

SCIENCE OF PRETERM BIRTH

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SynAptiv and the Colorado Hospital
Association

Safe Deliveries Project Partnership

- Colorado Hospital Association
- Anthem Blue Cross and Blue Shield Foundation
- March of Dimes Colorado/Wyoming Chapter
- Colorado Perinatal Care Quality Collaborative

Conflict of Interest Disclosure Statement

I have no financial interest or other relationships with the industry relative to the topics being discussed.



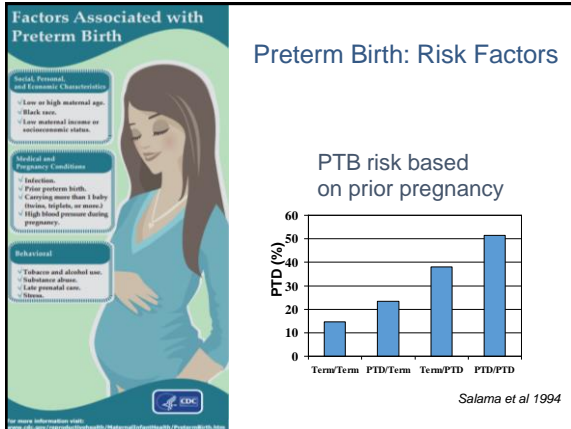
Overview of Today's Topics



- Causes and predictors of preterm birth
- Prevention of preterm birth
- Future NICHD research projects to inform preterm birth



Causes and Predictors of Preterm Birth

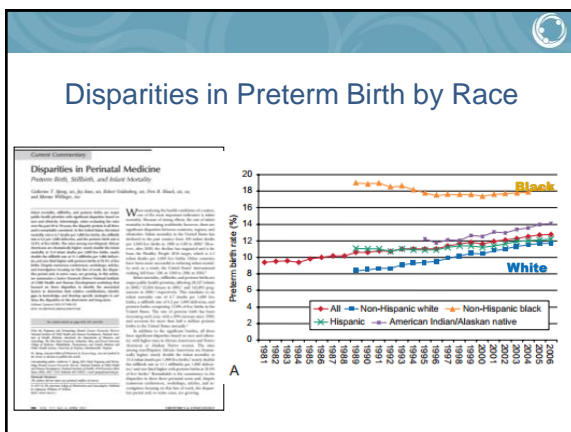


Recurrence Risk

- Preterm delivery is a significant risk factor for subsequent preterm birth
 - Recurrence in 15-20% of white women and 26% black women*
- Early preterm delivery increases the risk
 - Recurrence in ~30% of white women and 37% of black women*

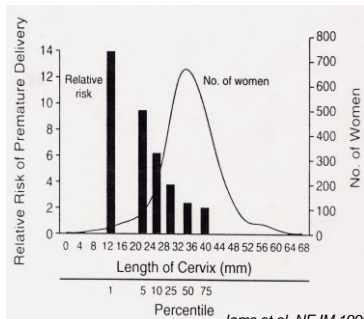
*Adams et al JAMA 2000 283:1591-1596
Ananth et al AJOG 2006 195:643-650
Bloom et al O&G 2001 98:379-85
Cnattingius et al NEJM 1999;341:943-8

Carr-Hill et al BJOG 1985; 92:921-928
Clark et al AJOG SMFM#542 2003
Kristensen et al O&G 1995; 86:800-4
Mercer et al AJOG 1999; 181:1216-21



Cervical Length Predicts Preterm Birth Risk

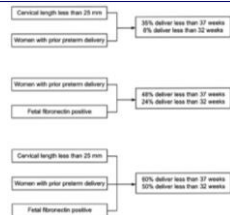
Relative risk of sPTD <35 wks by % of cervical length at 24 wks



Biomarkers to Predict Preterm Delivery

- Serum biomarkers
- Fetal fibronectin
- Clinical factors
- Proteomic studies
 - Serum serpin B7
- Genomic studies

Combination of markers modeled to predict risk of PTD



Spong, *Obstet Gynecol* 2007:110
Parry et al *Am J Obstet Gynecol* 2014
Monangi et al *Sem Perinatol* 2015

Birth Spacing

- <12 months between pregnancies
 - Increased risk of preterm birth
 - Placental abruption
 - Placenta previa (in women who had a first by CD)
- < 18 months
 - Increased risk of uterine rupture in women who attempt vaginal birth after cesarean (VBAC)
 - Low birth weight
 - Small size for gestational age
 - Preterm birth

DeFranco et al, *BJOG* 2014



Prevention of Preterm Birth

PTB
Prevention

We've come a long way baby!





