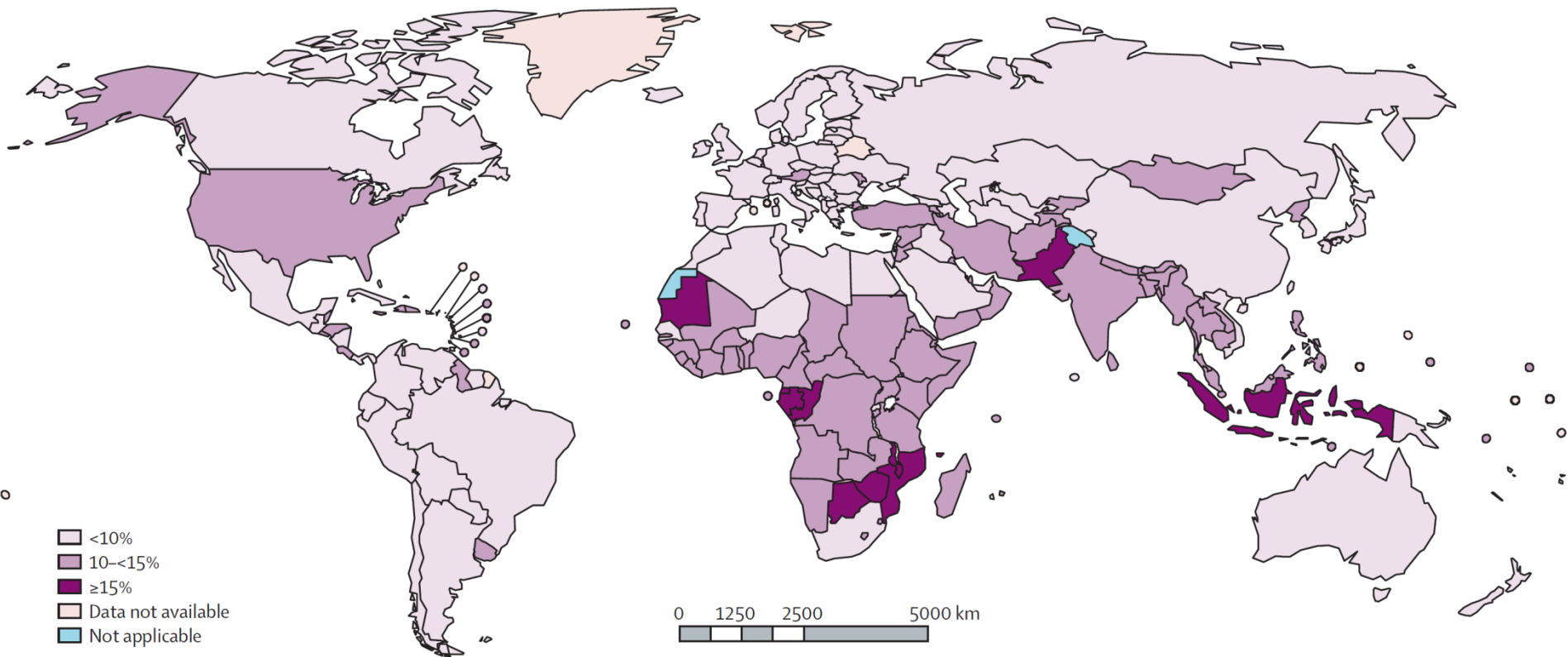




# **Improving Pregnancy Outcomes: The Challenge of Prematurity**

**Geeta K. Swamy, MD**  
**Duke Maternal Fetal Medicine**

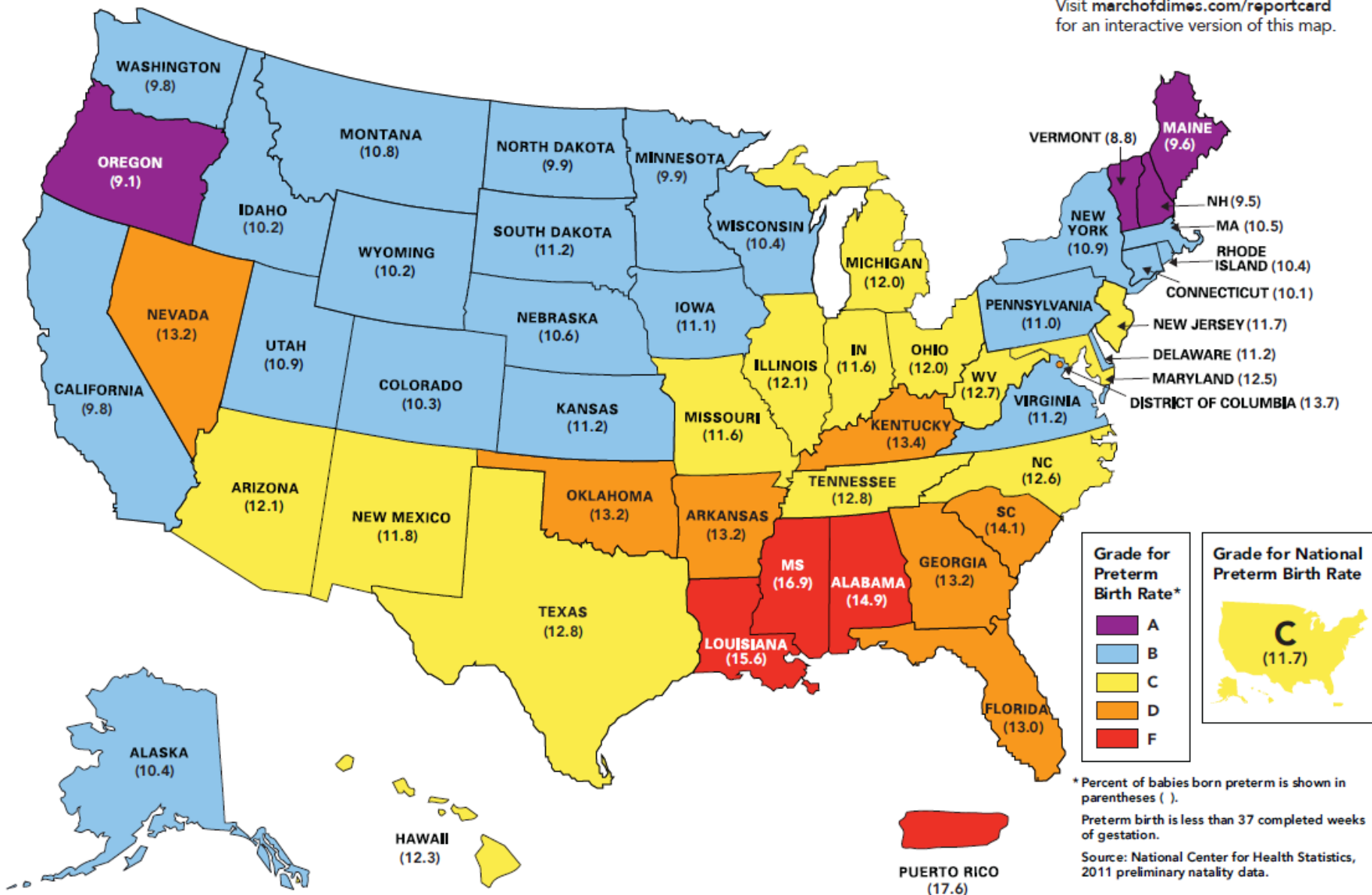
# Preterm Birth: A Global Issue



Estimated preterm birth rates by country for the year 2010

