Non-Invasive Prenatal Screening

and

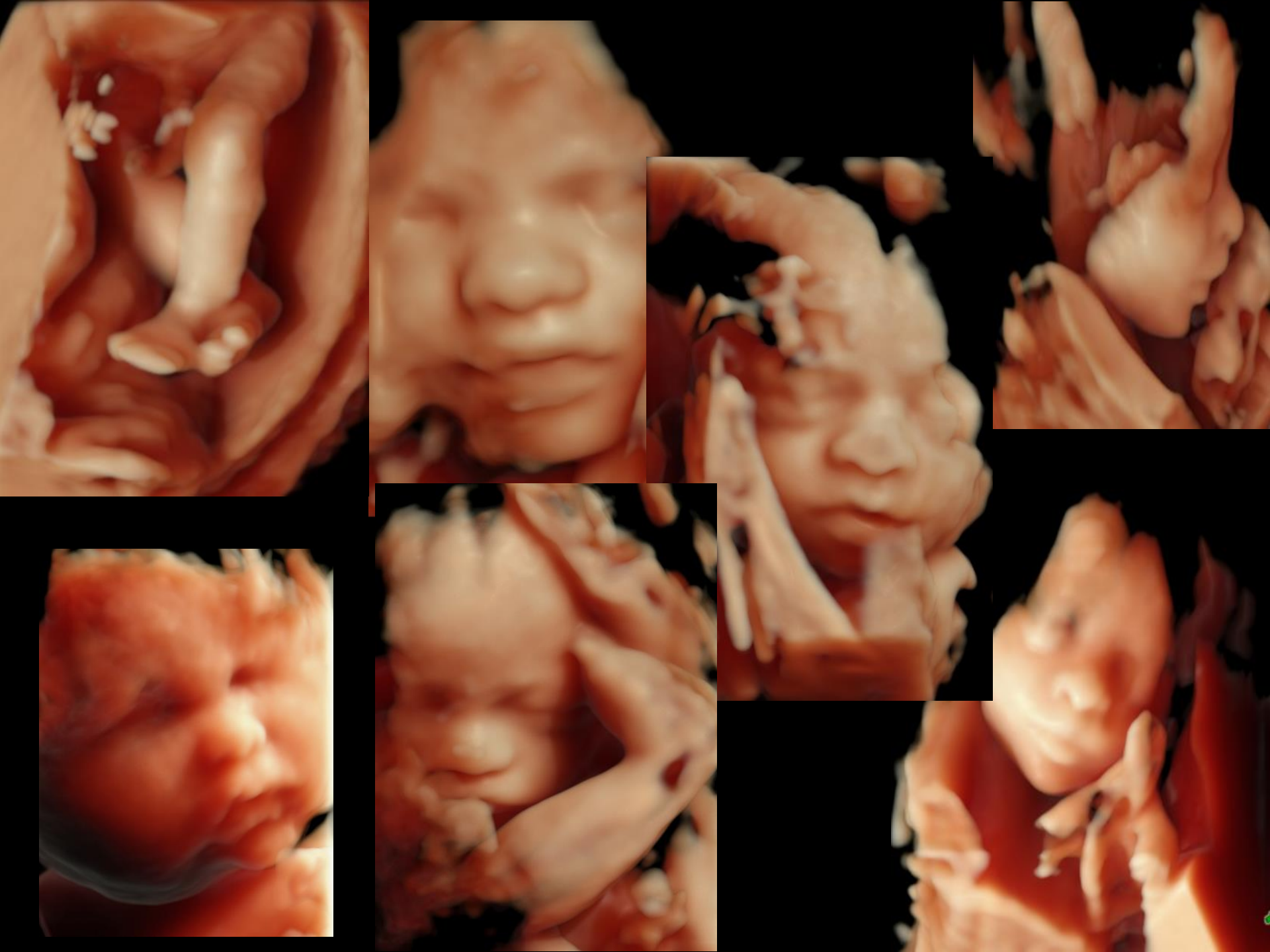
Other Screening

Dr Jay Marlow

Obstetrician and

Maternal Fetal Medicine

Sub-Specialist



Choice

- Nothing
- Combined Screening
- NIPT

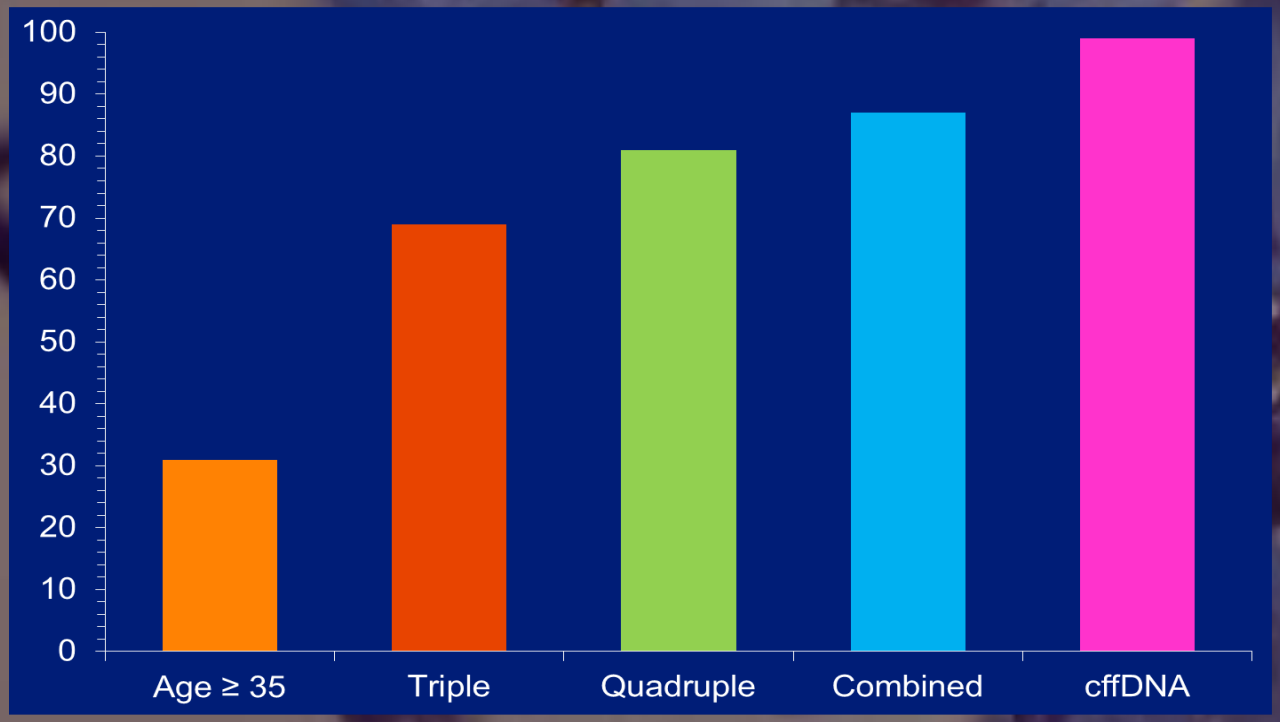
- Why? Knowledge? Options? Change care?

COMBINED FIRST TRIMESTER SCREEN

Maternal Risk of T21 increase with age

Age (yrs)	Risk for trisomy 21	
	At Birth	At 12 weeks
20	1 in 1527	1 in 898
25	1 in 1352	1 in 795
30	1 in 895	1 in 526
32	1 in 659	1 in 388
34	1 in 446	1 in 262
36	1 in 280	1 in 165
38	1 in 167	1 in 98
40	1 in 97	1 in 57
42	1 in 55	1 in 32
44	1 in 30	1 in 18

Aneuploidy Screening Approach: Observed Detection Rates

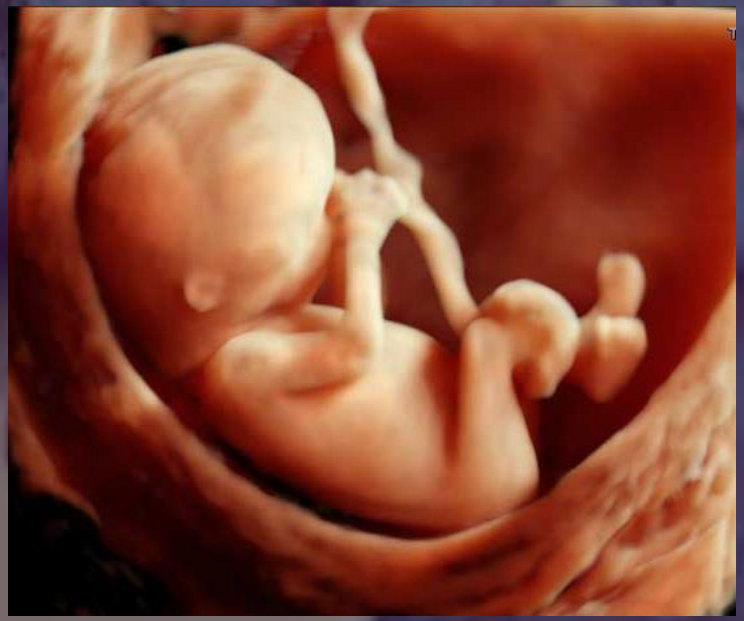


1960 1980 1990 2005 2011

CFTS

- Maternal bloods
  - From 10 weeks
  - PAPP-A
  - Free HCG
- Nuchal translucency
  - 11-13^{+6} weeks
- Combined
  - DR of 91-92%
  - FPR 5%

- However NSU
  - DR 72-75%

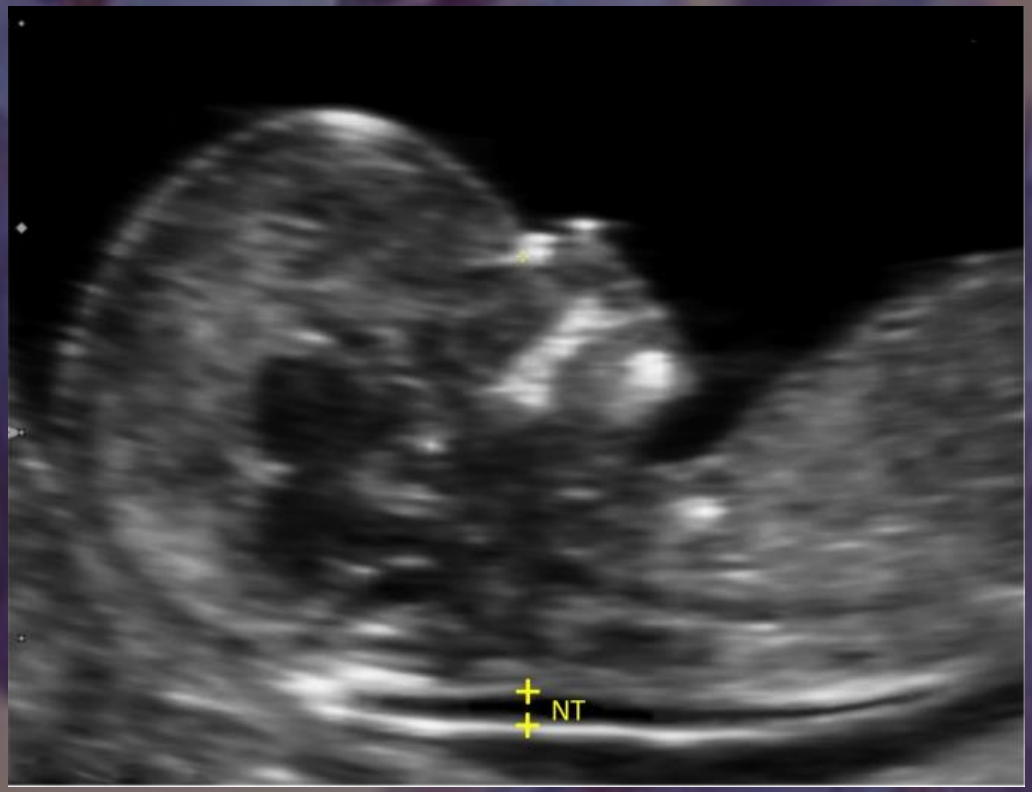


Nuchal Translucency

- Subcutaneous fluid-filled space located between back of fetal neck and skin
- Measured on USS between 11-13^{+6} weeks
  - *measurement is not valid outside of this time period*
- NT increases with gestational age

NT Standard (FMF)

- CRL 45 – 84mm
- Midline- Sagittal plane
- Mid sag face echogenic tip of nose
- Neutral position
  - not extended or flexed
- Away from amnion
- Head and thorax occupy >1/3 of the image
- Widest part of translucency measured
  - “on-to-on technique”



