RACE-BASED OBSTETRICS: ASPIRIN PROPHYLAXIS & RACIAL DISPARITIES IN PREECLAMPSIA

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High-Risk Obstetrics for the Family Physician: Racial Equity in Obstetrics
March 26, 2021
OBJECTIVES

1) Review a framework for interpreting race-based clinical guidelines
2) Evaluate possible causes of racial disparities in preeclampsia
3) Review the evidence for including race in clinical decision-making about aspirin prophylaxis
<table>
<thead>
<tr>
<th>Domain</th>
<th>Description</th>
<th>Representative Examples</th>
</tr>
</thead>
<tbody>
<tr>
<td>Semantics</td>
<td>Using imprecise and nonbiologic labels that inaccurately conflate race and</td>
<td>Widespread use of “Caucasian,” “Black,” “African American,” and “Asian” as labels to</td>
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<tr>
<td></td>
<td>ancestry</td>
<td>denote biologic differences between patients</td>
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<tr>
<td></td>
<td></td>
<td>Describing a Nigerian patient as “African American” in a clinical vignette</td>
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<tr>
<td>Prevalence without</td>
<td>Presenting racial/ethnic differences in disease burden without contextual-</td>
<td>Teaching students that “Black” patients have higher rates of asthma than “White”</td>
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<tr>
<td>context</td>
<td>ization</td>
<td>patients, without reference to the effects on asthma prevalence of residential</td>
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<td></td>
<td></td>
<td>segregation and unequal access to high-quality housing and health care</td>
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<td></td>
<td></td>
<td>Teaching students that “Black” patients have higher rates of hospital readmission,</td>
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<tr>
<td></td>
<td></td>
<td>without any discussion of the underlying causes of these disparities</td>
</tr>
<tr>
<td>Race-based diagnostic</td>
<td>Presentation of links between racial groups and particular diseases</td>
<td>Priming students to view sickle cell disease as affecting only Black people,</td>
</tr>
<tr>
<td>bias</td>
<td></td>
<td>rather than as common in populations at risk for malaria</td>
</tr>
<tr>
<td>Pathologizing race</td>
<td>The tendency to link minorities with increased disease burden</td>
<td>In a slide showing the incidence of 13 types of brain tumors in Black patients and</td>
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<tr>
<td></td>
<td></td>
<td>White patients, using the title “Incidence rates are higher among Blacks than among</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Whites,” even though 10 of the tumors occurred more frequently in White patients</td>
</tr>
<tr>
<td>Race-based clinical</td>
<td>Teaching of guidelines that endorse the use of racial categories in the</td>
<td>Teaching students to use different first-line antihypertensive drugs in Black patients</td>
</tr>
<tr>
<td>guidelines</td>
<td>diagnosis and treatment of diseases</td>
<td>than in White patients, without any exposure to literature that questions these</td>
</tr>
<tr>
<td></td>
<td></td>
<td>practices and misleading interpretations of information</td>
</tr>
</tbody>
</table>

SOCIAL CONSTRUCTION OF RACE IN OBSTETRICS

- Medical superbody\(^1\) – physically superior, socially inferior
- Obstetrical hardiness\(^2\) – pelvimetry and pain tolerance
- Wily patient\(^3\) – dumb and duplicitous
- Black maternal unfitness\(^4\) - Welfare queen, family structure, etc.
- Menacing mothers and hardy babies\(^5\) – threat and responsibility

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RACE-BASED OBSTETRICS

- Aspirin for preeclampsia prophylaxis
- VBAC calculator\(^1\)
- 17-OHP\(^2\)
- Anemia\(^3\)

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Should I be offering aspirin to all G1P0 Black pregnant people?

If so, how do I explain my recommendation to a patient?

“Race-based clinical guidelines”

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**RACIAL DISPARITIES IN PREECLAMPSIA**

Black birthing people compared to white people have:

- At least 60% greater incidence of preeclampsia¹
- Greater incidence of preeclampsia-related stroke, pulmonary edema, heart failure, renal failure²
- 3x the case fatality rate³

“Prevalence without Context”       “Pathologizing Race”

CAUSES OF PREECLAMPSIA RACIAL DISPARITIES

- Higher prevalence of chronic hypertension, diabetes, obesity, sleep apnea, etc.
- Genetic predisposition  “Semantics”
- Exposure to racism

Allelic variations in angiogenic pathway genes are associated with preeclampsia

Presented orally at the 30th Annual Meeting of the Society for Maternal-Fetal Medicine, Chicago, IL, Feb. 1-6, 2010. The racing flag logo above indicates that this article was rushed to press for the benefit of the scientific community.