# March of Dimes 2012 Premature Birth Report Card

Visit [marchofdimes.com/reportcard](http://marchofdimes.com/reportcard) for an interactive version of this map.



**Grade for Preterm Birth Rate\***

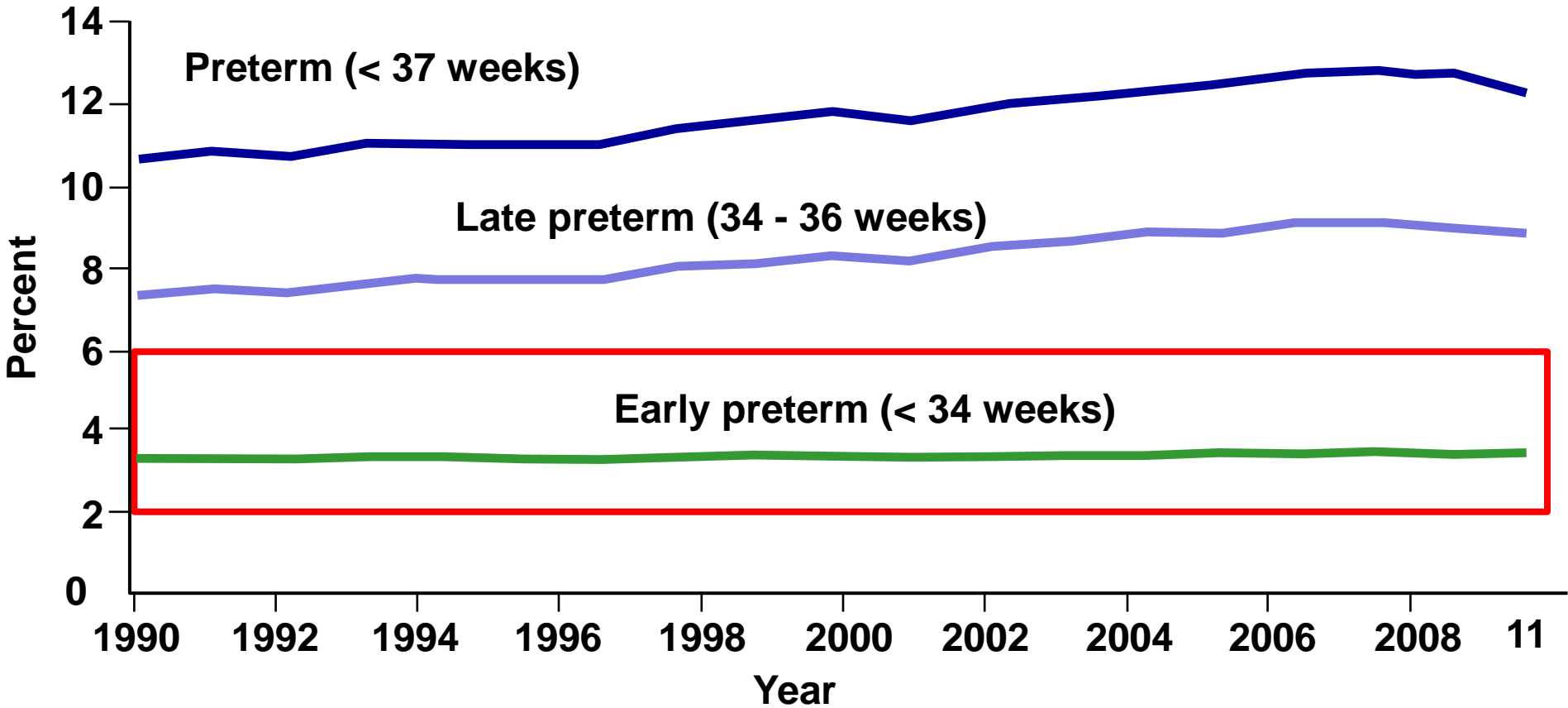
- A
- B
- C
- D
- F

**Grade for National Preterm Birth Rate**

C  
(11.7)

