Our State, Our Challenge: Preterm Birth In North Carolina

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Preterm Birth

25 Week neonate 265 gms (9 oz)
Preterm Birth

- **Preterm**
  - Infant born before 37 weeks of pregnancy
  - Very preterm birth < 32 weeks
  - Extreme preterm birth < 28 weeks

- 12,500 preterm births in North Carolina per year
  - $70-75 million annually

Source: NC Department of Health and Human Services State Center for Health Statistics (2016)
## Cost of Prematurity

### Table 1. Neonatal and Maternal Costs and Outcomes by Week of Gestation for Surviving Infants

<table>
<thead>
<tr>
<th>Gestational age (wk)</th>
<th>n</th>
<th>Neonatal LOS (d) Mean Median</th>
<th>Neonatal cost $1000/case</th>
<th>$ million RDS (%)</th>
<th>Ventilation (%)</th>
<th>C/D rate (%)</th>
<th>Nonnormal DRG (%)</th>
<th>Maternal LOS (d) Mean Median</th>
<th>Maternal cost $1000/cases*</th>
<th>$1000*</th>
</tr>
</thead>
<tbody>
<tr>
<td>25</td>
<td>192</td>
<td>92.0 87</td>
<td>202.7 38.9</td>
<td>82.3</td>
<td>89.6</td>
<td>43.2</td>
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<td>26</td>
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<td>146.6 36.8</td>
<td>70.9</td>
<td>81.7</td>
<td>49.4</td>
<td>100.0</td>
<td>6.9 5</td>
<td>7.8 1958</td>
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<td>27</td>
<td>328</td>
<td>66.8 66</td>
<td>119.6 39.2</td>
<td>69.8</td>
<td>71.3</td>
<td>47.3</td>
<td>99.7</td>
<td>7.0 4</td>
<td>8.1 2648</td>
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<tr>
<td>28</td>
<td>402</td>
<td>52.3 51</td>
<td>86.2 34.7</td>
<td>58.5</td>
<td>62.2</td>
<td>50.7</td>
<td>97.3</td>
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<tr>
<td>29</td>
<td>585</td>
<td>39.5 40</td>
<td>62.6 36.6</td>
<td>48.7</td>
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<td>43.9</td>
<td>93.2</td>
<td>6.1 4</td>
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<tr>
<td>30</td>
<td>797</td>
<td>30.4 29</td>
<td>46.4 37.0</td>
<td>38.4</td>
<td>41.2</td>
<td>43.0</td>
<td>88.6</td>
<td>6.1 3</td>
<td>7.2 5713</td>
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<tr>
<td>31</td>
<td>1194</td>
<td>21.5 18</td>
<td>29.8 35.5</td>
<td>31.2</td>
<td>27.3</td>
<td>39.1</td>
<td>81.7</td>
<td>5.2 3</td>
<td>6.2 7461</td>
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<tr>
<td>32</td>
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<tr>
<td>33</td>
<td>3172</td>
<td>9.0 3</td>
<td>11.0 34.7</td>
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<td>29.6</td>
<td>63.6</td>
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<td>4.5 14,389</td>
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<tr>
<td>34</td>
<td>5788</td>
<td>5.9 2</td>
<td>7.2 41.4</td>
<td>7.4</td>
<td>6.3</td>
<td>24.6</td>
<td>57.0</td>
<td>3.3 2</td>
<td>3.8 22,082</td>
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<tr>
<td>35</td>
<td>9898</td>
<td>3.9 2</td>
<td>4.2 41.1</td>
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<td>23.8</td>
<td>51.3</td>
<td>3.2 2</td>
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<td>36</td>
<td>16,609</td>
<td>2.8 1</td>
<td>2.6 42.8</td>
<td>2.3</td>
<td>2.3</td>
<td>22.1</td>
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<td>2.5 2</td>
<td>3.1 51,259</td>
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<tr>
<td>37</td>
<td>34,477</td>
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<td>1.7 58.2</td>
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<td>1.3</td>
<td>21.2</td>
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<td>71,610</td>
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<td>1.1 81.7</td>
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<td>0.7</td>
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<td>23.6</td>
<td>1.9 2</td>
<td>2.5 175,916</td>
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</tr>
</tbody>
</table>

LOS = length of stay; RDS = respiratory distress syndrome; C/D = cesarean delivery; DRG = diagnosis-related group.

