Hospitalization Characteristics and Survival of Children with Down Syndrome through Age 3

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Tuesday, Feb. 24th from 1:30-3:30 PM.

History

- J. Langdon Down, MD (1828-1896)
- Observations on an Ethnic Classification of Idiots, London Hospital Reports, 3:259-262, 1866

http://www.neonatology.org/classics/default.html
History

- Jerome Lejeune
- Identified Trisomy 21 in Down syndrome 1959
- "it would take less effort to find a cure for Down syndrome than to send a man to the moon."
- Folic acid and neural tube defects
- 5p- Cri du Chat (1963)

Over 140 years of research on Down syndrome?

- Maternal Age
- Health & Life Expectancy
Maternal Age

![Graph showing the risk of Down syndrome according to maternal age.](image)

- Age = 25
  - 1/1300
  - 0.08%
- Age = 35
  - 1/365
  - 0.27%
- Age = 30
  - 1/30
  - 3.5%

Still true?

- “New era, new worry: New tests for Down syndrome could lead to more abortions and less support for families”, *Newsweek*, Dec. 15, 2008
- Highlights how little we know about these families
Mortality

- Longer life spans from early years
  - Penrose, 1912—9 years
  - Recent studies—58-60 years

Increasing Life Expectancy in Down Syndrome

Bittles & Glasson, 2004
Racial Disparities in Age of Death

Other Health Issues

- Congenital Heart Defects—40-60%
- In-patient hospitalizations within first 3 years (Frid et al., 2004)
- Infant Mortality rates—many times higher than general population
Our Studies

- I-Maternal-Family Characteristics
- II-Newborn-Infant Health
  - Adverse Birth Outcomes
  - Early Hospitalizations
  - Infant Mortality

Methodology

- Identify TN Individuals with DS
- TN Births 1990 - 2006
- Hospital Discharge Data 1997-2005
- N=1,311
Birth Records

- 140+ pieces of information
- Mom (Age, Race/Ethnicity, marital status, education, prior live births, inter-delivery interval)
- Infant (gender, birthweight, gestational age, APGAR, birth complications, congenital anomalies)

Birth Records

- Prenatal Practices (smoking, mom weight gain, number of prenatal doctor visits, month prenatal visits began)
Hospital Discharge Records

- All inpatient and outpatient hospitalizations
- Principal and 8 secondary ICD9 diagnosis codes
- Services and procedures
- Patient address
- Hospital location

Expected and Observed Number of Children with Down Syndrome

![Graph showing expected and observed numbers of children with Down Syndrome from 1990 to 2002.](image)
Death Records

- Child Age (Months, Hours, Minutes)
- Child TN Birth Certificate Number
- DOB, DOD
- Gender, Race, Ethnicity
- Underlying Cause of Death
- Multiple Cause of Death Codes

Findings-I: Demographics

- Demographics of Mothers of Newborns with Down syndrome, 1990-2002
  - Hodapp, Urbano, & Rosenbloom, submitted
- Demographics of African-American & White Mothers, 1990-2002
  - Hodapp & Urbano, 2008
Percentages of DS Births at Different Maternal Ages

Maternal Age Distributions: TN Population v DS Births
Potential Racial Differences

- On average, African-American mothers give birth 2 years earlier than do Euro-American mothers.
- Age at birth relates to:
  - Marital status
  - Education levels
- In other studies, maternal age, race, and education levels have all been linked to ability to know about and access services.

Ages of Af-Am. v. White Mothers of Infants with DS

![Graph showing age density functions for European-heritage and African-American mothers.](image)

**Figure 1**
Kernel density functions by age and race.
Summary of Demographics Findings

- Mothers of children with DS continue to be older—more older, fewer younger
- Age-curves differ based on whether mother is African-American or White
- More younger mothers in African-American group
- In both groups, younger = less educated and less often married

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**TABLE 2**

Educational and marital status for European-heritage vs. African-American mothers of newborns with Down syndrome

<table>
<thead>
<tr>
<th>Age groups</th>
<th>African-American mothers</th>
<th>European-heritage mothers</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>≤23</td>
<td>24-31</td>
</tr>
<tr>
<td>Age (Mean)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>SD</td>
<td>1.60</td>
<td>1.25</td>
</tr>
<tr>
<td>% Not HS graduate</td>
<td>44.4%</td>
<td>9.8%</td>
</tr>
<tr>
<td>% Some college</td>
<td>13.0%</td>
<td>29.3%</td>
</tr>
<tr>
<td>Marital status %</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Married at birth</td>
<td>14.8%</td>
<td>41.5%</td>
</tr>
</tbody>
</table>