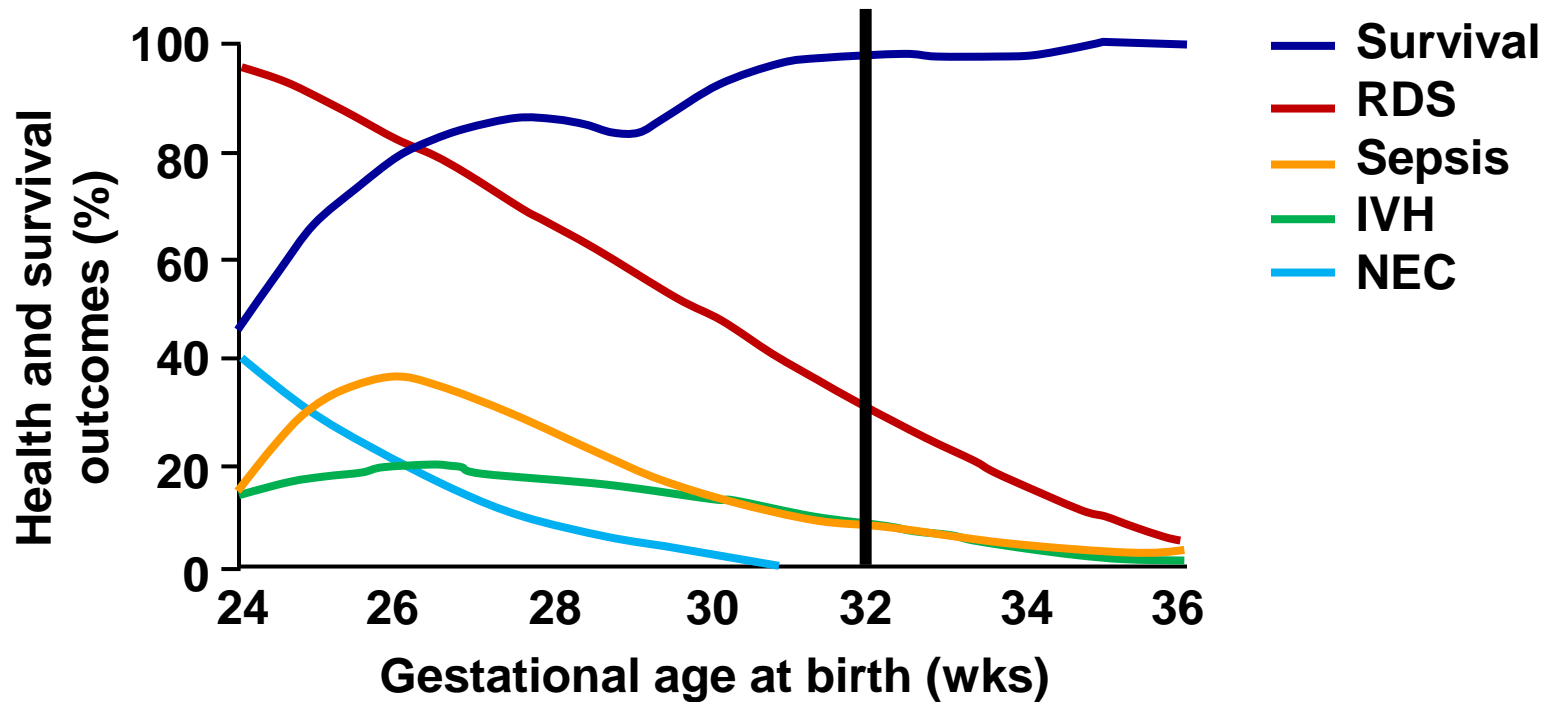
\* Percent of babies born preterm is shown in parentheses ( ).  
 Preterm birth is less than 37 completed weeks of gestation.  
 Source: National Center for Health Statistics, 2011 preliminary natality data.  
 Report card grades calculated by March of Dimes Perinatal Data Center, November 2012.  
 See Technical Notes for more information.

# Preterm Birth: Trends in in the US





# Preterm Birth: Short-term Morbidity & Mortality by Gestational Age



# Preterm birth: Long-term Effects



- Childhood sequelae
  - Chronic lung disease
  - Visual and hearing impairments
  - Neurodevelopmental disabilities
- Adolescent & adult sequelae
  - Increased mortality risk
  - Reduced reproductive capacity/potential
  - Increased risk for psychiatric conditions

# Preterm Birth is an unusual . . .



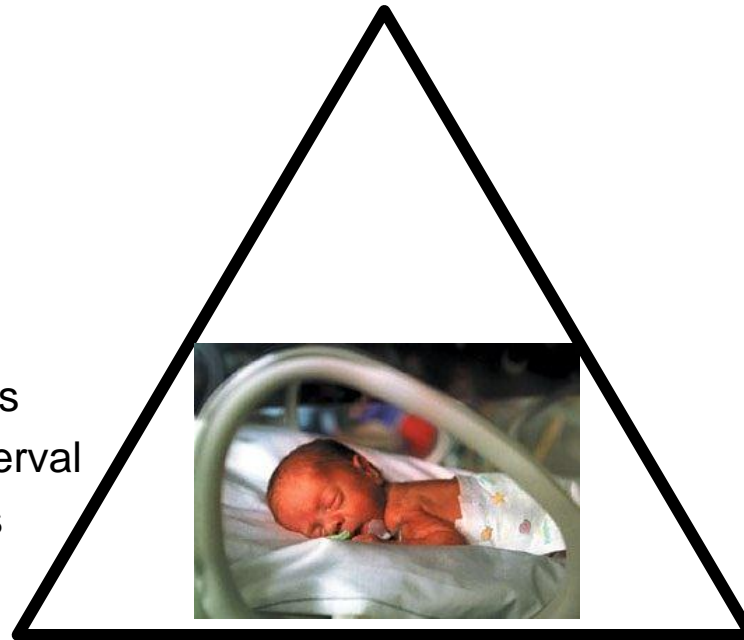
- Disease?
- Syndrome?
- Health Outcome?
- Condition defined by time rather than a distinct clinical phenotype