Nuchal Translucency

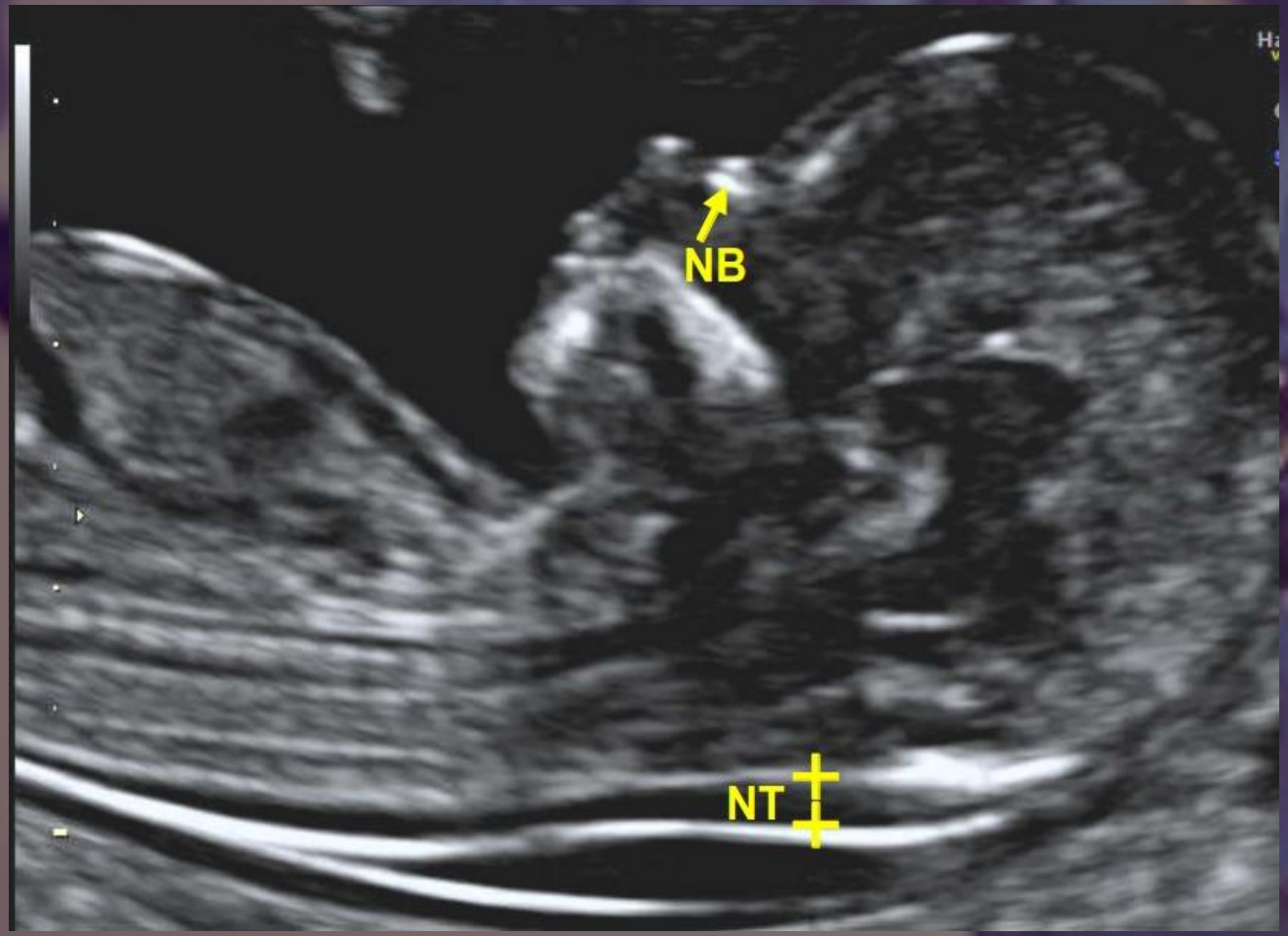
- Between 11-13^{+6} weeks >3.5mm considered elevated
  - Diagnostic testing indicated
  - Tertiary anatomy scan at 18-20 weeks
  - Fetal screening echocardiogram indicated ~24 weeks
- Increased NT thickness is associated with:
  - Trisomies 21, 18, 13, triploidy and Turner syndrome
  - Spontaneous fetal loss
  - With normal chromosomes:
    - *cardiac defects, diaphragmatic hernia, pulmonary defects, skeletal dysplasias*
    - *congenital infection*
    - *metabolic/haem disorders*
    - *rare single gene disorders*

Nicolaides. *Am J Obstet Gynecol* 2004;191:45
Souka *et al. Ultrasound Onstet Gyncol* 2001;18:9

Nuchal Translucency (mm)	Chromosomal abnormality (%)	Normal Karotype group			Alive and well given original NT (%)
		Fetal Death (%)	Major Anomaly (%)	Cardiac Anomaly (%)	
3.5-4.4	21.1	2.7	10	3	70
4.5-5.4	33.3	3.4	18.5	7	50
5.5-6.4	50.5	10.1	24.2	20	30
>6.5	64.5	19	46.2	30	15

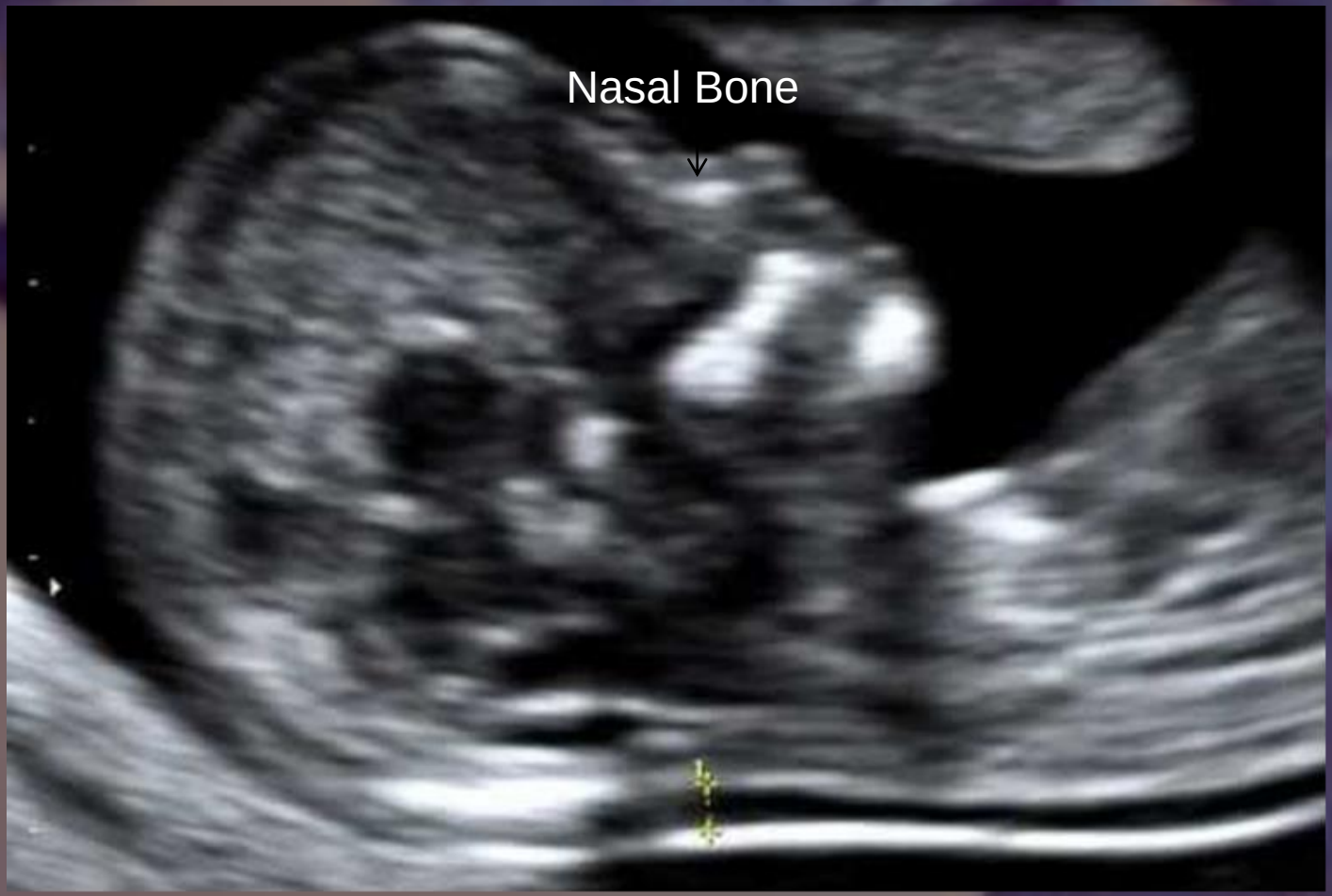
Chance of a normal birth varies with size of NT measurement

Nasal Bone

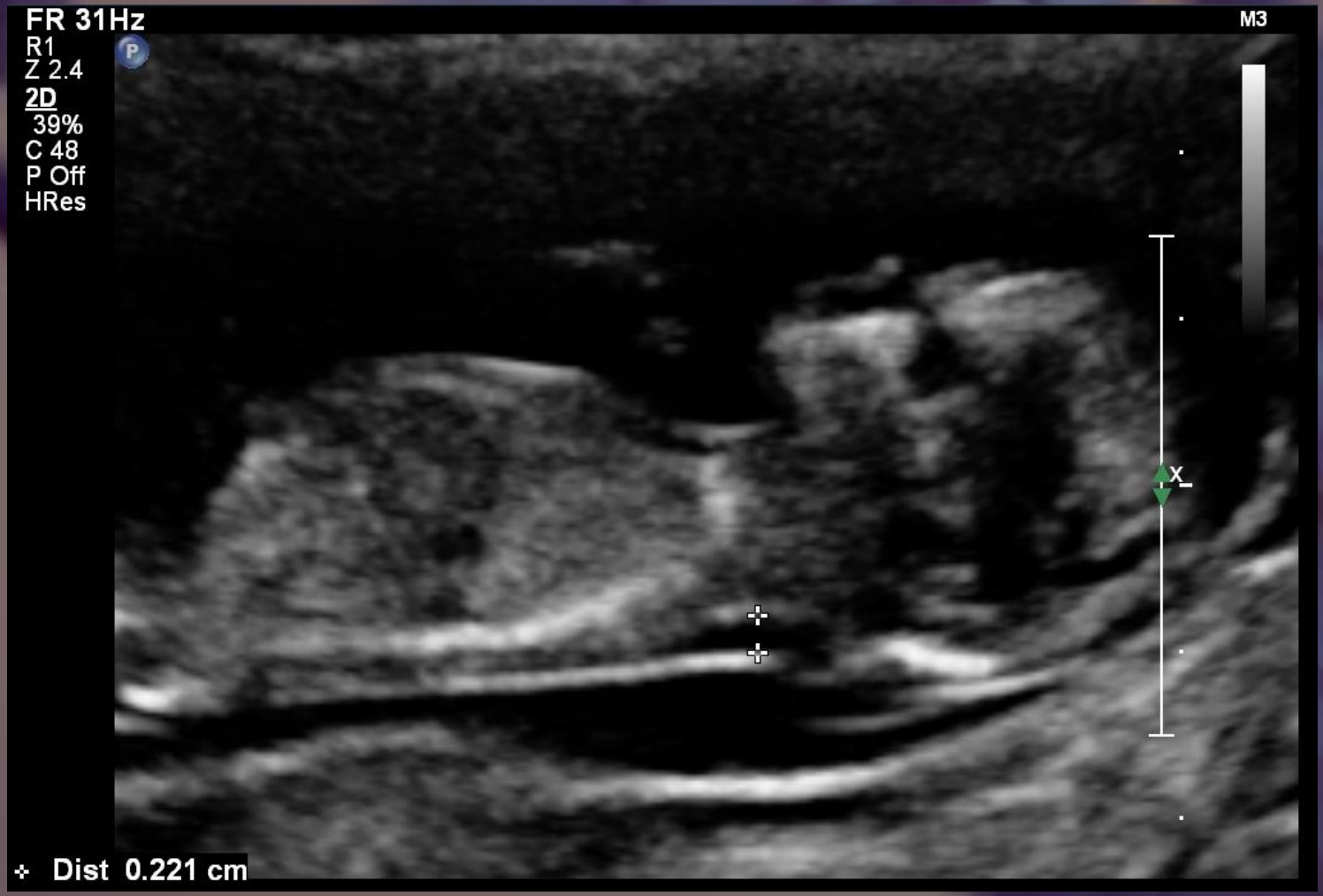



WHY IS OUR DETECTION
RATE SO LOW?