* Includes any prenatal admissions and delivery admission and possible subsequent transfers until mother was sent home.

Gilbert W, Obstet Gynecol 2003;102:488
Preterm Birth

- Leading cause of neonatal mortality (35%)
- NICU care has improved survival for extreme preterm deliveries but increased the proportion of survivors with disabilities
Preterm Birth

- Cerebral palsy
- Developmental delay
- Vision problems
- Hearing impairment
Infant Mortality Rate (Deaths per 1,000 Live Births) – 2013

- United States: 6.0
- North Carolina: 7.0

## Infant Mortality Rate (Deaths per 1,000 Live Births) by Race/Ethnicity – 2011-2013

<table>
<thead>
<tr>
<th>Location</th>
<th>Non-Hispanic White</th>
<th>Non-Hispanic Black</th>
<th>American Indian or Alaska Native</th>
<th>Asian or Pacific Islander</th>
<th>Hispanic</th>
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<tbody>
<tr>
<td>United States</td>
<td>5.1</td>
<td>11.3</td>
<td>8.1</td>
<td>4.2</td>
<td>5.1</td>
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<tr>
<td>Alabama</td>
<td>6.9</td>
<td>12.9</td>
<td>NSD</td>
<td>NSD</td>
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</tr>
<tr>
<td>Massachusetts</td>
<td>3.5</td>
<td>6.9</td>
<td>NSD</td>
<td>3.3</td>
<td>5.5</td>
</tr>
<tr>
<td>Minnesota</td>
<td>4.3</td>
<td>8.9</td>
<td>11.3</td>
<td>4.6</td>
<td>5.4</td>
</tr>
<tr>
<td>Mississippi</td>
<td>6.8</td>
<td>12.4</td>
<td>NSD</td>
<td>NSD</td>
<td>6.4</td>
</tr>
<tr>
<td><strong>North Carolina</strong></td>
<td><strong>5.4</strong></td>
<td><strong>12.6</strong></td>
<td><strong>10.6</strong></td>
<td><strong>4.3</strong></td>
<td><strong>5.6</strong></td>
</tr>
<tr>
<td>South Carolina</td>
<td>5.3</td>
<td>11.5</td>
<td>NSD</td>
<td>NSD</td>
<td>5.0</td>
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<tr>
<td>Virginia</td>
<td>4.8</td>
<td>11.7</td>
<td>NSD</td>
<td>5.0</td>
<td>5.8</td>
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</tbody>
</table>

### Infant Mortality Rate by County – North Carolina, 2010-2014

#### North Carolina Infant Mortality Rates by County 2010 - 2014

<table>
<thead>
<tr>
<th>Residence</th>
<th>White Rate</th>
<th>African American Rate</th>
<th>Disparity Ratio</th>
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<tbody>
<tr>
<td>Cabarrus</td>
<td>4.6</td>
<td>6.6</td>
<td>1.43</td>
</tr>
<tr>
<td>Craven</td>
<td>7.8</td>
<td>8.0</td>
<td>1.03</td>
</tr>
<tr>
<td>Iredell</td>
<td>4.2</td>
<td>24.1</td>
<td>5.74</td>
</tr>
<tr>
<td>Mecklenburg</td>
<td>3.5</td>
<td>9.9</td>
<td>2.83</td>
</tr>
<tr>
<td>New Hanover</td>
<td>2.9</td>
<td>9.0</td>
<td>3.10</td>
</tr>
<tr>
<td>Robeson</td>
<td>10.9</td>
<td>15.1</td>
<td>1.39</td>
</tr>
<tr>
<td>Rockingham</td>
<td>7.1</td>
<td>23.2</td>
<td>3.27</td>
</tr>
<tr>
<td>Scotland</td>
<td>12.8</td>
<td>13.3</td>
<td>1.04</td>
</tr>
<tr>
<td>Union</td>
<td>2.7</td>
<td>15.7</td>
<td>5.81</td>
</tr>
</tbody>
</table>