# Risk factors for Preterm Birth



## Lifestyle-Societal factors

Inadequate prenatal care  
Tobacco, alcohol, illicit substances  
Domestic violence  
Poor social support  
Psychosocial stress  
Excessive work hours  
Low socioeconomic status  
Short inter-pregnancy interval  
Environmental exposures



## Medical risk factors:

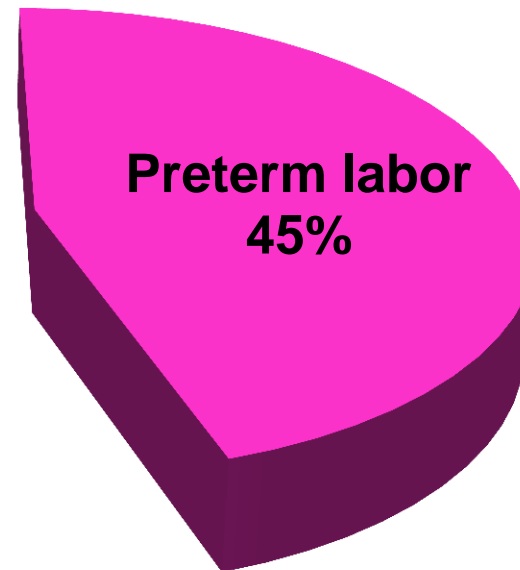
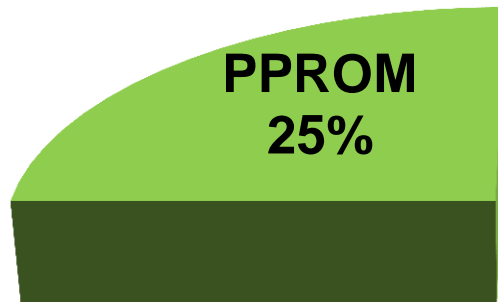
Hypertension  
Diabetes  
Clotting disorders  
Extremes of maternal weight  
Genitourinary Infections  
Fetal congenital anomalies  
Vaginal bleeding  
Prior preterm birth/poor outcome  
Multiple gestation  
Uterine/cervical anomalies  
Decreased cervical length

## Host factors

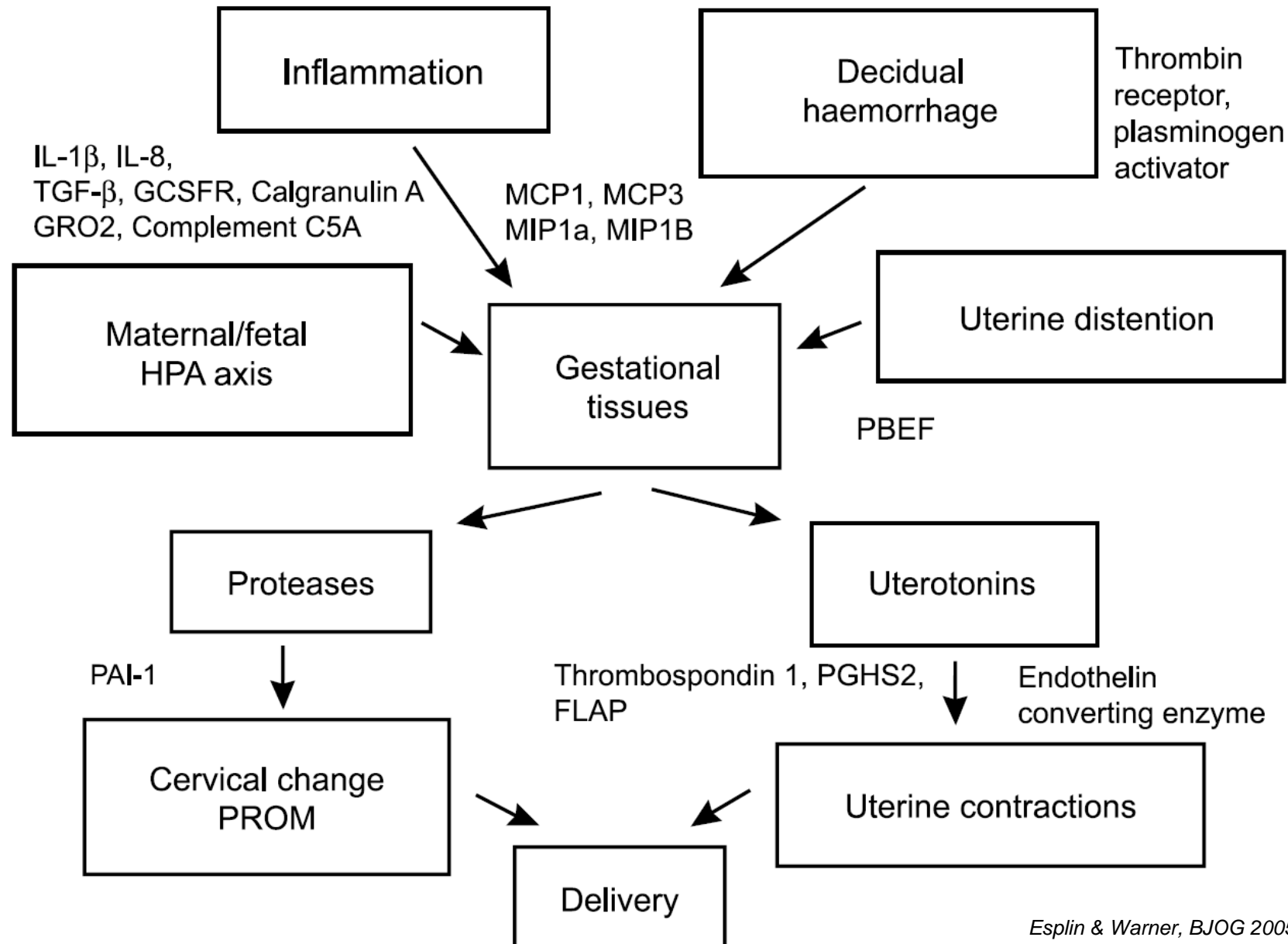
Extremes of maternal age  
Minority race  
Hereditary trait



