INTERGENERATIONAL BLOOD PRESSURE Study

A Systematic Review of Preterm Birth and DNA Methylation in African American women

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Faculty Disclosure

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Conflicts of Interest	None
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Goals and Objectives

Session Goal:

- Describe findings of a systematic analysis of existing studies on DNA methylation and preterm birth among African American women

Session Objectives:

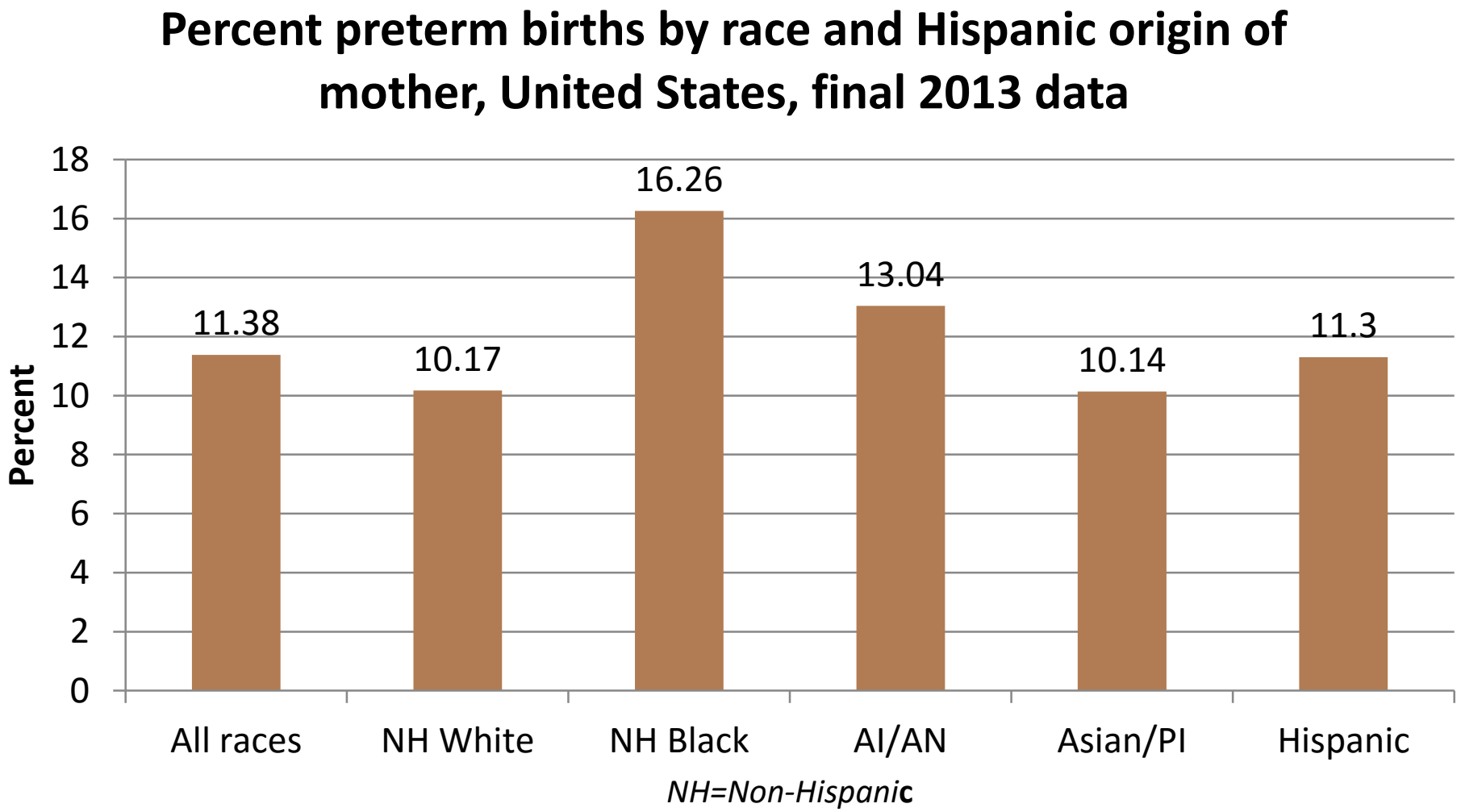
- Identify three limitations of existing studies on DNA methylation and preterm birth among African American women
- Discuss recommendations for future research in this area

Background

Preterm birth

- Definition
- Prevalence
- Significance
- Risk factors

Prevalence


Percent preterm births by race and Hispanic origin of mother, United States, final 2013 data
Percent
18
16
14
12
10
8
6
4
2
0
11.38
10.17
16.26
13.04
10.14
11.3
All races
NH White
NH Black
AI/AN
Asian/PI
Hispanic
NH=Non-Hispanic

