Prevention of Preterm Birth

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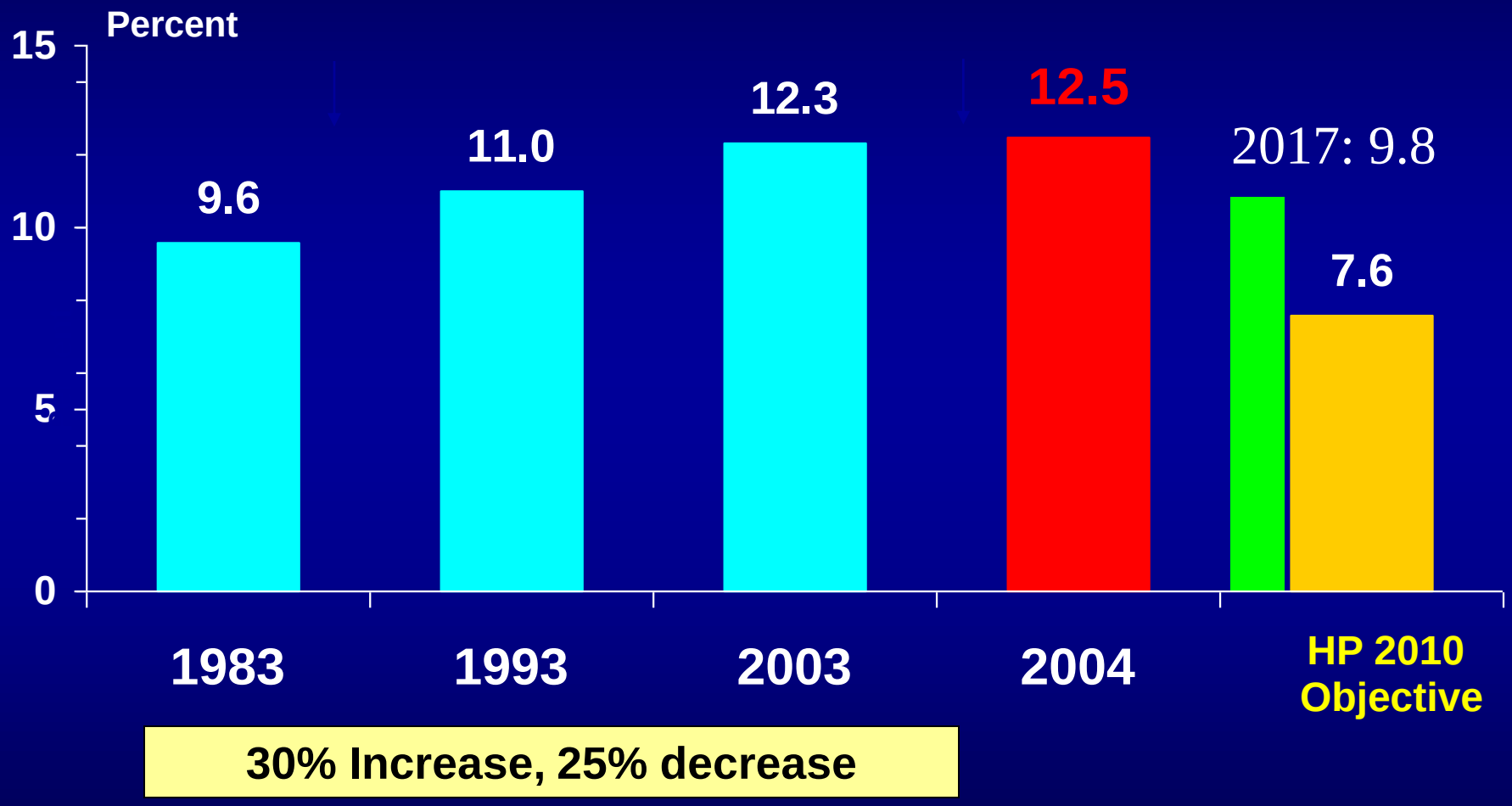
Preterm birth is one of the greatest frustrations of modern obstetrics, in particular and modern medicine, in general

While advances in neonatal medicine have led to progressively better survival rates for preterm infants, there has only been a modest improvement in the proportion of surviving infants without neurological impairment, and no change in the proportion with severe disability.

If preterm birth can be stopped, it was not preterm birth!

