

**Prenatal and Postnatal Diagnoses of Down Syndrome: Delivering Results in our New Age of Genetic Testing**

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Band of Angels Foundation

www.massgeneral.org/downsyndrome

### Disclosure Statement

- I volunteer in a non-paid capacity to non-profits: Massachusetts Down Syndrome Congress, Band of Angels Foundation, National Center for Prenatal and Postnatal Down Syndrome Diagnoses Resources
- I have a sister with Down syndrome

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### Activity Objectives

Describe the **current prenatal testing on Down syndrome** available and soon to be available to expectant parents.

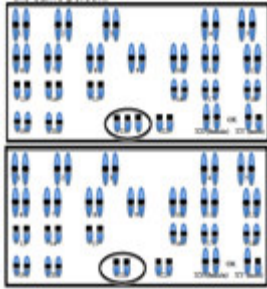
Define the **components of effective communication** between healthcare providers and parents when receiving a prenatal or postnatal diagnosis of Down syndrome.

Identify the **resources available to health care providers** wanting to improve their communication skills in this arena.

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### Down Syndrome

- Trisomy, chromosome 21
- Translocation Down syndrome
- Mosaic Down syndrome
- ~ 1 / 792 liveborns
- About 210,000 families in U.S.
- About 5,000 children born / yr



Dr. David G. Reardon & Heather E. Reardon MD, 2015, *Diagnosis of the Newborn, neonatal issues, and genetic inheritance with down syndrome in the United States*, *doi:10.1007/978-1-4939-7617-7*

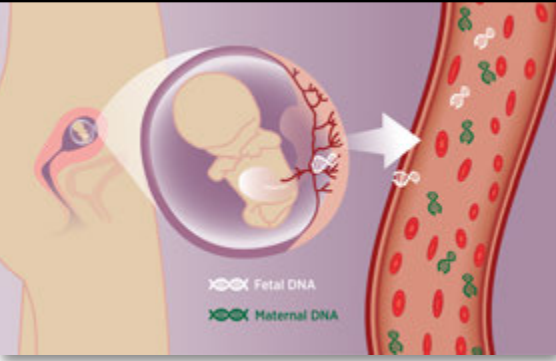
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### Prenatal Testing for Down Syndrome

Prenatal Screening	Prenatal Diagnosis
Triple Screen (βhCG, AFP, uE <sub>3</sub> ) Quadruple Screen (βhCG, AFP, uE <sub>3</sub> , inhibin-A) First-trimester Combined (Ultrasound, βhCG, PAPP- A) Integrative Screen Sequential Screen Independent Stepwise Contingent <b>~72%</b>	Chorionic Villus Sampling: ~99.9% (10-14 weeks, ≤ 1% spont termin) Amniocentesis: ~99.9% (after 15 <sup>th</sup> week; ≤ 0.25% spont term) <b>~2%</b>