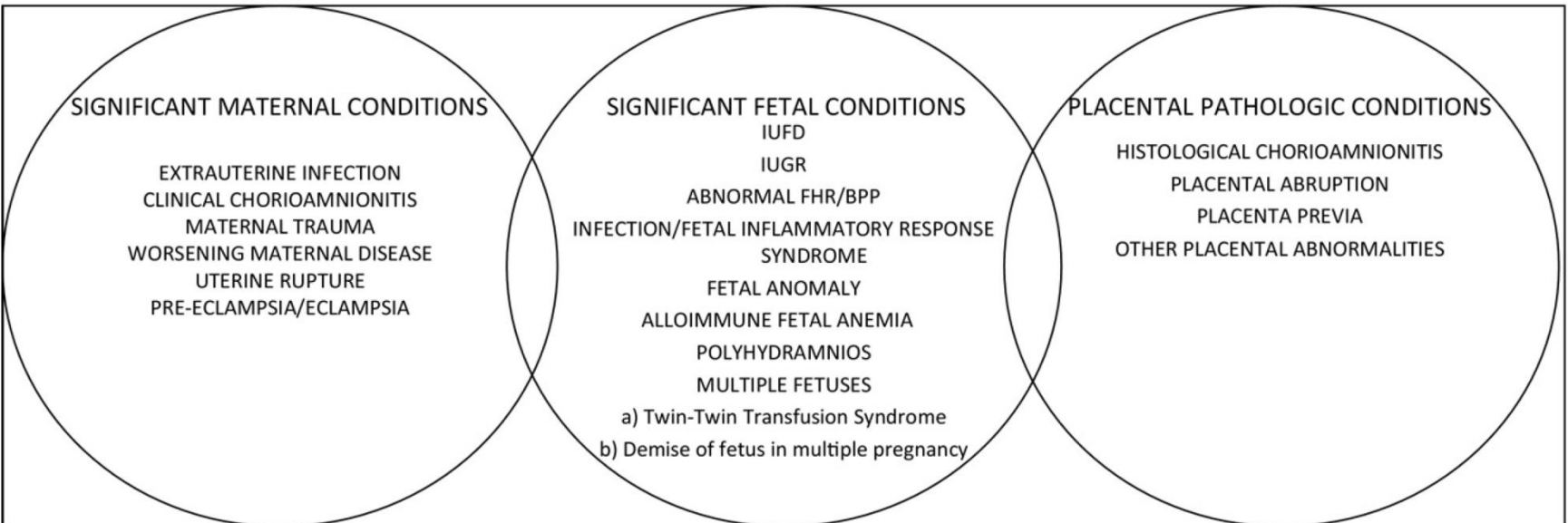
# Preterm Birth Phenotype



# Multifactorial Etiology of Preterm Birth



# Phenotypic components of preterm birth



## SIGNS OF INITIATION OF PARTURITION

NO EVIDENCE OF INITIATION PARTURITION

EVIDENCE OF INITIATION OF PARTURITION

- CERVICAL SHORTENING
- PPROM
- REGULAR CONTRACTIONS
- CERVICAL DILATATION
- BLEEDING
- UNKNOWN INITIATION

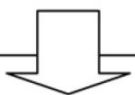
## PATHWAY TO DELIVERY

CAREGIVER INITIATED

SPONTANEOUS

- CLINICALLY MANDATED
- CLINICALLY DISCRETIONARY
- IATROGENIC OR NO DISCERNABLE REASON
- PREGNANCY TERMINATION
- NO DOCUMENTED CLINICAL INDICATION

- REGULAR CONTRACTIONS
- AUGMENTED



Preterm Birth

# Interventions to Reduce Preterm Birth



- Primary – directed to all women
- Secondary – aimed at eliminating or reducing existing risk
- Tertiary – aimed at improving outcomes in preterm infants