However, some improvement has been made in the US:



30% Increase, 25% decrease

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

March of Dimes
Saving babies, together

Objectives

- Discuss risk factors and clinical approaches to preterm birth
- Outline genetics and genomics principles
- Introduce preterm birth as a common complex disorder
- Propose a framework for a genomic approach to research in preterm birth

Major Categories of Risk for Preterm Birth

Extremes of maternal age

Unintended pregnancy

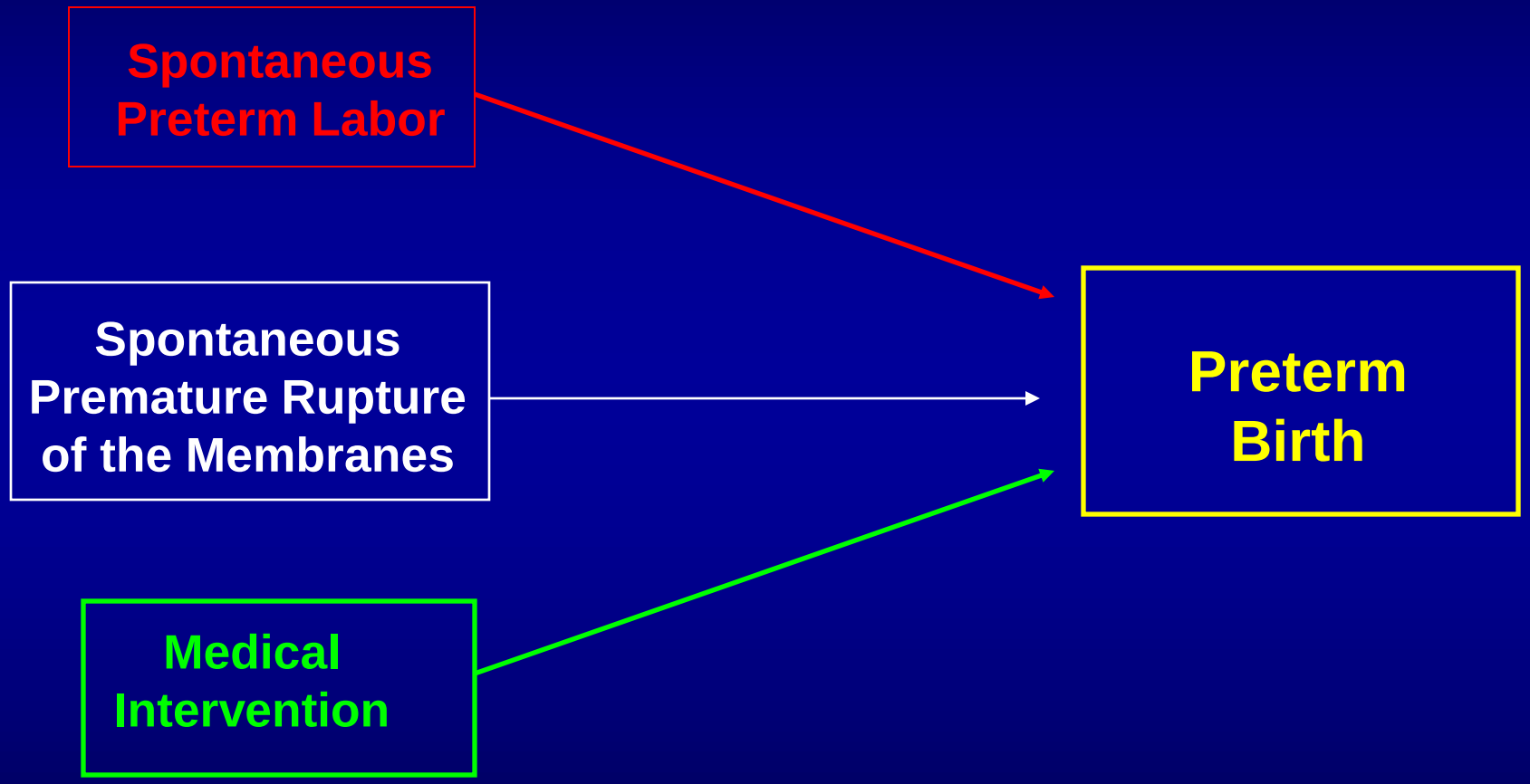
34, 35, 36 weeks

Maternal race

Multiple gestation

Cesarean section

Types of Preterm Birth

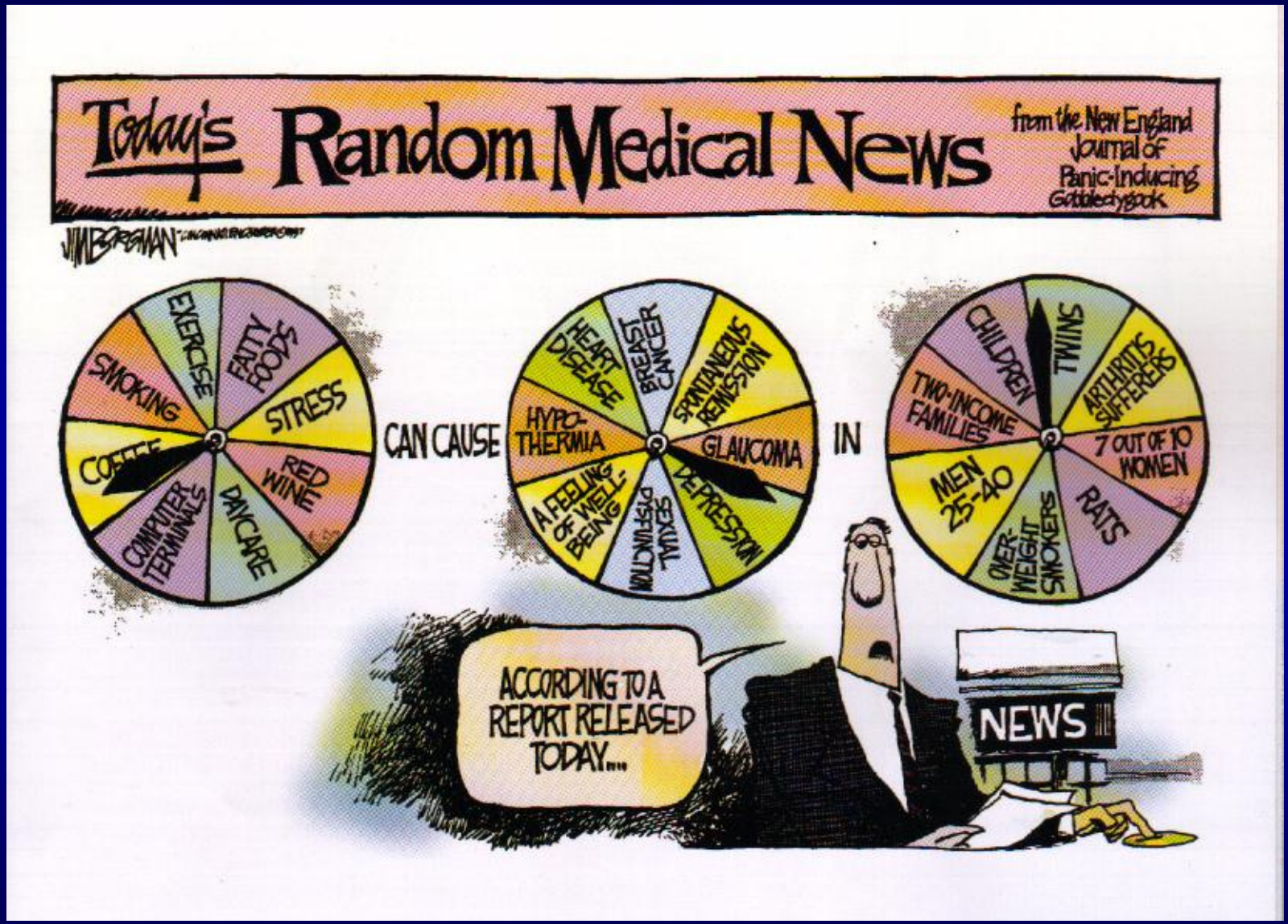


While this suggests distinct pathways, many of the risk factors for all 3 are similar.

Major Categories of Risk for Preterm Labor/Delivery

General maternal issues:

- Medical and Obstetric History
- Behaviors
- Genetics
- Environmental



American Journal of Public Health, March 2004

Risk Factors for Preterm Labor/Delivery

- **The best predictor of having a preterm birth is multifetal gestation or history of preterm labor/delivery**
- ***Other risk factors:***

–multifetal pregnancy
–maternal age (<17 and >35 years)
–black race
–low SES
–unmarried
–previous fetal or neonatal death
–3+ spontaneous losses
–uterine abnormalities
–incompetent cervix
–genetic predisposition

–low pre-pregnant weight
–obesity
–infections
–bleeding
–anemia
–major stress
–lack of social supports
–tobacco use
–illicit drug use
–alcohol abuse
–folic acid deficiency

The Risk of Preterm Birth Across Generations

Objective: To examine the risk of preterm birth for mothers who themselves were born before term.