Risk factors

- Medical
- Obstetric
- Social
- Environmental

Epigenetic inquiry

- Shared maternal/fetal environment
- DNAm common biomarker for preterm birth
- Racial differences in DNAm may contribute to outcome
- Epigenomic paths of inquiry are relevant

DNA Methylation

How environment turns genes on or off

DNA- 4 nucleotides (C,G,A,T)

Addition of methyl groups to Cytosine on DNA signals genes to turn on or off

Important for healthy cell development, and can also lead to disease (hypermethylation and CA)

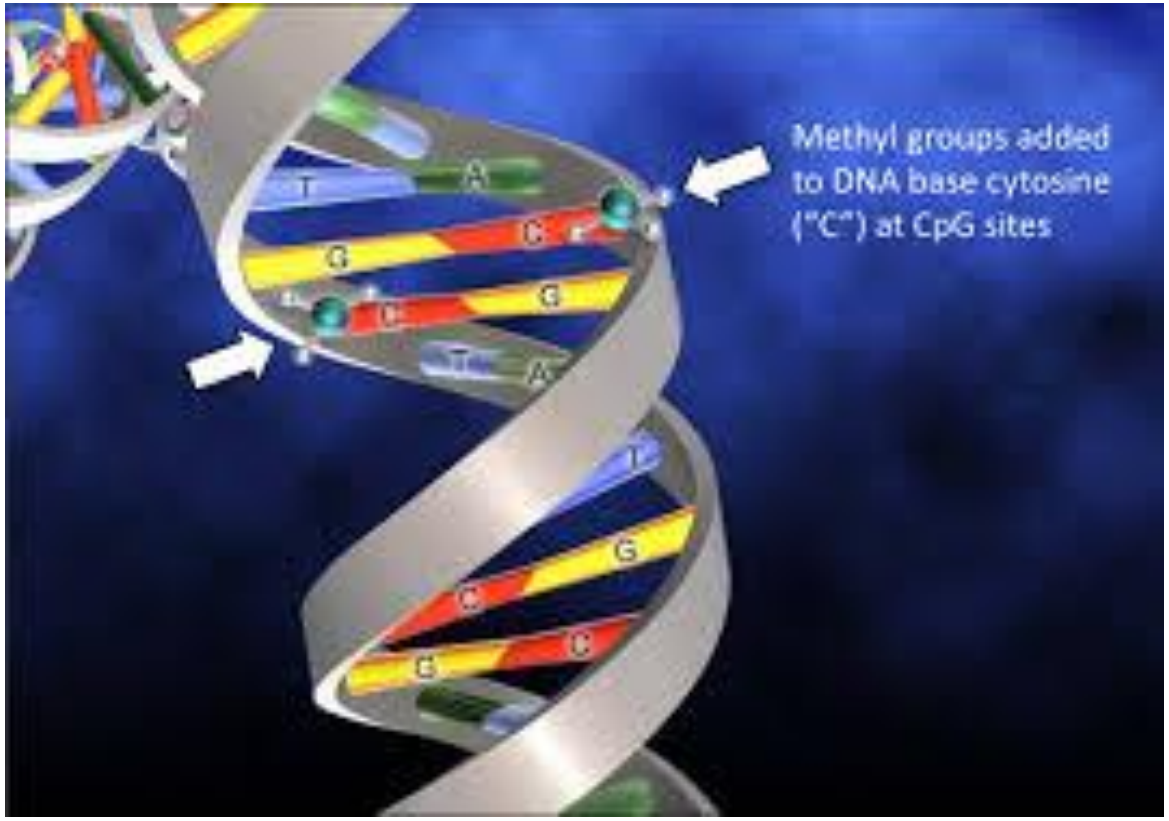
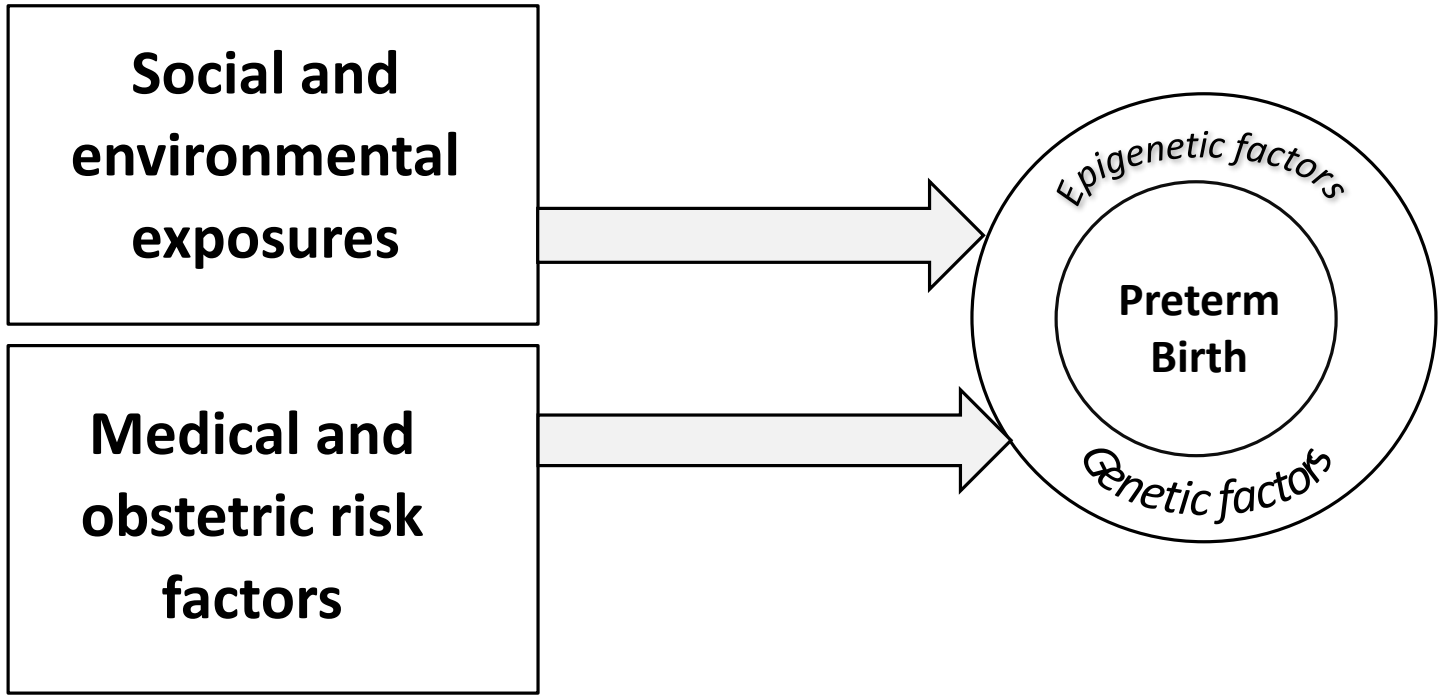