# Tertiary Interventions for women with immediate risk of preterm birth

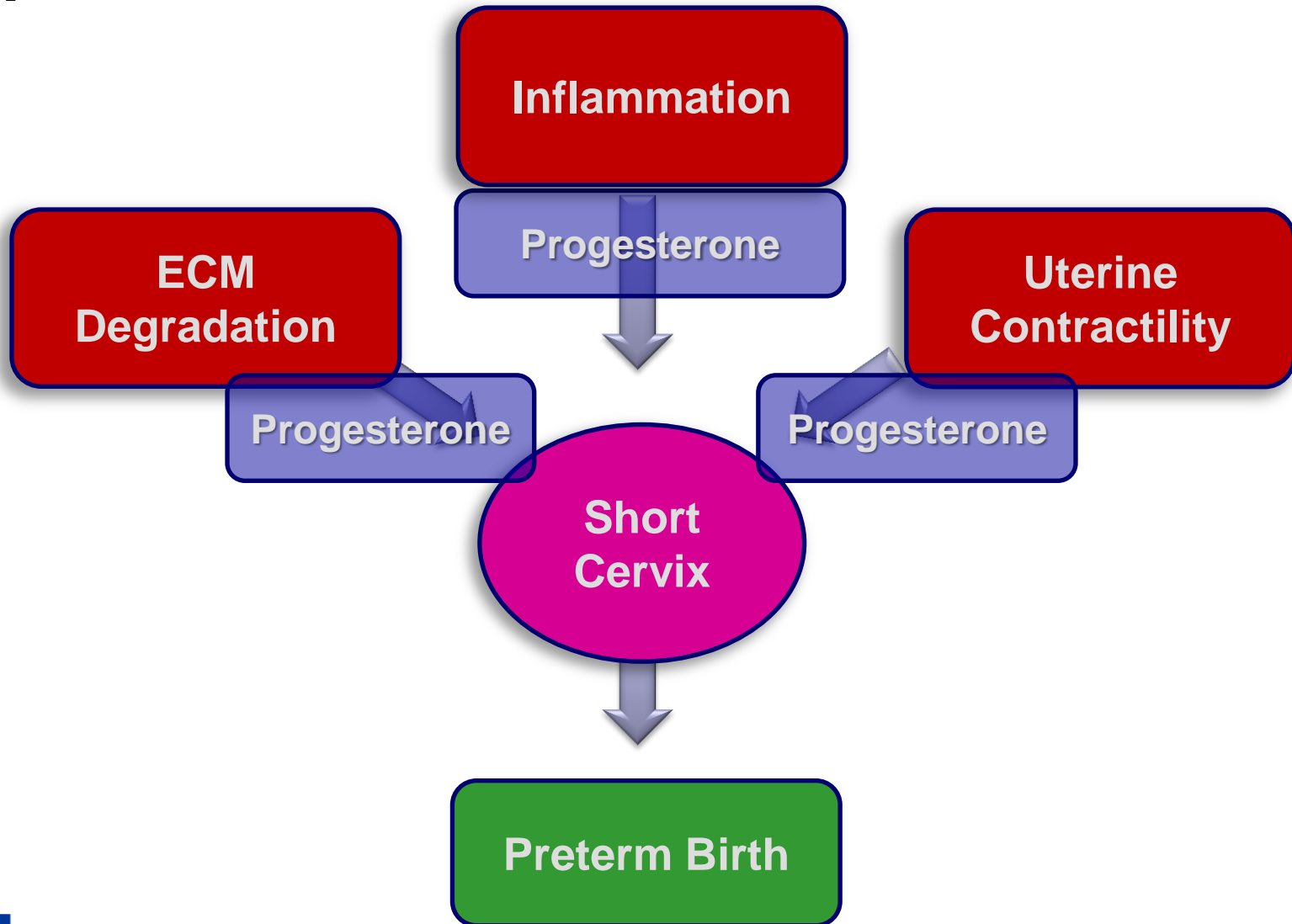
- Regionalized care
- Antenatal corticosteroids
- Tocolytic agents
- Antibiotics
  - PPROM latency
  - GBS prophylaxis
- Magnesium sulfate for CP prophylaxis
- While these measures have reduced perinatal morbidity and mortality, they have had no significant impact on preterm birth incidence

# Secondary prevention for women at risk for preterm birth



- Prevention of indicated preterm birth
  - Low dose aspirin, calcium supplementation
- Modified maternal activity
- Nutritional supplementation
- Improved prenatal care
- Antibiotics
- Cervical cerclage
- Cervico-Vaginal Pessary
- Progesterone

# Secondary prevention for women at risk for preterm birth



# Progesterone use in singleton gestation with history of spontaneous PTB



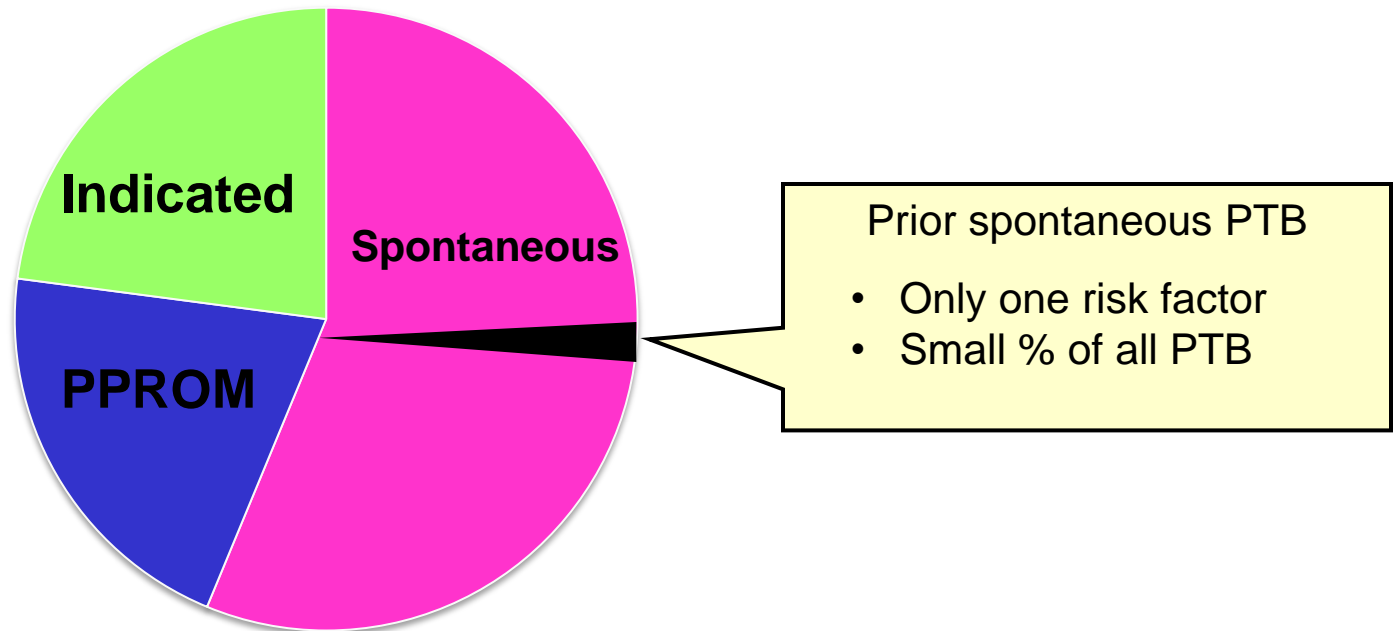
Author	N	Primary Outcome	Intervention	Delay in Delivery	Improved Infant outcome
Meis	463	PTB < 37wks	17-OHP from 16 - 36 wks	Yes	Yes
Fonseca	142	PTB < 37wks	Vaginal progesterone 24 - 34 wks	Yes	Unclear
O'Brien	659	PTB < 32wks	Vaginal progesterone 18 – 37 wks	No	No



