Down Syndrome Prenatal Testing:
Everything Your Group Should Know and Should Be Doing

Brian G. Skotko, MD, MPP
Clinical Fellow in Genetics

Children’s Hospital Boston
Massachusetts General Hospital
Brigham & Women’s Hospital
Dana Farber Cancer Institute
Disclosures

• No financial disclosures

• Volunteer in a non-paid capacity to National Down Syndrome Society National Down Syndrome Congress Massachusetts Down Syndrome Congress Band of Angels Foundation

• I have a sister with Down syndrome.
Goals

• Review the current and upcoming Down syndrome prenatal tests

• Review the national efforts regarding prenatal testing.

• Offer suggestions on what your affiliate organization can be doing
Down Syndrome

- Trisomy, chromosome 21
- Translocation, 14 and 21
- Mosaicism, chromosome 21
- 1 / 733 children
- About 400,000 families in US
- About 5,000 children born / yr

(National Down Syndrome Society & CDC)
Prenatal Diagnosis

Old recommendation: all pregnant women over the age of 35 be offered an amniocentesis

1978: National Institutes of Health (NIH)


New recommendation: “screening and invasive diagnostic testing should be available to all women . . . regardless of age.”

2007: American College of Obstetrics and Gynecology

2008: American College of Medical Genetics
Prenatal Diagnosis of Down syndrome

Prenatal Screening*

Triple Screen:
(βhCG, AFP, uE₃)

Quadruple Screen:
(βhCG, AFP, uE₃, inhibin-A)

First-trimester Combined:
(Ultrasound, βhCG, PAPP-A)

Integrative Screen:

Sequential Screen:
  Independent
  Stepwise
  Contingent

Prenatal Diagnosis

Chorionic Villus Sampling: ~99.9%
(10-14 weeks, ≤ 1% spont termin)

Amniocentesis: ~99.9%
(after 15th week; ≤ 0.25% spont term)

Upcoming Prenatal Tests for Down syndrome

1. Allele Ratio Analysis

2. Shotgun Sequencing
Allele Ratio Analysis

- **Risk:** A simple blood test, no risk to the fetus
- **Accuracy:** data questioned
- **Eligibility:** data questioned
- **Timing:** performed as early as 12 weeks of gestation
- **Availability:** perhaps as early as this year
- **Cost:** List price of $2,000; real cost for insurers about $700, less expensive than CVS or amniocentesis
- **Large-scale trial launched:** 10,000 pregnant women, 30 worldwide clinical sites, results available after product made available
- **Limitations:** not reliable for translocation or mosaicism
Shotgun Sequencing

- **Risk:** A simple blood test, no risk to the fetus
- **Accuracy:** so far, 100% sensitive, but data small sample sizes
- **Eligibility:** 100% of the population will be eligible for the test
- **Timing:** performed as early as 10 weeks of gestation
- **Availability:** Only in research labs right now
- **Cost:** Costs about $700, less expensive than CVS or amniocentesis
- **Advantages:** possible for translocation or mosaicism
Prenatal Diagnosis of Down syndrome

**Prenatal Screening***

- **Triple Screen:**
  - ($\beta$hCG, AFP, $uE_3$)

- **Quadruple Screen:**
  - ($\beta$hCG, AFP, $uE_3$, inhibin-A)

- **First-trimester Combined:**
  - (Ultrasound, $\beta$hCG, PAPP-A)

- **Integrative Screen:**

- **Sequential Screen:**
  - Independent
  - Stepwise
  - Contingent

**Prenatal Diagnosis**

- **Chorionic Villus Sampling:** $\sim$99.9%
  - (10-14 weeks, $\leq$ 1% spont termin)

- **Amniocentesis:** $\sim$99.9%
  - (after 15th week; $\leq$ 0.25% spont term)

- **cffDNA/RNA Test:** $\sim$100%

* *NEJM (2005), 353:2001-2011.*
With new prenatal testing, will babies with Down syndrome slowly disappear?