Progesterone to Prevent Preterm Birth

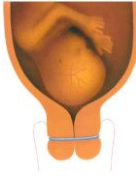
- Weekly progesterone injections helped prevent recurrent preterm birth in specific women (those with a prior spontaneous birth at <37 weeks) and improved the neonatal outcome for pregnancies at risk.



Meis et al, *NEJM* 2003

Cerclage to Prevent Preterm Birth

- Cerclage reduced PTB in women with prior preterm birth and short cervical length <15mm
- Periviable birth and perinatal mortality were reduced with short cervical length <25mm



- Singleton
- Prior sPTB < 34 weeks
- CL < 25 mm prior to 24 weeks



Owen et al, AJOG 2009; 201375:e1-8

Pessary to Prevent Preterm Birth

- Arabin pessary reduced PTB in an open label study of women with short cervix <25mm
- Pessary did not prevent preterm birth in twins



Goya et al, *Lancet* 2012 1800-6
Liem et al, *Lancet* 2013

Low-Dose Aspirin

Annals of Internal Medicine



LOW-DOSE ASPIRIN USE FOR THE PREVENTION OF MORBIDITY AND MORTALITY FROM PREECLAMPSIA CLINICAL SUMMARY OF U.S. PREVENTIVE SERVICES TASK FORCE RECOMMENDATION

Population	Asymptomatic pregnant women who are at high risk for preeclampsia
Recommendation	Prescribe low-dose (81 mg/d) aspirin after 12 weeks of gestation. Grade: B
Risk Assessment	Pregnant women are at high risk for preeclampsia if they have 1 or more of the following risk factors: <ul style="list-style-type: none"> • History of preeclampsia, especially when accompanied by an adverse outcome • Multifetal gestation • Chronic hypertension • Type 1 or 2 diabetes • Renal disease • Autoimmune disease (i.e., systemic lupus erythematosus, the antiphospholipid syndrome)
Preventive Medication	Low-dose aspirin (60 to 150 mg/d) initiated between 12 and 28 weeks of gestation reduces the occurrence of preeclampsia, preterm birth, and IUGR in women at increased risk for preeclampsia. The harms of low-dose aspirin in pregnancy are considered to be no greater than small.
Balance of Benefits and Harms	There is a substantial net benefit of daily low-dose aspirin to reduce the risk for preeclampsia, preterm birth, and IUGR in women at high risk for preeclampsia.

Reducing Elective Deliveries Prevents Preterm Birth



COMMITTEE OPINION

Number 561 • April 2013

The American College of Obstetricians and Gynecologists Committee on Obstetric Practice
The Society for Maternal-Fetal Medicine

The opinions expressed herein are those of the committee members and do not necessarily represent the opinions of the American College of Obstetricians and Gynecologists or the Society for Maternal-Fetal Medicine.

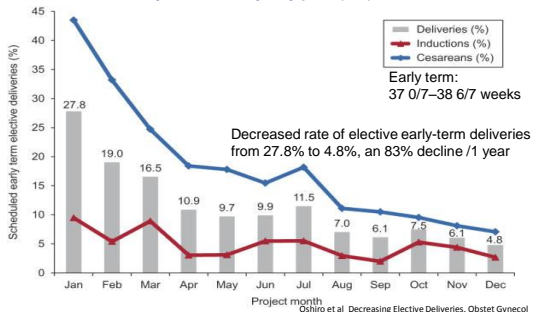
Nonmedically Indicated Early-Term Deliveries

ABSTRACT: For certain medical conditions, available data and expert opinion support optimal timing of delivery in the third trimester or early-term period for improved neonatal and infant outcomes. However, for nonmedically indicated early-term deliveries such an improvement has not been demonstrated. Morbidity and mortality rates are elevated for these deliveries compared to those between 39 and 40 weeks.

