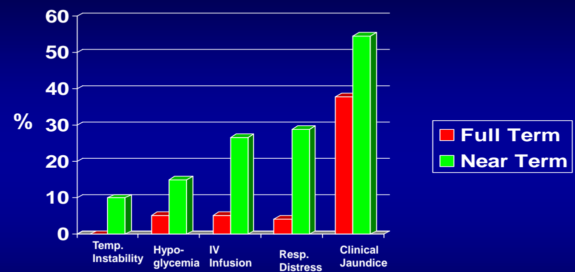
Morbidities associated with Late PTB?

Need to separate causes and effects

- Increased immediate morbidities:
  - Respiratory distress
  - Jaundice
  - Feeding difficulties
  - Hypoglycemia
  - Temperature instability
  - Sepsis
- Increased NICU use (and re-admissions)
- Increased cost
- Long term outcome - *??* - **NO DATA!**

NICHD Invitational Conference , July 2005

Clinical Outcomes of Late- Preterm Infants

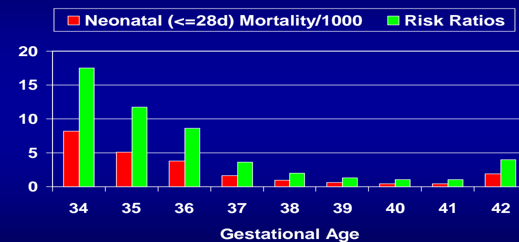


Graph of clinical outcomes in near-term and full-term infants as percentage of patients studied.

Wang et al. Clinical Outcomes of Near-Term Infants. *Pediatrics.* 2 Aug 2004; 114: 372-276.

Mortality of Late-Preterm (Near-Term) Newborns in Utah

Young P et al. Pediatrics 2007;119;659-665



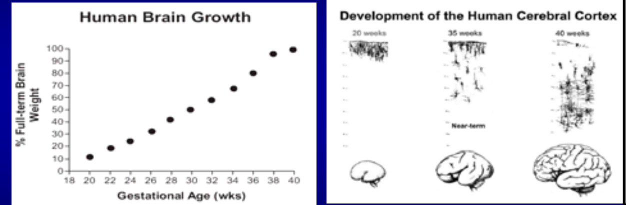
Late Prematurity Facts

- **Late preterm delivery is increasing**
  - **up at least 16% from 1993**
  - **straining the Public Health system**
  - **52% of late preterm infants are delivered by cesarean, a much higher rate than term infants**
- **Late-Preterm infants are:**
  - **a majority of NICU admissions**
  - **the greatest percentage of NICU patients to receive respiratory support**
  - **the majority of NICU economic costs**

Late Prematurity Facts

- often the sickest babies in a NICU
- more likely than a full term baby to be rehospitalized in the first year of life
- twice as likely to die in the first year of life as a full term baby
- at risk for long term health issues

Human Brain Growth in Gestation

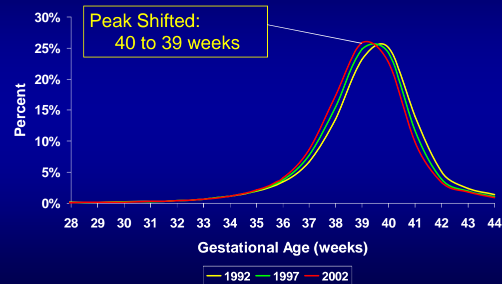


Kinney, 2006

Singletons by Birth Category

	1992	1997	2002
• Spontaneous:	68.1%	63.4%	56.8%
• PROM:	3.0%	2.7%	2.2%
• Intervention:	28.9%	33.9%	41.0%

Gestational Age-Specific Distribution Singleton Live Births, Spontaneous *United States, 1992, 1997, 2002*



U.S. Late Preterm live births are on the rise: % Change 1992-2002

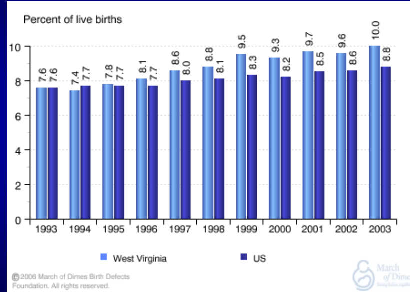
United States Live Births MOD: Davidoff 2005

Percent Change, Gestational Age-Specific Distribution Singleton Live Births, Spontaneous *United States, 1992, 1997, 2002*

