

Noninvasive Prenatal Screening A Genetic Counselor's Perspective

Background

- Genetic Counseling defined:

“Professionals who have specialized education in genetics and counseling to provide personalized help patients may need, as they make their decisions about genetic health.”

– National Society of Genetic Counselors

- Certification from American Board of Genetic Counseling and State Licensure
- In the US, >4,000 board certified genetic counselors (GCs) currently practice in various specialties
- Prenatal genetic counselors comprise (~30%) of practicing GCs

Aneuploidy Testing: The Patient Experience

- Genetic counseling consultations (Why are patients seen and what to expect?)
- Screening tests vs. Diagnostic tests are often misunderstood
- Following abnormal screening results, patients often faced with anxiety over diagnostic odyssey.
 - Often be a delay waiting for appointment with specialist
 - Confirmation through invasive procedure has pregnancy risks
- Emotional attachment amplifies the stress

Clinical Experience in General Population

NEXT Study (2015) Cell-free DNA Analysis for Noninvasive Examination of Trisomy








Cohort	T21 Findings (Primary Analysis)			Clinical Outcomes			
	<i>N</i>	<i>Detection Rate</i>	<i>False Positive Rate</i>	<i>TP</i>	<i>FP</i>	<i>PPV</i>	<i>NPV</i>
NIPT <35 years	11,994	100% (82.4-100)	0.05% (N=6)	19	6	76.0%	100% (99.9-100)
NIPT All Patients	15,841	100% (90.7-100)	0.06% (N=9)	38	9	80.9%	100% (99.9-100)
Standard Screening All patients	15,841	78.9% (62.7-90.4)	5.4% (N=854)	30	854	3.4%	99.9% (99.9-100)
NIPT Performance			~100x lower FPR			~20x better PPV	Very high NPV

Norton, ML et al Cell free DNA analysis for noninvasive examination of trisomy. The New England Journal of Medicine April 2015; 372: 1589-1597.

One standard of care for all patients

- ~20% of pregnancies in US are to women considered high risk (>35yrs)
 - NIPS is available as a screening strategy and is well utilized
- ~80% of pregnancies are to women considered average/low risks (<35yrs)
 - NIPS access is sporadic and this potentially sets up two different standards of care.
- GOAL is to ensure that all patients are receiving best patients care but also to establish a single standard of care

