Aneuploidy Screening and Invasive Testing in Western North Carolina in the Era of Cell-free Fetal DNA Testing

Jennifer E. Warren, MD[a], Carol C. Coulson, MD[a], Rick M. Loftis, MD[a], Anna Beth Parlier, BA[b], Shearon F. Roberts, MS, CGC[c], Shelley L. Galvin, MA[b]
[a]Department of Obstetrics and Gynecology, Mountain Area Health Education Center, Asheville, NC
[b]Center for Research, Mountain Area Health Education Center, Asheville, NC
[c]Fullerton Genetics Center, Mission Health, Asheville, NC

Abstract

Noninvasive prenatal testing (NIPT) offers accurate screening for fetal aneuploidy, primarily trisomies 21, 18, and 13. Invasive diagnostic testing (IT) carries a risk of fetal loss but remains the standard for definitive diagnosis. We describe our experience with NIPT and subsequent IT in a regional referral center in western North Carolina. Decisions about NIPT, IT and the results were assessed prospectively for patients presenting for prenatal genetic counseling from November 2012 through November 2013. We compared NIPT and IT rates between women presenting in their first trimester [W1 ≤ 12wks: n = 74 (18.9)] versus later trimesters (W2-3 > 12wks: n = 318 (81.1%)] using Chi square or Fisher's exact test. Data are presented: n(%). Women presenting in the first trimester chose NIPT significantly more often than women later in pregnancy [W1 = 59 (79.7) vs. W2-3 = 140 (44); $p < 0.001$], and they chose IT significantly more often [9(12.2) vs. 11(3.5); $p = 0.005$). Indications for genetic counseling and reasons for declining NIPT were also significantly different. Our experience was different for women presenting for genetic counseling early versus later in pregnancy. There remains a subgroup of women who desire definitive and comprehensive information available only by invasive testing. These results provide more relevant and specific information when counseling patients.

Key Words: Prenatal genetic counseling; Non-invasive prenatal testing; Invasive prenatal testing

Introduction

Cell-free fetal DNA testing is a non-invasive prenatal screening test (NIPT) that primarily indicates if a woman is at increased risk of having a fetus with trisomies 21, 18, and 13. Its use in identifying risk for other genetic conditions is rapidly increasing.

NIPT measures the relative amount of free fetal DNA in the mother's blood and can be performed any time after 10 weeks gestation. The sensitivity and specificity of this test is higher than traditional analyte serum screening and is thought to detect greater than 99% of all Down Syndrome (T21) pregnancies and 97% of all trisomy 18 (T18) pregnancies. It detects about 92% of all trisomy 13 pregnancies (T13; see Table I).[1] This offers a much better detection rate for these aneuploidies in high risk populations than other screening tests currently available.[1-2] Better detection through screening seems to have reduced patients' desire for invasive diagnostic testing (IT), which carries a risk of fetal loss.[3]

Table I. Pooled Rates from the 2015 Meta-analysis[1]

	Detection rates	False positive rates
Trisomy 21	99% (95%CI, 98.2-99.6)	0.08% (95%CI, 0.03-0.14)
Trisomy 18	96.8% (95%CI, 94.5-98.4)	0.15% (9%CI, 0.08-0.25)
Trisomy 13	92.1% (95%CI, 85.9-96.7)	0.20% (95%CI, 0.04-0.46)

Use of NIPT has some limitations compared to traditional analyte screening as it does not give information about neural tube or ventral wall defects.[4] Further, Norton, et al. found of the 26,059 invasive tests results from the California Program, 2993 were abnormal (11.5%); of these, 83.1% were predictable based on current NIPT methods but 16.6% were not.[5] Across 29 French clinics, NIPT identified 100% of Down Syndrome, 88% of T18 and 100% of T13. Both ultrasound and NIPT missed 0.4% of other abnormal karyotypes. In another study, NIPT performed for the indication of abnormal ultrasound findings missed 7.9% of other abnormal karyotypes.[6]

In addition, use in low risk pregnancies is still controversial as data are limited. A recent study reported low false positive rates in detection of T21, but it was underpowered to compare detection rates to traditional testing in low risk populations.[6]