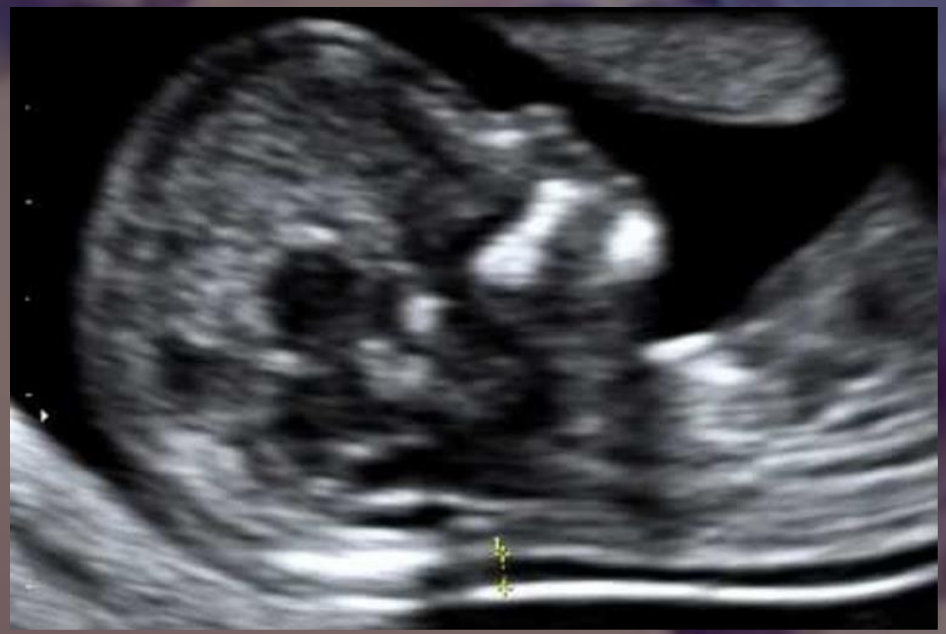
Standard View

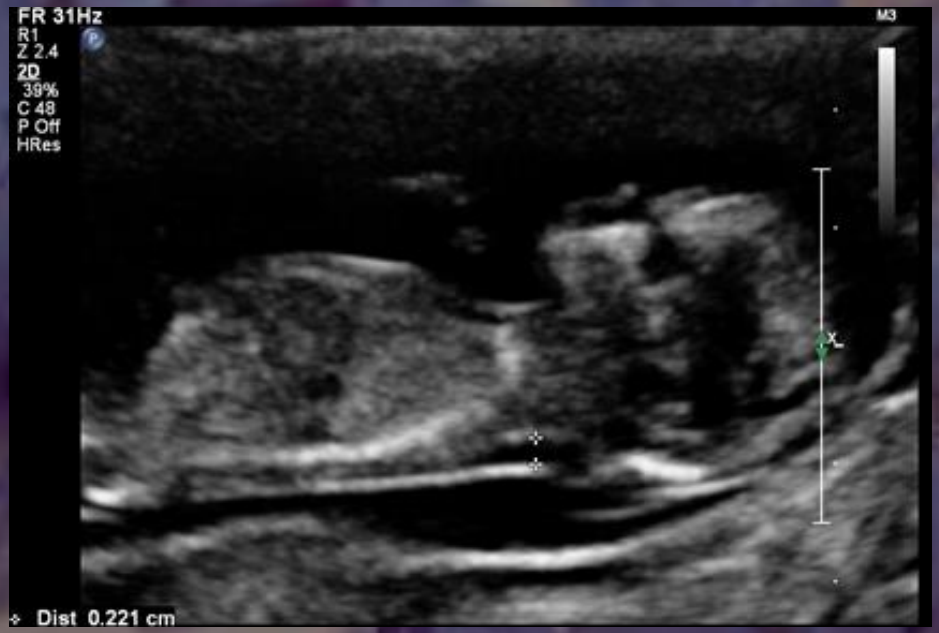


Case



Nuchal Comparison





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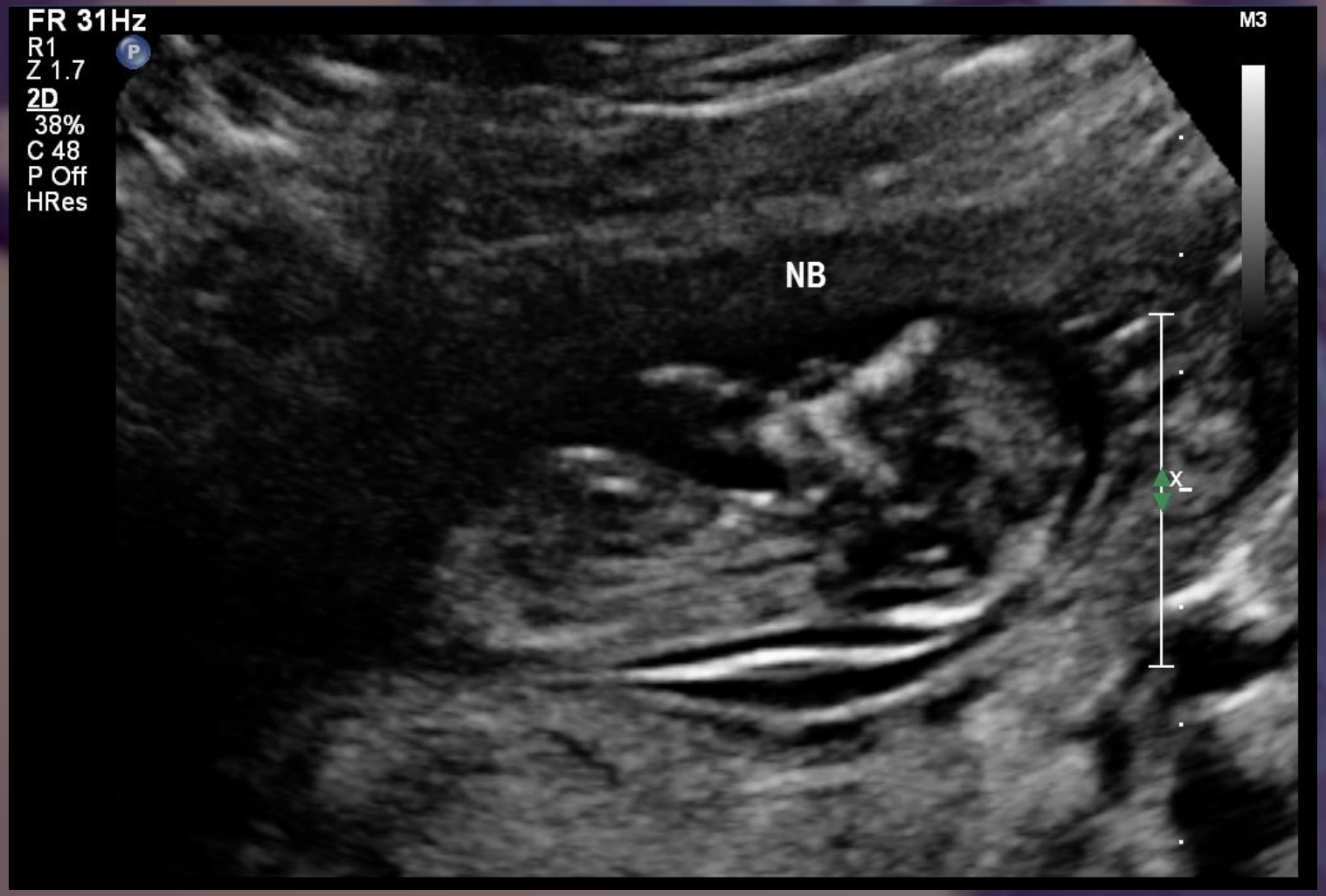
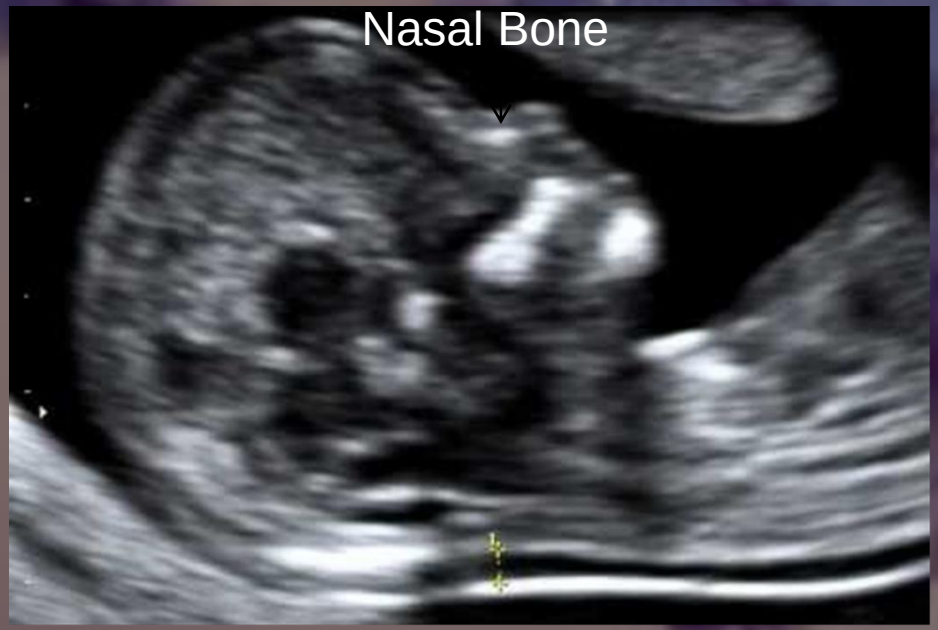
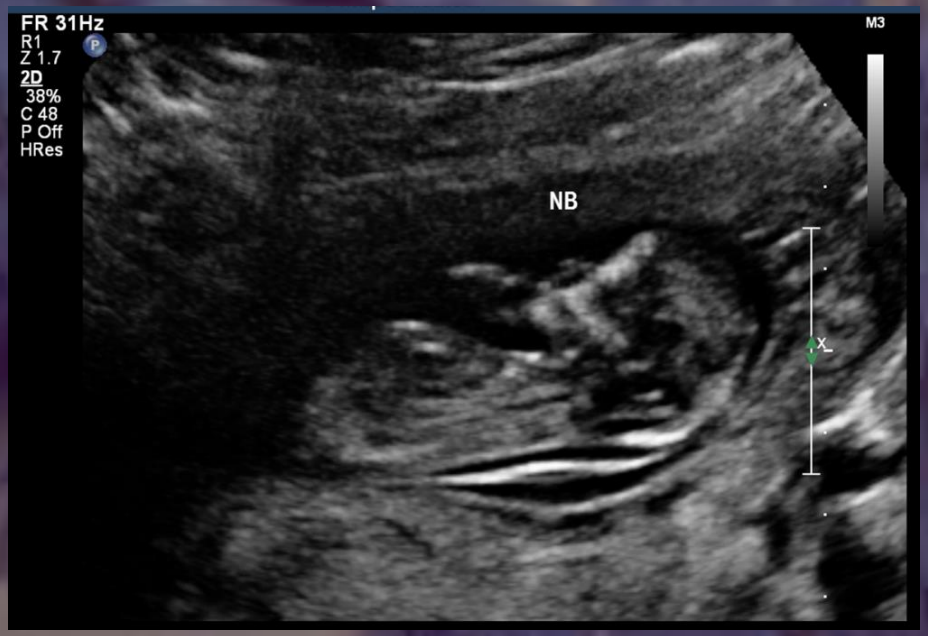