1405 preterm mothers

2781 term mothers

Table 2. Premature Birth for Preterm Mothers Stratified by Gestational Week at Birth

Gestational age (wk)	No. of offspring of preterm/term mothers	OR	95% CI
<37	773/13,340	1.18	1.02, 1.37
<36	375/5677	1.36	1.13, 1.64
<35	250/3480	1.47	1.17, 1.84
<34	173/2505	1.45	1.10, 1.96
<33	145/2035	1.68	1.25, 2.27
<32	94/1282	2.02	1.30, 2.94
<31	79/996	2.44	1.61, 3.78
<30	45/592	2.38	1.37, 4.16

OR = odds ratio; CI = confidence interval.

Conclusions: An increased risk of preterm delivery exists for women who themselves were born before 37 weeks gestation. This risk is inversely correlated with the maternal gestational age at birth and is influenced by maternal age and parity.

Porter et al. Obstetrics & Gynecology. 1997;90:63-67.

Maternal and Paternal Influences on Length of Pregnancy

Methods: 77,452 boys and girls in the Medical Birth Registry of Norway who later became parents themselves. Records were linked between parents and children.

Results: Gestational age of the child at birth increased on average 0.58 days for each additional week in the father's gestational age (0.48-0.67) and 1.22 days for each additional week in the mother's gestational age (1.21-1.32).

Lie et al. Obstet Gynecol 2006;107:880-5.

Complex Disorders

- **Environmental influences**
  - **Smoking**
  - **Infection**
  - **Stress**

Complex Disorders

- Genetic contribution
- Environmental influences
- Gene-environment interactions

Maternal Cigarette Smoking, Metabolic Gene Polymorphism, and Infant Birth Weight

Objective: To investigate whether the association between maternal cigarette smoking and infant birth weight differs by polymorphisms of 2 maternal metabolic genes: CYP1A1 and GSTT1.

741 mothers with singleton livebirths
- 174 ever smokers
- 567 never smokers

207 cases low-birth-weight or preterm

534 controls

Wang et al. JAMA. 2002;287:195-202.

Maternal Cigarette Smoking, Metabolic Gene Polymorphism, and Infant Birth Weight

Smoking	CYP1A1	GSTT1	#	Gestation, Week β (SE)	P value
Never	AA	Present	251	Referent	
Never	AA	Absent	72	0.9 (0.4)	.03
Never	Aa/aa	Present	182	0.2 (0.3)	.46
Never	Aa/aa	Absent	62	0.2 (0.5)	.64
Continuous	AA	Present	58	-0.4 (0.5)	.40
Continuous	AA	Absent	177	0.3 (0.8)	.75
Continuous	Aa/aa	Present	38	-0.01 (0.6)	.99
Continuous	Aa/aa	Absent	11	-5.2 (1.0)	<.001
Test of interaction Crude				-5.5 (1.0)	<.001
Test of interaction Adjusted				-5.4 (1.0)	<.001

Conclusions: Maternal CYP1A1 and GSTT1 genotypes modified the association between maternal cigarette smoking and infant birth weight, suggesting an interaction between metabolic genes and cigarette smoking.

Wang et al. JAMA. 2002;287:195-202.

A polymorphism in the promoter region of TNF and bacterial vaginosis: Preliminary evidence of gene-environment interaction in the etiology of spontaneous preterm birth

Objective: To assess if the presence of symptomatic bacterial vaginosis amplifies the risk of spontaneous preterm birth in those with a “susceptible” TNF genotype (TNF-2).

125 cases: delivered before 37 weeks
as a result of ruptured membranes
or preterm labor

250 controls: delivered after 37 weeks

Macones et al. AJOG. 2004;190:1504-8.

A polymorphism in the promoter region of TNF and bacterial vaginosis: Preliminary evidence of gene-environment interaction in the etiology of spontaneous preterm birth