Sindhu K. Srinivas MD, MSCE 1, Alanna C. Morrison PhD 2, Christina M. Andrela MS 1, Michal A. Elowitz MD 1
NOT JUST SOCIOECONOMIC STATUS

- N = 718,604 from California birth cohort database (2007-2012)
- SES proxies: insurance status and education
- Exclusions: cHTN, age<18, extreme BMIs
- Controls: age, parity, prenatal care, tobacco use, diabetes, BMI
- Outcomes:
  - White birthing people’s risk of preeclampsia decreased as SES improved
  - Black birthing people’s risk of preeclampsia did not decrease as SES improved

PREECLAMPSIA & Racial Stress Disparity

- N = 9,470 nulliparous, singleton, uncomplicated pregnancies
- Assess for association between subjective stress and adverse pregnancy outcomes (including hypertensive disorders of pregnancy)
- Controlled for medical risks (BMI, smoking, medical co-morbidities) but not SES
- Outcomes:
  - Black pregnant people are most likely to have all adverse pregnancy outcomes
  - Black pregnant people are most likely to score high on stress measures
  - Stress scores did not modify racial disparity in hypertensive disorders of pregnancy
  - Latent profile analysis showed that racism exposure scores also did not modify risk

FIGURE 3
The health equity framework

The framework describes the way racism works through social determinant of health to impact maternal health along the life course.

ASPIRIN IN MUDDY WATER

• What is the best dose?
• What time of day should aspirin be taken?
• When is it too late to benefit from starting aspirin?
• Does aspirin help prevent preterm and/or term preeclampsia?
• How important is adherence?
• What risk factors warrant aspirin treatment?
Although clinical risk assessments were not systematically reviewed for this recommendation, a pragmatic approach is described in the Table. This approach may help to identify a patient population with an absolute risk for preeclampsia of at least 8%, which is consistent with the lowest preeclampsia incidence observed in control groups in studies reviewed by the USPSTF (1). Women with 1 or more high-risk factors should receive low-dose aspirin. Women with several moderate-risk factors may also benefit from low-dose aspirin (Table, but the evidence is less certain for this approach. Clinicians should use clinical judgment in assessing the risk for preeclampsia and discuss the benefits and harms of low-dose aspirin use with their patients.

COMPETING RISKS MODEL

- Data from 3 studies (Ns = 35,948; 8,775; 16,451)
- “Triple test”
  - Maternal demographic factors (age, weight, height, race, parity, personal and family history of preeclampsia, chronic hypertension, diabetes mellitus, SLE or APS, method of conception, interpregnancy interval)
  - Biomarkers (MAP, uterine artery pulsatility index, and serum placental growth factor)
- Detection rates of:
  - Preeclampsia <34w = 90%
  - Preeclampsia 34-37w = 75%
  - All preeclampsia = 50%

**RACE WEIGHTING**


**Table 2**

Fitted regression model for the mean gestational age at delivery with preeclampsia