The American College of Obstetrics and Gynecology (ACOG),[4] the Society for Maternal Fetal Medicine (SMFM),[7] the International Society for Prenatal Diagnosis (ISPD),[8] the American College of Medical Genetics and Genomics (ACMG),[9] and the National Society of Genetic Counselors (NSGC)[10] have all issued statements recommending the use of NIPT for aneuploidy screening in women at increased risk of aneuploidy. The ACOG Committee Opinion on cell-free DNA screening states that this method of testing has great potential when used appropriately to screen for fetal aneuploidy to guide counseling, but does not replace definitive testing by amniocentesis or chorionic villus sampling (CVS).[4] All women who screen positive are recommended to undergo invasive, confirmatory testing using either amniocentesis or CVS, as the predictive value of NIPT varies widely based on the population screened.[11] The NSGC indicated in 2012 that offering of NIPT must include comprehensive genetic counseling.[8,10]

The incorporation of NIPT has impacted prenatal genetic counseling significantly.[12-13] As the biometric proprieties of NIPT approach that of a diagnostic test, NIPT has caused a paradigm shift in prenatal testing as it exists somewhere between screening and diagnostic tools.[13-14] Horsting, et al. report that 75% of genetic counselors surveyed indicated their patients use NIPT for a diagnosis.[12] Further, the number of women seeking genetic counseling has increased, along with the need for highly trained genetic counselors who understand their patients' motives and choices for prenatal testing.[12-13]

The objective of this project is to describe our experience with patients presenting for genetic counseling since the introduction of NIPT at our regional referral center for high-risk pregnancies in the western North Carolina.

Methods

During our data collection time period, four genetic counselors provided counseling in our regional referral center two half-days a week. Our center was staffed by two full-time maternal-fetal medicine specialists and four full-time sonographers. A total of 392 women presented for prenatal genetic counseling and ultrasound in our high-risk obstetrical ultrasound unit from November 2012 through November 2013.

This is a cross-sectional study. The protocol was approved by the institutional review board at our tertiary care hospital. Data were gathered prospectively by a resident; reasons, decisions, and indications, dates or gestational ages, and results of maternal-fetal medicine specialist

consultation, ultrasound (US), genetic counseling visits, NIPT, IT, and pregnancy termination were recorded (see Appendix A). Data were entered and verified by the Project Manager.

Data Analysis

We described patients, indications for referral, and rates of NIPT and IT between women presenting in their first trimester (W1 $\leq$12wks) versus later trimesters (W2-3 $>$12wks). Comparisons, including women who chose testing in the first trimester versus later trimester and women who elected NIPT versus those who did not, were done with Chi square or Fisher's exact test with significance $p<0.05$.

Results

Seventy-four women (18.9%) presented for counseling in the first trimester and 318 women (81.1%) presented in the second/third trimester. Women who had genetic consultation in the first trimester all had consults with a maternal-fetal medicine specialist and an ultrasound at the same visit. Among women who came in the second or third trimesters for consultation, all but three had concurrent ultrasounds [315(99.1%)].

Overall, 235 women (59.9%) presented with advanced maternal age (AMA) as their only indication for counseling and testing; 123 (31.4%) presented with other risk factors, including abnormal ultrasound findings or screening results, a personal history of abnormal findings or teratogen exposure, and 34 (8.7%) presented with both AMA and another risk factor.

Overall, 199 (50.8%) of the women chose to undergo NIPT. Overall, 20 (5.1%) women chose an invasive test; 15 (3.8%) chose amniocentesis and six (1.5%) chose CVS.

Indications for referrals to genetic counseling were significantly different between the group of women presenting in the first trimester versus those presenting in the second or third trimesters (see Table II; $p=0.023$), as were the percentages of women opting for NIPT and/or IT ($p<0.001$, $p=0.005$, respectively) and the reasons for declining NIPT (see Table III; $p<0.001$).

Table II. Indications for Genetic Counseling for Singleton Pregnancies, N = 392

	Gestational Age at Consult	
	$\leq$ 12 weeks **N = 74**	$>$12 weeks **N = 318**
	n (%)	n (%)
AMA	58 (78.4)	177 (55.7)
Other Risk Factors	6 (8.2)	117 (36.8)
Abnormal US	3	59
Abnormal Screen	0	50
Previous Child/ Pregnancy w/ abnormal finding	3	7
Teratogen Exposure in pregnancy	0	1
AMA and Another Risk Factor	10 (13.5)	24 (7.5)
Abnormal US	2	5
Abnormal Screen	0	7
Teratogen exposure	0	3
Previous child/pregnancy with abnormal finding	4	4
Family history	4	3
Carrier status	0	2

Note. $X^2 = 23.26$ (df = 2), $p<0.00001$

Decision trees and discussion of these results are presented separately for the two groups of women.