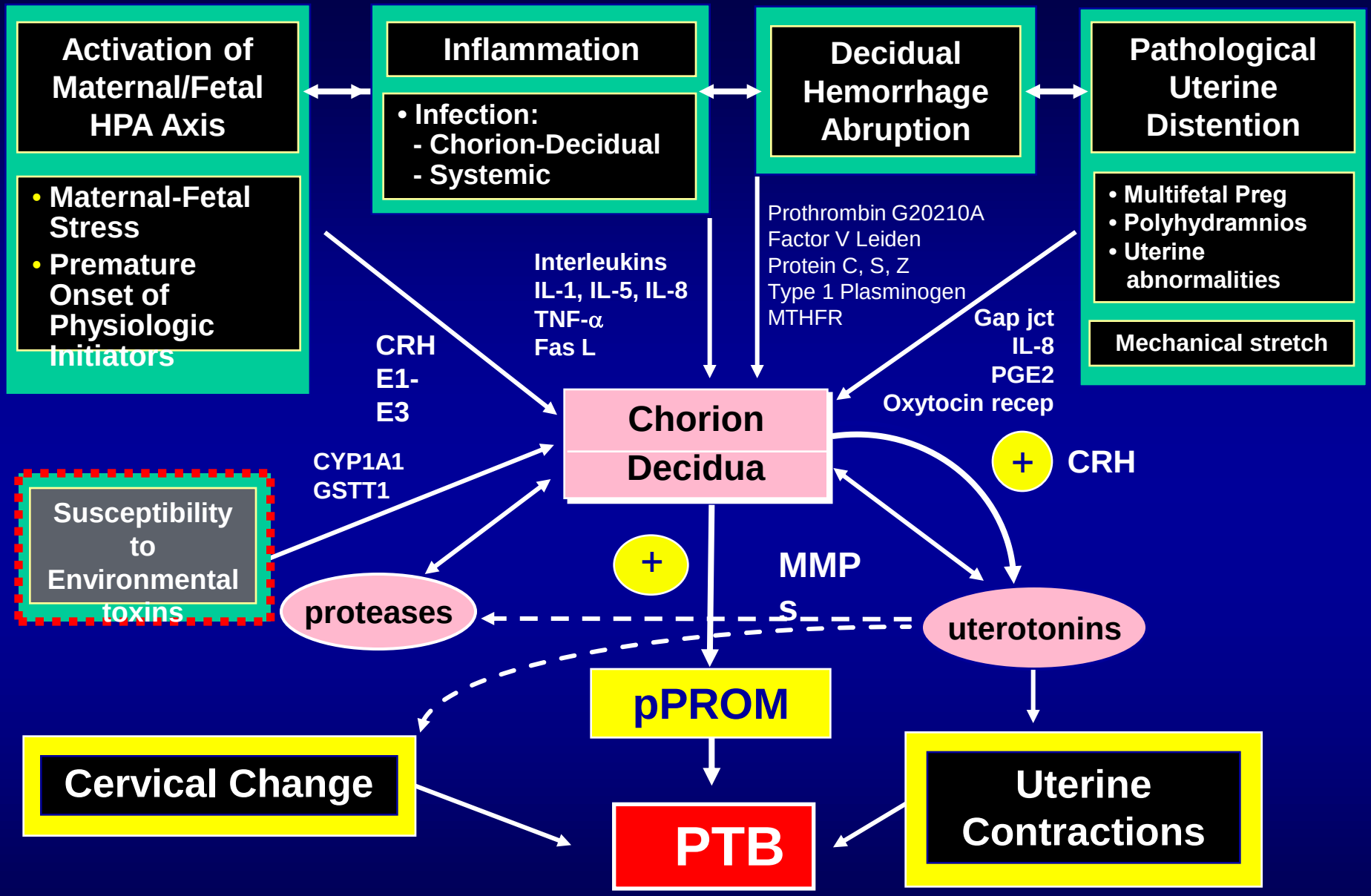
Group	% TNF-2 carriers in cases	%TNF-2 carriers in controls	OR (95% CI)
Overall	45%	23%	2.1 (1.7-4.5)
BV Positive	69%	27%	6.1 (1.9-21.0)
BV Negative	34%	22%	1.7 (1.0-3.1)

Conclusion: This study provides preliminary evidence that an interaction between genetic susceptibilities (TNF-2 carriers) and environmental factors (BV) is associated with an increased risk of spontaneous preterm birth.

Macones et al. AJOG. 2004;190:1504-8.

