Lives Worth Living

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Lives Worth Living

• My journey
• Clinical Issues related to Children with trisomy 13 or 18
• Attitudes of healthcare providers
• New modes of perinatal testing
• What we can (should) learn from history
• Perceptions, bioethics and language
• Regaining our humanity
Survival For Children With Trisomy 13 and 18
Metropolitan Atlanta, 1968–1999

Lethal and incompatible with life...

Survival History of Trisomy 13 and 18

- 114 families with trisomy 18 children
- 48 families with trisomy 13 children

Problems With Trisomy Survival Data

- Most center based studies small, suffer from rare incidence
- Large registry studies unable to comment on care provided
- When interventions compared no studies report on non-feeding of infants as part of palliative care
- When interventions are described no details regarding care after postnatal diagnosis made (withdrawal of previously “aggressive” care)
- Inclusion of mosaics (though generally only 2-4% of trisomy cases)
- In old studies: Later diagnosis...some cases missed that had died
- In old studies: Later diagnosis...infants supported who today might not be
- In new studies: Maybe increased terminations for more severely affected babies so higher survivals
Survival of Trisomy 13 and 18 in the Current Era

- Largest population-based study of survival among children with T13 or T18 published to date
- 693 infants with Trisomy 13, 1113 infants with Trisomy 18
- Includes all trisomies (full, mosaic)

Living With Trisomy 13 and 18

Trisomy 13: Survival from 28 Days to 1 Year is 45%
Trisomy 18: Survival from 28 Days to 1 Year is 36%

Living With Trisomy 13 and 18

Trisomy 13: Survival from 28 Days to 5 Year is 38%
Trisomy 18: Survival from 28 Days to 5 Year is 33%

Variation in Survivals Trisomy 13

Variation in Survivals Trisomy 18

Survival of Individuals With Trisomy

<table>
<thead>
<tr>
<th></th>
<th>Ages</th>
<th>1 week</th>
<th>1 month</th>
<th>1 year</th>
<th>5 years</th>
<th>10 years</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Trisomy 13</strong></td>
<td></td>
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<tr>
<td>Birth</td>
<td>53% (45-60%)</td>
<td>42% (35-49%)</td>
<td>20% (14-26%)</td>
<td>15% (10-21%)</td>
<td>13% (8-19%)</td>
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<tr>
<td>1 week</td>
<td>75% (85-83%)</td>
<td>75% (85-83%)</td>
<td>36% (26-45%)</td>
<td>27% (19-36%)</td>
<td>23% (15-32%)</td>
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<tr>
<td>1 month</td>
<td>47% (35-57%)</td>
<td>35% (25-46%)</td>
<td>35% (25-46%)</td>
<td>30% (20-41%)</td>
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<tr>
<td>6 months</td>
<td>77% (64-88%)</td>
<td>59% (44-73%)</td>
<td>59% (44-73%)</td>
<td>51% (35-86%)</td>
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<tr>
<td>1 year</td>
<td>76% (58-87%)</td>
<td>76% (58-87%)</td>
<td>76% (58-87%)</td>
<td>65% (46-79%)</td>
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<tr>
<td>5 years</td>
<td>86% (62-95%)</td>
<td>86% (62-95%)</td>
<td>86% (62-95%)</td>
<td>86% (62-95%)</td>
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<tbody>
<tr>
<td><strong>Trisomy 18</strong></td>
<td></td>
<td></td>
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<td></td>
</tr>
<tr>
<td>Birth</td>
<td>50% (44-56%)</td>
<td>35% (29-41%)</td>
<td>13% (9-17%)</td>
<td>11% (8-16%)</td>
<td>10% (8-14%)</td>
<td></td>
</tr>
<tr>
<td>1 week</td>
<td>67% (58-74%)</td>
<td>67% (58-74%)</td>
<td>25% (17-32%)</td>
<td>22% (15-30%)</td>
<td>19% (13-26%)</td>
<td></td>
</tr>
<tr>
<td>1 month</td>
<td>36% (26-46%)</td>
<td>32% (23-42%)</td>
<td>32% (23-42%)</td>
<td>28% (19-38%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>6 months</td>
<td>78% (63-89%)</td>
<td>70% (54-83%)</td>
<td>70% (54-83%)</td>
<td>60% (44-75%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1 year</td>
<td>90% (71-97%)</td>
<td>90% (71-97%)</td>
<td>90% (71-97%)</td>
<td>77% (58-89%)</td>
<td></td>
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</tr>
<tr>
<td>5 years</td>
<td>86% (63-95%)</td>
<td>86% (63-95%)</td>
<td>86% (63-95%)</td>
<td>86% (63-95%)</td>
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</tbody>
</table>