Table III. Reasons for Declining NIPT

	Gestational Age at Consult	
	≤ 12 weeks N=15	>12 weeks N=178
	n (%)	n (%)
Desired definitive testing	6 (40)	8 (4.5)
Amnio	5	5
CVS	1	3
No insurance and/or too expensive	5 (33.3)	11 (6.2)
No screening desired	2 (13.3)	125 (70.2)
Other Reasons	1 (6.7)	34 (19.1)
Already had/tried Harmony elsewhere	0	3 (1.7)
Already had QUAD	0	19 (10.7)
Already had targeted ultrasound	0	8 (4.5)
Desired targeted ultrasound first	0	4 (2.2)
Desired to discuss with doctor	0	2 (1.1)
Desired time to consider/discuss with fathers	0	7 (3.9)
Results would not affect course of pregnancy	0	3 (1.7)
Perceived self to be low-risk	0	1 (0.6)
Termination chosen	1 (6.7)	0
Unknown	0	4 (2.2)

Note. Multiple responses allowed, thus percentages may add up to greater than 100%.

Women Presenting in the First Trimester (W1 ≤12wks)

Figure 1 summarizes the indications for and testing choices of the 74 women presenting early in pregnancy. Most women, 58 (78.4%), presented with AMA as their only indication. Regardless of the indications, most women chose NIPT (81% of AMA, 83.3% of Other Risk Factors, and 70% of combined AMA and Other Risk Factors); there was no significant difference in indications ($p=0.706$). In all, 59 of the 74 women chose NIPT (79.7%). Fifteen women did not choose NIPT; one woman (1.7%) chose an alternative screen, and 14 (18.9%) chose no screen. The vast majority of those choosing NIPT did not go on to undergo IT (94.8%); only 3 women did choose IT. Conversely, 40% of the women opting to forgo screening with NIPT, went on to choose IT ($p=0.002$). In all, nine women (12.2%) chose to undergo IT. Most women who came early in pregnancy either wanted definitive testing or were concerned about expense (see Table III).

A case summary of all women with genetics consultation in the first trimester is shown in Table IV; shown are women choosing IT and those opting for termination based on other abnormal results in absence of NIPT.

Table IV. Cases Summary of Women Seeking Genetics Counseling at ≤12 Weeks Gestation

Gestational Age at Genetics Consult ≤ 12 weeks					
Patient	**Indication**	**NIPT Result**	**US Findings**	**IT Result**	**Outcome**
1	Previous child or fetus w/ abnormality	Inconclusive	EIF	Amnio-nl	Delivery
2	AMA	Low risk	Nothing identified	Amnio-nl	Delivery
3	AMA	Low risk	EIF	Amnio-nl	Delivery
4	AMA & Hygroma	Declined	Declined	CVS - T21	Termination
5	AMA & Hygroma	Declined	Hygroma	CVS-nl	Delivery
6	AMA & Previous child or fetus w/ abnormality	Declined	Nothing identified	CVS-nl	Delivery
7	AMA	Declined	Hygroma	CVS-nl	Delivery
8	AMA	Declined	Nothing identified	CVS-nl	Delivery
9	AMA	Declined	Nothing identified	Amnio-nl	Delivery
10	AMA	T18	Nothing identified	Declined	Termination
11	Abnormal US: Worsening pleural effusion	Declined	Declined	Declined	Termination
12	Abnormal US: Hygroma	Declined	Declined	Declined	Termination

Among the 74 women presenting in their first trimester, one inconclusive NIPT, two negative NIPT and six forgoers chose IT. All but one had AMA as an indication. The one screen that returned with inconclusive results was normal on amniocentesis (patient #1); and one unscreened patient underwent CVS and had a positive result for T-21 (patient #4). One screen positive (T18) declined further testing opting for termination (patient #10).