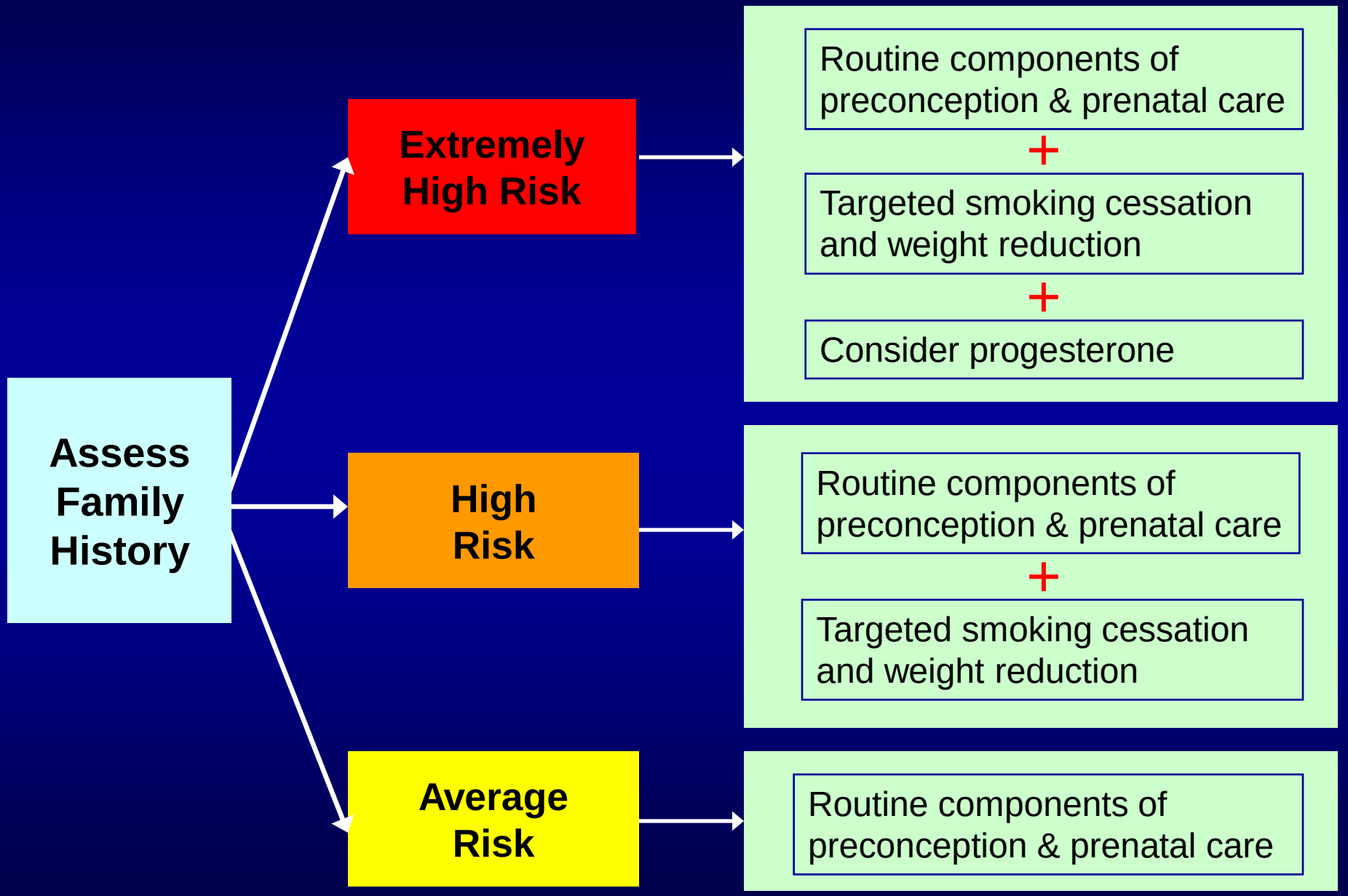
Pathways to Preterm Birth

- **Inflammation / Infection (ascending), 40%**
- **Stress (maternal/fetal), 25%**
- **Bleeding / Clotting Abnormality (thrombophilia, decidual hemorrhage, abruption), 25%**
- **Abnormal Uterine Distension (stretching), 10%**