<table>
<thead>
<tr>
<th>Term</th>
<th>Coefficient</th>
<th>Standard error</th>
<th>95% confidence interval</th>
</tr>
</thead>
<tbody>
<tr>
<td>For all women</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Constant</td>
<td>54.3637</td>
<td>0.24355</td>
<td>53.9–54.8</td>
</tr>
<tr>
<td>Age (y) –35 if age ≥35 y</td>
<td>–0.206886</td>
<td>0.03003</td>
<td>–0.27 to –0.145</td>
</tr>
<tr>
<td>Age (y) –0 if age &lt;35 y</td>
<td>–0.214935</td>
<td>0.03003</td>
<td>–0.27 to –0.145</td>
</tr>
<tr>
<td>Height in cm – 164</td>
<td>0.117110</td>
<td>0.00969</td>
<td>0.098–0.136</td>
</tr>
<tr>
<td>Afro-Caribbean racial origin</td>
<td>–2.6786</td>
<td>0.14373</td>
<td>–2.96 to –2.40</td>
</tr>
<tr>
<td>South Asian racial origin</td>
<td>–1.1290</td>
<td>0.26584</td>
<td>–1.65 to –0.61</td>
</tr>
<tr>
<td>Chronic hypertension</td>
<td>–7.2897</td>
<td>0.23379</td>
<td>–7.87 to –6.71</td>
</tr>
<tr>
<td>Systemic lupus erythematosus or antiphospholipid syndrome</td>
<td>–3.0519</td>
<td>0.95407</td>
<td>–4.92 to –1.18</td>
</tr>
<tr>
<td>Conception by in vitro fertilization</td>
<td>–1.6327</td>
<td>0.32653</td>
<td>–2.27 to –0.99</td>
</tr>
<tr>
<td>Parous with previous preeclampsia</td>
<td>–8.1867</td>
<td>0.54937</td>
<td>–9.24 to –7.09</td>
</tr>
<tr>
<td>Parous with previous preeclampsia (previous gestation in weeks, −24)²</td>
<td>0.0271988</td>
<td>0.00261</td>
<td>0.0221–0.0325</td>
</tr>
<tr>
<td>Parous with no previous preeclampsia</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Intercept</td>
<td>–4.3350</td>
<td>0.75185</td>
<td>–5.81 to –2.86</td>
</tr>
<tr>
<td>Interval 1</td>
<td>–4.15137651</td>
<td>1.30364</td>
<td>–6.71 to –1.60</td>
</tr>
<tr>
<td>Interval 2</td>
<td>9.21473572</td>
<td>1.8435</td>
<td>5.60–12.83</td>
</tr>
<tr>
<td>(Previous gestation in weeks, −24)²</td>
<td>0.01549673</td>
<td>0.00186</td>
<td>0.0119–0.0191</td>
</tr>
</tbody>
</table>

**Screening results**

<table>
<thead>
<tr>
<th>Group</th>
<th>Prevalence (%)</th>
<th>Screen positive (%)</th>
<th>False positive (%)</th>
<th>DR (%)</th>
<th>Screen positive (%)²</th>
<th>Screen negative (%)²</th>
</tr>
</thead>
<tbody>
<tr>
<td>Preeclampsia &lt;37 w</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>All pregnancies</td>
<td>0.64</td>
<td>11.4</td>
<td>10.4</td>
<td>85</td>
<td>4.77</td>
<td>0.11</td>
</tr>
<tr>
<td>Nulliparous</td>
<td>0.76</td>
<td>14.7</td>
<td>13.7</td>
<td>84</td>
<td>4.37</td>
<td>0.14</td>
</tr>
<tr>
<td>Parous</td>
<td>0.52</td>
<td>8.0</td>
<td>7.2</td>
<td>85</td>
<td>5.50</td>
<td>0.08</td>
</tr>
<tr>
<td>No previous PE</td>
<td>0.34</td>
<td>5.9</td>
<td>5.4</td>
<td>78</td>
<td>4.45</td>
<td>0.08</td>
</tr>
<tr>
<td>Previous PE</td>
<td>3.32</td>
<td>41.6</td>
<td>37.8</td>
<td>97</td>
<td>7.76</td>
<td>0.16</td>
</tr>
<tr>
<td><strong>Afro-Caribbean</strong></td>
<td><strong>1.47</strong></td>
<td><strong>23.3</strong></td>
<td><strong>21.1</strong></td>
<td><strong>91</strong></td>
<td>5.78</td>
<td><strong>0.17</strong></td>
</tr>
<tr>
<td>Nulliparous</td>
<td>1.64</td>
<td>30.0</td>
<td>27.8</td>
<td>92</td>
<td>5.03</td>
<td>0.20</td>
</tr>
<tr>
<td>Parous</td>
<td>1.36</td>
<td>18.8</td>
<td>16.8</td>
<td>91</td>
<td>6.58</td>
<td>0.15</td>
</tr>
<tr>
<td>No previous PE</td>
<td>0.93</td>
<td>15.4</td>
<td>14.1</td>
<td>86</td>
<td>5.20</td>
<td>0.15</td>
</tr>
<tr>
<td>Previous PE</td>
<td>6.83</td>
<td>62.6</td>
<td>57.1</td>
<td>100</td>
<td>10.87</td>
<td>0.07</td>
</tr>
<tr>
<td><strong>White</strong></td>
<td><strong>0.46</strong></td>
<td><strong>8.8</strong></td>
<td><strong>8.2</strong></td>
<td><strong>80</strong></td>
<td>4.20</td>
<td><strong>0.10</strong></td>
</tr>
<tr>
<td>Nulliparous</td>
<td>0.62</td>
<td>12.1</td>
<td>11.4</td>
<td>81</td>
<td>4.12</td>
<td>0.13</td>
</tr>
<tr>
<td>Parous</td>
<td>0.29</td>
<td>5.2</td>
<td>4.7</td>
<td>78</td>
<td>4.41</td>
<td>0.07</td>
</tr>
<tr>
<td>No previous PE</td>
<td>0.19</td>
<td>3.4</td>
<td>3.2</td>
<td>66</td>
<td>3.65</td>
<td>0.07</td>
</tr>
<tr>
<td>Previous PE</td>
<td>2.01</td>
<td>34.1</td>
<td>31.5</td>
<td>95</td>
<td>5.61</td>
<td>0.14</td>
</tr>
</tbody>
</table>