Figure 1. Contributors to preterm birth



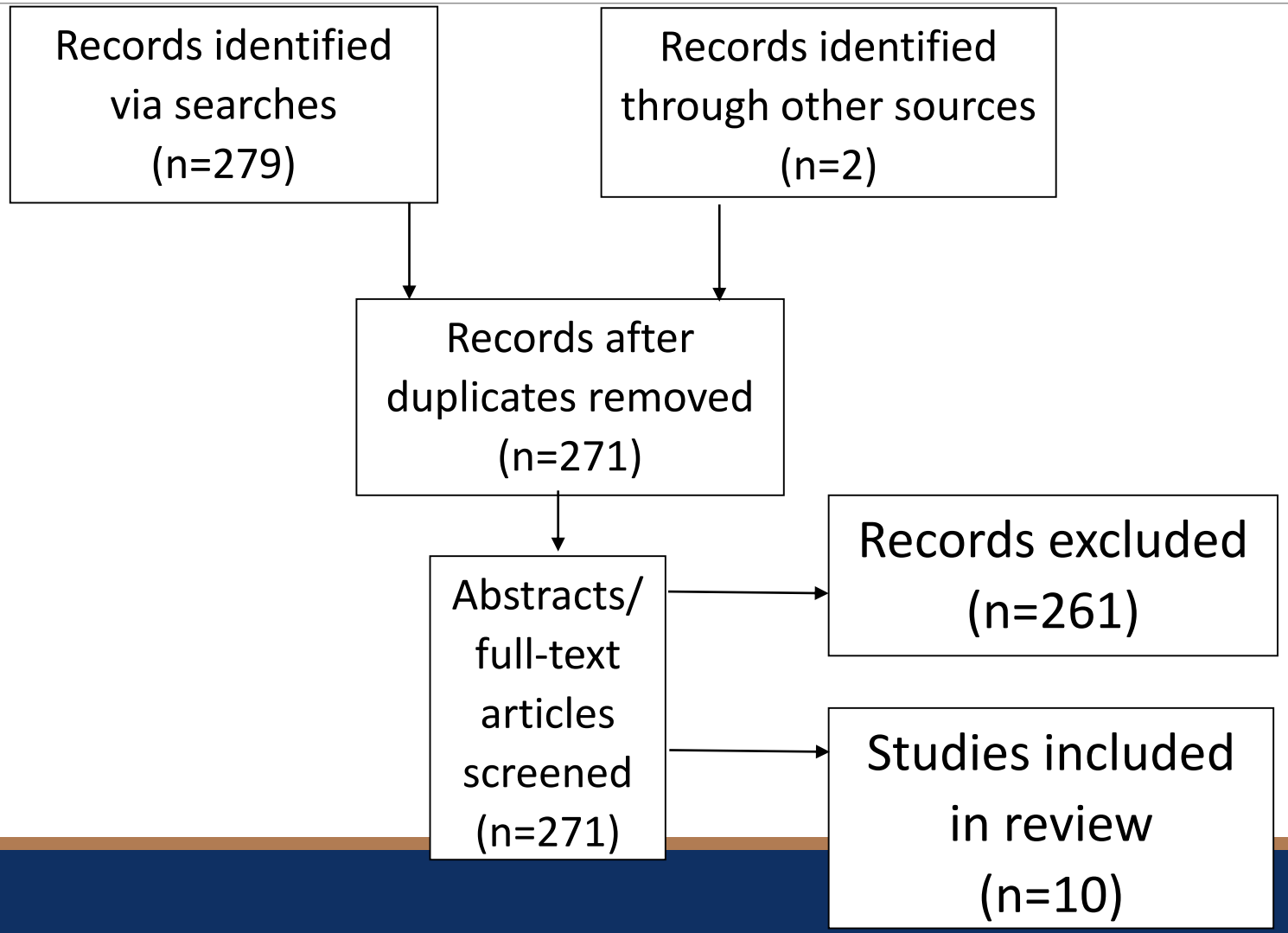
Methods

- Systematic review of Medline and CINAHL

- Inclusion criteria

- Search terms: DNA methylation, preterm birth, gestational age, preterm birth

PRISMA flow diagram



Results

- N=10 studies reviewed
- All included African Americans
- Overall, DNAm was associated with preterm birth

Author	Population	Sample size	Preterm birth	Tissue source	Epityping	Findings
Behnia, 2015	Nashville, TN Nashville Biobank	N=70 (13% AA)	22-36 weeks gestation (+ contractions/ cervical changes	Placental fetal membranes (amniochorion)	Candidate gene/ targeted	Higher methylation status of CpG islands within the OXTR promotor in infants born preterm
Burris, 2012	Boston, MA Project Viva	N=1160 (10% AA)	<37 weeks gestation	Maternal and umbilical cord, DNAm	LINE-1	Preterm birth is associated with lower LINE-1 in cord blood
Filiberto, 2011	Providence, RI	N=480 (10% AA)	SGA, LGA	Placenta	Candidate gene/ targeted	Significant relationship between differential (increased) methylation and large for gestational age
Lee, 2012	Baltimore, MD	N=141 (64% AA)	<37 weeks	Umbilical cord blood	EWAS	Gradual changes in DNAm associated with gestational age

Author	Population	Sample size	Preterm birth	Tissue	Epityping	Findings
Liu 2013	Durham, NC	N=73 (54%)	<37 weeks	Umbilical cord blood	Candidate gene/ targeted	No DNAm difference found between types of PTB