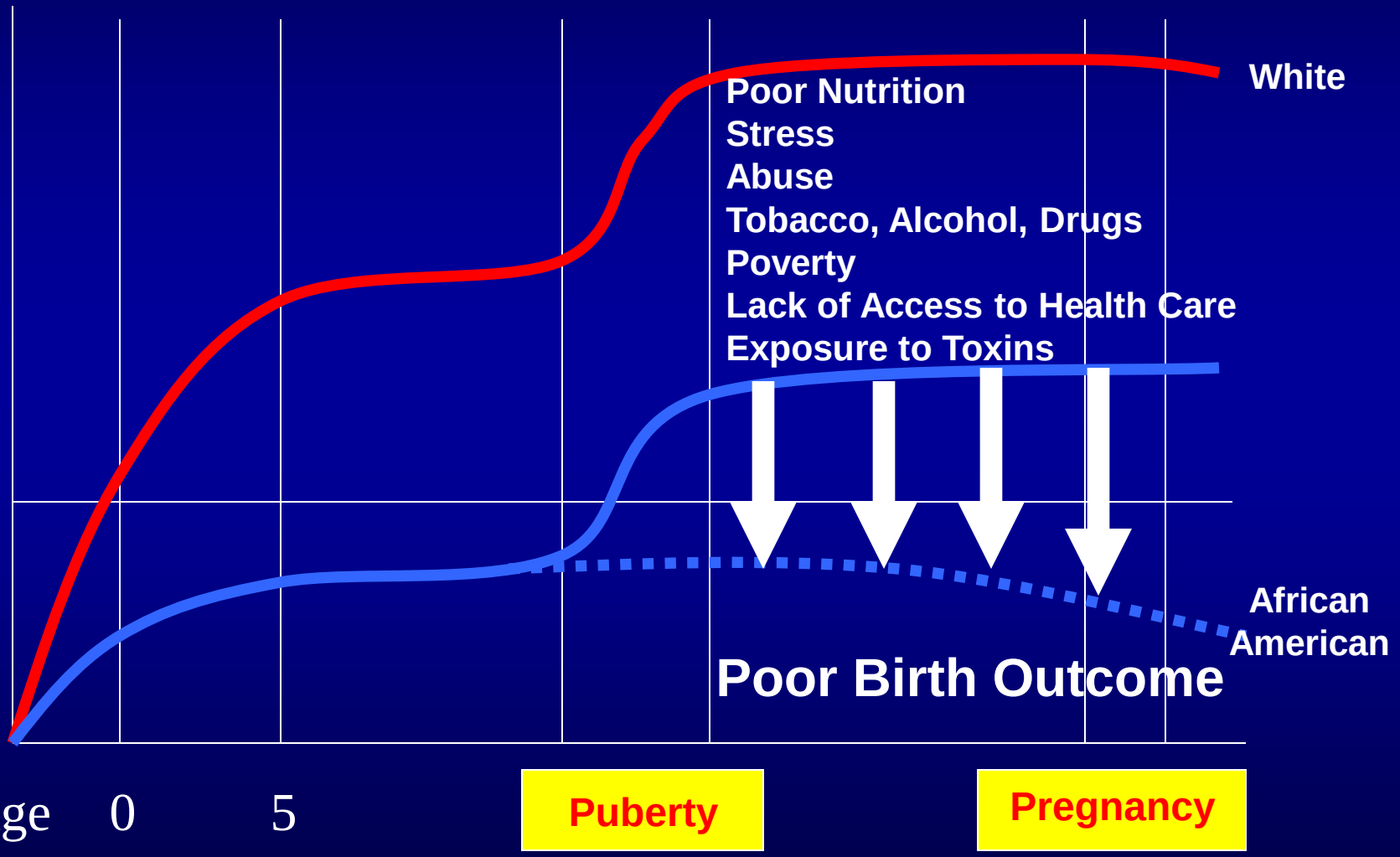


Adapted from: Lockwood CJ, Paediatr Perinat Epidemiol 2001;15:78 and Wang X, et al. Paediatr Perinat Epidemiol 2001; 15: 63

Hypothetical Protocol for Preterm



Life Course Perspective



Genetic and Genomic approaches do not replace but can add to:

- Community based interventions
- Patient / Consumer education
- Provider education
- Equity in health outcomes and health care

How can I help, if I am part of a kangaroo program?