*p < 0.001; *p for Education levels = 3 (no high school, high school graduate, some college) × 4 age levels (≤6 degrees of freedom )

HSD (high school diploma), SD (standard deviation)
Results: II-Health Issues

• A-Adverse Birth Outcomes
  • Hodapp, Urbano, & Rosenbloom, submitted

• B-Early Hospitalization
  • So, Urbano, & Hodapp, 2007

• C-Infant Mortality
  • Goldman, Urbano, & Hodapp, in preparation

A-Adverse Birth Outcomes

• Preterm < 37 weeks gestational age
• Low Birthweight < 2500 grams
• Small-for-gestational-age
Adverse Birth Outcomes

- TN resident births 1990-2005
  N=1,220,717
- DS N= 1,043.
Adverse Birth Outcomes

- Low birth weight
  - OR=3.1; 95%CI: 2.6-3.5
- Preterm
  - OR=2.2; 95%CI: 1.9-2.6
- Small-for-gestational age
  - OR=2.6; 95%CI: 2.3-3.1

Predict ABOs Non-DS

<table>
<thead>
<tr>
<th>low maternal education</th>
<th>maternal age</th>
</tr>
</thead>
<tbody>
<tr>
<td>unmarried marital status</td>
<td>race</td>
</tr>
<tr>
<td>few prenatal visits (0 to 5)</td>
<td>late start of prenatal care</td>
</tr>
<tr>
<td>maternal weight gain of less than 25 pounds</td>
<td>maternal smoking</td>
</tr>
<tr>
<td>child gender</td>
<td>index child first born</td>
</tr>
</tbody>
</table>
Adverse Birth Outcomes

• Predict ABOs, DS
  • Weight Gain < 25 pounds
  • < 5 prenatal visits (for 2 of 3 ABO’s)

B-Early Hospitalization

• Rates
• Reasons (Diagnoses)
• Congenital Heart Defects
Hospitalizations

- N = 212 newborns, from birth to 3
- Newborns with DS identified through birth hospitalization
- "Birth forward" = conservative strategy to avoid "stacking the deck" with later hospitalized infants

Hospitalizations

- 50% admitted at least once
- 12 (11%) hospitalized 5-9 times
- Under Age 1 rate 4 times non-DS population
Connections to Congenital Heart Defects

Cardiac Surgery (Dx CHD N = 112)
- 67% Hospitalized
- 36% Cardiac Surgery

<table>
<thead>
<tr>
<th>Number of children admitted to the hospital*</th>
<th>0 times</th>
<th>1 time</th>
<th>2-4 times</th>
<th>5-9 times</th>
</tr>
</thead>
<tbody>
<tr>
<td>CHD</td>
<td>33 (33.0%)</td>
<td>33 (28.7%)</td>
<td>33 (28.7%)</td>
<td>11 (9.6%)</td>
</tr>
<tr>
<td>non-CHD</td>
<td>69 (70.4%)</td>
<td>15 (15.3%)</td>
<td>14 (14.2%)</td>
<td>0 (0%)</td>
</tr>
</tbody>
</table>

* Excludes birth hospitalizations.
Hospitalizations
CHD vs non-CHD

Most frequent condition: Respiratory Infections
- 65% CHD
- 71% without CHD
- Even infants with CHD are often entering hospital for pneumonia, bronchitis, and other respiratory problems

C-Infant Mortality in DS

- How Many:
  - Deaths per 1,000 live births
  - N = 103
- When:
  - Age of Death
    - 1st day
    - Less than 28 day
    - Less than 1 yr
- Why:
  - Causes-correlates of death
How many: Infant Mortality in Down syndrome