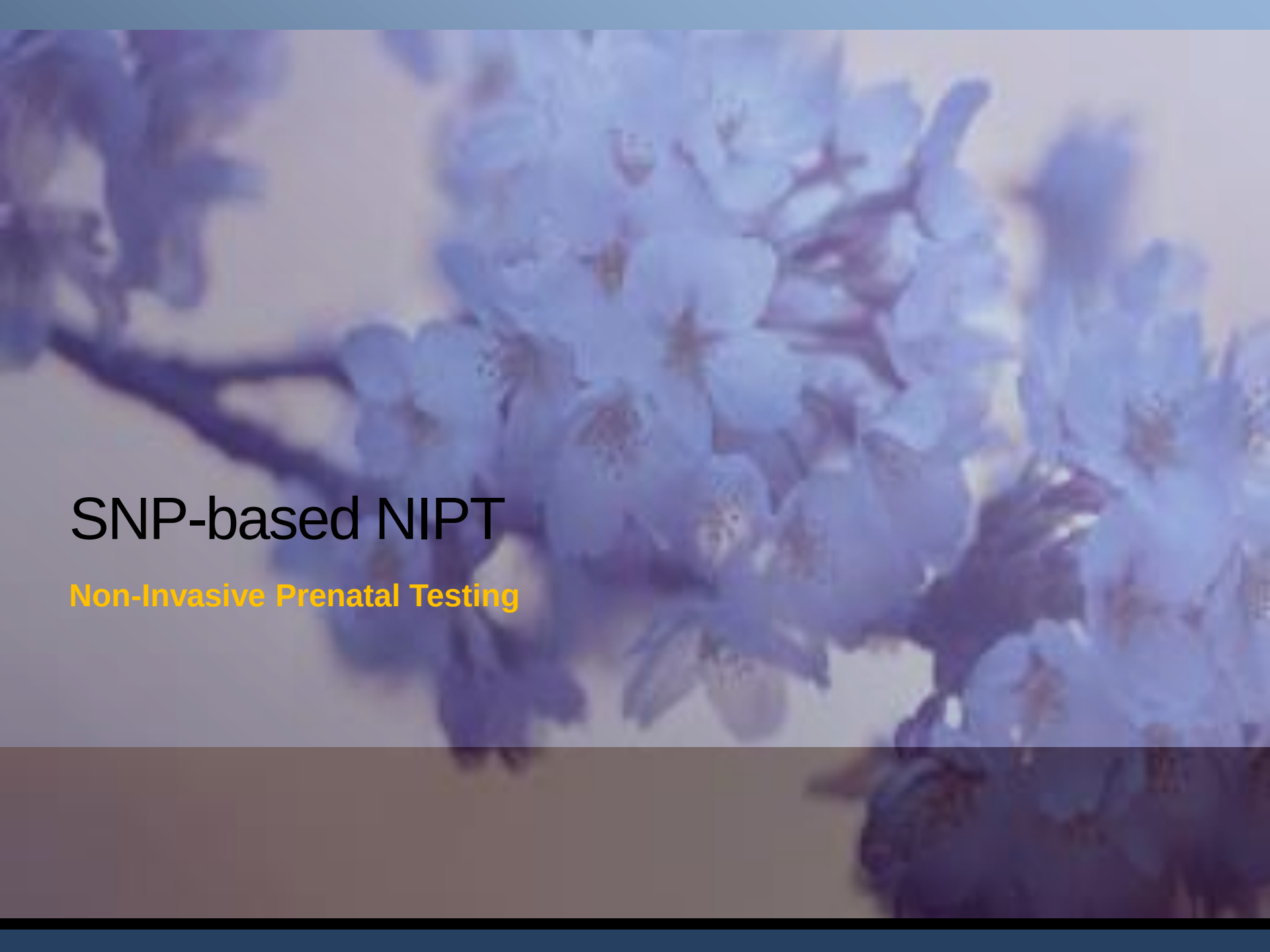
Nasal Bone Comparison





Why is our detection rate so low?

- Incorrect maternal data
- Lack of certification/quality control for nuchal
- Erroneous reporting of the nasal bone
- Self reported postnatal diagnosis of T21.



SNP-based NIPT

Non-Invasive Prenatal Testing

What's in a name?

- NIPTest
- NIPScreen
- Down Syndrome blood test

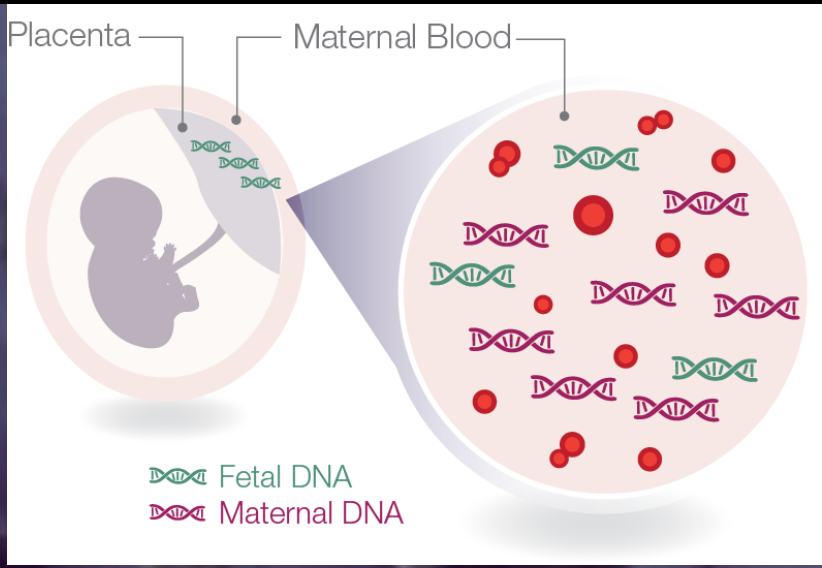
SCREENING TEST

What is NIPT?

- Screening test to prenatally detect
  - Down syndrome
  - other aneuploidies (extra or missing chromosomes)
    - *trisomy 21, 18, 13*
    - *trisomy of sex chromosomes (XXX, XXY, XYY)*
    - *Turner syndrome (monosomy X)*
    - *triploidy (extra copy of all chromosomes)*
  - Microdeletions
  - Chorionicity in twins

NIPT

- Measures circulating cell-free DNA (cfDNA) from placenta present in maternal blood
- ~10% of DNA in maternal blood
  - *Increases with gestational age*
- As early as 9-10 weeks gestation
  - *(company specific)*
- Dating U/S –
  - *viability, accurate GA, exclude multiples*



cfDNA comes from apoptotic cells derived from:

Maternal Circulation

- *Adipocytes*
- *White Blood Cells*

- *Fetal*
  - *Placental cells (trophoblasts) in the maternal circulation*

The Evolution of NIPT

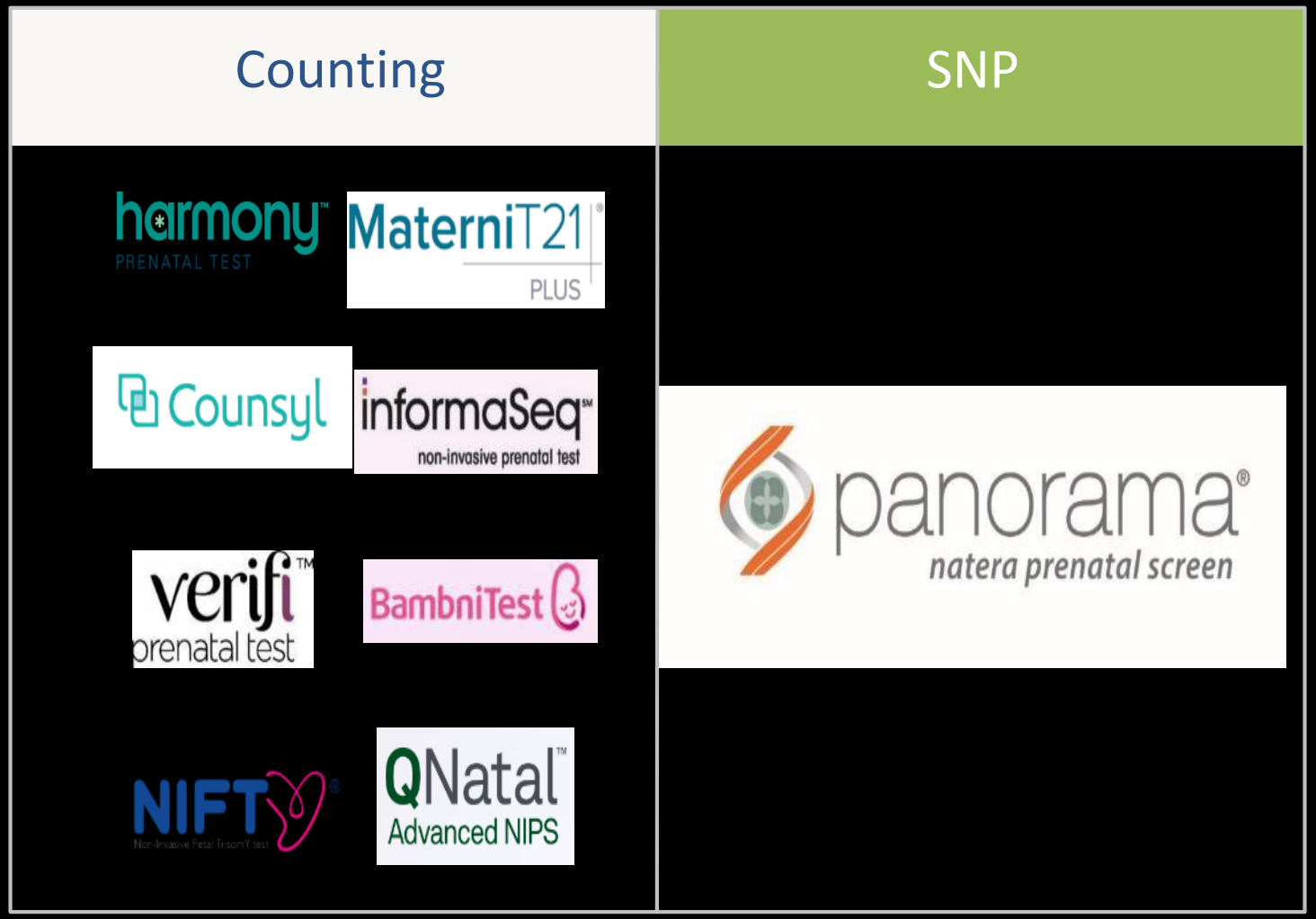
2011 2012 2013 2014-2017

1st generation: Quantitative or "Counting"

2nd generation: Qualitative or "SNP-based"

Other labs enter domestic NIPT space using 1st generation counting technologies

NIPT Methodologies



SNP-based NIPT

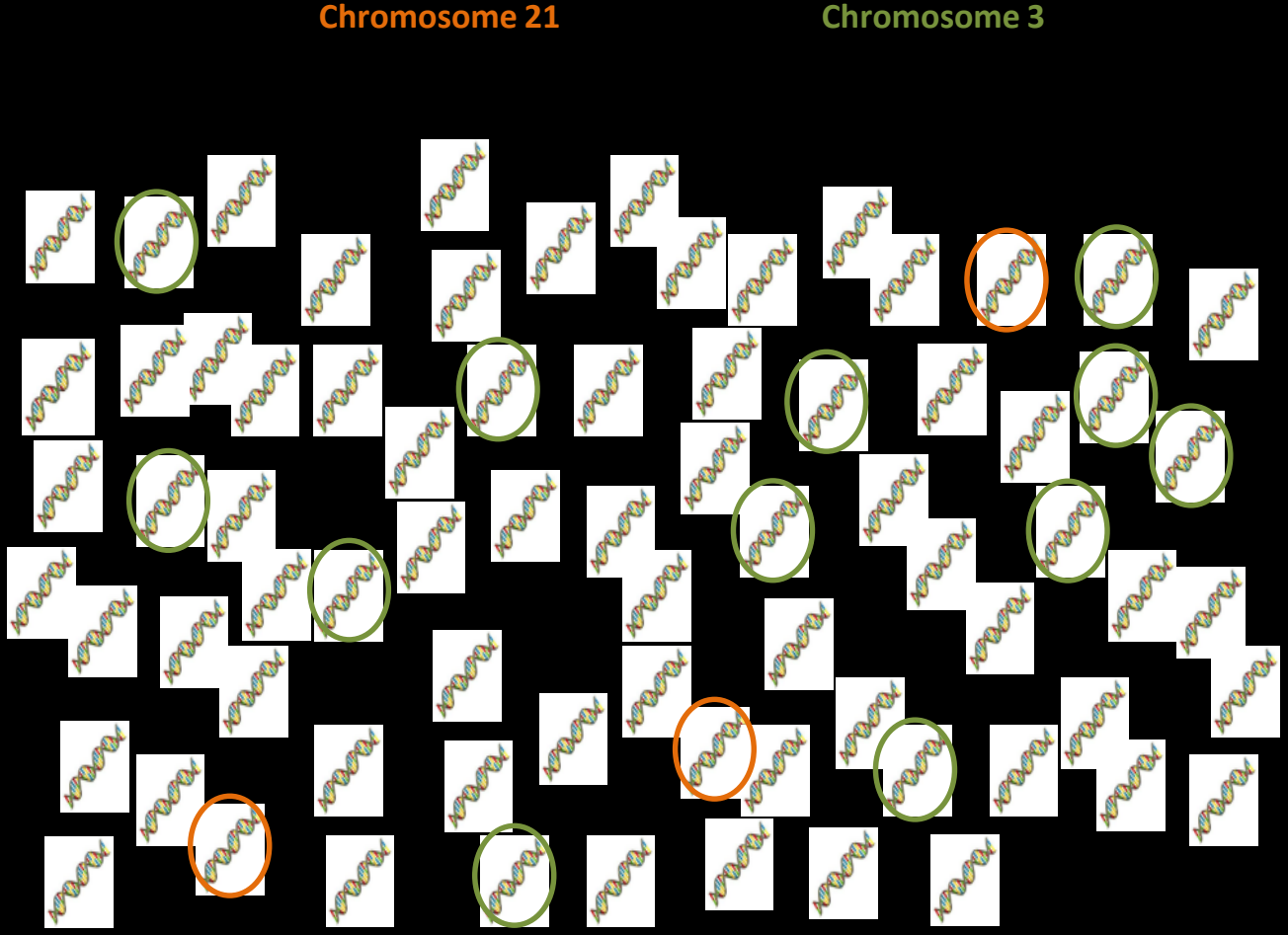
Whole chromosome conditions

- Trisomy 21, 18, 13
- Monosomy X
- Sex chromosome trisomies
- Triploidy
- Complete molar pregnancy