Morbidity and mortality rates > early-term period compared to those between 39 and 40 weeks

Nonmedically indicated early-term deliveries. CO No. 561. Obstet Gynecol 2013;121:911–5

Scheduled Elective Singleton Early-term Deliveries by Delivery Type (%)



Wolters Kluwer Health

OvidSP

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National Child & Maternal Health Education Program (NCMHEP)

- Coalition of the nation's most prominent health care provider associations, federal agencies, nonprofit maternal and child health organizations, and other partners to review, translate, and disseminate new research in the field of maternal and child health
- First topic: late preterm birth and reducing elective deliveries before 39 weeks of pregnancy



Is It Worth It? Initiative to Reduce Elective Deliveries Before 39 Weeks

- Created 30-second, 60-second, and 4-minute versions of educational video for pregnant women and their families
- Continuing education course: Raising Awareness: Late Preterm Birth and Non-Medically Indicated Inductions Prior to 39 Weeks for physicians and nurses



Some studies have shown that common medical practices do not benefit patients after all...



Antibiotic Use During Pregnancy

- In two trials, researchers found that antibiotic treatment for pregnant women with asymptomatic bacterial vaginosis did not reduce preterm delivery or adverse perinatal outcomes.
- Moreover, treatment of asymptomatic trichomonas vaginalis actually increased the risk of preterm delivery.
- These results have helped decrease the indiscriminate use of antibiotics in pregnancy.

BV: Carey et al, *N Engl J Med* 2000
TV: Klebanoff et al, *N Engl J Med* 2001

Home Uterine Activity Monitoring Not Beneficial in Predicting PTD

- Monitoring uterine contractions at home does not predict who will deliver preterm



ACOG PRACTICE BULLETIN
Clinical Management Guidelines for Obstetrician-Gynecologists
Number 31, October 2001
(Replaces Technical Bulletin Number 286, June 1995, Consensus Opinion Number 112, May 1994, Consensus Opinion Number 141, September 1993, Consensus Opinion Number 195, February 1996, and Consensus Opinion Number 219, January 2000)

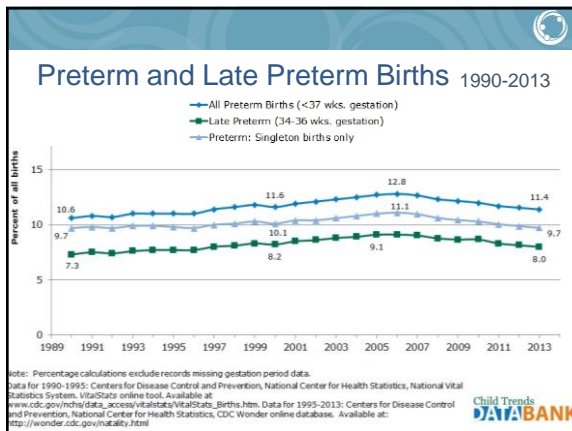
Assessment of Risk Factors for Preterm Birth

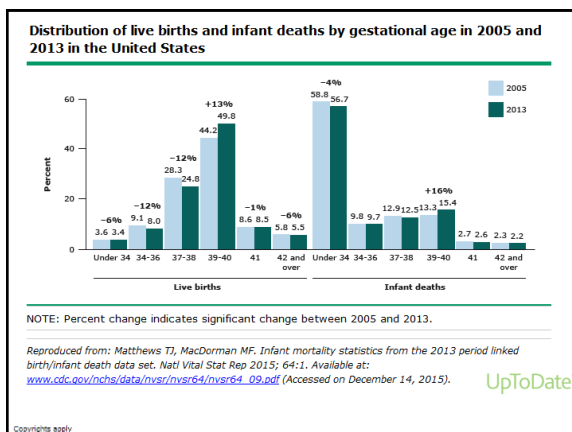
CHUMS AIOG 2005
Dyston et al NEJM 1998
Iams et al NEJM 2002

approved a BRACAM study

The U.S. Perinatal Society's independent review found that HUAM was not effective (56%) in predicting preterm birth.

HUAM not clinically useful to predict patients who will deliver preterm





Preterm Birth



Don't let the pendulum swing too far...

Preterm birth may not be all bad...

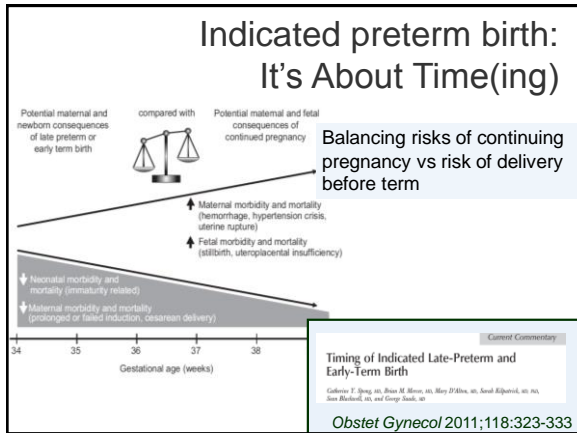
Prevents fetal death and prolonged exposure of fetus to hostile intrauterine environment



Photo credit: [hudsontheguy](#) via [Complight.co](#)

In some specific conditions such as placenta previa and multifetal gestation, preterm birth or early term birth is optimal for the mother, baby or both, because of maternal and/or fetal risks with continued pregnancy.