Survival of Individuals With Trisomy

- Tracking Rare Incidence Syndromes (TRIS) project database based on TRIS Survey (2004)
- Recruitment procedures included parent-to-parent contact, listservs, Facebook, SOFT conferences, articles in the SOFT newsletter, blog posts through the Global Genes Project, and the TRIS project brochure.
- Focus is children living 2 months or longer
- “Hospice or no intervention”, “necessary interventions (enteral feeding, ventilator use)”, and “aggressive interventions (surgery)”

<table>
<thead>
<tr>
<th>Status at time of survey completion</th>
<th>Living n (%)</th>
<th>Deceased n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hospice care or no interventions (n = 5)</td>
<td>3 (60)</td>
<td>2 (40)</td>
</tr>
<tr>
<td>Necessary interventions (n = 46)</td>
<td>33 (71.7)</td>
<td>13 (28.3)</td>
</tr>
<tr>
<td>Aggressive interventions (n = 31)</td>
<td>23 (74.2)</td>
<td>8 (25.8)</td>
</tr>
</tbody>
</table>

a Categories are based upon highest level of care provided. For example, those who have received hospice have not received necessary or aggressive interventions and those who have received necessary interventions did not receive aggressive interventions.

Congenital Heart Disease (CHD) Surgery in Trisomy 13 & 18

- Cases reviewed from 1982-2008 in US Pediatric Cardiac Care Consortium (PCCC)
- 50 patients with trisomy 13 and 121 patients with trisomy 18
- 29 patients with trisomy 13 and 69 patients with trisomy 18 underwent intervention for CHD
- In-hospital mortality rates for patients with trisomy 13 or trisomy 18 were high: 27.6% and 13%
- In-hospital mortality rate for all surgical risk categories higher than that reported for the general population (10x higher)
- For discharges survivals far longer than previously reported

And.....in the US...STS Reporting

STS Congenital Heart Surgery
- 117 participants
- 57% publicly reporting

https://www.sts.org/congenital-public-reporting-module-search
Survival Without Severe Morbidity for ELBW Infants

One-Year Net Survival, Selected Cancers, Adults (Aged 15-99), England and Wales, 2010-2011

Breast is for female only. Laryngeal is for male only.

Five- and ten-year survival for 2010-2011 is predicted using an excess hazard statistical model. Survival for bowel cancer is a weighted average derived from data for colon (C18) and rectum cancer (C19-C20, C21.8).

Source: cruk.org/cancerstats
Breast is for female only.
Laryngeal is for male only

Five- and ten-year survival for 2010-2011 is predicted using an excess hazard statistical model.
Survival for bowel cancer is a weighted average derived from data for colon (C18) and rectum cancer (C19-C20, C21.8). Source: cruk.org/cancerstats.
### Developmental Progression for Trisomy 18 and 13

Mean chronological ages, developmental ages and developmental quotients for trisomy 18 and trisomy 13