*Source: North Carolina State Center for Health Statistics, August 2015 – retrieved May 21, 2016*

March of Dimes: 2015 PREMATURE BIRTH REPORT CARD

National Preterm Birth Rate of 9.6%

Percent of Preterm Births by Mother’s Education Level – NC, 2014

Source: NC Department of Health and Human Services State Center for Health Statistics (2016)
## Preterm Birth By State

<table>
<thead>
<tr>
<th>State</th>
<th>All Races</th>
<th>Non-Hispanic Black</th>
<th>Non-Hispanic White</th>
<th>Disparity Ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alabama</td>
<td>11.7</td>
<td>15.2</td>
<td>10.3</td>
<td>1.48</td>
</tr>
<tr>
<td>South Carolina</td>
<td>10.8</td>
<td>13.9</td>
<td>9.5</td>
<td>1.46</td>
</tr>
<tr>
<td>North Carolina</td>
<td>9.7</td>
<td>13.3</td>
<td>8.8</td>
<td>1.51</td>
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<tr>
<td>Virginia</td>
<td>9.2</td>
<td>12.6</td>
<td>8.4</td>
<td>1.50</td>
</tr>
<tr>
<td>North Dakota</td>
<td>8.4</td>
<td>8.5</td>
<td>8.1</td>
<td>1.05</td>
</tr>
<tr>
<td>Minnesota</td>
<td>8.7</td>
<td>8.9</td>
<td>8.6</td>
<td>1.03</td>
</tr>
</tbody>
</table>

Kaiser Family Foundation 2014
Preterm Birth

Percentage of Preterm Births: 2014 North Carolina Resident Births
(NC Statewide Average = 9.7%)

Legend

- ≥ 14.6% (6 Counties)
- 9.7 - 14.5% (55 Counties)
- 8.2 - 9.6% (30 Counties)
- ≤ 8.1% (9 Counties)

Source: NC Department of Health and Human Services State Center for Health Statistics (2016)
What have we learned about preventing preterm birth?
Preterm Birth
Corticosteroids Before Delivery

• Respiratory distress reduced by 44%
• Bleeding in the brain reduced by 46%
• Neonatal risk of death reduced by 31%
Preterm Birth Successes

- Magnesium Sulfate given prior to 32 weeks decreases the risk of cerebral palsy by 29%
Preterm Birth: What Does Not Work

- Bedrest/Pelvic rest
- Maintenance tocolytics
- Broad spectrum antibiotics
- Screening and treating asymptomatic high risk women for lower genital tract infection
- Screening and treating gingivitis
The Progression to Preterm Birth

- Inflammation
- Decidual Hemorrhage
- Stress
- HPA axis activation
- Common Pathway
- Uterine Distension
Preterm Labor: Major Known Pathways

- Inflammation/infection
- Hemorrhage
- Stress
- Uterine distension
- Immune dysregulation

Decidua and fetal membrane activation

Prostaglandins/matrix metalloproteinases

Uterine contractions/cervical ripening

Preterm birth
Recurrent Preterm Birth

- Only 10-15% of all PTD
- Risk increases from 1 to 2 to 3 prev PTD from 16%, 41%, & 67%
- Previous Delivery 13-24 wks risk 38%, (Goldenberg 1993)

Bloom SL, Obstet Gynecol 2001;98:379
Relative Risk of Spontaneous Preterm Delivery < 35 Weeks by Percentile of Cervical Length at 24 Weeks

Preterm Birth Prevention

- In a patient with a prior preterm birth, progesterone reduces the risk by 33%
- In a patient with a prior preterm birth and a short cervix, a cerclage reduces the risk by 30%
- In a patient without a prior preterm birth and a short cervix, progesterone reduces the risk by 40-45%
Aspirin Preventing Preterm Birth

Meta-analysis

Coomarasamy A, Obstet Gynecol 2003;101:1319
## Prevention of Prematurity
### Low Dose Aspirin Cost-Benefit