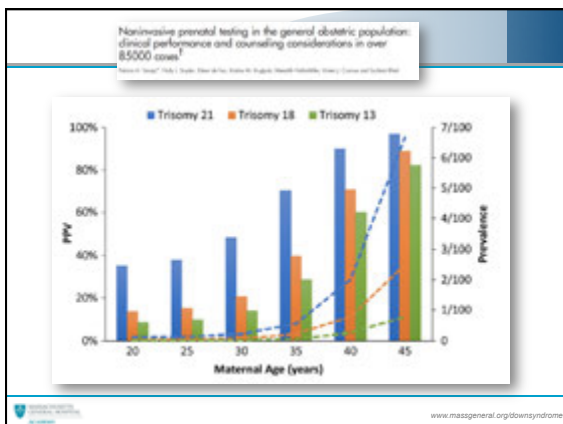
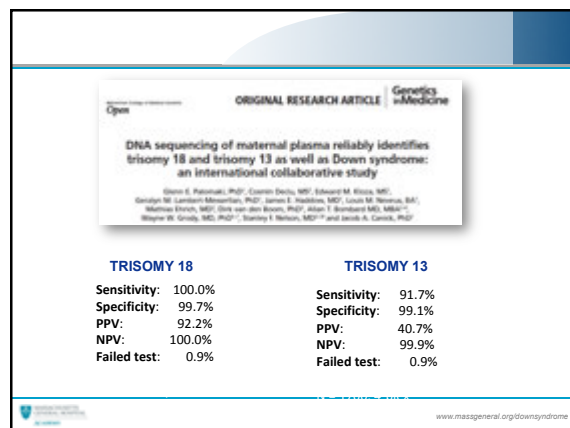
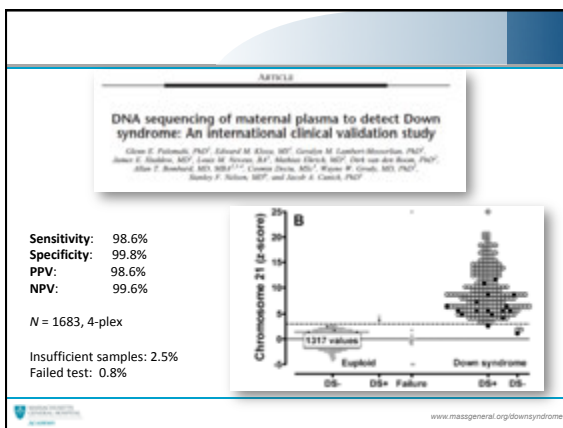
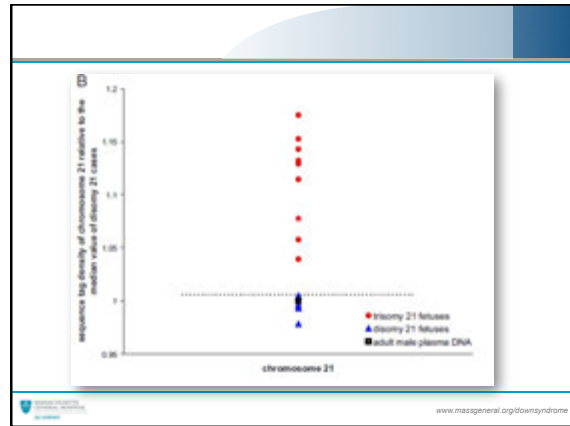
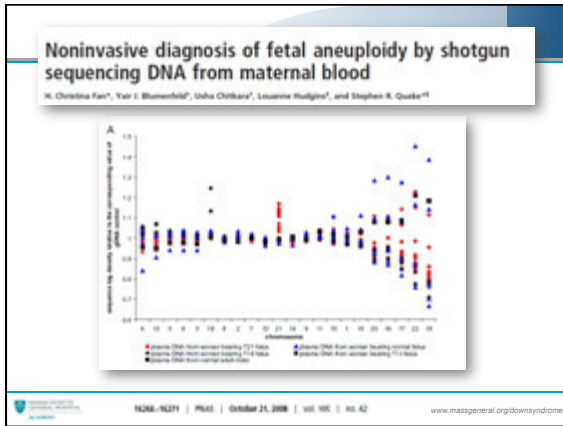
NEJM (2005), 353:2001-2011  
 APLM (2013), 137:921-926  
 Nature (2011), 469:289-291

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Courtesy of Ariosa Diagnostics

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- ### Shotgun Sequencing: cfDNA
- **Risk:** A simple blood test, no risk to the fetus
  - **Accuracy:** varies per condition
  - **Timing:** performed as early as 10 weeks of gestation
  - **Availability:** Now multiple companies in U.S. and world
  - **Cost:** dependent, in part, on insurance coverage
  - **Turn-around time:** ~10 days
  - **Advantages:** will pick up trisomy 21, translocation Down syndrome, and high-level mosaic Down syndrome
  - **Disadvantage:** doesn't distinguish types of Down syndrome
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### Other NIPS Limitations

- Unbalanced translocations from non-tested chromosomes, microduplications, microdeletions not validated
- Not able to distinguish specific forms of aneuploidy
- Does not screen for single-gene mutations
- Uninformative test results could lead to a delay in diagnosis or eliminate the availability of information for risk assessment
- Must keep timing of results in mind
- Does not screen for neural tube defects
- Does not replace the utility of first-trimester ultrasound
- Limited data on twins and higher-order pregnancies
- No role in predicting late-term pregnancy complications