# Effectiveness of Progesterone in women with prior sPTB



- 5-6 women need to be treated to prevent 1 birth <37 weeks
- 12 women need to be treated to prevent 1 birth <32 weeks



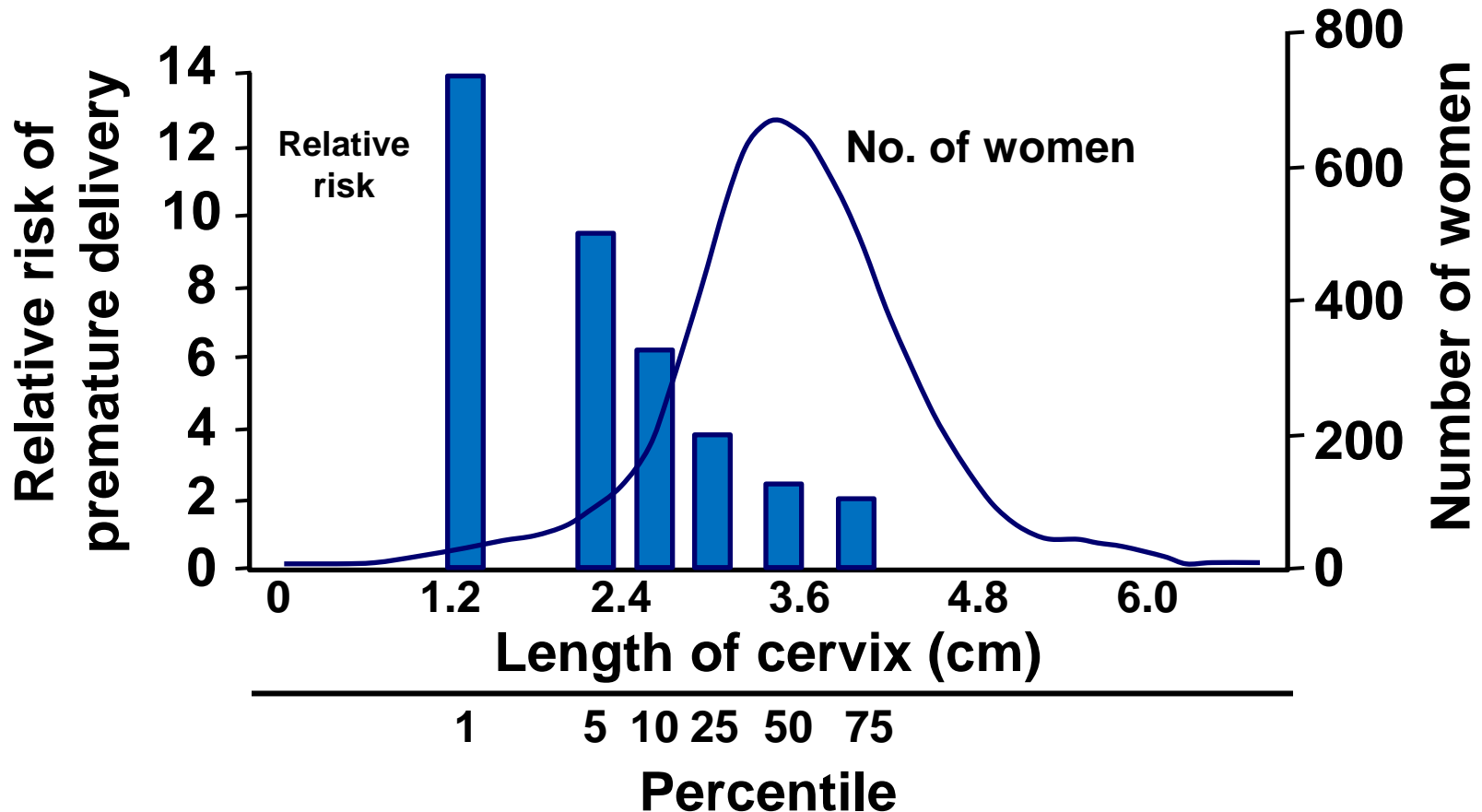
# Primary prevention during pregnancy



- Primary - directed to all women
- Nutritional supplementation
- Smoking cessation
- Periodontal care
- Screening-treatment
  - Benefit in cancer and cardiovascular disease
  - Involves decades of effort through education and public policy built on sound science
  - Cervical length
  - Maternal serum proteomic profiling