Semantics

“Race-based diagnostic bias” and “Pathologizing race”
SUMMARY SO FAR

• Black pregnant people are more like to be diagnosed with preeclampsia
• Inconclusive research on why preeclampsia racial disparity exists.
  • Avoid genetic inquiry
  • SES and psychosocial stress don’t have strong associations
  • Structural racism model for preeclampsia is theoretical
• Clinical risk assessments are fraught
  • USPSTF algorithm is not evidence based
  • Newer prediction models improve detection rate, but also increase false positive rate
• Does risk for preeclampsia correlate with benefit from aspirin?
HOW EFFECTIVE IS ASPIRIN?

USPSTF review (13 RCTs) in 2014¹
- “High risk” population: 24% RR reduction, ARR 2-5%
- “Risk reductions closer to 10%.... represent a more conservative interpretation of the results.”
- No evaluation of race

Cochrane review (60 RCTs, N=36,716) in 2019²
- General population: 18% RR reduction; NNT=61
- Weak evidence for differential impact when risk stratified
- No evaluation of race

AJOG metanalysis (16 RCTs, N=18,907) in 2018³
- RR = 0.62 for preterm preeclampsia if aspirin:
  - Started <16w
  - Dose >100mg
- No effect on term preeclampsia
- No evaluation of race

ASPIRIN EFFICACY USING THE COMPETING RISKS MODEL

ASPRE trial

• Uses the same trial population as one of the “competing risks model” trials

• N=1620 at “high risk”

• Aspirin dose 150 mg, started <16w

• Reduced incidence of preterm but not term preeclampsia

No heterogeneity in aspirin efficacy in high risk subgroups, except chronic hypertension.

**Interpretation:** Great! In high risk subgroups, Afro-Caribbean pregnant people respond to aspirin just as well as white people.

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MFMU: SECONDARY ANALYSIS

- Data from 1990s, reanalyzed in 2020
- Aspirin dose 60 mg, started as late as 26w
- Stated goal: “…stratifying results by ethnicity and race as a first-pass approximation of pharmacogenomics.”

Low risk trial
- **White people benefit (RR=0.19) but black people don’t**
- Aspirin associated with increased risk of stillbirth in Black people (1.4% vs 0.4%, p=0.048)

High risk trial
- “High risk” - Pregestational insulin-treated diabetes mellitus, chronic hypertension, multiple gestation, history of preeclampsia
- Aspirin didn’t help or hurt anyone, and racial stratification didn’t change that.

Authors’ hypothesis: **Non-response in low risk Black people may be explained by race-related genetic polymorphisms causing aspirin resistance.**

RACE-CONSCIOUS ASPIRIN PRESCRIBING

• The identity of the prescriber should shape counseling language about “race-as-risk” for preeclampsia
• If patients benefit from mechanistic explanation, err toward structural racism exposure and avoid genetics
• Acknowledge uncertainty in risk assessment and predicted benefit
• Acknowledge the risks of aspirin
  • Minimal adverse maternal/fetal outcomes
  • BUT “At-risking” pregnancies and racializing pregnancies can be harmful
• Advocate to address structural racism
ACKNOWLEDGMENTS

• Dr. Anne Marie Williams
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