Optional

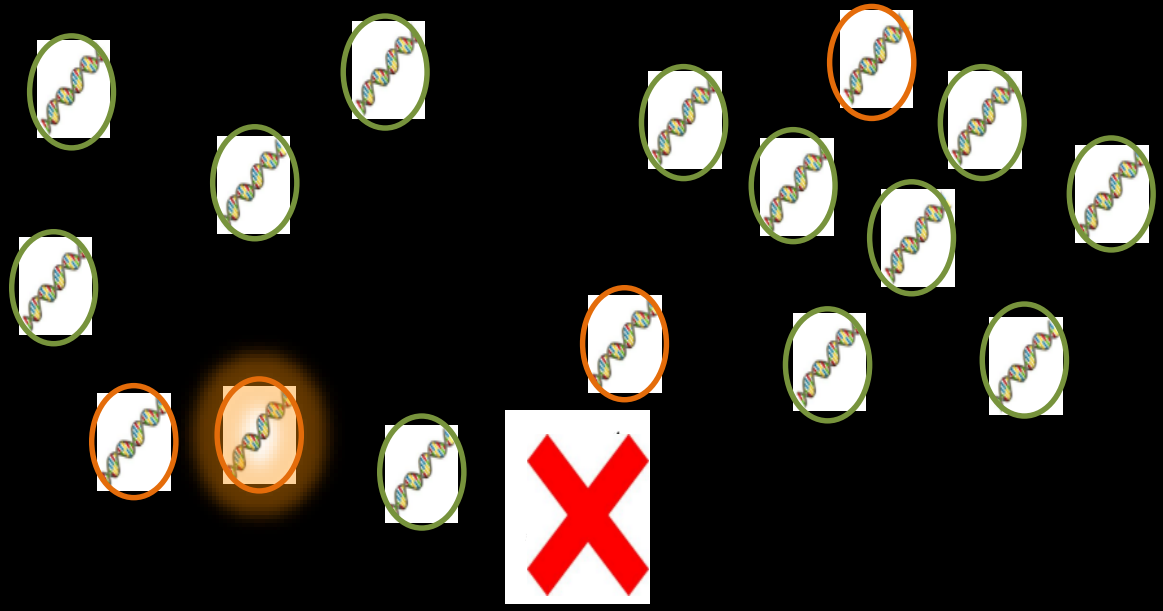
- 22q11.2 deletion syndrome
- Additional microdeletions
- Fetal sex

Counting

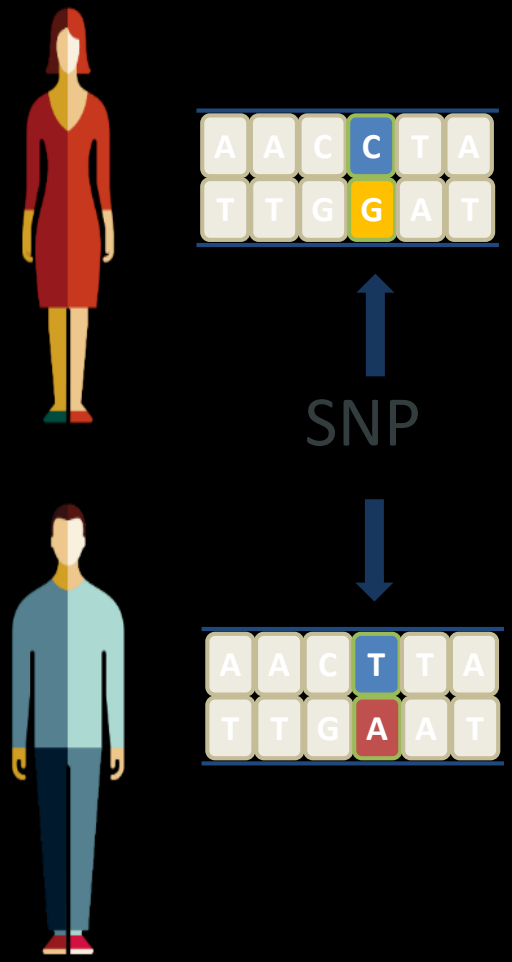


Counting

	Chromosome 21	Chromosome 3
Expected Amount:	20%	80%
Observed Amount:	25%	75%



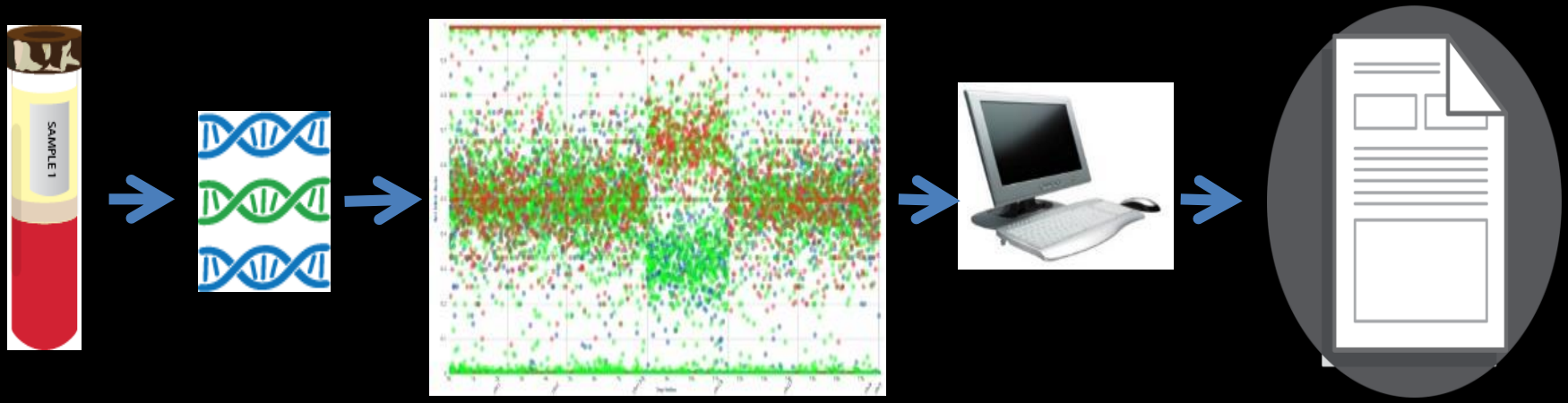
SNP = Single Nucleotide Polymorphism



- A DNA sequence variation occurring when a single base pair is changed
- Normal genetic changes that occur in every person
- SNP-based NIPT analyzes more than 13,000 SNPs

SNP-based NIPT Technology

Proprietary SNP analysis distinguishes between maternal & fetal DNA



Clinical Advantages of SNP-based NIPT

Uniquely differentiates between maternal and fetal DNA

- Fetal fraction
- Maternal contribution
- Vanishing twins
- Fetal sex accuracy
- Triploidy/complete mole

SNP-based Aneuploidy Screening for Twins

Benefits of NIPT

- Fewer women having diagnostic tests
  - *associated risk of pregnancy loss*
- Early test result (drawn at ≥ 9-10 weeks at earliest)
- No risk of miscarriage
- Detects the most common chromosomal aneuploidies
- Higher detection rates and lower false positive rates than CFTS

What can go wrong with NIPT?

- Unusual result
- Not a true result

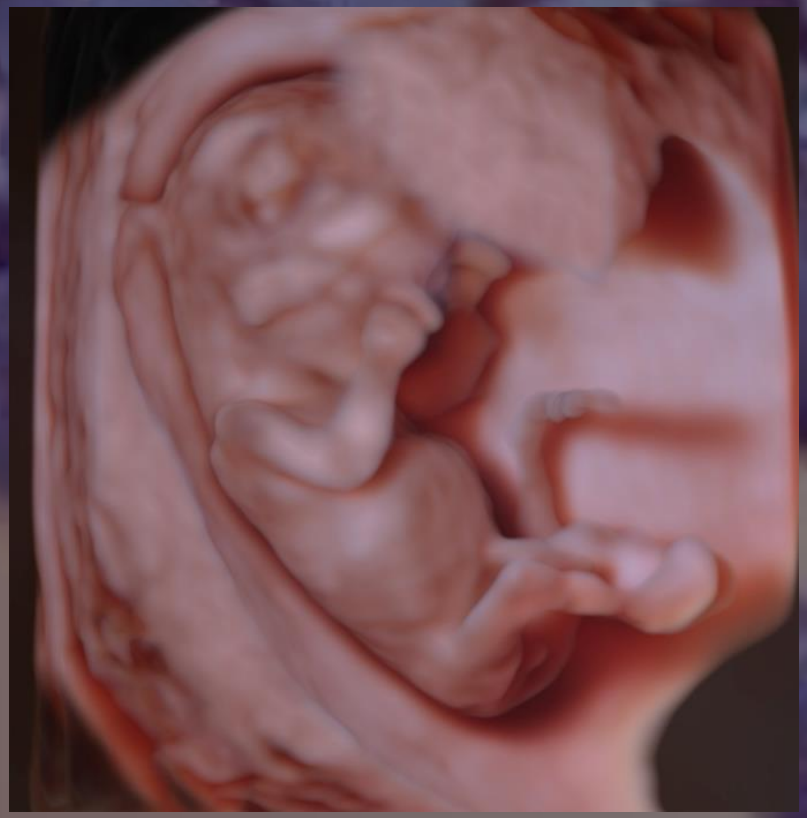
- Only detects those conditions it tests for

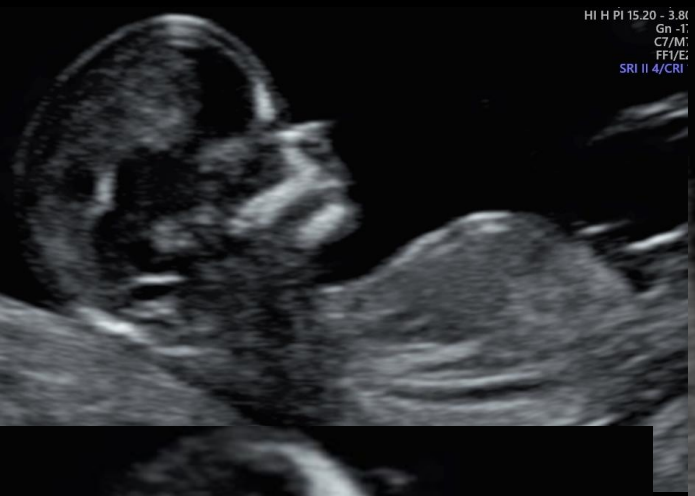
False negative/positive

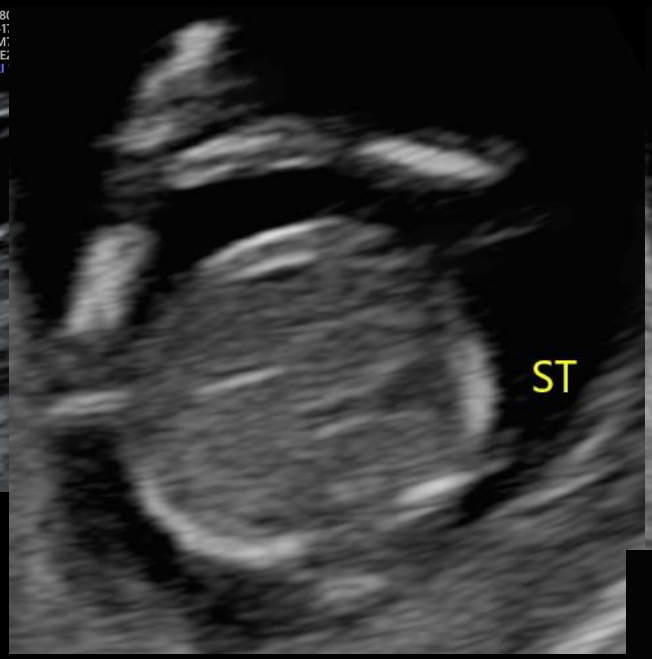
- Check with invasive testing if you are going to act on the result

Do I still need a nuchal scan?

