Spectrum Health Maternal Fetal Medicine

*Non-Invasive Prenatal Screening Guidelines*

**Policy Overview**

1. Cell free fetal DNA non-invasive screening (NIPS) is the most accurate screening tool for traditional aneuploidies (trisomies 13, 18, and 21) in pregnancy and may be offered to ***all women (at the provider’s discretion)***, along with traditional serum screening and invasive testing.
   1. Pre-testing counseling regarding the benefits and limitations of testing is recommended for every woman.
   2. Post-test counseling is recommended in the event of a positive or high-risk result. Diagnostic testing should be offered in order to confirm an abnormal screening result.
   3. In the case of multiple congenital anomalies, diagnostic testing should be offered.
2. **Microdeletions/microduplications**: Current guidelines do not recommend routine screening for copy number variants. 22q11.2 deletion syndrome may be ordered, at the provider’s discretion, if there is *a family history* of this condition or *a heart defect present*. Please note, follow-up for an abnormal microdeletion/duplication is with a microarray, which is traditionally more costly than standard chromosome analysis and may not be covered by insurance in a prenatal setting.
3. **Multiples:** Current guidelines do not recommend NIPS for multiple gestations. NIPS may be ordered for twins, at the provider’s discretion, along with specific pre-test counseling discussion the limitations and reporting of results. Twin gestations will receive one report for the pregnancy, rather than a risk score for each twin.
4. **Sex Determination:** Current guidelines do not recommend NIPS for sex determination.
5. **Whole Genome:** Current guidelines do not recommend NIPS for genome-wide gains or losses.

**What do abnormal results mean?**

Positive or high-risk results can represent the following:

* Fetal aneuploidy
* Confined placental mosaicism
* Residual cffDNA from a vanishing twin
* Maternal aneuploidy (in the case of sex chromosome abnormalities- this depends on the specific testing technology)
* Limitations of the technology
* Maternal medical conditions (in rare cases, maternal malignancy has been detected through NIPS)
* Other unknown biological factors

**Benefits of NIPS**

* Non-invasive, so there are minimal risks to the pregnancy
* Increased accuracy with lower false positive and false negative rates than traditional maternal serum screening
* Able to perform testing at a wider range of gestational ages
* Typically, only one blood draw is required
* Provides risk estimate for the most common aneuplodies in pregnancy

**Limitations of NIPS**

* Still a screening test – abnormal results should be confirmed with diagnostic testing
* Risk asseessment is limited to specific fetal aneuplodies - approximately 50% of cytogenetic abnormalities routinely identified by amniocentesis will not be detected when trisomy 21, 18, and 13 are the only aneuploidies being screened (unbalanced translocations, deletions, duplications, triploidy (depending on the lab), or if Down syndrome is due to a translocation vs real trisomy)
* Uninformative test results due to insufficient isolation of cell-free fetal DNA could lead to a delay in diagnosis or eliminate the availability of information for risk assessment. Biologic factors associated with reduced available cell-free fetal DNA include a high body mass index and early gestational age (<10 weeks gestation)
* Does not screen for open neural tube defects. Maternal serum α-fetoprotein testing should still be offered at 15–20 weeks gestation to screen for open neural tube defects
* Does not replace the utility of a first-trimester ultrasound examination

**Professional Statement Summaries**

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|  | **ACMG**  **(American College of Medical Genetics and Genomics)** | **ACOG**  **(American Congress of Obstetricians and Gynecologists)** | **SMFM**  **(Society for Maternal-Fetal Medicine)** | **NSGC**  **(National Society of Genetic Counselors)** |
| **Statement Release** | **2016**  <http://www.acmg.net/docs/NIPS_AOP.pdf> | **2015**  [http://www.acog.org/Resources-And-Publications/Committee- Opinions/Committee-on-Genetics/Cell-free-DNA-Screening-for-Fetal-Aneuploidy](http://www.acog.org/Resources-And-Publications/Committee-%20Opinions/Committee-on-Genetics/Cell-free-DNA-Screening-for-Fetal-Aneuploidy) | **2015**  <https://www.smfm.org/publications/157-smfm-statement-maternal-serum-cell-free-dna-screening-in-low-risk-women> | **2016 (brief update)**  <http://nsgc.org/p/bl/et/blogaid=33> |
| **Low-risk populations** |  |  |  |  |
| **High-risk populations\*** |  | x | x |  |
| **Microdeletions/duplications (ie 22q11.2)** | x | x | x | x |
| **Multiple gestations (ie twins)** | x | x | x | x |
| **Sex determination** | x | x | x | x |
| **Pre-test education** | Discuss risks, benefits, alternative screening options, diagnostic testing, and the option of no testing. | Discuss risks, benefits, alternative screening options, diagnostic testing, and the option of no testing. | Discuss risks, benefits, alternative screening options, diagnostic testing, and the option of no testing. | Discuss risks, benefits, alternative screening options, diagnostic testing, and the option of no testing. |
| **Abnormal Results Follow-up** | Offer diagnostic testing and targeted ultrasound.  Offer genetic counseling. | Offer diagnostic testing and targeted ultrasound.  Offer genetic counseling. | Offer diagnostic testing and targeted ultrasound.  Offer genetic counseling. | Offer diagnostic testing and targeted ultrasound.  Offer genetic counseling. |

**\*high-risk populations include those with the following indications:**

* Maternal age 35 years or older at delivery
  + Sonographic findings indicating an increased risk of aneuploidy
  + History of a prior pregnancy with a trisomy (13, 18, or 21)
  + Positive screening results for aneuploidy (first trimester, sequential, integrated, or quad screen)
  + Parental balanced Robertsonian translocation (involving chromosomes 13, 18, or 21)