<table>
<thead>
<tr>
<th>Age (years)</th>
<th>Trisomy</th>
<th>Chronological age (months)</th>
<th>Developmental age (months)</th>
<th>Developmental quotient</th>
<th>Number of children</th>
</tr>
</thead>
<tbody>
<tr>
<td>1–3</td>
<td>18</td>
<td>25.2</td>
<td>3.9</td>
<td>0.17</td>
<td>15</td>
</tr>
<tr>
<td></td>
<td>13</td>
<td>26.3</td>
<td>7.7</td>
<td>0.31</td>
<td>5</td>
</tr>
<tr>
<td>3–5</td>
<td>18</td>
<td>46.8</td>
<td>8.2</td>
<td>0.18</td>
<td>7</td>
</tr>
<tr>
<td></td>
<td>13</td>
<td>44.1</td>
<td>7.3</td>
<td>0.17</td>
<td>5</td>
</tr>
<tr>
<td>All ages</td>
<td>18</td>
<td>48.5</td>
<td>5.7</td>
<td>0.18</td>
<td>26</td>
</tr>
<tr>
<td></td>
<td>13</td>
<td>42.9</td>
<td>8.4</td>
<td>0.25</td>
<td>8</td>
</tr>
</tbody>
</table>

Modified and adapted from [18].

Obstetrician Attitudes Towards Trisomy 18

Attitudes towards T18, and expectations of outcome

<table>
<thead>
<tr>
<th>Attitudes towards T18 (n = 962)</th>
<th>Strongly/moderately disagree, n (%)</th>
<th>Strongly/moderately agree, n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>T18 is a lethal abnormality</td>
<td>72 (7.5)</td>
<td>813 (84.5)</td>
</tr>
<tr>
<td>A fetus with T18 should be treated no differently from any other fetus</td>
<td>721 (75.0)</td>
<td>110 (11.4)</td>
</tr>
<tr>
<td>Active treatment of a fetus or newborn with T18 is futile</td>
<td>163 (16.9)</td>
<td>601 (62.5)</td>
</tr>
<tr>
<td>T18 is compatible with the child having a meaningful life</td>
<td>759 (78.9)</td>
<td>79 (8.2)</td>
</tr>
<tr>
<td>T18 is incompatible with life</td>
<td>274 (28.5)</td>
<td>521 (54.2)</td>
</tr>
<tr>
<td>Infants with T18 should not be resuscitated at birth (n = 948)</td>
<td>269 (28.4)</td>
<td>421 (44.4)</td>
</tr>
</tbody>
</table>

Care not futile...the life is futile

Neonatology Attitudes Towards Resuscitation of An Infant With Trisomy 18 and Congenital Heart Disease

- “A significant proportion of providers seem to be willing to put aside professional responsibility to direct the treatment decision and instead concede to any decision that parents may make.”
- “There is a changing approach, largely driven by physicians' desires to honor parents' preferences.”
- “Causes some degree of pain and suffering without offering any reasonable hope of benefit.”
- Lethal 4 times, futile/futility 7 times
- “Abandoning the best-interest standard...and instead are adopting an ethic of abdication.”

Providers and % Choosing Termination for Different Fetal Anomalies

<table>
<thead>
<tr>
<th></th>
<th>DR</th>
<th>NICU-MAT</th>
<th>NICU-CH</th>
<th>Paeds</th>
<th>Obs</th>
</tr>
</thead>
<tbody>
<tr>
<td>n</td>
<td>31</td>
<td>38</td>
<td>46</td>
<td>99</td>
<td>65</td>
</tr>
<tr>
<td>Trisomy 21</td>
<td>58</td>
<td>58</td>
<td>61</td>
<td>43</td>
<td>73</td>
</tr>
<tr>
<td>Trisomy 18</td>
<td>71</td>
<td>74</td>
<td>83</td>
<td>74</td>
<td>75</td>
</tr>
<tr>
<td>Turner syndrome</td>
<td>47</td>
<td>58</td>
<td>54</td>
<td>19</td>
<td>38</td>
</tr>
<tr>
<td>CLCP</td>
<td>7</td>
<td>6</td>
<td>8</td>
<td>5</td>
<td>5</td>
</tr>
<tr>
<td>HLHS</td>
<td>55</td>
<td>58</td>
<td>80</td>
<td>61</td>
<td>62</td>
</tr>
</tbody>
</table>