- Yes…..Early anatomy scan



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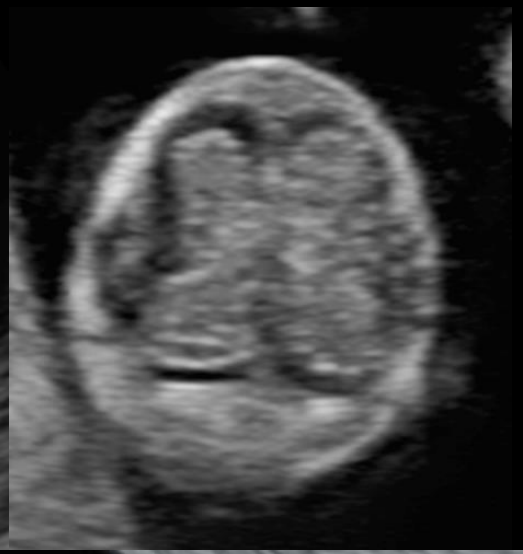
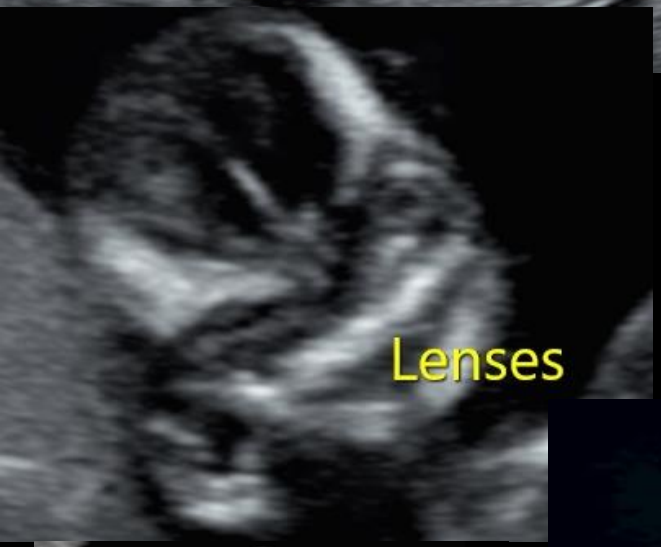
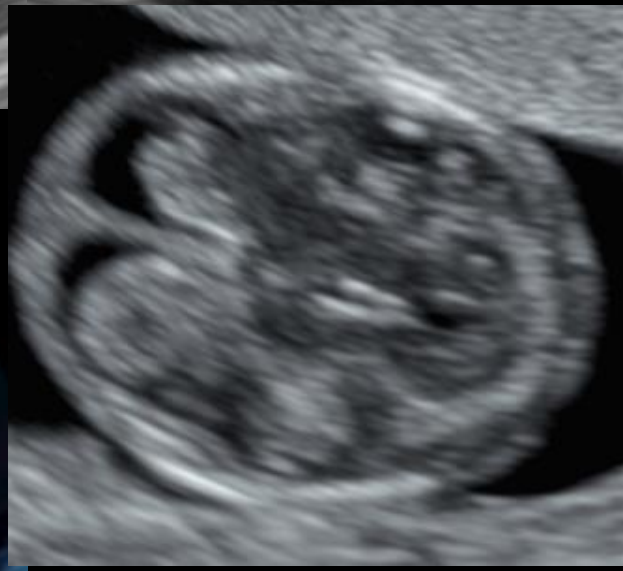
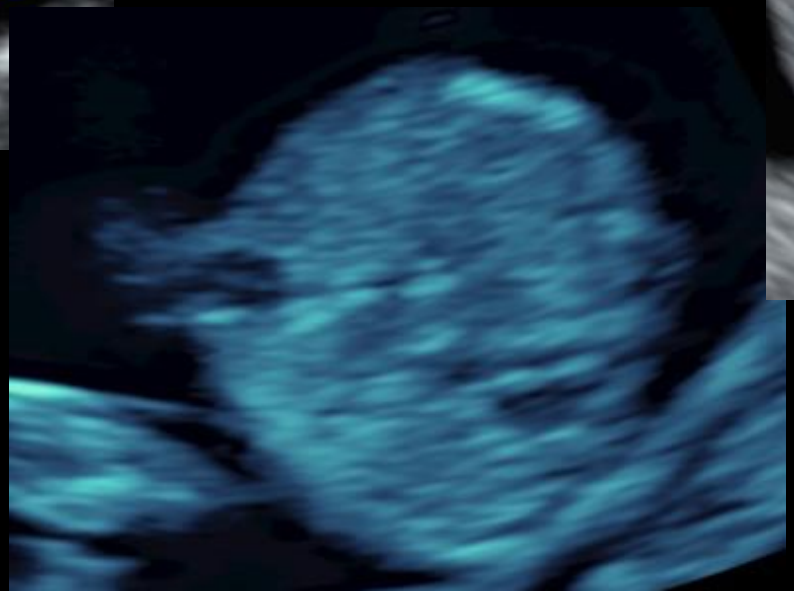
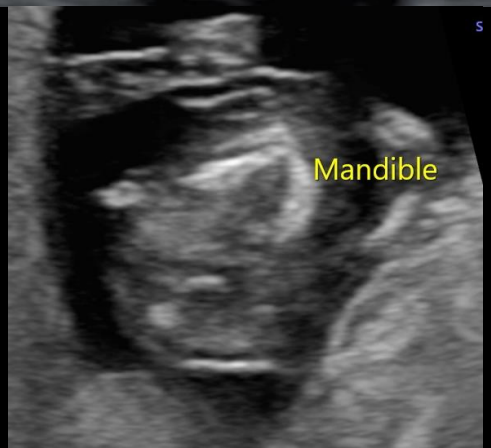
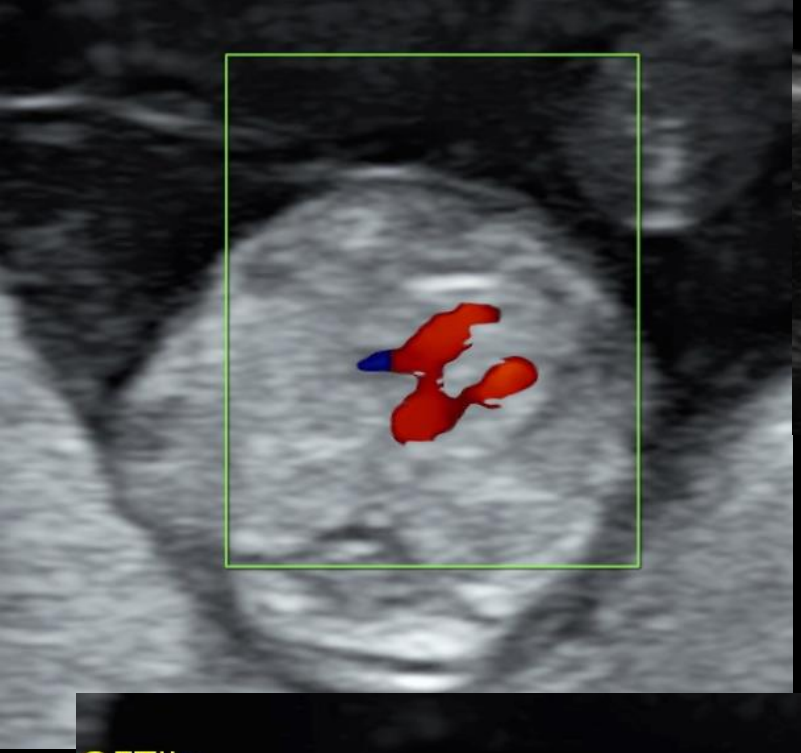


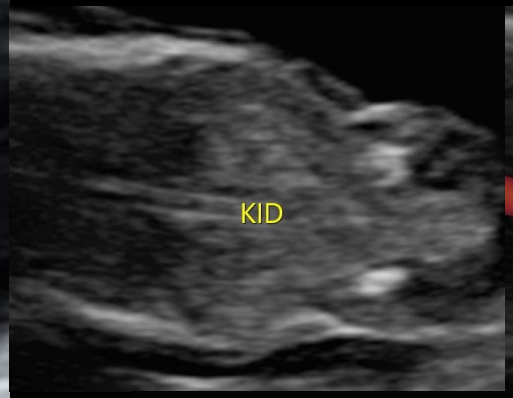

Lenses






Mandible

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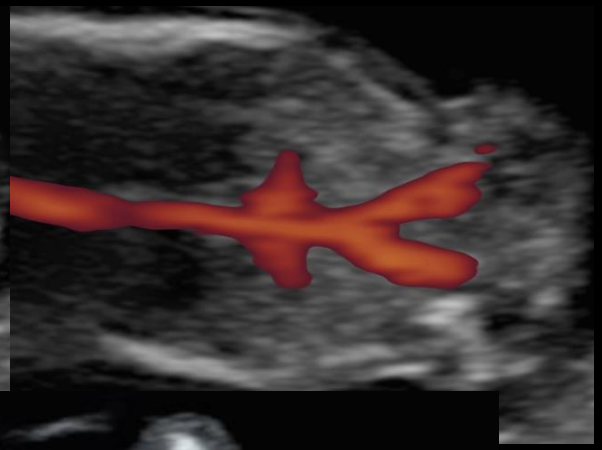
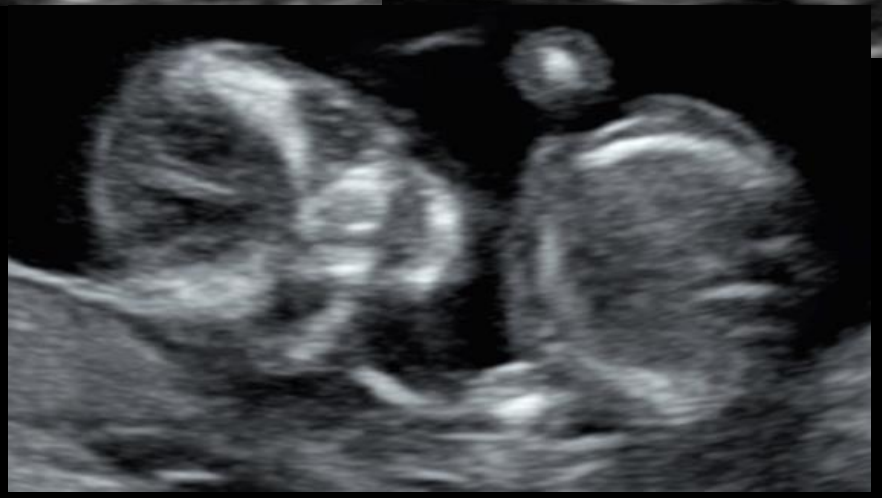
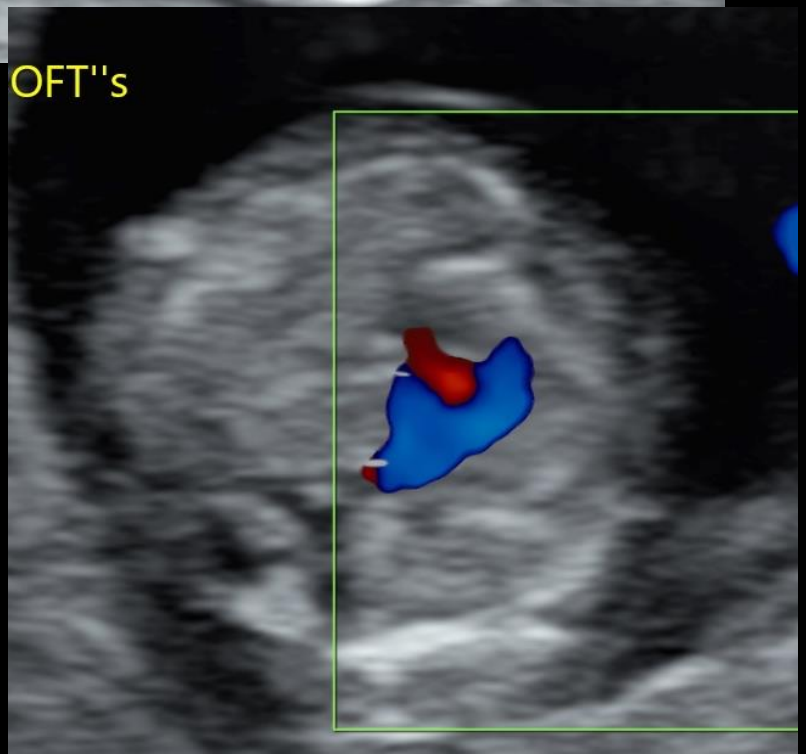
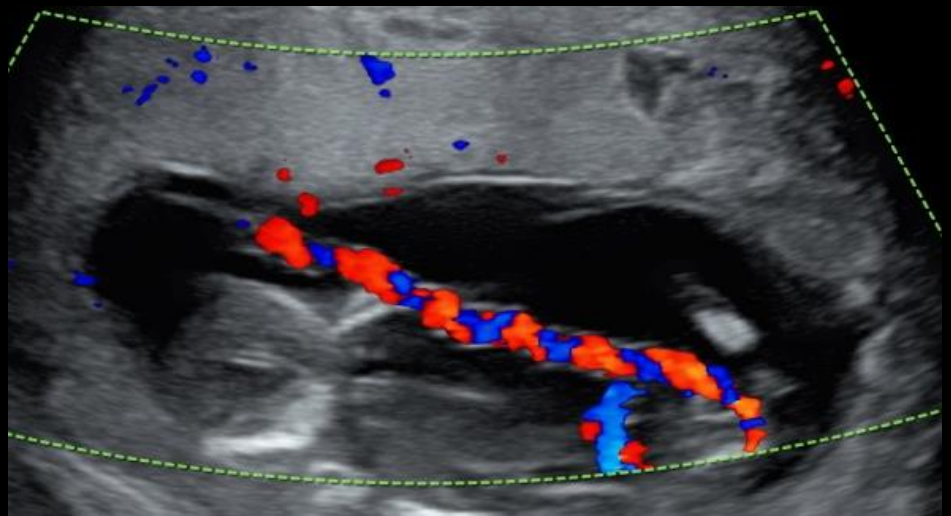