U.S. Preventive Services Task Force

<table>
<thead>
<tr>
<th>Preterm birth</th>
<th>RR</th>
<th>95% CI</th>
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<tbody>
<tr>
<td>High-risk</td>
<td>0.86</td>
<td>0.71-0.98</td>
</tr>
<tr>
<td>Moderate-risk</td>
<td>0.93</td>
<td>0.71-0.98</td>
</tr>
</tbody>
</table>

Werner EF, Obstet Gynecol 2015;126:1242
North Carolina
Preterm Birth Rate, 2003-2013

March of Dimes Perinatal Data Centers
Primate Social Structure
Primate Social Status

- Social status is one of the most important predictors of quality of an individual’s social environment and affects gene regulation
- Subordinates have little social support leading to chronic stress, immune compromise and reproductive dysregulation

Tung J, PNAS 2012;109:6495
Maternal Stress

- Defined as a state that threatens or is perceived to threatened an individual’s physiological equilibrium
- Associated with adverse outcomes such as cardiovascular disease, cerebrovascular disease and immunosuppression
- The classic mediators are cortisol, norepinephrine and inflammatory markers including cytokines
- Women in lower socioeconomic groups have an increased risk of stress and complications during pregnancy independent of other factors

Borders AE, Obstet Gynecol 2007;109:331
Cardwell MS, Obstet & Gynecol Surv 2013; 68:119
Maternal Stress

- Economic, communication and geographic barriers
- Safety issues
- Unstable housing
- Poor nutrition
- Substance abuse
- Depression symptoms
Overall Poverty 2015

Map Key
- Less than 10%
- 10.1 - 12.8%
- 12.9 - 15.6%
- 15.7 - 18.5%
- More than 18.5%

Talkpoverty.org
Overall Poverty vs Infant Mortality

Overall Poverty

Infant Mortality
Race and Infant Mortality

Figure 19. Black Population

Black Population
Percent of Total Population

- ≥ 50%
- 25.0 - 49.99
- 10.0 - 24.99
- 5.0 - 9.99
- ≤ 4.99

Note: N.C. population = 21.6 percent Black.
Sources: U.S. Census.

North Carolina Infant Mortality Rates by County
2010 - 2014

Rates Per 1,000 Live Births

3.9 - 6.2
Reduce the Risk of Stress Related Illness

- Spiritual belief
- Loving relationship
- Enjoy work
- Play every day (music, art)
- Exercise

Hsing-Chi C, Complimentary Ther Med 2015;23:509
Health Disparity
Preventing Preterm Birth

- Tobacco cessation
- Programs to reduce obesity
- Reduce multiple gestations
- Prevent unintended pregnancy
- Outreach: make access to preterm birth prevention interventions easy, (ultrasound, progesterone, ASA)
March of Dimes Prematurity Campaign
Goal: 8.1% by 2020

- North Carolina 9.7%
- Oregon 7.7%; Mississippi 12.3%
- PTD rate Idaho’s Kootenai county 6.2%
- Maine: White 8.0% and Black 8.2%
How Does Your Patient Get Progesterone

- 36 y/o G-6 P-3-1-1-4 at 24 + 0 weeks
- Previous 32 week delivery
- School teacher with private insurance
- 1 vial (5 doses) of commercial 17-OHP $3381
- $5000 deductible after that 20% copay
- Makena: $95 per 1250 mg vial, (5 weeks)
- Prometrium: $135 for 5 weeks ($27 co pay)
- Started PNC at 19 weeks
- First injection at 25 weeks
## Preterm Birth

<table>
<thead>
<tr>
<th></th>
<th>Very Preterm Birth (%)</th>
<th>Preterm Birth (%)</th>
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<tbody>
<tr>
<td>Singleton</td>
<td>1.2</td>
<td>9.74</td>
</tr>
<tr>
<td>Twins</td>
<td>10.6</td>
<td>58.7</td>
</tr>
<tr>
<td>Triplets</td>
<td>39.3</td>
<td>98.4</td>
</tr>
</tbody>
</table>
Percent of Preterm Births within each Racial and Ethnic group – NC, 2014

Source: NC Department of Health and Human Services State Center for Health Statistics (2016)
Preterm Birth

North Carolina, 2010-2013 Average

Preterm birth

Source: March of Dimes Peristats