ACMG statement on noninvasive prenatal screening for fetal aneuploidy | GREGG et al | www.massgeneral.org/downsyndrome

### Many Professional Position Statements

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### “High-risk” Expectant Mothers

**Box 1. Indications for Considering the Use of Cell Free Fetal DNA**

- Maternal age 35 years or older at delivery
- Fetal ultrasonographic findings indicating an increased risk of aneuploidy
- History of a prior pregnancy with a trisomy
- Positive test result for aneuploidy, including first trimester, sequential, or integrated screen, or a quadruple screen.
- Parental balanced robertsonian translocation with increased risk of fetal trisomy 13 or trisomy 21.

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### Prenatal Testing for Down Syndrome

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NIPS: ~99%  
~20%

NEJM (2005), 353:2001-2011

### Prenatal Testing for Down Syndrome

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### Prenatal Testing for Down Syndrome

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NIPS: ~99%

NEJM (2005), 353:2001-2011

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ARTICLE **Genetics in Medicine**

**Adherence of cell-free DNA noninvasive prenatal screens to ACMG recommendations**

Brian G. Skotko, MD, MPP<sup>1,2</sup>, Megan A. Alyse, PhD<sup>2</sup>, Kamal Raju, MD, MS, MPH<sup>1,2</sup>, Robert G. Best, PhD<sup>2</sup>, Susan Klugman, MD<sup>2</sup>, Mark Leach, JD, MA<sup>2</sup>, Stephanie Meredith, MA<sup>2</sup>, Mantha Michic, PhD<sup>2</sup>, Katie Stoll, MS<sup>2</sup> and Anthony R. Gregg, MD, MBA<sup>2</sup>

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**No NIPS Lab Fully Adherent to ACMG**

For the latest version of our analyses to adherence to ACMG recommendations:  
<https://prenatalinformation.org/table/>

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**Termination Rates High After CVS or Amnio**

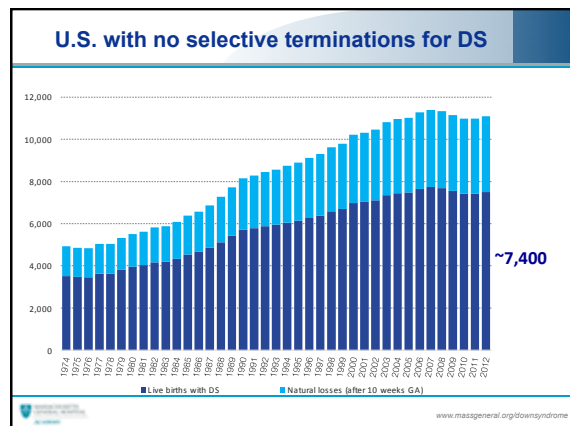
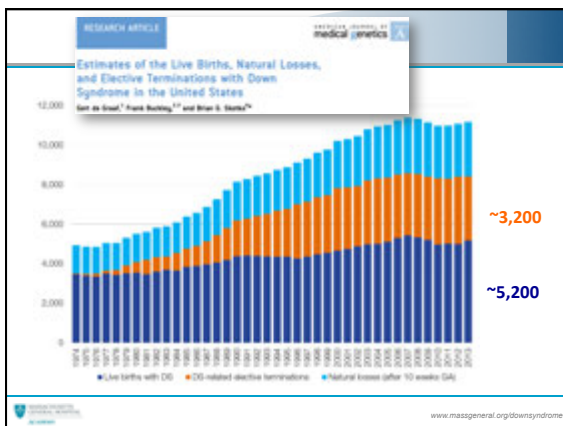
**Prenatal diagnosis of Down syndrome: a systematic review of termination rates (1995–2011)**