Brian G Skotko
Table 2  Worldwide effects of prenatal testing on the birth incidence of Down syndrome (DS)

<table>
<thead>
<tr>
<th>Reference</th>
<th>Location</th>
<th>Timeframe</th>
<th>Observed change in DS incidence (%)</th>
<th>Expected change in DS incidence* (%)</th>
<th>Realised change† (%)</th>
<th>Average realised change/year‡ (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cheffins et al 2000</td>
<td>South Australia</td>
<td>1982–1996</td>
<td>↓ 42</td>
<td>↑ 60</td>
<td>↓ 102</td>
<td>↓ 7</td>
</tr>
<tr>
<td>Bell et al 2003</td>
<td>North England</td>
<td>1985–1999</td>
<td>0</td>
<td>↑ 43</td>
<td>↓ 43</td>
<td>↓ 3</td>
</tr>
<tr>
<td>Ekelund et al 2008</td>
<td>Denmark</td>
<td>2000–2006</td>
<td>↓ 50</td>
<td>↑ 12</td>
<td>↓ 62</td>
<td>↓ 10</td>
</tr>
<tr>
<td>Egan et al 2008</td>
<td>USA</td>
<td>1989–2005</td>
<td>↓ 15</td>
<td>↑ 34</td>
<td>↓ 49</td>
<td>↓ 3</td>
</tr>
</tbody>
</table>

*Predicted or calculated change in the incidence of babies born with DS, reflecting advancing maternal age of pregnant women, absent prenatal testing. Not all papers adjusted for small changes attributable to spontaneous terminations between prenatal diagnosis and birth.
†Difference between observed change and predicted change in incidence of babies born with DS.
‡Average realised change per year based on the timeframe of the study.
NA, not available.
Are expectant mothers making “informed decisions”?

- non-directive counseling
- accurate information
- up-to-date information
- balanced information
Education of Medical Professionals

81% of medical students report they “are not getting any clinical training regarding individuals with Down syndrome”¹

58% of medical school deans say such training not a high priority¹

45% of ACOG fellows and junior fellows rated their residency training as “barely adequate or nonexistent.”²

Only 28% of ACOG fellows felt “well qualified” in prenatal genetic counseling.²

Emphasize positive aspects so that parents will favor carrying to term without suggesting it directly

Emphasize negative aspects so that parents will favor termination without suggesting it directly

Urge parents to carry to term

Try to be unbiased as possible

Urge parents to terminate

<table>
<thead>
<tr>
<th></th>
<th>Genetic Professionals</th>
<th>Physicians</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>(N = 1,084)</td>
<td>(N = 499)</td>
</tr>
<tr>
<td>Emphasize positive</td>
<td>2%</td>
<td>4%</td>
</tr>
<tr>
<td>Emphasize negative</td>
<td>86%</td>
<td>10%</td>
</tr>
<tr>
<td>Urge to carry to term</td>
<td>13%</td>
<td>13%</td>
</tr>
<tr>
<td>Urge to terminate</td>
<td>10%</td>
<td>10%</td>
</tr>
</tbody>
</table>

Mothers Who Chose to Terminate

• In Netherlands, women recruited prospectively before or during hospital admission for termination ≤ 24 wks

• 4 months after termination: 71 women completed survey (77% response rate)
  \[M = 38 \text{ years, not religious (44%), Catholic (27%), college (47%)}\]

• 97% of women described pregnancy as formerly wanted

<table>
<thead>
<tr>
<th>Percentage</th>
<th>Motivation</th>
</tr>
</thead>
<tbody>
<tr>
<td>92%</td>
<td>I believed the child would never be able to function independently</td>
</tr>
<tr>
<td>90%</td>
<td>I considered the abnormality too severe</td>
</tr>
<tr>
<td>83%</td>
<td>I considered the burden for the child <em>itself</em> too heavy</td>
</tr>
<tr>
<td>82%</td>
<td>I worried about the care of the child after my/our death</td>
</tr>
<tr>
<td>78%</td>
<td>I considered the uncertainty about the consequences of the abnormality too high</td>
</tr>
<tr>
<td>73%</td>
<td>I considered the burden too heavy for my other children</td>
</tr>
</tbody>
</table>
Reasons for Doubt

65% of women expressed some level of doubt

49%: My reason was in conflict with my feelings
43%: I had the feeling of killing the child
38%: My partner and I disagreed
“Medical caregivers are among the most important persons for women who decide to terminate pregnancy because of Down syndrome.”
Are expectant mothers making “informed decisions”? 
Toward Concurrence:
Understanding Prenatal Screening and Diagnosis of Down Syndrome from the Health Professional and Advocacy Community Perspectives

