

Prenatal Cell-free DNA Screening

cfDNA screening

- Not a diagnostic test
- High sensitivity for trisomy 21, 18, 13, sex chromosomes
- Also tests for microdeletions, rare trisomies, single-gene disorders (accuracy unknown)
- Adequate fetal fraction is critical for accurate results
- Guidelines vary on who to test and what conditions to screen for

How does it work?

- Detects placental DNA fragments in maternal blood
- Measurable placental DNA is detectable from 10 weeks gestation to end of pregnancy
- 'Counts' DNA fragments to look for overabundance from one or more chromosomes

Age	Risk for trisomy 21	Positive result PPV	Negative result NPV
21	1/1160	49%	>99%
30	1/700	61%	>99%
40	1/86	93%	>99%

Understanding results | Concerns

- +** **Positive results: Increased chance for specific aneuploidy**
 - Chance for a false positive
 - Must be interpreted in context of positive predictive value
- **Negative result: Decreased chance for aneuploidy**
 - Chance for false negative
 - Still a small residual risk
- ?** **Indeterminate or 'no call' result**
 - Increased BMI or incorrect pregnancy dating
 - Indicates increased risk for aneuploidy

Who's at high risk?

- Over age 35
- Abnormal ultrasound
- Abnormal screening test
- Family history of aneuploidy
- Personal history of aneuploidy

Management

- Pre- and post-test counseling recommended
- Offer patients with a positive or 'no-call' result a diagnostic test (amniocentesis)
- Declining all prenatal testing/screening is an option

To learn more:

Prenatal cell-free DNA screening: <https://www.pathlms.com/ashg/course/4595>

Important Definitions

Sensitivity: detection rate, the proportion of individuals with the condition who test positive
Specificity: the proportion of individuals without the condition who test negative
Positive predictive value (PPV): the likelihood that someone with a positive test truly has the condition; related to the incidence of the condition in the population