Gestational Age Category	1992	1997	2002	% Change	Adjusted* % Change
<32	1.2%	1.1%	1.0%	-16.7%	-9.1%
32-34	2.2%	2.2%	2.2%	0.0%	0.0%
35-36	5.4%	5.8%	6.2%	14.8%	16.7%
37-39	43.4%	48.1%	51.8%	19.4%	18.6%
40	25.0%	24.3%	22.7%	-9.2%	-9.2%
41-44	22.8%	18.6%	16.0%	-29.8%	-29.1%

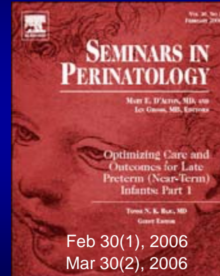
* Adjusted for maternal race/ethnicity and maternal age. All rates significantly different ($p < 0.05$) between 1992 and 2002, except at 32-34 weeks.

Late Preterm Births (34-36 weeks) WV and US, 1993-2003



WV LPTB increase 31.6%
US LPTB increase 15.8%

July 2005- Invitational NICHD Workshop on Near Term/Late Preterm births (34-36 weeks)



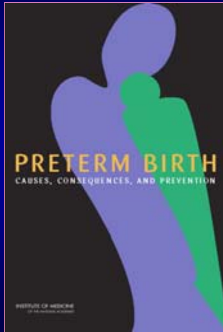
Feb 30(1), 2006
Mar 30(2), 2006

Optimizing Care and Outcome for Late-Preterm (Near-Term) Infants: A Summary of the Workshop Sponsored by the National Institute of Child Health and Human Development

Peds, 118(3):1207-14, 2006

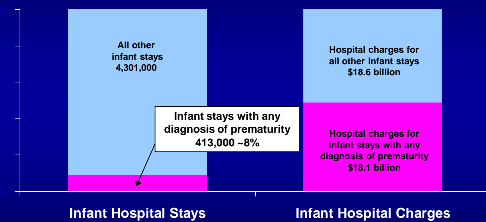
Clinics in Perinatology, Dec 2006

Institute of Medicine Report, July 2006



The IOM estimates the total national cost of premature births to be ***at a minimum*** **$26.2 billion**. This estimate includes many costs, such as in-patient hospital costs, lost wages and productivity and early intervention programs.

Costly: Distribution of Hospital Stays and Hospital Charges, United States, 2003



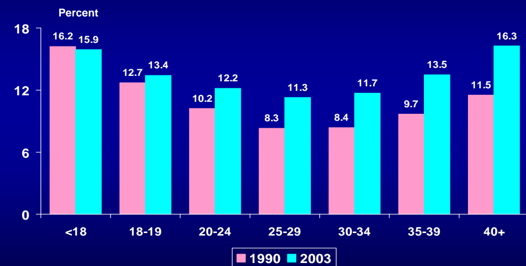
Agency for Healthcare Research and Quality, 2003. Nationwide Inpatient Sample.
Prepared by March of Dimes Perinatal Data Center, 2005.

Factors that Contribute to Increasing Rates of Preterm Birth

- Increasing rates of births to women 35+ years of age
- Increasing rates of multiple births
- Indicated deliveries
  - Induction
  - Management of maternal and fetal conditions
  - Patient preference/consumerism (CDMR)
- Substance abuse
  - Tobacco
  - Alcohol
  - Illicit drugs
- Bacterial and viral infections
- Increased stress (catastrophic events, DV, racism)

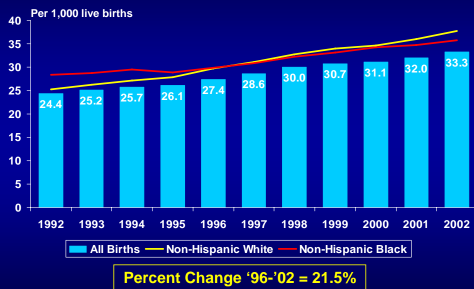
MATERNAL AGE

Preterm Births by Maternal Age Among Singletons, US, 1990 and 2003



Source: National Center for Health Statistics, final natality data
Prepared by March of Dimes Perinatal Data Center, 2005

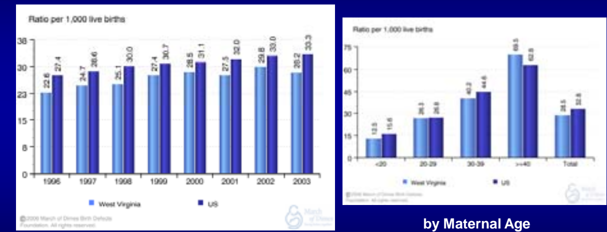
Multiple Birth Ratios by Maternal Race/Ethnicity United States, 1992-2002