CLCP Cleft lip and palate; HLHS Hypoplastic left heart syndrome. DR Delivery room nurse; NICU-MAT Maternity neonatal intensive care unit nurse; NICU-CH Children’s hospital NICU nurse; Peds paediatric residents; OB obstetric residents

The Bioethical Revolution

• Abandonment of Hippocratic Oath
  – Prohibited abortion and euthanasia
  – Total duty to the sick individual

• New Oaths
  – No mention of abortion or euthanasia
  – Variable references to “higher interest”, “justice”, “it may be within my power to take a life; this awesome responsibility must be faced with great humbleness.”
  – “I treat a sick human being whose illness may affect the person’s family and economic stability.”
  – “I am a member of society with special obligations to all my fellow human beings, those of sound mind and body as well as the infirmed.”

The Bioethical Revolution
Sanctity of Life vs Relativism (Human vs Person)

• All lives are not created equally
• Utilitarian
  – The welfare of the family or community
  – A duty for some to die
• Futile Care Theory
• Bioethics historian Albert R. Jonsen has called bioethics a “social movement.”
• Daniel Callahan, founder of the Hastings Center on the Bioethic Revolution
  – “The first thing those in bioethics had to do was push religion aside.”
  – “The final factor of great importance was the emergence ideologically of a form of bioethics that dovetailed nicely with the reigning political liberalism of the educated classes in America”

The Bioethical Revolution
Sanctity of Life vs Relativism (Human vs Person)

• “The traditional hard choices will have to be made with respect to what is to be preserved and strengthened and what is not, and that this will of necessity violate and ultimately destroy the traditional Western ethic with all that this portends. It will become necessary and acceptable to place relative rather than absolute values on such things as human lives, the use of scarce resources, and the various elements which are to make up the quality of life or of living which is to be sought. This is quite distinctly at variance with the Judeo-Christian ethic.”

• “Because many humans lack properties of personhood or are less than full persons, they are equal or inferior in moral standing to some non-humans. If this conclusion is defensible we will need to rethink our traditional view that these unlucky humans cannot be treated in the same ways we treat similar nonhumans. For example, they might be aggressively used as human research subjects and sources of organs.”

2. Beauchamp T. The failure of theories of personhood. Kennedy Institute of Ethics Journal. 9(1999);309-324
The Bioethical Revolution
Sanctity of Life vs Relativism (Human vs Person)

• “If criteria such as the costs (social, psychological, economic) for the potential parents are good enough reasons for having an abortion even when the fetus is healthy, if the moral status of the newborn is the same as that of the foetus and if neither has any moral value by virtue of being a potential person, then the same reasons which justify abortion should also justify the killing of the potential person when it is at the stage of a newborn.

• “When we decided to write this article about after-birth abortion we had no idea that our paper would raise such a heated debate. ‘Why not? You should have known!’ people keep on repeating everywhere on the web. The answer is very simple: the article was supposed to be read by other fellow bioethicists who were already familiar with this topic and our arguments [as] ... this debate has been going on for 40 years.

The Bioethical Revolution

• Georgetown Mantra\(^1\)
  – Autonomy, beneficence, justice, non-malfeasance\(^2\)
  – Practiced without any mooring in sanctity of life
  – In a relativistic world can be used to justify any outcome
• The “mantra” has been taught in medical, nursing schools for decades.
• Autonomy appears to rule increasingly in cases where individuals seek to end the lives of a child, loved one or themselves. (Brittany Maynard)
• Beneficence, justice and non-malfeasance are increasingly employed to override decisions to continue medical care in difficult cases. (Charlie Gard)
• Many ethics committees have assumed the role of quasi-judicial bodies.
• Is mainstream bioethics rational analysis with no predetermined ideology?
• Or as noted bioethicist Albert Jonsen writes is Bioethics a “social movement with a view toward the formation of public policy”\(^3\)

What Do We Say to Parents Whose Baby Has A Trisomy?

