# A look at cell-free DNA performance at 9 weeks gestation, stratified by patient weight ranges

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## 1. Introduction

Cell-free DNA (cfDNA) is an established first-line screen for common fetal aneuploidies in all pregnant patients, regardless of age or risk.[1] Patient weight is known to have an inverse relationship to fetal fraction (FF) while FF is directly related to gestational age (GA).[2] A previous study showed a non-reportable rate due to low FF between 9-12 weeks GA ranged from 0.14% in patients weighing <150 lbs to 17.39% in those weighing >400 lbs.[3] Little data exists on the success of cfDNA screening at 9 weeks GA stratified by patient weight. The benefit of drawing a patient for cfDNA screening between 9.0-9.9 weeks GA is earlier access to results. However, a high success rate is imperative in order for the patient to benefit from earlier access to diagnostic testing to help guide appropriate education and pregnancy management. This study evaluates the success rate of prenatal cfDNA screening results obtained between 9.0-9.9 weeks GA across different patient weight ranges at one laboratory.

## 2. Methods

A retrospective statistical analysis of >29,000 patient blood samples submitted to one laboratory, drawn between 9.0-9.9 weeks GA for traditional or expanded genome-wide prenatal cfDNA screening with available weights was performed. Traditional cfDNA screening includes screening for the common trisomies 21, 18 and 13 with opt-in choices for sex chromosome aneuploidy and/or select microdeletion syndromes and trisomies 16 and 22. Expanded genome-wide cfDNA screening samples were not included for analysis for study. Samples underwent DNA extraction, library preparation, and genome-wide massively parallel sequencing as described by Jensen et al.[4] Patients weighing <80lbs (n=59) were excluded as outliers likely related to errors on the test requisition form or with transcription. Samples with the indication for testing marked as NA/No known increased risk, or had no indication provided, were changed to "Maternal age" if the patient was ≥35 years of age at the time of the blood draw; if they were <35 years they were classified as "No known high risk". FF was analyzed on reportable cases (n=27,940) only. Total non-reportable samples (n=532) included QNS (low FF) (n=370) and technical failures (n=162); as technical failures are not expected to increase with increasing maternal weight, success rates in this study were calculated using non-reportables due to QNS only.

## 3. Results

The overall success rate for reporting on samples submitted between 9.0-9.9 weeks GA across all different patient weights was 98.69%. The average patient age in the cohort was 31 years and the average patient weight was 165 lbs (range 80-456 lbs), with most patients weighing <200 lbs (81.32%) (**Figure 1**). The average FF for reportable samples (n=27,940) was 7.41%, see **Figure 2** for FF distribution by patient weight. The most common indications for screening (**Table 1**) were "No known high risk" (66.71%) and "Maternal age" (32.28%). Singletons accounted for 98.80% of cases, and the overall positivity rate for the common trisomies was 0.78%. Stratifying by patient weight shows the majority of patients received a result when drawn between 9.0-9.9 weeks GA (**Table 2**), although a decrease in success rate as patient weight increased was observed. Success rate, when stratified by weight, was highest for patients weighing <100 lbs (99.53%). Success rate for patients weighing between 100-200 lbs was 99.22%, 96.64% for patients weighing between 200-300 lbs, and 91.70% for patients weighing ≥300 lbs.

## 4. Conclusions

The success rates stratified by patient weight as reported in this study are similar to those reported by Wardrop et al.[5] between 10-12 weeks GA, and by Hopkins et al.[3] between 9-12 weeks GA. The overall success rate of 98.69% is slightly higher than what was previously reported in a smaller 9.0-9.9 weeks cohort by Fanelli et al. 2018[6], perhaps related to implementation of assay enhancements since 2018. While the likelihood of a no-call result increases with patient weight, the high success rate in this cohort further supports use of cfDNA early in pregnancy. Earlier access to results can lead to earlier patient education and access to prenatal diagnosis when indicated. Limitations of this study include a lack of outcome data to further assess cfDNA screening performance at 9 weeks GA. Additionally, indications for referral were limited to the information provided on the test requisition form. As such, an indication of "abnormal serum biochemical screening" in the current pregnancy should not have been an indication for testing so early in pregnancy; however, it was reported as an indication for testing in 17 samples. This highlights the importance of including accurate and complete information on test requisition forms. Areas of future research could include exploring pregnancy outcomes from cfDNA screening samples drawn in the 9th week of gestation.