Impact

Implementing known interventions: potential for only modest reductions in PTB


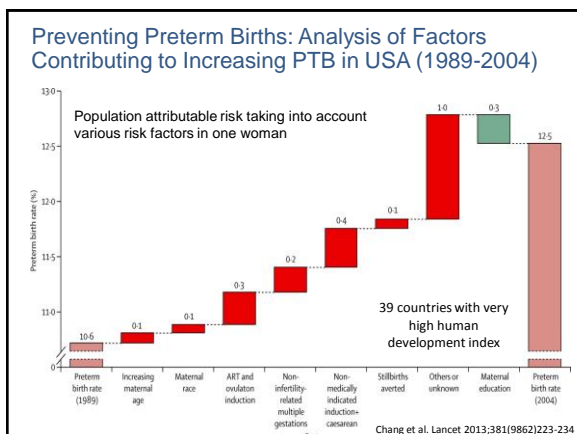
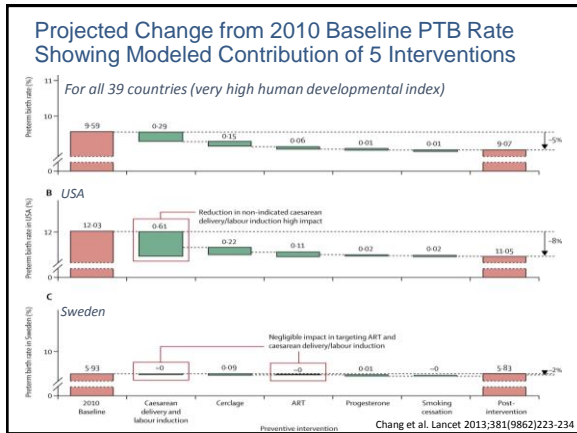
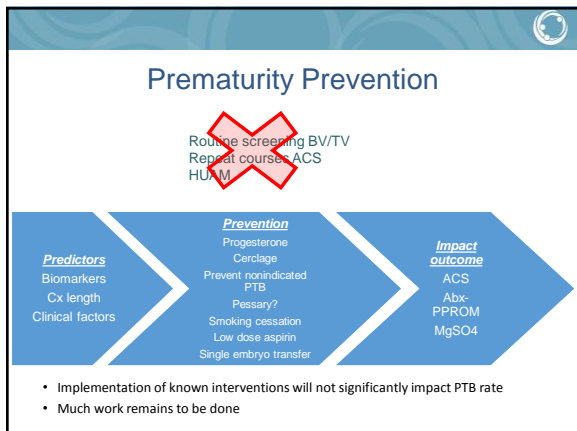


Photo Credit: [bradleygo](#) via [Comstock](#)









PROSPECT – PROgesterone & Pessary for Cervical Shortening in Twins

- The PROSPECT Trial will compare pessary use to vaginal progesterone or placebo as a potential means to reduce the risk of preterm delivery prior to 35 weeks in women pregnant with twins and having a short cervix, beginning from the 16th through the 23rd week of gestation.
- Recruiting now



Human Placenta Project

Overarching goal:
Understanding human placental
development and function in real time

NIH Eunice Kennedy Shriver National Institute
of Child Health and Human Development



PregSource: Crowdsourcing to Understand Pregnancy

- A crowd-sourced, interactive, mobile app to:
 - Detail the natural history – and variations - of human pregnancy
 - Provide accurate info about pregnancy from trusted sources
 - Let pregnant women know about opportunities to participate in targeted research
- In early developmental stage with >15 partner organizations

PregSource
Crowdsourcing to Understand Pregnancy



Summary

- Identifiable risk factors and markers for PTB
- Research has identified preventative therapies and ineffective interventions
- Prevention strategies
 - Tailor the plan to the population
 - Facilitate research and advances for prevention, identification, treatment
- Much work remains to be done

Implications

The prevention of preterm birth will not only improve pregnancy outcome and outcome for families, but healthier babies, will result in improved health of the nation: less heart disease, diabetes and potentially even cancer as these children grow.




Questions?