• Your baby will likely die before or at the time of birth (94%)
• Your baby will not live for more than a few months (88%)
• Your baby’s condition is lethal or incompatible with life (93%)
• Your child will be a vegetable (55%)
• Your baby will destroy your family or marriage (28%)
• If your baby survives his/her life will be meaningless (55%) or a life of suffering (68%)

“I found out that my daughter had Full T-18 when i was 18 weeks pregnant. OBs asked me 3 times to terminate, told me none of these babies survive to birth and if they did it was only for a few hours. I was even asked ‘Why would you want to give birth to a baby that is going to be no use to society?’"

“Who got the diagnosis I was asked if I minded waiting until tomorrow for the termination!?!?”

“An OB asked me if I wanted to burden my other kids with such a sibling. Another doctor (Ob/Gyn) told me these children lacked all will to live, that they were without a soul, unable to experience being alive.”
Language Which Pressures Parents Not to Pursue Newborn Interventions

• “I was told by a neo no one with trisomy 18 had EVER survived. I was told if somehow he did survive he would ruin my life. I was told he would have no quality of life.”

• “We found out about trisomy 18 days before we left for a trip to Africa. We were told ‘It doesn't matter where you give birth, the outcome will be the same for the baby - whether an elite hospital or the African bush.’”

• A GYN asked me if I had any children and I told him I had a daughter, about 9 mos old at the time, with F T18. "Oh”, he said with a sad face, “So you're just like counting down the days huh?“

• “There’s a dark cloud coming for her.”
What is Palliative Care?

• Palliative care is care given to improve the quality of life of patients who have a serious or life-threatening disease
  – Treatment continues as medical condition continues to be assessed

• Hospice offers medical care toward a different goal: maintaining or improving quality of life for someone whose illness, disease or condition is unlikely to be cured.
  – Focus on caring not curing
  – Generally not concurrent care in the US

Palliative Care for Trisomy 13 and 18 Patients

- Surveyed 332 parents on trisomy support social networks
- Answered questions about their 272 children
- Healthcare providers recommended comfort care at birth in all prenatally diagnosed cases
- Life-sustaining interventions "as for any other child" was chosen as a plan of care by 25% of parents
- Prenatal diagnosis strongest independent factor negatively associated with longevity
  - 64% with a prenatal diagnosis died in <24 hr, only 47% were DC’d home
  - With postnatal diagnosis 1% died in < 24 hr and 87% DC’d home (P < 0.01)

Palliative Care for Trisomy 13 and 18 Patients

• Palliative care elements
  – Prenatal diagnosis: Warmth, skin to skin care, medication for comfort and bereavement/psychological support
  – Postnatal diagnosis (median age of 6 days): Various interventions, including oxygen, ventilation, tube feeding and intravenous fluids,

• With one exception, death in the first 24 hr of life was exclusively seen in children with a prenatal diagnosis

Palliative Care for Trisomy 13 and 18 Patients

• “It seems palliative care for children with prenatal diagnosis is directed to a goal of having as short a survival as possible delivery.”

• “Survival for trisomy infants is possible after a short trial of respiratory support.”

• “Parents of almost half the children discharged on comfort care later decided to consider surgical interventions, because their child exceeded expectations. Most parents had been told their child was ‘incompatible with life’ and would live a meaningless life of suffering.”

Palliative Care for Trisomy 13 and 18 Patients

• “It seems to us that neither a universal imposition of comfort-care nor a universal application of intensive care and invasive surgery is appropriate.”

• As clinicians
  – With equipoise carefully examine available data
  – Current status of practices related to care from palliation to intensive interventions
  – Rise above personal prejudices
  – Listen to the voices of families imploring us to consider their opinions regarding the value of the life of a child with trisomy 13 or 18.

The Tyranny of the Self Fulfilling Prophecy in Trisomy 13 and 18

• A false description of a circumstance evokes behavior that makes the original false conception come true.
  – “The specious validity of the self-fulfilling prophecy perpetuates a reign of error.” (Robert Merton)

• When a condition is predicted as lethal, potentially lifesaving treatments are withheld. As a result, patients who might have survived will then die, perpetuating the belief that the condition is lethal.