# Relative Risk of sPTB < 35 wks by cervical length at 24 wks



# Progesterone for Short cervix



Author	N	Primary Outcome	Intervention	Delay in Delivery	Improved Infant outcome
Fonseca	250 CL 15mm	PTB < 34wks	Vaginal progesterone 24 – 34 wks	Yes	+/-
Hassan	458 CL 10-20mm	PTB < 33 wks	Vaginal progesterone 20 – 36 wks	Yes	Yes
Grobman	657 CL 30mm	PTB < 37wks	17-OHP 16 - 36 wks	No	No

# Maternal Serum Proteomics



- Secondary analysis of Preterm Prediction Study for validation of biomarker + novel proteomics for sPTB prediction
- Samples selected from 160 asymptomatic participants
  - 24 and 28 weeks – 40 spontaneous PTB, 40 term births
- 3 peptides from inter-alpha-trypsin inhibitor heavy chain (ITIH)-4 protein were significantly reduced in women having subsequent sPTB
- Predictive value at 28 weeks

Measure	Sensitivity	Specificity
Single ITIH-4 peptide	65%	82.5%
ITIH-4 peptides + 6 biomarkers	86.5%	80.6%
Cervix length $\leq$ 25mm	49.5%	86.8%

# Proteomic Assessment of Preterm Birth (PAPR)



- Sera Prognostics, Inc.
- Observational cohort study n = 4000
- Proteomic profiles comparison of women who deliver preterm and term
- Inclusion Criteria – 18+ years of age, singleton gestation, no known fetal congenital anomalies
- Estimated Study Completion Date: April 2013

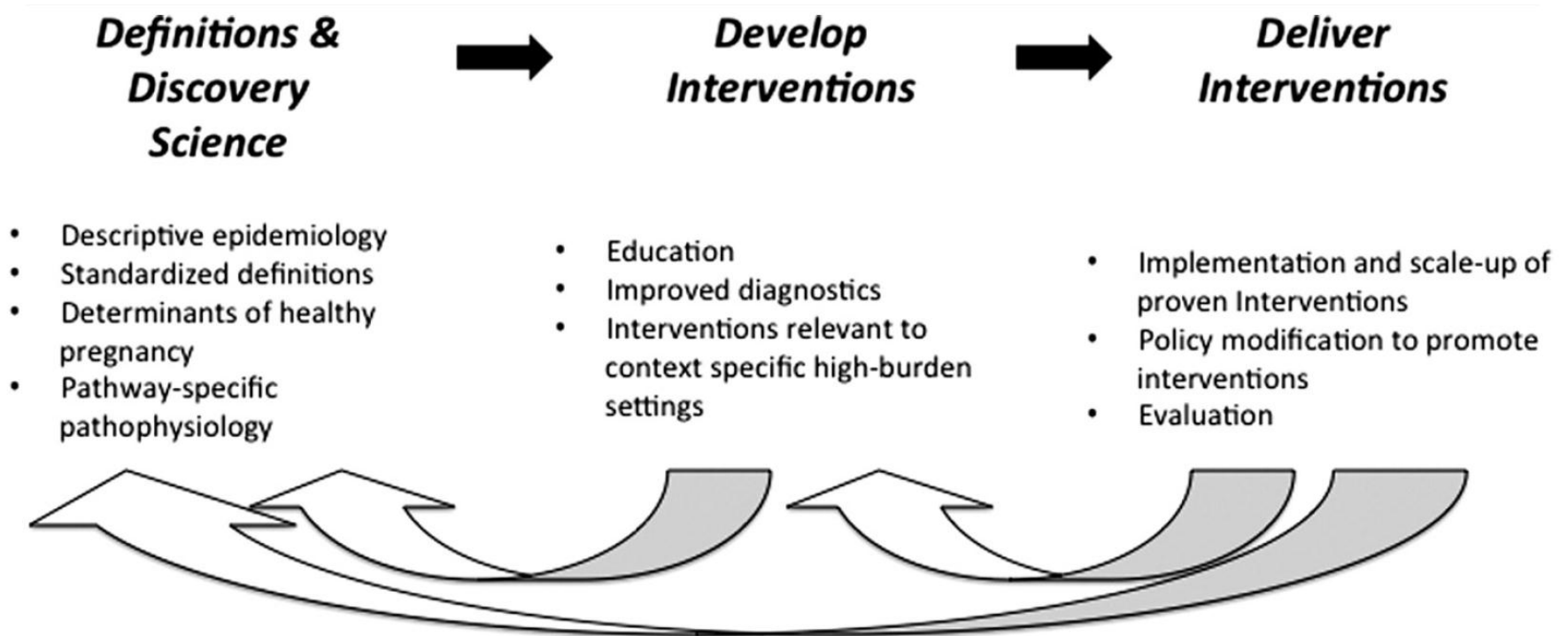
# Summary



- Preterm birth is complex, multifactorial, and affected by host, societal, and environmental factors
- Despite intensive research efforts, our increased knowledge of the disease process and etiology has not translated into effective strategies for disease reduction
- Significant impact on prematurity prevention can only occur with advances in primary and secondary interventions



# Integrated approach to research & implementation to promote healthy pregnancy & reduce PTB and stillbirth



Improved understanding of determinants of healthy pregnancy and of risk factors and pathways for poor pregnancy outcomes are prerequisites to developing and implementing effective population-specific interventions and to promote rational health care policies. In turn, evaluation of effective interventions will further facilitate research into pathways, mechanisms, and identification of unique populations at risk.

Gravett. *Strategic investments to reduce preterm birth. Am J Obstet Gynecol* 2012.