- Identify and refer
- Talk about it
- Increase awareness
- Preconceptional care

The Preconception Care Initiative

A Collaborative Effort of over 35 National Organizations

National Summit on Preconception Care

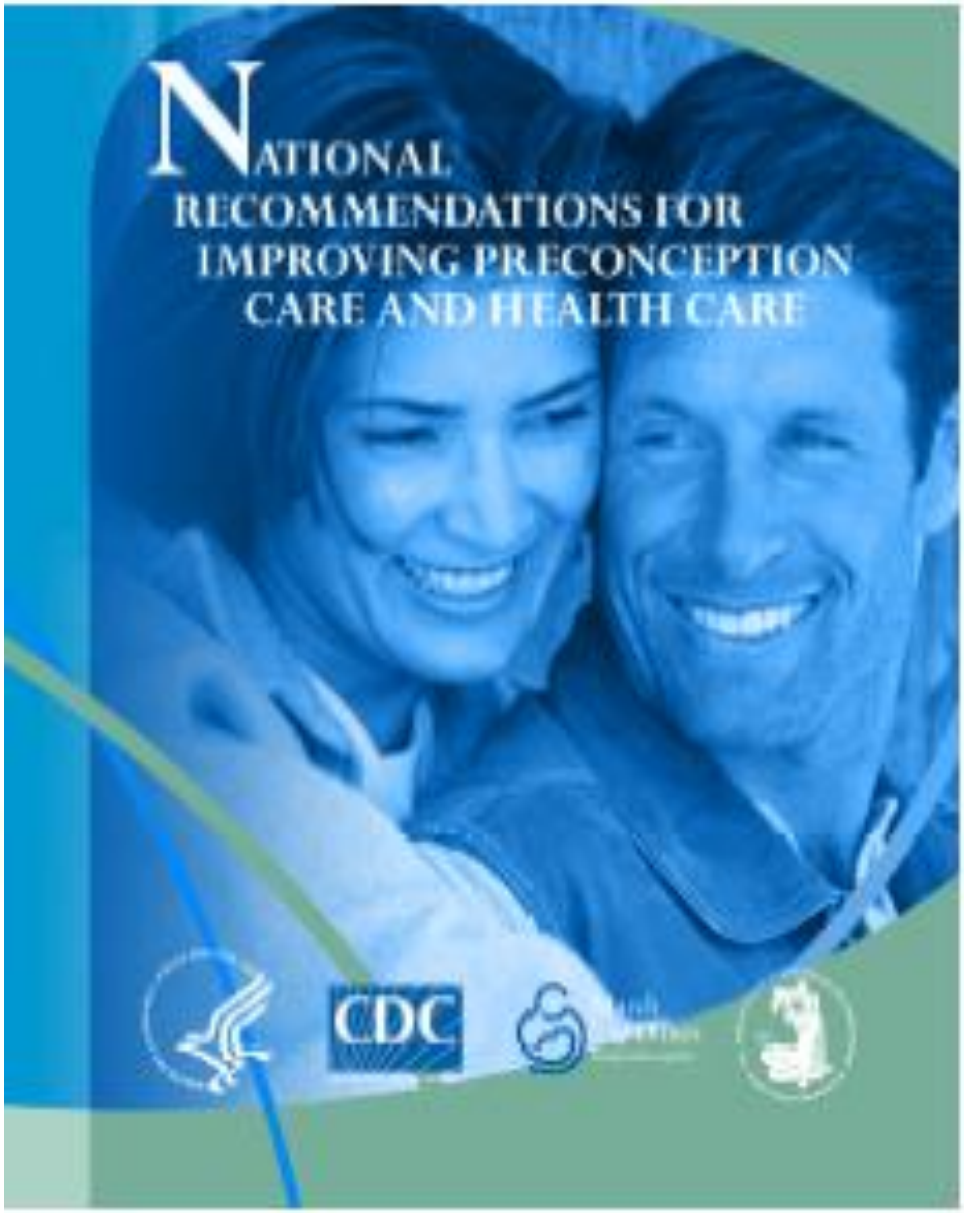
June 21 - 22, 2005

The Atlanta Marriott Century Center
Atlanta, Georgia

CDC

March of Dimes

National Recommendations for Improving Preconception Care and Health Care



CDC

ACOG

Committee on Gynecologic Practice

Committee Opinion

Number 313, September 2005

The Importance of Preconception Care in the Continuum of Women's Health Care

ABSTRACT: The goal of preconception care is to reduce the risk of adverse health effects for the woman, fetus, or neonate by optimizing the woman's health and knowledge before planning and conceiving a pregnancy. Because reproductive capacity spans almost four decades for most women, optimizing women's health before and between pregnancies is an ongoing process that requires access to and the full participation of all segments of the health care system.

This document reflects emerging clinical and scientific advances as of the date issued and is subject to change. The information should not be construed as dictating an exclusive course of treatment or procedure to be followed.

The Committee wishes to thank the ACOG Preconception Care Work Group co-chairs, Michele G. Curtis, MD, and Paula J. Adams Hillard, MD, and members, Hani K. Atrash, MD, MPH; Alfred Brann Jr, MD; Siobhan M. Dolan, MD, MPH; Ann Lang Dunlop, MD; Ann Weathersby, CNM, MSN; and Gerald Zelinger, MD, for their assistance in the development of this opinion.

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–illicit drug use
–alcohol abuse
–folic acid deficiency

Preconception Care Today

CDC Centers for Disease Control and Prevention
CDC 24/7: Saving Lives, Protecting People™

SEARCH

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- Women
- Men
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Before Pregnancy Home

Planning for Pregnancy

Language: English (US)

If you are trying to have a baby or are just thinking about it, it is not too early to start getting ready for pregnancy. Preconception health and health care focus on things you can do before and between pregnancies to increase the chances of having a healthy baby. For some women, getting their body ready for pregnancy takes a few months. For other women, it might take longer. Whether this is your first, second, or sixth baby, the following are important steps to help you get ready for the healthiest pregnancy possible.

1. Make a Plan and Take Action

Whether or not you've written them down, you've probably thought about your goals for having or not having children, and how to achieve those goals. For example, when you didn't want to have a baby, you used effective birth control methods to achieve your goals. Now that you're thinking about getting pregnant, it's really important to take steps to

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Recommendations for Preconception Counseling and Care

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