Women Presenting in the Second or Third Trimester (W2-3 >12wks)

Figure 3 summarize the indications for and testing choices of the 318 women counseled later in pregnancy. A slight majority, 177(55.7%), presented with AMA, and 141 (44.3%), presented with other risk factors with or without AMA. Indications for counseling did differ significantly between those who chose NIPT and those who did not ($p=0.023$); 50.8% of AMA, 35% of Other Risk Factors, and 37.5% of combined AMA and Other Risk Factors chose NIPT.

In all, 140 (44%) chose NIPT; 178 (56%) opted to forego NIPT; 9 (2.8%) women chose an alternative screen, and 169 (53.1%) chose none. The primary reason for declining NIPT was the desire for no screening at all in 125 women (70.2%; see Table III).

The vast majority opted not to undergo IT; 97.8% of those with NIPT findings of low risk; 96.1% of women who did not have NIPT screening; and 60% of those with elevated risk on the NIPT. In all, 11 women (3.5%) chose to undergo IT. Opting for IT was not related to forgoing NIPT ($p=0.761$).

Among all 318 women presenting later in pregnancy, two NIPT positive, two NIPT negative, and seven forgoers chose IT; only five had advanced maternal age as an indication (see Table V).

Cases among women presenting in the second or third trimester of pregnancy for counseling are shown in Table V; included are women who chose IT and those with positive NIPT

findings who decline IT. Three screen positives (T-21) opted not to undergo invasive testing (patients #12-14) while two (T-21) were confirmed by amniocentesis (patients #1 and 2); two screen negatives were confirmed (patients #3 and 4), and one unscreened positive (T-21) was identified (patient #9).

Table V. Case Summary of Women Seeking Genetics Counseling at >12 Weeks Gestation

Gestational Age at Genetics Consult > 12 weeks					
Patient	**Indication**	**NIPT Result**	**US findings**	**IT Results**	**Outcome**
1	Abnormal US – increased nuchal	T21	Declined	Amnio – T21	Termination
2	Abnormal MSS	T21	Short long bones	Amnio – T21	Delivery
3	AMA	Low risk	EIF	Amnio - nl	Delivery
4	Previous child w/abnormality	Low risk	Multiple anomalies	Amnio - nl	Delivery
5	Previous child w/abnormality	Declined	No findings	Amnio - nl	Delivery
6	Abnormal US – EIF & 2 vessel cord	Declined	Multiple markers & anomalies	Amnio - nl	Delivery
7	AMA	Declined	CP cysts	Amnio - nl	Delivery
8	AMA	Declined	No findings	Amnio - nl	Delivery
9	Abnormal MSS & Abnormal US – multiple findings	Declined	Multiple markers & anomalies	Amnio – T21	Delivery
10	AMA & Previous child w/abnormality	Declined	Renal hydronephrosis	Amnio - nl	Delivery
11	AMA	Declined	No findings	CVS - nl	Delivery
12	AMA	T21	Declined	Declined	Termination
13	Abnormal MSS	T21	Multiple anomalies & markers	Declined	Delivery
14	Abnormal Quad	T21	EIFs & CP cysts	Declined	Delivery

Conclusions

Uptake of NIPT was 50.9% and our overall IT rate was 5.3%. However, our experience with NIPT and IT was very different for women presenting for genetic counseling early versus later in pregnancy. Approximately 3.5 times as many women counseled early in their first trimester desired definitive testing as compared to women later in their pregnancies. Further, most of the women counseled early who went on to choose IT declined NIPT (8 of 12).

Friel, et al.,'s looked at reduction of IT uptake after NIPT and found a significant reduction among women counseled between 14 and 22 weeks gestation, but not among women counseled at <14 weeks gestation.[15] They did not find, however, any difference in the rate of IT between the two groups of women (14% and 17.9%, respectively). Our rate of IT among women counseled early in pregnancy was similar at 12.2%, but among those later in pregnancy the rate was much lower at 5.3%. We did not find any other reports separating analyses by trimester of testing.

A multi-site study across multiple locations in the United States concluded the reductions in IT post-NIPT were likely not a regional phenomenon but were associated with abnormal NIPT results.[16] Further, over half of genetic counselors also perceive that an abnormal NIPT is associated with choosing IT.[12] However, our center, in western North Carolina, a region of Appalachia, found only two of six women with abnormal NIPT chose to undergo amniocentesis.

