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 (the percentage of patients whose results are not reported, indeterminate, or uninterpretable, because of laboratory technical issues). Its validated technology delivers 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

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

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

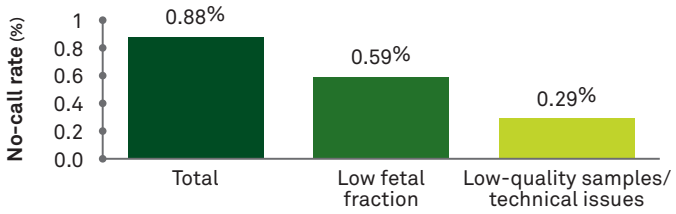
High positive predictive value (PPV)

In real-world data on the first 10,000 patients, QNatal Advanced has high PPVs.

Positive Test Result	Prevalence	QNatal Advanced PPV[1]
Trisomy 21	1:185	97%
Trisomy 18	1:470	90%
Trisomy 13	1:1500	75%
Sex aneuploidy	1:1000	87%
Microdeletions	1:3000	100%

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]



While noninvasive prenatal screening test is for screening purposes only and not diagnostic, reducing the "no-call" rate can help provide[2,3]:

- reduction in patient anxiety
- decrease in invasive diagnostic testing referrals
- fewer invasive 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.[3]

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.

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. Morris S, et al. Model-based analysis of costs and outcomes of non-invasive prenatal testing for Down's syndrome using cell free fetal DNA in the UK National Health Service. *PLoS ONE.* 2014;9:e93559. 3. 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, Noninvasive Prenatal Screening Test for Trisomy 21, 18, 13 in Singleton and Twin Gestations

Oral Presentation at FIGO

What is already known?

- Noninvasive prenatal screening tests use cell-free DNA in the blood of a pregnant woman to detect fetal chromosome aneuploidies (eg, trisomies and sex chromosome aneuploidies)
- Compared to traditional screening methods, such as maternal serum marker screening and ultrasound imaging, the noninvasive prenatal screening test has a lower false-positive rate. Thus, multiple organizations recommend the noninvasive prenatal screening test for screening high-risk pregnancies for chromosome aneuploidies
- The noninvasive prenatal screening test in general has 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 noninvasive prenatal screening test 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 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 noninvasive prenatal screening test 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

Authors

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