**Key Points:**

- Success rate for samples drawn between 9.0-9.9 weeks GA was 98.69%, indicating that the majority of samples drawn in the 9th week of pregnancy are likely to result with the first draw. Earlier access to results can allow earlier access to prenatal diagnosis.
- Similar success rates at different patient weights at 9 weeks gestation compared to samples drawn between 10 and 12 weeks.
- Improved success rate compared to a previous review in 2018 of success rates in cfDNA screening samples drawn at 9 weeks GA.

## References

1. Screening for Fetal Chromosomal Abnormalities. Practice Bulletin of the American College of Obstetrics and Gynecologists & Society for Maternal Fetal Medicine Obstetrics & Gynecology. Number 226, October 2020.
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3. Hopkins MK, Koelper N, Caldwell S, et al. Obesity and no call results: optimal timing of cell-free DNA testing and redraw. *Am J Obstet Gynecol* 2021;225:417.e1-10.
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5. Wardrop J et al. Success of NIPT based on Maternal Weight and Gestational Age. Poster presented at: NSGC Annual Conference; 2016 September 28-October 1; Seattle, WA.
6. Fanelli et al. Cell free DNA screening at 9 weeks: A clinical laboratory experience. Poster presented at: NSGC Annual Conference; 2018 November 14-17th; Atlanta, GA.

## Tables + Figures

**Table 1. Indication for screening**

| Indication | % |
|---|---|
| No known high risk | 66.71 % |
| Maternal age | 32.28% |
| Personal or family history | 0.57% |
| Ultrasound finding | 0.13% |
| Abnormal serum biochemical screening | 0.06% |
| Multiple indications | 0.25% |

**Table 2. Success rate at 9.0-9.9 weeks GA by patient weight**

| Gestational Age | Patient Weight (lbs) | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | <100 | ≥100 - <125 | ≥125 - <150 | ≥150 - <175 | ≥175 - <200 | ≥200 - <225 | ≥225 - <250 | ≥250 - <275 | ≥275 - <300 | ≥300 - <325 | ≥325 - <350 | ≥350 |
| 9.0-9.9 weeks | 99.53% | 99.72% | 99.55% | 99.08% | 98.36% | 97.67% | 95.73% | 95.69% | 94.50% | 91.67% | 89.47% | 95.00% |

**Figure 1. Patient weight distribution**

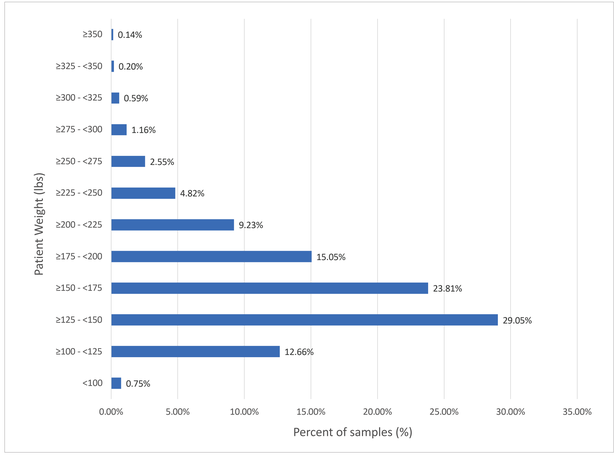
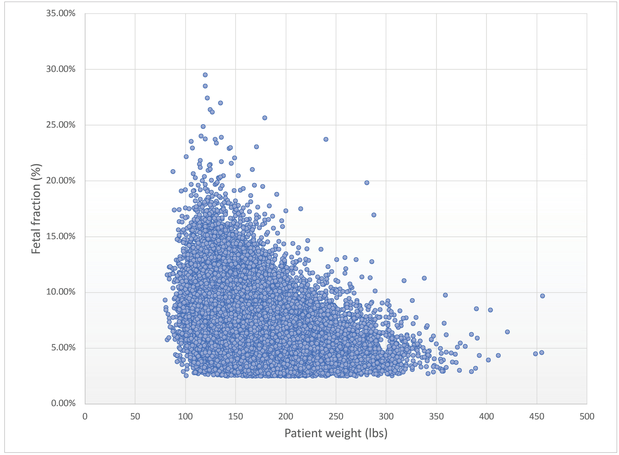



**Figure 2. Fetal fraction distribution by patient weight**

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