ACMG: American College of Medical Genetics
ACOG: American College of Obstetricians & Gynecologists
NSGC: National Society of Genetic Counselors
NDSS: National Down Syndrome Society
NDSC: National Down Syndrome Congress

June 17, 2009
Misperceptions Clarified

1. OBs recommend prenatal tests to reduce number of individuals in society with genetic conditions.

2. Purpose of offering prenatal diagnosis to all women is to decrease the number of children born with DS.

3. 90% of pregnancies prenatally diagnosed with DS are terminated.

4. NDSS and NDSC are pro-life organizations.

5. Genetic counselors with a master’s degree influence parents to terminate.

6. Prenatal screening and testing are performed exclusively to detect DS.
What Change is Needed?

1. Develop **standardized practice guidelines** on how to deliver prenatal diagnosis

2. Train **healthcare professionals** of today and tomorrow to deliver complete, consistent, nonjudgmental, noncoercive information.

3. Develop consistent, **gold-standard information** about prenatal testing for Down syndrome.

4. **Public education** about the lives and values of people with DS
Prenatal Diagnosis of Down Syndrome: How Best to Deliver the News

Brian G. Skotko,¹* Priya S. Kishnani,² George T. Capone³
and for the Down Syndrome Diagnosis Study Group

¹Division of Genetics, Department of Medicine, Children's Hospital Boston, Boston, Massachusetts
²Division of Medical Genetics, Department of Pediatrics, Duke University Medical Center, Durham, North Carolina
³Division of Neurology & Developmental Medicine, Department of Pediatrics, Kennedy Krieger Institute, Johns Hopkins Medical Institutions, Baltimore, Maryland
Prenatal Recommendations

1. Results of prenatal screening should be clearly explained as a risk assessment, not a “positive” or “negative” result.

2. Prior to CVS or amnio, discuss all reasons for prenatal diagnosis.

3. Healthcare professional(s) most knowledgeable about DS should deliver the news—most likely OB and genetic professional together.

4. If in-person visit not possible, news should be delivered over phone at pre-arranged time.

5. Answer: What is DS? What causes the condition?


7. Use non-directive language.

8. Offer up-to-date materials or bibliography.

9. Make follow-up appts, including specialists, as needed.
Postnatal Diagnosis of Down Syndrome: Synthesis of the Evidence on How Best to Deliver the News

AUTHORS: Brian G. Skotko, MD, MPP,a George T. Capone, MD,b and Priya S. Kishnani, MD,c for the Down Syndrome Diagnosis Study Group
Postnatal Recommendations

1. OBs and pediatricians should coordinate their messaging. Ideally, they would meet together with parent(s) to deliver the news.

2. Inform parents of suspicion for DS immediately, even if diagnosis is not yet confirmed.

3. Deliver diagnosis in a private room.

4. Parents should be informed together

5. The infant with DS should be present and referred to by name.
Postnatal Recommendations

6. Begin conversation with positive words, such as congratulations on the birth of the child.

7. Provide accurate, up-to-date information.

8. Limit discussions to medical conditions that the infant has or might develop within 1 year of age.

9. Connect to local parent support groups and/or other families.

10. Follow-up appointments should be arranged, as desired and needed.
What Change is Needed?

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4. **Public education** about the lives and values of people with DS.
Training Modules

• *Brighter Tomorrows* is an interactive online simulation that asks medical professionals to view virtual patient-doctor sessions and provide responses to questions and situations

• Developed in collaboration between physicians and parents

• In tests with 30 residents in OB/GYN and Pediatrics showed significant improvement in knowledge and level of comfort

• Access to online simulation: [www.brighter-tomorrows.org](http://www.brighter-tomorrows.org).

Prenatally and Postnatally Diagnosed Condition Awareness Act

**Purpose:** to ensure that more accurate, up-to-date information is given to mothers who have fetuses or children with Down syndrome

**October 8, 2008:** President Bush signed into law (Public Law 110-374)

**Funding Opportunities:** Once funds are available, hospital and departments could apply for competitive grants

**State version of the law:** Missouri and Virginia
Parent Advocacy Groups

- First Call Programs across the country
- Parents and persons with Down syndrome are serving as speakers at medical schools and residency lectures
- Parents and persons with Down syndrome are being invited to serve on hospital committees
What Change is Needed?