Pettit, et al. reported the indications for testing in most of their patients were positive aneuploidy screen and abnormal ultrasound findings (79%), which is similar to the proportion of patients who opted for NIPT in our study for these same indications (74%).[17] Furthermore, they reported advanced maternal age was related to choosing IT. We also found AMA women among the vast majority of women presenting early in pregnancy who wanted definite testing.

Reasons for choosing IT over NIPT may include: presence of more than one indication for testing, concern over financial implications of multiple tests, desire to have the most comprehensive information early to aid in decisions about pregnancy, and anxiety surrounding any uncertainty in the ultimate diagnosis. Financial implications on choice of testing have been demonstrated in other studies. In a study in New York, 40% of 235 patients accepted NIPT, and those that accepted this testing were more likely to be white, with private insurance, and to have more than one indication for testing. Once controlling for other factors, insurance coverage was the only reason for declining NIPT as it was not covered by public insurance options at that time.[18] Fifty percent of genetic counselors report patients decline NIPT due to cost concerns.[12]

Belief that IT is the preference of patients' obstetricians is perceived to be a reason for patients declining NIPT among 71.1% of genetic counselors. Conversely, perceiving that patients accept NIPT due to their obstetricians' preferences is believed to be so for only 0.5% of genetic counselors.[12]

Anxiety surrounding uncertainty about fetal well-being may also have an impact. In one study, IT decreased from 49% to 12% in response to availability of NIPT, however maternal anxiety increased from 22% to 55% in this population.[19] Other psychosocial factors related to choosing IT included: having a supportive attitude towards testing, perceiving testing as reliable, and requesting more scientific information about testing.[20]

Despite the low rate of IT found in our study, there remains a subgroup of women in our population, primarily among women who present in the first trimester for counseling, who ultimately choose IT due to risk factors including AMA, a history with fetal abnormalities, or abnormal ultrasound findings. We cannot say why this is so – a thorough tracing of the individual time lines and reasons for decisions were beyond the scope of this project. Further, generalization of our results is limited by the inclusion of only one site – it is, however, the only site in the western 16 counties of the state that offers access to this care and is thus representative of our region.

Genetic counselors must have the knowledge and confidence to provide necessary prenatal counseling to women regarding their options for screening and diagnostic testing and how these options differ with respect to the accuracy of information provided.[10,12-13] Understanding the different perspectives and patterns of testing chosen by women presenting for prenatal genetic counseling earlier in pregnancy compared to those presenting later in pregnancy is important to consider in the counseling process. Improved understanding of the patient's perspective may help the counselor provide more relevant and useful information to aid in decision making.

