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Prenatal screening for chromosome abnormalities has evolved over the past several decades, but the intention remains the same: provide pregnant women and their health care providers the opportunity for informed-decision making. Most women are healthy with healthy pregnancies, but approximately 1 in 150 pregnancies have chromosome abnormalities, and a primary purpose of screening is to identify those patients who would most benefit from additional diagnostic testing (ACOG/SMFM 2016 Practice Bulletin #163).

Since 2001, the American College of Obstetricians and Gynecologists (ACOG) and the Society for Maternal-Fetal Medicine (SMFM) have recommended offering all pregnant women the option of prenatal screening or prenatal diagnosis for chromosome abnormalities (ACOG Practice Bulletin #27). The screening options evolved from the single AFP test, to the quadruple marker screen and the integrated screen.

Noninvasive prenatal screening (NIPS) became available in 2011 and while some initially perceived this testing as diagnostic, the truth is that NIPS has always been a screening test. The latest 2016 Practice Bulletin (#163) from ACOG/SMFM includes screening by cell-free DNA as one of the screening options that should be considered for all patients interested in prenatal screening.

What is NIPS?
Small bits of DNA freely float in all plasma samples. This is called cell-free DNA, or cfDNA. During pregnancy, a portion of that cfDNA originates from the placenta. When there is an extra or missing chromosome in the pregnancy, there is a difference in the observed pattern of cfDNA found in maternal plasma. A venipuncture at about 10 weeks gestation or later can screen for common chromosome abnormalities, such as Down syndrome, trisomy 18 and monosomy X (Turner syndrome).

3 things you should know:
NIPS is the most accurate screen for common chromosome abnormalities - Both ACOG and SMFM state that NIPS has the highest sensitivity and specificity for the common chromosome abnormalities for which screening is intended. A screen-positive NIPS result is ten-fold more likely to be a truly affected pregnancy than a screen-positive maternal serum screen. That means more affected pregnancies are correctly identified, while fewer women are referred for unnecessary invasive procedures. This is true for all women, both those considered to be at high risk for chromosome problems as well as average risk (ACOG/SMFM 2015 Committee Opinion #640; ACOG/SMFM 2016 Practice Bulletin #163).
**No call rates matter -** The latest 2015 Committee Opinion #640 from ACOG and SMFM states, “Women whose results are...a ‘no call’ test result...should receive further genetic counseling and be offered comprehensive ultrasound evaluation and diagnostic testing because of an increased risk of aneuploidy.” Essentially, this protocol is the same as that for a screen-positive NIPS or serum screen result. And while ACOG/SMFM made this recommendation because there is an increased chance of aneuploidy in these pregnancies with a ‘no call’ result, the reality is the vast majority of women who receive these results are carrying a healthy pregnancy. Therefore the goal of screening, to maximize sensitivity and minimize invasive procedures, is undermined by significant ‘no call’ rates which can range from <1% to 8% according to the statement from ACOG/SMFM ([ACOG/SMFM 2015 Committee Opinion #640](https://www.acog.org).)

**Clear reporting leads to clear understanding -** While the sensitivity and specificity of NIPS is very high, patients and healthcare providers should remember that it is a screening test. The concept of positive predictive value (PPV) describes the likelihood that a screen-positive result is reflective of a truly affected pregnancy, and is an important figure to include in discussions with patients. And it depends on how likely that pregnancy was to be affected to begin with. Therefore a 40 year old woman at 12 weeks gestation is going to have a higher PPV than a 25 year old woman at 16 weeks gestation. Neither should be counseled that their screen-positive NIPS result means there is a >99% chance the pregnancy is actually affected. Instead, refer to the laboratory report or [calculate](https://www.counsyl.com) the PPV for that particular patient based on her age and gestational age ([ACOG/SMFM 2015 Committee Opinion #640](https://www.acog.org).)

For all providers who care for women during their pregnancies, knowledge of the wide availability (and insurance coverage) for NIPS is essential. Equally important is to understand that while NIPS is the latest and greatest screening tool, it is still screening; therefore, awareness of limitations and resources for assistance help ensure patients accurately understand their results.

**Bio:**

Carrie Haverty is the Clinical Product Director for prenatal screening at Counsyl. Prior to joining Counsyl, she had 15 years experience caring for patients and leading teams in both prenatal and pediatric settings at Boston University Medical Center, Massachusetts General Hospital, and California Pacific Medical Center. Carrie has a Masters of Science in Genetic Counseling from the University of California at Irvine Medical School and is certified by the American Board of Genetic Counseling.