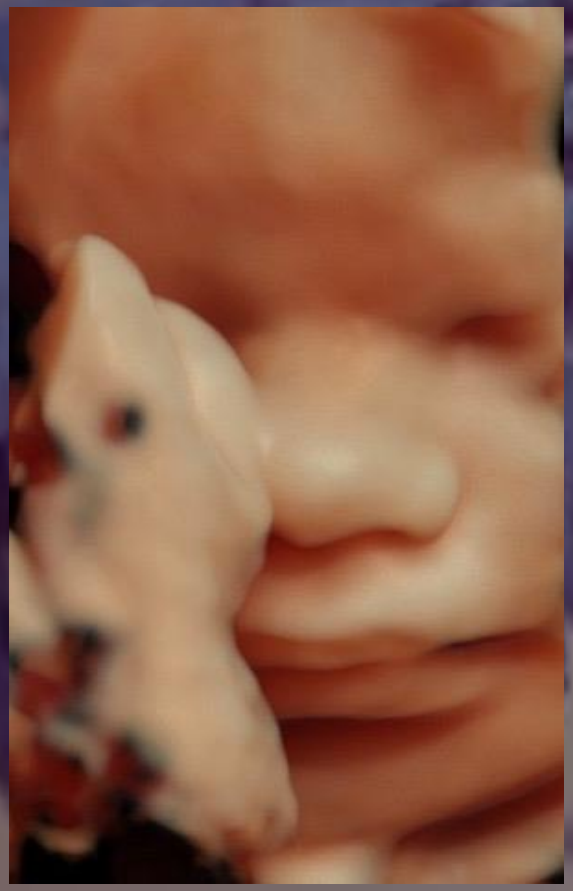

OFT''s



What if an anomaly occurs later?

- False negative
- Another anomaly
- A non-genetic syndrome

How do I counsel?



Results

Patient Information

Patient Name:	Jane Doe
Date of Birth:	11/08/1975
Maternal Age at EDD:	37
Gestational Age:	11 weeks/0 days
Maternal Weight:	N/A
Patient ID:	P99457
Medical Record #:	M84555
Collection Kit:	123233-2-N
Reference ID:	254233-2-N
Accessioning ID:	C47695
Case File ID:	159466

Test Information

Ordering Physician:	Dr. Matthew Goodbirth, M.D. (G123456)
Clinic Information:	Natera, Inc.
Additional Reports:	N/A
Report Date:	02/01/2013
Samples Collected:	01/31/2013
Samples Received:	02/01/2013
	Mother Blood

panorama
natera prenatal screen

ABOUT THIS SCREEN: Panorama™ is a screening test, not diagnostic. It evaluates genetic information in the maternal blood, which is a mixture of maternal and placental DNA, to determine the chance for specific chromosome abnormalities. The test does NOT tell with certainty if a fetus is affected, and only tests for the conditions ordered by the healthcare provider. A low risk result does not guarantee an unaffected fetus.

TEST SELECTED: Sex of Fetus

FINAL RESULTS SUMMARY

Result	*Fetal Sex*	*Fetal Fraction*
LOW RISK	**Male**	**8.3%**

Notes by the clinical reviewer, if any, will be shown here.

RESULTS DETAILS: ANEUPLOIDIES

Condition tested[1]	*Result*	*Risk Before Test*[2]	*Panorama Risk Score*[3]
Trisomy 21	Low Risk	1/152	<1/10,000
Trisomy 18	Low Risk	1/111	<1/10,000
Trisomy 13	Low Risk	1/357	<1/10,000
Monosomy X	Low Risk	1/256	<1/10,000
Triploidy	Low Risk		

1. Excludes cases with evidence of fetal and/or placental mosaicism. 2. Based on maternal age, gestational age, and/or general population, as applicable. References available upon request. 3. Based on a priori risk and results of analysis of circulating placental DNA.

Approved By: Gregory M. Enns, MB, ChB, FAAP **Approved By:** Susan Zneimer, Ph.D., FACMGG, Laboratory Director

IF THE ORDERING PROVIDER HAS QUESTIONS OR WISHES TO DISCUSS THE RESULTS, PLEASE CONTACT US AT 650-249-9090 #3. Ask for the NIPT genetic counselor on call.

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OVERALL TEST SPECIFICATIONS FOR PANORAMA

The Panorama risk score shown on page 1 reflects the confidence of the algorithm for the result reported for an individual sample.

The information in the table below relates to the general performance of the test.

Sensitivity is the ability to correctly identify a truly high risk case as high risk. For example, in a group of Trisomy 21 cases, Panorama will correctly identify more than 99% of those cases.

Specificity is the ability to correctly identify an unaffected case as low risk.

Positive Predictive Value is the likelihood the result says high-risk and the fetus is actually affected. For example, when Panorama shows a high-risk result for Trisomy 21, there is a 91% chance that the fetus is affected by Trisomy 21. In other words, 9% of the time, you may get a high-risk result when the fetus is not affected by Trisomy 21.

Negative Predictive Value is the likelihood the result says low-risk and the fetus is truly not affected.

Condition	*Sensitivity (95% CI)*	*Specificity (95% CI)*	*Positive Predictive Value*	*Negative Predictive Value*
Trisomy 21[1,2,3,4]	>99% (CI 97.8-99.9)	>99 (CI 99.7-100)	91%	>99.99%*
Trisomy 18[1,2,3,4]	98.2% (CI 90.4-99.9)	>99% (CI 99.7-100)	93%	>99.99%*
Trisomy 13[1,2,3,4]	>99% (CI 87.2-100)	>99% (CI 99.8-100)	38%	>99.99%*
Monosomy X[1,2,3,4]	94.7% (CI 74.0-99.9)	>99% (CI 99.7-100)	50%	>99.99%*
Triploidy[5,6]	>99% (CI 66.4-100)	>99% (CI 99.5-100)	5.3%	>99.99%*
XXX, XXY, XYY[4]	N/A-Reported when identified	N/A-Reported when identified	89%	N/A-Reported when identified
22q11.2 deletion syndrome[7,8,9]	95.7% (CI 85.5-99.5)	>99 (CI 98.6-99.9)	20%**	99.97-99.99%***
1p36 deletion syndrome[7,8]	>99% (CI 2.5-100)	>99% (CI 99.1-100)	7-17%***	99.98-99.99%***
Angelman syndrome[7,8]	95.5% (CI 77.2-99.9)	>99% (CI 99.1-100)	4%	>99.99%
Cri-du-chat syndrome[7,8]	>99% (CI 85.8-100)	>99% (CI 99.1-100)	2-5%***	>99.99%
Prader-Willi syndrome[7,8]	93.8% (CI 69.8-99.8)	>99% (CI 99.1-100)	5%	>99.99%
Female	>99.9% (CI 99.4-100)	>99.9% (CI 99.5-100)		
Male	>99.9% (CI 99.5-100)	>99.9% (CI 99.4-100)		

1. Nicolaides KH et al. Prenat Diagn. 2013 June;33(6):575-9
2. Pergament E et al. Obstet Gynecol. 2014 Aug;124(2 Pt 1):210-8
3. Ryan A et al. Fetal Diagn Ther. 2016;40(3):219-223
4. Dar P et al. Am J Obstet Gynecol. 2014 Nov;211(5):527.e1-527.e17
5. Nicolaides KH et al. Fetal Diagn Ther. 2014;35(3):212-7.
6. Curnow KJ et al. Am J Obstet Gynecol. 2015 Jan;212(1):79.e1-9
7. Wapner RJ et al. Am J Obstet Gynecol. 2015 Mar;212(3):332.e1-9
8. Ryan A et al. EUR J Hum Genet. 2016 May;24(E-supplement 1):53
9. Natera. Panorama: SNP-Based Non-Invasive Prenatal Screening Test, white paper V3. 2017 Feb.

* Ongoing clinical follow-up is performed to ensure the NPV does not fall below the quoted value but follow up is not obtained for all low risk calls.

** PPV for 22q11.2 deletion syndrome in published studies was 20% when no ultrasound anomalies were seen and was up to 100% when ultrasound anomalies were seen prior to testing.

*** Dependent upon fetal fraction, see Panorama Risk score on report for accurate PPV/NPV for a specific patient.

For additional information, please visit: www.natera.com/panorama-test/test-specs

Testing Methodology: DNA isolated from the maternal blood, which contains placental DNA, is amplified at specific loci using a targeted PCR assay, and sequenced using a high-throughput sequencer. Sequencing data is analyzed using Natera's proprietary algorithm to determine the fetal copy number for chromosomes 13, 18, 21, X, and Y, thereby identifying whole chromosome abnormalities at these locations, and if ordered, the microdeletion panel will identify microdeletions at the specified loci only. If a sample fails to meet the quality threshold, no result will be reported for the specified chromosome(s). The test requires sufficient fetal fraction to produce a result. Fetal fraction is determined using a proprietary algorithm incorporating data from single nucleotide polymorphism-based next-generation sequencing. Estimates of fetal fraction may differ when measured by different laboratories and/or methodologies.

Disclaimers: This test has been validated on women with a singleton pregnancy and of at least nine weeks gestation. A result will not be available where the maternal blood cells and oocytes are not of the same genetic lineage, as in the case of an egg donor, surrogate, or bone marrow transplant recipient. Findings of unknown significance will not be reported. As this assay is a screening test and not diagnostic, false positives and false negatives can occur. High risk test results need diagnostic confirmation by alternative testing methods. Low risk results do not fully exclude the diagnosis of any of the syndromes nor do they exclude the possibility of other chromosomal abnormalities or birth defects, which are not a part of this test. Potential sources of inaccurate results include, but are not limited to, mosaicism, low fetal fraction, limitations of current diagnostic techniques, or misidentification of samples. This test will not identify all deletions associated with each microdeletion syndrome. This test has been validated on full region deletions only and may be unable to detect smaller deletions. Microdeletion risk score is dependent upon fetal fraction, as deletions on the maternally inherited copy are difficult to identify at lower fetal fractions. Test results should always be interpreted by a clinician in the context of clinical and familial data with the availability of genetic counseling when appropriate. The Panorama prenatal test was developed by Natera, Inc., a laboratory certified under the Clinical Laboratory Improvement Amendments (CLIA). This test has not been cleared or approved by the U.S. Food and Drug Administration (FDA).

OVERALL TEST SPECIFICATIONS FOR PANORAMA

The Panorama risk score shown on page 1 reflects the confidence of the algorithm for the result reported for an individual sample.

The information in the table below relates to the general performance of the test.

Sensitivity is the ability to correctly identify a truly high risk case as high risk. For example, in a group of Trisomy 21 cases, Panorama will correctly identify more than 99% of those cases.

Specificity is the ability to correctly identify an unaffected case as low risk.

Positive Predictive Value is the likelihood the result says high-risk and the fetus is actually affected. For example, when Panorama shows a high-risk result for Trisomy 21, there is a 91% chance that the fetus is affected by Trisomy 21. In other words, 9% of the time, you may get a high-risk result when the fetus is not affected by Trisomy 21.

Negative Predictive Value is the likelihood the result says low-risk and the fetus is truly not affected.

Condition	*Sensitivity (95% CI)*	*Specificity (95% CI)*	*Positive Predictive Value*	*Negative Predictive Value*
Trisomy 21[1,2,3,4]	>99% (CI 97.8-99.9)	>99 (CI 99.7-100)	91%	>99.99%*
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XXX, XXY, XYY[4]	N/A-Reported when identified	N/A-Reported when identified	89%	N/A-Reported when identified
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Female	>99.9% (CI 99.4-100)	>99.9% (CI 99.5-100)		
Male	>99.9% (CI 99.5-100)	>99.9% (CI 99.4-100)		

1. Nicolaides KH et al. Prenat Diagn. 2013 June;33(6):575-9
2. Pergament E et al. Obstet Gynecol. 2014 Aug;124(2 Pt 1):210-8
3. Ryan A et al. Fetal Diagn Ther. 2016;40(3):219-223
4. Dar P et al. Am J Obstet Gynecol. 2014 Nov;211(5):527.e1-527.e17
5. Nicolaides KH et al. Fetal Diagn Ther. 2014;35(3):212-7.
6. Curnow KJ et al. Am J Obstet Gynecol. 2015 Jan;212(1):79.e1-9
7. Wapner RJ et al. Am J Obstst Gynecol. 2015 Mar;212(3):332.e1-9
8. Ryan A et al. EUR J Hum Genet. 2016 May;24:E-supplement 1:53
9. Natera. Panorama: SNP-Based Non-Invasive Prenatal Screening Test, white paper V3. 2017 Feb.