References

1. Gil MM, Quezada MS, Revello R, Akolekar R, Nicolaides KH. Analysis of cell-free DNA in maternal blood in screening for fetal aneuploidies: Updated meta-analysis. *Ultrasound Obstet Gynecol*. 2015;45(3):249-266. doi: 10.1002/uog.14791 [doi]. PubMed PMID: 25639627.
2. Verweij EJ, van den Oever JM, de Boer MA, Boon EM, Oepkes D. Diagnostic accuracy of noninvasive detection of fetal trisomy 21 in maternal blood: A systematic review. *Fetal Diagn Ther*. 2012;31(2):81-86. doi: 10.1159/000333060 [doi]. PubMed PMID: 22094923.
3. Warsof SL, Larion S, Abuhamad AZ. Overview of the impact of noninvasive prenatal testing on diagnostic procedures. *Prenat Diagn*. 2015;35(10):972-979. doi: 10.1002/pd.4601 [doi]. PubMed PMID: 25868782.
4. American College of Obstetricians and Gynecologists. Committee opinion no. 640: Cell-free DNA screening for fetal aneuploidy. *Obstet Gynecol*. 2015;126(3):e31-7. PubMed PMID: 26287791.
5. Norton ME, Jelliffe-Pawlowski LL, Currier RJ. Chromosome abnormalities detected by current prenatal screening and noninvasive prenatal testing. *Obstet Gynecol*. 2014;124(5):979-986. doi: 10.1097/AOG.0000000000000452 [doi]. PubMed PMID: 25437727.
6. Bianchi DW, Rava RP, Sehnert AJ. DNA sequencing versus standard prenatal aneuploidy screening. *N Engl J Med*. 2014;371(6):578. PubMed PMID: 24571752.
7. Society for Maternal-Fetal Medicine. SMFM statement: Maternal serum cell-free DNA screening in low risk women [Internet]. Washington: Society for Maternal-Fetal Medicine; 2015 [cited 2016 Mar 21]. Available from: https://www.smfm.org/publications/157-smfm-statement-maternal-serum-cell-free-dna-screening-in-low-risk-women.
8. Benn P, Borell A, Chiu R, et al. Position statement from the aneuploidy screening committee on behalf of the board of the International Society for Prenatal Diagnosis. *Prenat Diagn*. 2013;33(7):622-629. PubMed PMID: 23616385.
9. Gregg AR, Gross SJ, Best RG, et al. ACMG statement on noninvasive prenatal screening for fetal aneuploidy. *Genet Med*. 2013;15(5):395-398. doi: 10.1038/gim.2013.29 [doi]. PubMed PMID: 23558255.
10. Devers PL, Cronister A, Ormond KE, Facio F, Brasington CK, Flodman P. Noninvasive prenatal testing/noninvasive prenatal diagnosis: The position of the national society of genetic counselors. *J Genet Couns*. 2013;22(3):291-295. PubMed PMID: 23334531.
11. American College of Obstetricians and Gynecologists. ACOG practice bulletin no. 88, December 2007. Invasive prenatal testing for aneuploidy. *Obstet Gynecol*. 2007;110(6):1459-1467. PubMed PMID: 18055749.
12. Horsting JM, Dlouhy SR, Hanson K, Quaid K, Bai S, Hines KA. Genetic counselors' experience with cell-free fetal DNA testing as a prenatal screening option for aneuploidy. *J Genet Couns*. 2014;23(3):377-400. doi: 10.1007/s10897-013-9673-4 [doi]. PubMed PMID: 24352524.

13. Wax JR, Cartin A, Chard R, Lucas FL, Pinette MG. Noninvasive prenatal testing: Impact on genetic counseling, invasive prenatal diagnosis, and trisomy 21 detection. *J Clin Ultrasound*. 2015;43(1):1-6. doi: 10.1002/jcu.22243 [doi]. PubMed PMID: 253031.
14. Allyse M, Sayres LC, King JS, Norton ME, Cho MK. Cell-free fetal DNA testing for fetal aneuploidy and beyond: Clinical integration challenges in the US context. *Hum Reprod*. 2012;27(11):3123-3131. PubMed PMID: 22863603.
15. Friel LA, Czerwinski JL, Singletary CN. The impact of noninvasive prenatal testing on the practice of maternal-fetal medicine. *Am J Perinatol*. 2014;31(9):759-764. doi: 10.1055/s-0033-1359717 [doi]. PubMed PMID: 24338115.
16. Platt LD, Janicki MB, Prosen T, et al. Impact of noninvasive prenatal testing in regionally dispersed medical centers in the United States. *Am J Obstet Gynecol*. 2014;211(4):368.e1-368.e7. doi: 10.1016/j.ajog.2014.03.065 [doi]. PubMed PMID: 24705127.
17. Pettit KE, Hull AD, Korty L, Jones MC, Pretorius DH. The utilization of circulating cell-free fetal DNA testing and decrease in invasive diagnostic procedures: An institutional experience. *J Perinatol*. 2014;34(10):750-753. doi: 10.1038/jp.2014.102 [doi]. PubMed PMID: 24875410.
18. Vahanian SA, Baraa Allaf M, Yeh C, Chavez MR, Kinzler WL, Vintzileos AM. Patient acceptance of non-invasive testing for fetal aneuploidy via cell-free fetal DNA. *J Matern Fetal Neonatal Med*. 2014;27(1):106-109. doi: 10.3109/14767058.2013.806477 [doi]. PubMed PMID: 23687914.
19. Comas C, Echevarria M, Rodriguez I, Serra B, Cirigliano V. Prenatal invasive testing: A 13-year single institution experience. *J Matern Fetal Neonatal Med*. 2014;27(12):1209-1212. PubMed PMID: 24131234.
20. Pivetti M, Melotti G, Morselli D, Olivieri M. Psychosocial factors affecting uptake of prenatal genetic testing: A pilot study. *Prenat Diagn*. 2013;33(13):1276-1282. doi: 10.1002/pd.4248 [doi]. PubMed PMID: 24122815.