• Lethality begets lethality.

Why Do Physicians Often Challenge Parents Fighting For The Life of a Child With A Trisomy Condition?

• Many of us taught these children do not survive to be born...beyond an hour...beyond a day...beyond a month....beyond a year...
• Many of us have not seen a child with trisomy survive
• Some do not believe that the mental disabilities characterizing trisomy are worth living with (beneficence)
• Some personally view severe disability as equal to suffering and pain (beneficence, non-malfeasance)
• Some believe they are able to see what parents cannot regarding the future
• Some do not believe resources should be “wasted” on these babies (justice)
A Tale of Three Trisomies: Selecting the Road Previously Not Taken

- Until the 1980s, Down syndrome was characterized as severely life limiting
- A life with little meaning and institutionalization encouraged
  - A life expectancy of 8–12 years in 1949 for individuals with Down syndrome
- Disability rights groups organize for those with special needs (1975: PL 94-142)
- Medical literature through the 1970s shifts terminology from “defective mongoloids” to “mongoloids” to trisomy 21 to Down syndrome
- Baby Doe case in 1982 (Indiana)
- Delays in diagnosis of AV Canal, and failure to offer repair despite acceptable levels of pulmonary vascular resistance, persisting into the 1990s

A Tale of Three Trisomies: Selecting the Road Previously Not Taken

• “Survival of infants with T18 is not improved with aggressive obstetric or neonatal care.”

• “The natural history of trisomy 18 is well studied, and our results are in keeping with the findings of others.”

• Similar statements were made by pediatricians regarding Down syndrome in 1980 when life expectancy was 25 years.

• As for Down syndrome families, trisomy 13/18 families are committed to loving potentially technology dependent children with significant impairments

• Trisomy families, with social media support, are mandating transparency and truth from us as medical providers

The Meaning of Words

• “Many clinicians object to life-sustaining treatment of infants with trisomy 13 and 18. These views are based on 2 ideas. First, that these trisomies are uniformly fatal or lethal conditions. Second, that the burdens of treatment under these circumstances outweigh the benefits. **These views are no longer tenable.** Many infants with these trisomies survive for years. Many parents report that infants with trisomies have an acceptable quality of life and are valued members of families.”
  — John Lantos

• An accurate generic description for the trisomy 13 and 18: life limiting conditions.

Parental Views of Their Children With Trisomy 13 and 18

- Survey of 332 families in trisomy support social networks...describing 272 children
- Of families with a full trisomy 13 or 18 child 40% lived > than a year, 21% lived at least 5 years
- For those whose children had died, 89% reported the overall experience of their child’s life was positive.
- In families where a child lived longer than 3 months, 50% stated that their child experienced more pain than other children
- 50% recognized that caring for a special needs child was more difficult than they thought it would be
- 98% reported that this child enriched their life.
- Of families with other children, 82% felt that this child had a positive effect on siblings.
- When all parents were asked if they would continue the pregnancy if they discovered they were expecting another child with trisomy 13 or 18:
  - 8% responded negatively
  - 9% were unsure
  - 83% responded positively or said they would not do prenatal testing to determine if this was the case

Clinical Challenges in Caring for Infants With Trisomy 13 and 18

• Optimal delivery...Cesarean or Vaginal Delivery?
• Administration of antenatal steroids for PTB (in US rec to 37 weeks GA)
• Central apnea...or is it?
  – Seizures or airway obstruction (tongue, PLTB malacia, subglottic stenosis)
  – A large percentage of trisomy 18 babies, in my experience, have airway obstruction.” (Dr. Glenn Green)
  – If central apnea is there a role for caffeine?
• Types of supportive measures and benefit
  – Use of non-invasive airway support in hospital and at home (HFNC, nasal cpap devices)
  – Tracheostomy
• Cardiac surgery
  – Coarc, PDA, VSD (STAT 1 and 2)
  – More complex surgeries
Non-Invasive Perinatal Testing (NIPT)