1. Develop **standardized practice guidelines** on how to deliver prenatal diagnosis

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4. **Public education** about the lives and values of people with DS
Gold-standard Prenatal Information

canisterbooks.com
What Change is Needed?

1. Develop *standardized practice guidelines* on how to deliver prenatal diagnosis

2. Train healthcare professionals of today and tomorrow to deliver complete, consistent, nonjudgmental, noncoercive information.

3. Develop consistent, *gold-standard information* about prenatal testing for Down syndrome.

4. Public education about the lives and values of people with DS
NDSS: My Great Story Campaign

SARA WOLFF
The PUBLIC SPEAKER

DO YOU HAVE A STORY? TELL US AT NDSS.ORG/StORIES

I have no fear of public speaking and have spoken to over 500 people.
I've been honored at the Waldorf Astoria.
I hosted events with Barbara Walters.
I starred in my own television commercial.
I believe in words like kindness and caring.
I have Down syndrome and this is my great story.

www.ndss.org
NDSS: My Great Story Campaign

TV Host Meredith Vieira:

TV Host Nancy O’Dell:

Actor John C. McGinley:

Actor Chris Burke:
WHO’S A BETTER TEAMMATE, YOU OR ME?

Did you know children with Down syndrome can excel in school and participate in team sports? Did you know they can live independent, rewarding lives as adults? What else don’t you know about Down syndrome? Contact your local Down syndrome organization or visit advocates.org to learn more.

WE’RE MORE ALIKE THAN DIFFERENT.

NDSC: More Alike Than Different Campaign

www.ndscccenter.org
What your group can do

• Education
• Legislation
• First Call Programs
• Media Opportunities
Promote a Continuum of Education
GRADE SCHOOL

• **Annual Library Book Drive**, donating books to local libraries and encouraging them to display copies during October (Down Syndrome Awareness Month)

• **Sponsoring social opportunities**, creating forums for children with and without Down syndrome to interact

• **Buddy Walks**, encourage families to get their children’s classmates to walk as a team!
Promote a Continuum of Education

HIGH SCHOOL & COLLEGE

• Bring parents and self-advocates to classrooms. Biology, embryology, genetics, biological anthropology, philosophy, and religion classes.

• Promote Best Buddy Programs. Providing resources, space, encouragement, www.bestbuddies.org

Professor Harris, UNC Professor of Embryology, “In my opinion, the moral thing for older mothers to do is to have amniocentesis, as soon during pregnancy as is safe for the fetus, test whether placental cells have a third chromosome #21, and abort the fetus if it does. The brain is the last organ to become functional. . . I know somebody who had a child like this, and it ruined their life.”

February 16, 2008
Promote a Continuum of Education

MEDICAL PROFESSIONALS

• Bring parents and self-advocates to classrooms. Genetics classes best option.

• Ask to sponsor a grand rounds session. Contact Pediatrics and OB/GYN Departments. Invite a scientists or physicians to present with support groups speaking at the end.

• Send copies of two research review papers to Pediatrics and OB/GYN Departments. Highlight the call to work collaboratively with parent support groups.

• Encourage local schools and hospitals to use Brighter Tomorrows. www.brighter-tomorrows.org
Prenatally and Postnatally Diagnosed Condition Awareness Act

1. Sign up for e-mails from the NDSS Policy Center and NDSC Policy Center.

2. Encourage your state to adopt a state version of the law.
First Call Programs & Projects

- Identify one volunteer per hospital. Contact should be re-made every 6 months with hospital.
- Hold trainings for first call responders. Best practices promoted; ideas exchanged.
- Update First Call packets. Sign-up at canisterbooks.com.
- Holiday campaigns. Parents and persons with Down syndrome are writing letters to their original obstetricians keeping them updated on their lives.
Media Opportunities

• Use controversies in the news to insert information about Down syndrome.

• Encourage your parents to write op-eds describing life with Down syndrome.

• Read www.patriciaebauer.com every day.
Acknowledgements

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www.brianskotko.com

Band of Angels Foundation