* Ongoing clinical follow-up is performed to ensure the NPV does not fall below the quoted value but follow up is not obtained for all low risk calls.

** PPV for 22q11.2 deletion syndrome in published studies was 20% when no ultrasound anomalies were seen and was up to 100% when ultrasound anomalies were seen prior to testing.

*** Dependent upon fetal fraction, see Panorama Risk score on report for accurrate PPV/NPV for a specific patient.

For additional information, please visit: ***www.natera.com/panorama-test/test-specs***

Sensitivity is the ability to correctly identify a truly high risk case as high risk. For example, in a group of Trisomy 21 cases, Panorama will correctly identify more than 99% of those cases.

Specificity is the ability to correctly identify an unaffected case as low risk.

Positive Predictive Value is the likelihood the result says high-risk and the fetus is actually affected. For example, when Panorama shows a high-risk result for Trisomy 21, there is a 91% chance that the fetus is affected by Trisomy 21. In other words, 9% of the time, you may get a high-risk result when the fetus is not affected by Trisomy 21.

Negative Predictive Value is the likelihood the result says low-risk and the fetus is truly not affected.

Patient Information

Patient Name:	Jane Doe
Date of Birth:	11/08/1975
Maternal Age at EDD:	37
Gestational Age:	11 weeks/0 days
Maternal Weight:	N/A
Patient ID:	P99457
Medical Record #:	M84555
Collection Kit:	254233-2-N
Accessioning ID:	C47695
Case File ID:	159466

Test Information

Ordering Physician:	Dr. Matthew Goodbirth, M.D. (G123456)
Clinic Information:	Natera, Inc.
Additional Reports:	N/A
Report Date:	02/01/2013
Samples Collected:	01/31/2013
Samples Received:	02/01/2013
	Mother Blood

panorama
natera prenatal screen

ABOUT THIS SCREEN: Panorama™ is a screening test, not diagnostic. It evaluates genetic information in the maternal blood, which is a mixture of maternal and placental DNA, to determine the chance for specific chromosome abnormalities. The test does NOT tell with certainty if a fetus is affected, and only tests for the conditions ordered by the healthcare provider. A low risk result does not guarantee an unaffected fetus.

TEST SELECTED: Sex of Fetus

FINAL RESULTS SUMMARY

Result	*Fetal Sex*	*Fetal Fraction*
HIGH RISK for Trisomy 21	**Male**	**8.3%**

This is a screening test only. Genetic counseling and diagnostic testing should be offered to further evaluate these findings.

The Panorama risk score reflects analysis of DNA from the placenta. The placental DNA may not accurately reflect the status of the fetus; therefore, no irreversible decisions should be made based upon results of this screening test alone.

RESULTS DETAILS: ANEUPLOIDIES

Condition tested[1]	*Result*	*Risk Before Test*[2]	*Panorama Risk Score*[3]
Trisomy 21	**High Risk**	1/152	**>99/100**
Trisomy 18	Low Risk	1/111	<1/10,000
Trisomy 13	Low Risk	1/357	<1/10,000
Monosomy X	Low Risk	1/256	<1/10,000
Triploidy	Low Risk		

1. Excludes cases with evidence of fetal and/or placental mosaicism. 2. Based on maternal age, gestational age, and/or general population, as applicable. References available upon request. 3. Based on a priori risk and results of analysis of circulating placental DNA.

POSITIVE PREDICTIVE VALUES (PPV)

Positive Predictive Value (PPV) is the likelihood that diagnostic testing will confirm a High Risk result. PPV provided is NOT personalized for this patient, but calculated from a published study of 17,885 women. PPV for an individual specimen will vary based on prior risk.

Trisomy 21	91%
Trisomy 18	93%
Trisomy 13	38%
Monosomy X	50%

Perinatology.com

National Society of Genetic Counselors

NIPT/Cell Free DNA Screening Predictive Value Calculator

Perinatal QUALITY .org

Overview | **PPV Calculator** | NPV Calculator | Definitions | FAQs | Resources | References

Please select the chromosome condition and maternal age at the time of EDD.
Alternatively you choose to enter Prevalence directly.

Trisomy 21 | 37

The estimated prevalence of Trisomy 21 at 16 weeks gestation for women who are 37 at EDD is 1 in 186. Where does this number come from? See the FAQs from the menu above for details.

Sensitivity: 99.2

Specificity: 99.91

The default performance metrics for Trisomy 21 are set at a sensitivity of 99.2 and specificity of 99.91 based on the weighted and pooled data from a meta-analysis by Gil et al (2015). The user may wish to change these inputs to reflect the performance statistics provided by the referral laboratory.

Calculate **Clear**

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NIPT/Cell Free DNA Screening Predictive Value Calculator

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Overview | **PPV Calculator** | NPV Calculator | Definitions | FAQs | Resources | References

The prevalence of Trisomy 21 at 16 weeks gestation for a woman who is 37 at EDD is 1 in 186.

The probability that result is a **true positive** (the fetus **is affected**). **PPV:** **86%**

Probability that it is a **false positive** (the fetus is **not affected**). **14%**

PPV (not rounded): 85.62796719896401%

PPV = (sensitivity x prevalence) / ((sensitivity x prevalence) + (1 – specificity)(1 – prevalence))

PPV = (0.992 x 0.005376344086021506) / ((0.992 x 0.005376344086021506) + (1 – 0.9991)(1 – 0.005376344086021506))

Please note: the post-test probability for an individual patient may differ based on other factors that influence her unique prior risk to have an affected pregnancy, such as gestational age of the patient, ultrasound findings and biochemical screening.

Calculate | Clear | Revise

NIPT/Cell Free DNA Screening Predictive Value Calculator

Overview | **PPV Calculator** | NPV Calculator | Definitions | FAQs | Resources | References

The prevalence of Trisomy 21 at 16 weeks gestation for a woman who is 20 at EDD is 1 in 1177.

The probability that result is a **true positive** (the fetus **is affected**). **PPV:** **48%**

Probability that it is a **false positive** (the fetus is **not affected**). **52%**

PPV (not rounded): 48.38080374561029%

PPV = (sensitivity x prevalence) / ((sensitivity x prevalence) + (1 – specificity)(1 – prevalence))

PPV = (0.992 x 0.0008496176720475786) / ((0.992 x 0.0008496176720475786) + (1 – 0.9991)(1 – 0.0008496176720475786))

Please note: the post-test probability for an individual patient may differ based on other factors that influence her unique prior risk to have an affected pregnancy, such as gestational age of the patient, ultrasound findings and biochemical screening.

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NIPT/Cell Free DNA Screening Predictive Value Calculator

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Overview | **PPV Calculator** | NPV Calculator | Definitions | FAQs | Resources | References

The prevalence of Trisomy 21 at 16 weeks gestation for a woman who is 44 at EDD is 1 in 28.

The probability that result is a **true positive** (the fetus **is affected**). **PPV:** **98%**

Probability that it is a **false positive** (the fetus is **not affected**). **2%**

PPV (not rounded): 97.60897372822981%

PPV = (sensitivity x prevalence) / ((sensitivity x prevalence) + (1 – specificity)(1 – prevalence))

PPV = (0.992 x 0.03571428571428571) / ((0.992 x 0.03571428571428571) + (1 – 0.9991)(1 – 0.03571428571428571))

Please note: the post-test probability for an individual patient may differ based on other factors that influence her unique prior risk to have an affected pregnancy, such as gestational age of the patient, ultrasound findings and biochemical screening.

Calculate | Clear | Revise

Patient Information

Patient Name:	Jane Doe
Date of Birth:	11/08/1975
Maternal Age at EDD:	37
Gestational Age:	11 weeks/0 days
Maternal Weight:	N/A
Patient ID:	P99457
Medical Record #:	M84555
Collection Kit:	254233-2-N
Accessioning ID:	C47695
Case File ID:	159466

Test Information

Ordering Physician:	Dr. Matthew Goodbirth, M.D. (G123456)
Clinic Information:	Natera, Inc.
Additional Reports:	N/A
Report Date:	02/01/2013
Samples Collected:	01/31/2013
Samples Received:	02/01/2013
	Mother Blood

panorama
natera prenatal screen

ABOUT THIS SCREEN: Panorama™ is a screening test, not diagnostic. It evaluates genetic information in the maternal blood, which is a mixture of maternal and placental DNA, to determine the chance for specific chromosome abnormalities. The test does NOT tell with certainty if a fetus is affected, and only tests for the conditions ordered by the healthcare provider. A low risk result does not guarantee an unaffected fetus.

TEST SELECTED: Sex of Fetus, 22q11.2 Deletion

FINAL RESULTS SUMMARY

Result	*Fetal Sex*	*Fetal Fraction*
HIGH RISK for Trisomy 13	**Male**	**8.3%**

This is a screening test only. Genetic counseling and diagnostic testing should be offered to further evaluate these findings.

The Panorama risk score reflects analysis of DNA from the placenta. The placental DNA may not accurately reflect the status of the fetus; therefore, no irreversible decisions should be made based upon results of this screening test alone.

RESULTS DETAILS: ANEUPLOIDIES

Condition tested[1]	*Result*	*Risk Before Test*[2]	*Panorama Risk Score*[3]
Trisomy 21	Low Risk	1/152	<1/10,000
Trisomy 18	Low Risk	1/111	<1/10,000
Trisomy 13	**High Risk**	1/357	**>99/100**
Monosomy X	Low Risk	1/256	<1/10,000
Triploidy	Low Risk		

RESULTS DETAILS: MICRODELETIONS

Condition tested[1]	*Result*	*Risk Before Test*[2]	*Risk After Test*
22q11.2 deletion syndrome	Low Risk	1/2,000	1/13,300

1. Excludes cases with evidence of fetal and/or placental mosaicism. 2. Based on maternal age, gestational age, and/or general population, as applicable. References available upon request. 3. Based on a prior risk and results of analysis of circulating placental DNA.

POSITIVE PREDICTIVE VALUES (PPV)

Positive Predictive Value (PPV) is the likelihood that diagnostic testing will confirm a High Risk result. PPV provided is NOT personalized for this patient, but calculated from a published study of 17,885 women. PPV for an individual specimen will vary based on prior risk.

Trisomy 21	91%
Trisomy 18	93%
Trisomy 13	38%
Monosomy X	50%

National Society of Genetic Counselors

NIPT/Cell Free DNA Screening Predictive Value Calculator

Perinatal QUALITY .org

Overview | **PPV Calculator** | NPV Calculator | Definitions | FAQs | Resources | References

Please select the chromosome condition and maternal age at the time of EDD.
Alternatively you choose to enter Prevalence directly.

Trisomy 13 | 37

The estimated prevalence of Trisomy 13 at 16 weeks gestation for women who are 37 at EDD is 1 in 1575. Where does this number come from? See the FAQs from the menu above for details.

Sensitivity: 91

Specificity: 99.87

The default performance metrics for Trisomy 13 are set at a sensitivity of 91 and specificity of 99.87 based on the weighted and pooled data from a meta-analysis by Gil et al (2015). The user may wish to change these inputs to reflect the performance statistics provided by the referral laboratory.

Calculate | Clear

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NIPT/Cell Free DNA Screening Predictive Value Calculator

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Overview | **PPV Calculator** | NPV Calculator | Definitions | FAQs | Resources | References

The prevalence of Trisomy 13 at 16 weeks gestation for a woman who is 37 at EDD is 1 in 1575.

The probability that result is a **true positive** (the fetus **is affected**). **PPV:** **31%**

Probability that it is a **false positive** (the fetus is **not affected**). **69%**

PPV (not rounded): 30.782761653474583%

PPV = (sensitivity x prevalence) / ((sensitivity x prevalence) + (1 – specificity)(1 – prevalence))

PPV = (0.91 x 0.0006349206349206349) / ((0.91 x 0.0006349206349206349) + (1 – 0.9987)(1 – 0.0006349206349206349))

Please note: the post-test probability for an individual patient may differ based on other factors that influence her unique prior risk to have an affected pregnancy, such as gestational age of the patient, ultrasound findings and biochemical screening.

Calculate | Clear | Revise

Questions???