- During pregnancy, the mother's blood contains fragments of the developing baby’s DNA
- Maternal blood can be analyzed for infant DNA fragments
- Analyzes fragments from specific chromosomes using specific DNA probes
- A variety of vendors with variable technologies
  - Harmony, Panorama, Verifi
- Greater sensitivity and specificity than prior screening, less false positive rates but...
  - SCREENING tests!
  - Positive Predictive Value (PPV)
• Sensitivity
  – Sensitivity measures the proportion of known positives that are correctly identified as such
  – 1,000 tested individuals are known to have a condition and 990 of them test “positive”, the sensitivity is 99%. Sensitivity = Detection Rate = 990/990 + 10 = 990/1000 = 99%

• Specificity
  – Specificity measures the proportion of known negatives that are correctly identified as such
  – If 99,000 out of 100,000 individuals are known not to have a condition and 98,000 test “negative”, the specificity is 99%. Specificity = 98,000/98,000 +1000 = 99%
NIPT Definitions

• False Positive Rate FPR)
  – The percentage of unaffected cases which test positive.
  – FPR=False Positives/False Positives + True Negatives
  – 1,000 of 99,000 unaffected individuals have a positive test result, the false positive rate is 1,000/1000 + 98,000 = 1000/99,000 = .01 or 1%.

• Positive Predictive Value (PPV)
  – PPV represents the proportion of positive test results that are truly positive. It answers the question: “If my test is positive, what is the chance my baby is truly affected?”
  – It includes consideration of how rare or common the condition is
  – PPV = (sensitivity x prevalence) / ((sensitivity x prevalence) + (1 – specificity)(1 – prevalence))

• NIPT PPV Calculator: https://www.perinatalquality.org/Vendors/NSGC/NIPT/
• 1,000,000 NIPT tests with reported sensitivity 97.4% and specificity 99.8%
• 30yo mothers, 367 infants with Trisomy 18
• Test reaches 50% PPV for mothers at 30, 37 and 40 years for Trisomy 21, 18 and 13 respectively
Transparency in NIPT

Exceptional positive predictive value (PPV)

Positive Predictive Value (PPV) is the likelihood that a positive test result is a true-positive. PPV varies by population.

Harmony’s extremely low false-positive rate of less than 0.1% gives it a high PPV for trisomy 21. Harmony has a PPV for trisomy 21 of 63% in pregnancies in women age 35, where the incidence of fetal trisomy 21 is 1 in 249. In contrast, for this same population, the PPV of traditional first trimester screening is 6%. 

<table>
<thead>
<tr>
<th></th>
<th>DETECTION RATE</th>
<th>FALSE-POSITIVE RATE</th>
<th>Positive Predictive Value for 30 YO Mother</th>
</tr>
</thead>
<tbody>
<tr>
<td>Trisomy 21</td>
<td>&gt;99%</td>
<td>&lt;0.1%</td>
<td>61%</td>
</tr>
<tr>
<td>Trisomy 18</td>
<td>97.4%</td>
<td>&lt;0.1%</td>
<td>22%</td>
</tr>
<tr>
<td>Trisomy 13</td>
<td>93.8%</td>
<td>&lt;0.1%</td>
<td>10%</td>
</tr>
</tbody>
</table>

Positive predictive value (PPV) and incidence

PPV depends on the incidence of the condition being tested. The rarer the condition, the higher the probability a positive result is a "false positive".