Disclosure: None of the authors have any conflicts of interest to disclose.
Funding: No external funding supported this project.

Authors' Contributions:

Jennifer E. Warren, MD, Maternal-Fetal Medicine Specialists and Faculty Mentor: Project conceptualization and design, interpretation, critical revision, and approval of the final manuscript
Carol C. Coulson, MD, Maternal-Fetal Medicine Specialists and Faculty Mentor: critical revision and final approval of manuscript
Rick Loftis, MD, MAHEC OB/GYN Resident: Data extraction, interpretation, and prior presentation
AnnaBeth Parlier, BS, Project Manager: Data management and final approval of manuscript
Shearon F. Roberts, MS, CGC, Genetic Counselor: Obtained data, interpretation, critical revision, and final approval of the manuscript
Shelley L. Galvin, MA, Director of Research: Data analysis and interpretation, manuscript drafts and critiques, final approval of the manuscript

Previous Presentation:

Warren JE, Loftis RM, Parlier AB, Roberts SF, Galvin SL, Coulson CC. Aneuploidy screening and invasive testing in the era of cell-free fetal DNA testing (NIPT). Poster session presented at: Annual Meeting of the American College of Medical Genetics; 2014 March 28; Nashville, TN.

Correspondence: Shelley L. Galvin, MA
MAHEC Center for Research 121 Hendersonville Road, Asheville, NC 28803
Phone: 828.771.5501
Email: Shelley.Galvin@mahec.net

Appendix A

Title: Aneuploidy Screening and Invasive Testing in Western North Carolina in the Era of Cell-free Fetal DNA Testing. Journal of Genetic Counseling

Authors: Jennifer E. Warren[1], Carol C. Coulson,[1] Rick M. Loftis[1], AnnaBeth Parlier[2], Shearon F. Roberts[3], Shelley L. Galvin[2]

Corresponding Author: Shelley L. Galvin
Center for Research, MAHEC; Email: Shelley.Galvin@mahec.net

Data Collection Sheet

Name:
DOB:
Referring provider:

1. EGA at time of visit: _____ weeks _____ days

2. EGA determined by:
   () LMP () LMP and _____ week ultrasound () _____ week ultrasound only

3. What was the reason for visit (please list specific reason next to appropriate category)?
   () AMA
   () Family history concerns : _____
   () Suspected fetal anomaly: _____
   () Ultrasound aneuploidy marker: _____
   () Abnormal serum screening test: _____
   () Other: _____

4. Did the patient have genetic counseling or consultation with MFM?
   () Yes () No

5. Did the patient have an ultrasound at the time of counseling/consultation?
   () Yes () No

6. Did the patient choose Harmony screen?
   () Yes () No

7. If yes to questions 6, please skip to question 11.
   If no to question 6, what was the reason for declining Harmony test?
   () No screening desired
   () Cost or insurance coverage concerns
   () Had another test in previous pregnancy
   () Desire to discuss with provider
   () Desired definitive invasive testing : (choose one) _____ Amnio _____CVS
   () Other: _____

8. Did the patient choose another screening test?
   () Yes () No

9. If yes to question 8, which other screening test was selected?
   () Quad screen
   () NT screen
   () Serum integrated screen
   () Targeted ultrasound

10. EGA at time of test: _____ weeks _____ days

11. Were initial results of the Harmony screen inconclusive?
   () Yes () No

12. If no to question 11, please skip to question 14.
   If yes to question 11, did the patient opt to redraw sample?
   () Yes () No

13. EGA at time of redraw: _____

14. What was the turn around time for results (including redraw if performed)?
   () 7-10 days
   () 11-14 days
   () 15-21 days
   () > 21 days: _____

15. Results of Harmony test for Trisomy 21: _____
16. Results of Harmony test for Trisomy 18: _____
17. Results of Harmony test for Trisomy 13: _____

18. Did the patient choose invasive testing at any time?
   () Yes: (choose one) ____Amnio _____CVS
   () No

19. If no to question 18, please skip to question 20.
   If yes to question 18, EGA at time of invasive testing: _____weeks _____ days

20. Did the patient ultimately choose to terminate pregnancy?
   () Yes () No