Michels 2011	Boston, MA Epigenetic Birth Cohort	N=319 dyads (12%)	<37 weeks, term ≥37w	Umbilical cord blood/ placenta	LINE-1	PTB associated with lower LINE-1 methylation compared to term
Parets 2013	Nashville, TN Nashville Biobank	PTB n=22, term n=28 (100%)	24-34 weeks, controls: >39 weeks	Umbilical cord blood	Candidate gene/ targeted	29 CpG sites associated with PTB
Parets 2015	Nashville, TN Nashville Biobank	PTB n=16, term n=24 (100%)	24-34 weeks, controls: >39 weeks	Maternal leukocytes	EWAS	No CpG sites associated with PTB, but DNAm between maternal-fetal pairs correlated
Schroeder 2011	Atlanta, GA, Nashville, TN	2 Cohorts: n=259 (10%), n=194 (57%)	<37weeks. LMP, OB estimate	Umbilical cord blood	Candidate gene/ targeted	CpG sites on several genes associated with gestational age
Vidal 2013	North Carolina, NEST Cohort	N=397 (41%)	LBW, Preterm: < 37 weeks	Umbilical cord blood	Candidate gene/ targeted	Increased DNAm at PLAGL1 DMR associated with higher birthweight

Discussion

- Exposure measurement:
  - Varying definitions of preterm birth
  - PTB vs. Gestational Age
- Limited inclusion of AA's
- Small sample sizes, no or small comparison groups
- Varying methodologies for methylation analysis
  - GWAS vs. sites vs. regions

Limitations

- Race in epigenetic studies
- Three studies: same biobank
- Need for more research

Recommendations

- Standardized definitions/methodologies
- Tissue types
- Maternal or fetal focus?