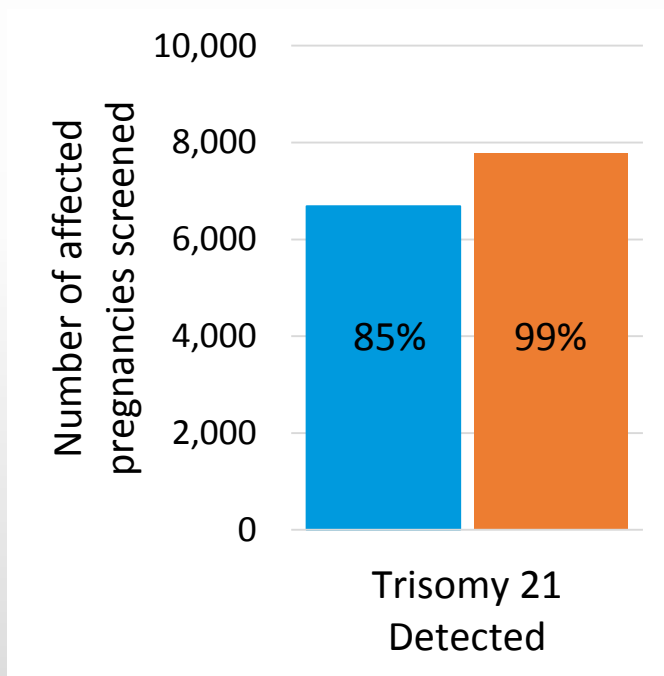
Professional Society Statements

 <p>ACOG THE AMERICAN CONGRESS OF OBSTETRICIANS AND GYNECOLOGISTS</p>	<p>Jan 2015</p>	<p>Any patient may choose cell-free DNA analysis as a screening strategy for common aneuploidies regardless of her risk status.</p>
 <p>ASHG THE AMERICAN SOCIETY OF HUMAN GENETICS</p> <p>ESHG EUROPEAN SOCIETY OF HUMAN GENETICS</p>	<p>March 2015</p>	<p>Comparably good results can be achieved in general obstetrical populations, making NIPT an alternative to current first-trimester screening protocols</p>
 <p>ispd International Society for Prenatal Diagnosis</p>	<p>April 2015</p>	<p>cfDNA screening as a primary test offered to all pregnant women [is currently considered an appropriate protocol option]</p>
 <p>ACOG THE AMERICAN CONGRESS OF OBSTETRICIANS AND GYNECOLOGISTS</p>	<p>May 2016</p>	<p>The sensitivity and specificity in the general obstetric population are similar to the levels previously published for the high-risk population</p>
 <p>ACMG</p>	<p>July 2016</p>	<p>Inform all pregnant women that NIPS is the most sensitive screening option for traditionally screened aneuploidies (i.e., Patau, Edwards, and Down syndromes)</p>
 <p>National Society of Genetic Counselors</p>	<p>October 2016</p>	<p>NSGC supports prenatal cell-free DNA (cfDNA) screening, also known as NIPT or NIPS, as an option for pregnant patients <risk not specified></p>
 <p>ACOG THE AMERICAN CONGRESS OF OBSTETRICIANS AND GYNECOLOGISTS</p>	<p>April 2017</p>	<p>For scenarios in which different testing options are acceptable alternatives, obstetrician-gynecologists and other health care providers should determine which tests will be offered as the standard in their practices</p>

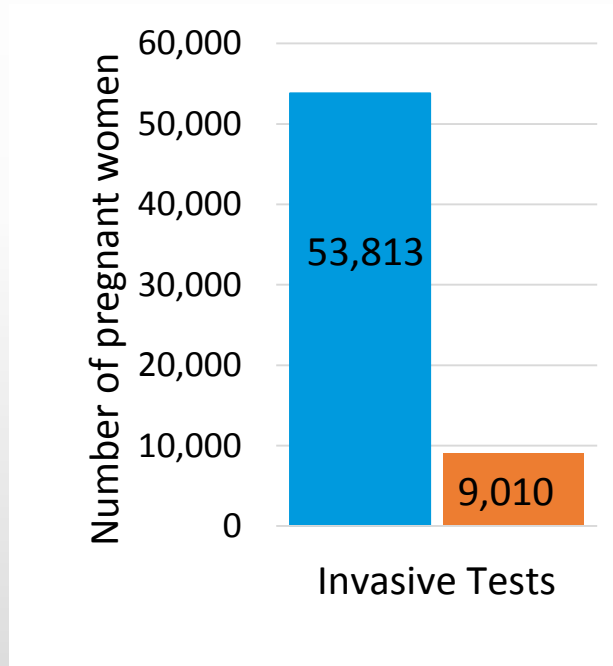
In Summary



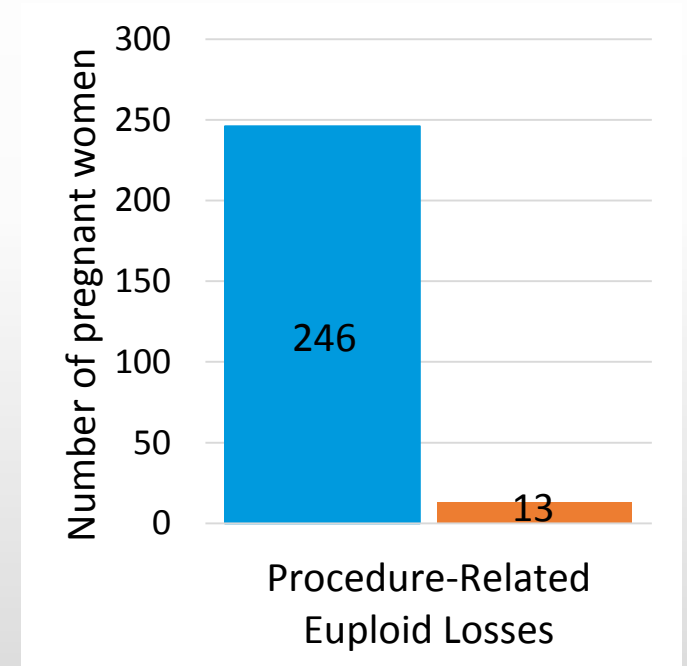
Better detection



Fewer false positives -> Fewer invasive procedures



Fewer procedure related losses



■ Conventional Screening ■ NIPS