Percent Change '96-'02 = 21.5%

Source: National Center for Health Statistics, final natality data
Prepared by March of Dimes Perinatal Data Center, 2005

Multiple Birth Ratios WV and US, 1996-2003

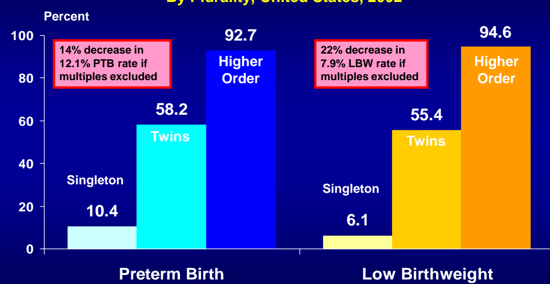


by Maternal Age

All Multiple Births

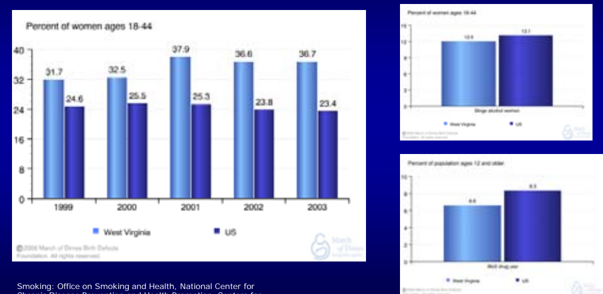
PLURALITY Preterm and Low Birthweight Births

By Plurality, United States, 2002



Preterm is less than 37 weeks gestation
Low birthweight is less than 2500 grams or 5 1/2 pounds
Source: National Center for Health Statistics, final natality data
Prepared by March of Dimes Perinatal Data Center, 2002

Substance Abuse WV and US, 1999-2003



Smoking: Office on Smoking and Health, National Center for Chronic Disease Prevention and Health Promotion, Centers for Disease Control and Prevention.

Smoking Cessation and Preterm Birth (Cochrane Review)

- 64 trials (51 RCTs of 20,931 women) and 6 cluster-randomised trials (over 7500 women) provided data on smoking cessation and/or perinatal outcomes
- Smoking cessation interventions reduced low birthweight (RR 0.81, 95% CI 0.70 to 0.94) and preterm birth (RR 0.84, 95% CI 0.72 to 0.98)
- One intervention strategy, rewards plus social support, resulted in a significantly greater smoking reduction than other strategies (RR 0.77, 95% CI 0.72 to 0.82).
- Smoking cessation programs in pregnancy reduce the proportion of women who continue to smoke, and reduce low birthweight and preterm birth.

Lumley J, et al. Interventions for promoting smoking cessation during pregnancy. The Cochrane Database of Systematic Reviews 2004, Oct 18;(4):CD001055.

Prevention of Preterm Labor, Preterm Delivery and Prematurity

- **Primary prevention**
  - **identifying and managing risks**
  - **risk reduction approach and strategies to reproductive health**
  - **prevent PTL**
- **Secondary prevention**
  - **prevent preterm delivery**
- **Tertiary prevention**
  - **prevent/minimize complications of prematurity**

Pre/Interconception Internatal Care

- Readiness for pregnancy (FP, prevent unintended pg, interval between pregnancies)
- Optimal management of medical conditions (diabetes, HBP, asthma, heart disease, addictions, depression)
- Infections and STIs
- Immunizations
- Family history, genetic counseling, carrier testing
- Substance abuse (smoking, alcohol, other drugs)
- Domestic violence (DV/IPV)
- Stress reduction
- Optimal weight and activity
- Good nutrition-- folic acid for men and women
- Avoid teratogens (work site, environment)
- Review all meds and home remedies with hcp

Prevent the Preventable

- Ø Unintended pregnancies
- Ø Folic acid deficiency
- Ø Alcohol
- Ø Tobacco
- Ø Illicit drugs
- Ø Infections (UTIs, STIs, periodontal disease)
- Ø Extremes of weight
- Ø Some medications (Rx, OTC, home remedies)
- Ø Environmental toxins
- Ø Known genetic/familial risks
- Ø Unnecessary interventions resulting in preterm birth
- Promote appropriate level designation and regionalization

Take Home Messages

- Preterm birth is a common complex disorder meeting criteria for high public health priority
- Intervene throughout the continuum of reproductive health for women and men with culturally sensitive, health literacy appropriate risk reduction interventions
- All providers have a major role in the success of primary and secondary prevention
- All pregnant women may be at risk for preterm labor and birth and should be taught the signs and symptoms beginning about 20 weeks of gestation
- A multidisciplinary approach is needed
- Everyone can make a difference