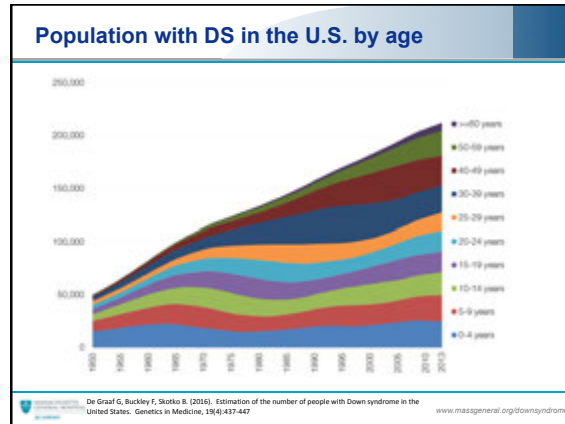
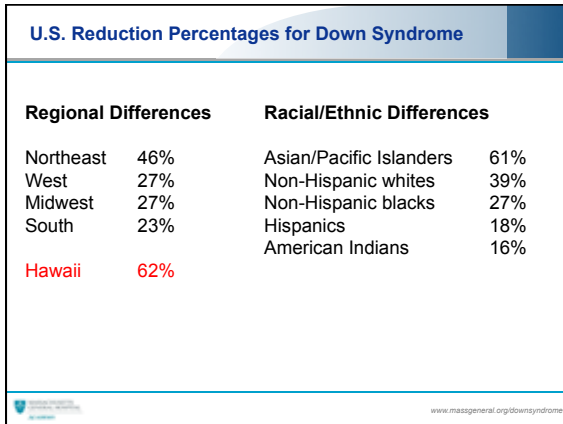
James L. Hank<sup>1\*</sup>, Deborah L. Ackema<sup>2</sup>, Suzanne McDermott<sup>3</sup> and Joyce G. Edrwick<sup>1</sup>

First author (Year)	State	Study years	Gestational age	N	Termination following PND of Down syndrome	%
Robinson (2004) <sup>17</sup>	CA	2000–2007	Second trimester (post-10 weeks)	466	265	57.1
Whe (2008) <sup>18</sup>	CA	1995–2000	Second trimester	1408	1036	73.3
Belin (2002) <sup>19</sup>	CA	1988–1991	Any time during pregnancy	531	469	88.2
Towse (2002) <sup>20</sup>	WI	1988–1990	Any time during pregnancy	173	135	77.9
Stevens (2008, 2009) <sup>11,12</sup>	WI	1987–2006	Any time during pregnancy	1371	1191	86.9
Hogan (2002) <sup>21</sup>	NE	2001–2002	Second trimester	15	14	93.3
Weighted average of all studies (n=14)				2724	2029	74.5
Weighted average of all studies from unique populations (n=12)				2263	1655	73.1
Weighted average of single race/ethnic study from each state (n=12)				614	429	69.9

*Prenatal Diagnosis* 2012, **32**, 142–153

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### Women Who Chose to Terminate

- In Netherlands, women recruited prospectively before or during hospital admission for termination  $\leq 24$  wks
- 4 months after termination: 71 women completed survey (77% response rate)  
[M = 38 years, not religious (44%), Catholic (27%), college (47%)]
- 97% of women described pregnancy as formerly wanted

Korenromp, et al. Maternal decision to terminate pregnancy after a diagnosis of Down syndrome. Am J Obstet Gynecol 2007;196:149.e1-149.e11.

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### Motivations for Termination

- 92%:** I believed the child would never be able to function independently
- 90%:** I considered the abnormality too severe
- 83%:** I considered the burden for the child *itself* too heavy
- 82%:** I worried about the care of the child after my/our death
- 78%:** I considered the uncertainty about the consequences of the abnormality too high
- 73%:** I considered the burden too heavy for my other children

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### Family Attitudes about Down Syndrome

Sent surveys to 4,924 families  
GA, MA, CO, NC, TX, and CA

2,044 **parents/guardians** from 1,407 households (29% response)  
822 **brothers/sisters**, ages 9 – 62 (19% response)  
284 **people with Down syndrome**, ages 12 – 52 (17% response)

3,150 TOTAL family members

Diversity among Hispanic origin and religion

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### Parents' Attitudes about Down Syndrome

**RESEARCH ARTICLE**  
**HAVING A SON OR DAUGHTER WITH DOWN SYNDROME: PERSPECTIVES FROM MOTHERS AND FATHERS**  
Brian G. Skotko,<sup>1,2\*</sup> Susan P. Levine,<sup>1†</sup> and Richard Goldstein<sup>3</sup>