<table>
<thead>
<tr>
<th>Authors and publication date</th>
<th>Location and year of study</th>
<th>Database used</th>
<th>DS infant mortality rate (%)</th>
<th>Population infant mortality rate (%)</th>
<th>Odds ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>Current study</td>
<td>Tennessee, 1990-2004</td>
<td>Tennessee Department of Health, Birth, Death Registry, and Population Proills, Metropolitan Atlanta Congenital Defects Program, Georgia vital records, State National Death Index</td>
<td>7.9%</td>
<td>27%</td>
<td>3.1</td>
</tr>
<tr>
<td>Li et al. (2010)</td>
<td>5 counties of metropolitan Atlanta, 1979-2003</td>
<td>Metropolitan Atlanta Congenital Defects Program, Georgia vital records, State National Death Index</td>
<td>6.4% (599/22)</td>
<td>1.1%</td>
<td>5.5</td>
</tr>
<tr>
<td>Whiting et al. (1993)</td>
<td>The Netherlands, January 1, 1979-December 31, 1998</td>
<td>Dutch Perinatal Surveillance Unit, Statistics Netherlands, National Death Registry, National Death Index</td>
<td>4.0% (100/22)</td>
<td>0.8%</td>
<td>1.7</td>
</tr>
<tr>
<td>Hasman et al. (1993)</td>
<td>5 counties of metropolitan Atlanta, 1979-1988</td>
<td>Metropolitan Atlanta Congenital Defects Program, State of Georgia Certificate of Live Birth, National Death Index</td>
<td>7.1%</td>
<td>1.1%</td>
<td>6.6</td>
</tr>
<tr>
<td>Leonard et al. (1993)</td>
<td>Western Australia, 1960-1994</td>
<td>Birth Defects Registry, Maternal and Child Health Research Database</td>
<td>0.3%</td>
<td>0.5%</td>
<td>1.6</td>
</tr>
<tr>
<td>Elliot et al. (1990)</td>
<td>Western Australia, 1975-1989</td>
<td>Disability Services Commission of Western Australia Database, Western Australia Cancer Registry, Western Australia Death Index</td>
<td>0.5%</td>
<td>0.5%</td>
<td>1.0</td>
</tr>
<tr>
<td>Materni et al. (1990)</td>
<td>Italy, 1971-1989</td>
<td>Italian National Civil Birth Registry, Deaths Registry, National Death Index</td>
<td>20.2%</td>
<td>1.4%</td>
<td>14.4</td>
</tr>
</tbody>
</table>

*General population mortality rate obtained from published sources.

When?: DS v. TN Population Deaths in 1st Year

- DS Population
- General Population
Why?: Causes-Correlates

Summary: II-Health Issues

- Although great advances have been made in DS health care, issues remain in terms of:
  - A-Adverse Birth Outcomes
  - B-Early Hospitalizations
  - C-Mortality throughout 1st year of life
A-Adverse Birth Outcomes

• High levels
  - 20-25% of all DS births
  - OR’s from 2.2 (preterm) – 3.1 (LBW)
  - M weight gain & (to some extent) # of prenatal visits = sole predictors
  - Many “usual” predictors do not predict

B-Early Hospitalizations

• Experienced by ½ of sample
  - Most before 1st birthday
  - More often in CHD infants, who often also have multiple in-patient stays
  - Often for respiratory problems
C-Mortality in 1\textsuperscript{st} Year

- Many times more likely than in non-DS population
- More often beyond 1\textsuperscript{st} month
- Early = preterm & “born too soon”
- Later = heart-respiratory
Acknowledgements

- The Vanderbilt Kennedy Center’s Nicholas Hobbs Society
- The Greenfield Discovery Grant
- NICHD grants P30HD 15052 and R03HD 050468
- HRSA grant R40MC08957
- Tennessee Department of Health, Office of Health Statistics

<table>
<thead>
<tr>
<th>Samantha Goldman</th>
<th>Trent Rosenbloom</th>
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<tr>
<td>Meghan Burke</td>
<td>Stephanie So</td>
</tr>
<tr>
<td>Cole Beck</td>
<td>Jeremy Stephens</td>
</tr>
</tbody>
</table>

Lucas

END
J. L. Down Quotes

• “The hair is not black, as in the real Mongol, but of a brownish colour, straight and scanty. The face is flat and broad, and destitute of prominence. The cheeks are roundish, and extended from on another. The eyes are obliquely placed, and the internal canthi more than normally distant from one another.....The lips are large and thick with transverse fissures. The tongue is long, thick, and is much roughened. The nose is small. The skin has a slight dirty yellowish tinge, and is deficient in elasticity, giving the appearance of being too large for the body.”

J. L. Down Quotes

• “They have considerable power of imitation, even bordering on being mimics. They are humorous, and a lively sense of the ridiculous often colours their mimicry...They are usually able to speak; the speech is thick and indistinct, but may be improved very greatly by a well-directed scheme of tongue gymnastics...”
• “…whatever advance is made intellectually in the summer, some amount of regression may be expected in the winter.”