A **high-performance** test in the **real world**

QNatal™ Advanced, an automated, noninvasive prenatal screening assay, demonstrates excellent performance characteristics, high positive predictive values and very low "no-call" rates. It's validated technology delivering accurate results with clear positive or negative reporting.

Unparalleled sensitivity and specificity

QNatal Advanced was verified and validated in a study of 2,752 pregnant women.[1]

Singletons	T21	T18	T13	Monosomy X
# Pos/# Specs	90/2,637	30/2,637	20/2,637	1/2,637
Positives Detected	90/90	30/30	20/20	1/1
Sensitivity (%)	>99.9	>99.9	>99.9	>99.9
Specificity (%)	>99.9	>99.9	>99.9	>99.9

Twins	T21	T18	T13	Monosomy X
# Pos/# Specs	10/115	4/115	1/115	N/A
Positives Detected	10/10	4/4	1/1	N/A
Sensitivity (%)	>99.9	>99.9	>99.9	N/A
Specificity (%)	>99.9	>99.9	>99.9	N/A

Singleton data are combined analysis of verification (n=2,085) and validation (n=552) sets

High positive predictive value (PPV)

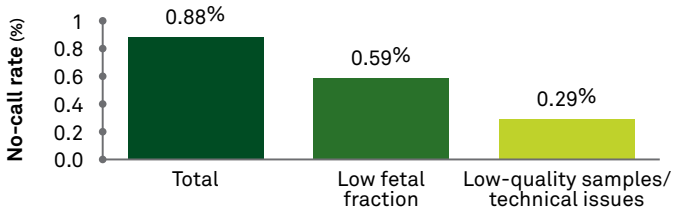
In real-world data on the first 10,000 patients, QNatal Advanced has higher PPVs than what is reported in the literature.

Positive Test Result	Prevalence	PPV	
		Cumulative*[2-7] (literature)	QNatal Advanced[1]
Trisomy 21	1:185	91%	97%
Trisomy 18	1:470	74%	90%
Trisomy 13	1:1500	41%	75%
Sex aneuploidy	1:1000	48%	87%
Microdeletions	1:3000	33%	100%

*Cumulative PPV is based on combined analysis of references 2 to 7 along with Quest unpublished data from third-party testing (excluding QNatal data).

A very low "no-call" rate

In commercial experience, including an analysis of the first 10,000 patients, QNatal Advanced demonstrated an overall "no-call" rate of 0.88%.[1]



Reducing the "no-call" rate means:

- Less uncertainty in referral to invasive diagnostic tests
- Less potential incidence of procedure-related miscarriages

American College of Obstetricians and Gynecologists guidelines (Committee Opinion No. 640, September 2015) recommend that women who receive a "no-call" test result from cfDNA prenatal screening should not only receive genetic counseling, but also be offered comprehensive ultrasound evaluation and diagnostic testing because of an increased risk of aneuploidy.†

QNatal Advanced validated technology and advanced bioinformatics generate low nonreportable rates, so you and your patients can count on test accuracy and avoid retesting or unnecessary invasive procedures.

Note: *Noninvasive prenatal screening (NIPS) is for screening purposes only and is not diagnostic.*

References:

1. Anderson B, *et al.* An automated, non-invasive prenatal screening assay (NIPS) for trisomy 21,18,13 in singleton and twin gestations [FIGO abstract FCS79.3.]. *Int J Gynaecol Obstet.* 2015;131(Suppl 5):E264. 2. Choy KW, *et al.* American Society of Human Genetics 2013 Annual Meeting; Boston, MA; 2013 [abstract 19]. 3. Meck JM, *et al.* American College of Medical Genetics and Genomics (ACMG) 2014 Annual Meeting; Nashville, Tennessee; 2014 [abstract 17]. 4. Zhang H, *et al.* Non-invasive prenatal testing for trisomies 21, 18 and 13: clinical experience from 146,958 pregnancies. *Ultrasound Obstet Gynecol.* 2015;45:530-538. 5. Yao H, *et al.* Detection of fetal sex chromosome aneuploidy by massively parallel sequencing of maternal plasma DNA: initial experience in a Chinese hospital. *Ultrasound Obstet Gynecol.* 2014;44:17-24. 6. Cheung SW, *et al.* Accurate description of DNA-based noninvasive prenatal screening. *N Engl J Med.* 2015;372:1675-1677. 7. Norton ME, *et al.* Cell-free DNA analysis for noninvasive examination of trisomy. *N Engl J Med.* 2015;372:1589-1597. † ACOG. Committee Opinion No. 640: Cell-free DNA screening for fetal aneuploidy. *Obstet Gynecol.* 2015;126:e31-e37.

Quest Diagnostics™

Scientific Publication/Presentation Key Summary

An Automated, Non-Invasive Prenatal Screening Assay (NIPS) for Trisomy 21, 18, 13 in Singleton and Twin Gestations

Oral Presentation at FIGO!

What is already known?

- Noninvasive prenatal screening (NIPS) assays use cell-free DNA in the blood of a pregnant woman to detect fetal chromosome aneuploidies (e.g., trisomies and sex chromosome aneuploidies)
- Compared to traditional screening methods, such as maternal serum marker screening and ultrasound imaging, NIPS has a lower false-positive rate. Thus, multiple organizations recommend NIPS for screening high-risk pregnancies for chromosome aneuploidies
- NIPS assays in general have good performance characteristics, but there is variability between assays; thus, it is important to validate each assay and report performance characteristics
- While sensitivity and specificity are important assay characteristics, the positive predictive value (PPV) is more clinically relevant. PPV describes the likelihood of a positive result being true in a specific population, which is especially important when a screen could lead to more invasive procedures that carry risk of miscarriage and other complications

What was done in this study?

- The investigators developed an automated NIPS assay for trisomy 21 (T21), T18, and T13; the assay incorporates advanced, proprietary statistical analyses and bioinformatics processes
- Performance characteristics of the assay were established for unaffected gestations using 1,288 plasma samples previously analyzed by another NIPS laboratory
- These characteristics were then verified using samples from 2,085 singleton gestations, which included T21, T18, and T13 samples
- The assay was then validated using samples from 552 singleton and 115 twin gestations, which included T21, T18, and T13 samples, as well as a sex chromosome aneuploidy (SCA; XO)
- Results from the first 10,000 clinical cases tested with this assay were analyzed

What were the findings of this study?

- In validation the assay identified all aneuploidy samples for both singleton and twin gestations. No false-positive results occurred in the validation study; thus, sensitivity and specificity were both 100%
- Analysis of the first 10,000 "real-world" clinical samples identified T21 in 103 pregnancies, T18 in 36, T13 in 21, sex chromosome aneuploidies (SCAs) in 17, and microdeletion in 1
- Within this 10,000 patient analysis, an overall no-call rate of 0.88% was reported:
  - 0.59% were due to a low fetal fraction
  - 0.29% were due to unmet quality metrics, uninformative DNA pattern or technical and sample-related issues
- For patients with available follow-up data, PPVs were 97% (34/35) for T21, 90% (18/20) for T18, 75% (9/12) for T13, and 87% (7/8) for SCA; the single microdeletion case was also confirmed

What were the conclusions from the study?

- A NIPS assay with excellent performance characteristics, including high PPVs, was developed and validated
- The assay also provided high PPVs and low no-call rates in a reference laboratory setting

Oral presentation at FIGO 2015

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FIGO World Congress of Gynecology and Obstetrics

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