\*Division of Genetics, Department of Medicine, Children's Hospital Boston, Boston, Massachusetts  
†Family Resource Associates, Inc., Stockbridge, New Jersey  
‡Department of Psychological, Behavioral, and Palliative Care, Dana-Farber Cancer Institute, Boston, Massachusetts

2,044 parents/guardians from 1,407 households (29% response)

- 99%** love their son/daughter with Down syndrome
- 97%** are proud of son/daughter with Down syndrome
- 79%** felt outlook on life was more positive because of son/daughter
- 5%** felt embarrassed, in general, by son/daughter with Down syndrome
- 4%** regret having their son/daughter with Down syndrome

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### Siblings' Attitudes about Down Syndrome




822 brothers/sisters, ages 9 – 62 (19% response)

- **97%** ages 9- 11, love their brother/sister with DS
- **94%** ages >12, are proud of brothers/sister with Down syndrome
- **88%** ages >12, felt they were better people because of sib
- **7%** ages > 12, felt embarrassed, in general, by sib with Down syndrome
- **4%** ages > 12, wish they could trade in sib with Down syndrome

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### Attitudes from People with Down Syndrome



284 people with Down syndrome, ages 12 – 52 (17% response)

- **99%** happy with their lives
- **99%** said that they love their families
- **97%** liked who they are
- **96%** liked how they look
- **86%** indicated they could make friends easily
- **4%** expressed sadness about their life

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### Expectant mothers making “informed decisions”?

- non-directive counseling
- accurate information
- up-to-date information
- balanced information

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### Toward Concurrence: Understanding Prenatal Screening and Diagnosis of Down Syndrome from the Health Professional and Advocacy Community Perspectives

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

June 17, 2009

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### 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

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### 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.

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### 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.

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### Pre-Test NIPS Pamphlet



Available in print, online, & in Spanish: <http://www.lettercase.org/prenataltesting>  
 Recognized by the National Society for Genetics Counselors for input by Genetic Counselors

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### Prenatal, Pre-Decision Info: Down syndrome



lettercase.org

www.massgenet.org/downsyndrome

### Prenatal, Pre-Decision Information

This booklet was prepared with assistance from the Down Syndrome Consensus Group which includes representatives of

- The National Society of Genetic Counselors*
- The American College of Medical Genetics and Genomics*
- The American College of Obstetricians and Gynecologists*
- American Academy of Pediatrics*
- Association of University Centers on Disabilities*
- Down Syndrome Education International*
- The National Down Syndrome Society*
- Down Syndrome Diagnosis Network*

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### Prenatal, Pre-Decision Information




It's digital. And free.

- English
- Korean
- Vietnamese
- Chinese
- Japanese
- Russian
- Somali
- Spanish

<http://www.understandingdownsyndrome.org/>

www.massgenet.org/downsyndrome

### Prenatal, Post-Decision to Continue



[www.downsyndromepregnancy.org](http://www.downsyndromepregnancy.org)

www.massgenet.org/downsyndrome



### Prenatally and Postnatally Diagnosed Condition Awareness Act



[www.downsyndromediagnosis.org](http://www.downsyndromediagnosis.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:**  
MA, MO, VA, KY, MD, DE, OH, PA, LA, FL, IL, MN, TX, IN



[www.massgeneral.org/downsyndrome](http://www.massgeneral.org/downsyndrome)

### MA Dept. of Public Health



[www.mass.gov/dph/downsyndrome](http://www.mass.gov/dph/downsyndrome)

[www.massgeneral.org/downsyndrome](http://www.massgeneral.org/downsyndrome)

### Massachusetts Down Syndrome Congress

**Parents' First Call Program** is a group of trained mothers and fathers available 24/7 for new and expectant parents

- Can match per religious, race, or language preference
- Can talk by phone, e-mail, or in-person
- Confidential discussions
- Free information given, different for prenatal and postnatal consultations

[www.mdsc.org](http://www.mdsc.org)

[www.massgeneral.org/downsyndrome](http://www.massgeneral.org/downsyndrome)

### Acknowledgements

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