Testing for extremely rare conditions (1 in 10,000 incidence rate) in a routine genetic test may:

- Increase the cumulative false-positive rate of the entire test
- Substantially lower the overall PPV of the test

PPV transparency at https://www.perinatalquality.org/Vendors/NSGC/NIPT/
Test reaches 50% PPV for mothers at 30, 37 and 40 years for Trisomy 21, 18 and 13 respectively.
The Parental Journey With A Life Limiting Condition

Personal Pregnancy Experience
- Grieving Multiple Losses
- Arrested Parenting
- “My Baby Is a Person”

Interactions with Others
- Fragmented Health Care
- Disconnected Family and Friends

• Utterly Alone

Acknowledged Dependence

• Given the uniqueness of the circumstances involving life limiting prenatal diagnoses, parents need a local community responsive to distinct needs
  – Prenatal vs postnatal support
• There are no private decisions; every choice affects the persons to whom they are bound
  – Family, friends
  – Local community...including the medical community
• The nature of these supports drive decisions
• This dependence can be a source of courage, love, and hope...or despair
• Which it is depends largely on the character of the community in which parents are embedded.

What About Us? Acknowledged Dependence

- A community that recognizes unique bond of trust and love between a parent and child
- A refusal to see the child merely as a medical complication or a constellation of limitations that produce suffering
- An appreciation for the suffering parents’ experience
  - False hope: This life will include suffering but it will summon love.
  - Terminating the pregnancy: The specter of conditional maternal/parental love
- A community that commits itself to assisting the parents in recovering meaning after the disappointment of unfulfilled hopes
- Goods grounded in the virtues of acknowledged dependence promote genuine human flourishing...they preserve our humanity

The Evolving UNC Approach

• Multidisciplinary leadership team to review current data on trisomy conditions and formulate approach to care of infants with trisomy
  • Includes OBs, MFM, Ethics, Chaplains, General Peds, Neos, Peds Surgery, Peds CT Surgery, OB and Peds Nurses, housestaff
• Elimination of “lethal” language
• All cases reviewed at High Risk Perinatal Conference
• Partner with individual families
  – Meet with family after initial workup completed (including prenatal echo)
  – Assignment to a perinatal Case Manager and referral to Supportive Care Team
  – Review current data and openly inform families
  – Acute and long term medical challenges with recognition of joy this life can also bring
  – Identify parental expectations for pregnancy
  – Develop prenatal, delivery and postnatal care plan that includes
    • Emphasis on the value of this pregnancy
    • Discussion of antenatal testing, intervention for distress, mode of delivery
    • Discussion of palliative care, resuscitation, intensive care and surgical interventions
Supporting Families Whose Child Is Diagnosed With A Life Limiting Disorder

• What is your baby’s name? Congratulations!
• Provide an honest appraisal of the data in conjunction with what is known about the baby
  – For infants with trisomy, every child is unique with variable medical challenges based on associated conditions
  – Discuss the range of limited survival and severity of developmental disabilities
  – Discuss the value of a limited life and attempt to support hope
• What do you hope for? What are your expectations?
  – A live birth?
  – Holding my baby? Having my family present to celebrate what may be a short life?
  – Supportive care (palliative care)?
  – Resuscitation, stabilization and postnatal assessment with planning based on these results?
• We will share this challenging journey with you
The Miracle of Life

"I know what you are thinking. You need a sign. What better one could I give but to make this little one whole and new? I could do it, but I will not. I am the Lord and not a conjurer. I gave this mite a gift I denied to all of you — eternal innocence. To you she looks imperfect — but to me she is flawless...She will never offend me, as all of you have done. She will never pervert or destroy the work of my Father’s hands. She is necessary to you. She will evoke the kindness that will keep you human. Her infirmity will prompt you to gratitude for your own good fortune.

"More! She will remind you every day that I am who I am, that my ways are not yours, and that the smallest dust mite whirled in the darkest spaces does not fall out of my hand ... I have chosen you.

"You have not chosen me.

"This little one is my sign to you.

"Treasure her!"

The Trisomy Touch: Preserving Our Humanity
Lives Worth Living

• “The moral test of government (and the people) is how they treat those who are in the dawn of life, the children; those who are in the twilight of life, the elderly; those who are in the shadows of life; the sick, the needy and the handicapped.”
  ~Last Speech of Hubert H. Humphrey

• “The two most important days in your life are the day you were born and the day you find out why.”
  ~Mark Twain
Lives Worth Living

Ethan

Moriah

Saskia

Danielle

Mareyah

Malakai

Brennagh