a tale of two studies

The Effects of Delivery Context on Women's Experiences of Prenatal cfDNA Screening

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Introduction

The clinical implementation of prenatal cfDNA screening has taken place very quickly and with little regulation. Commercial marketing, a lack of provider and patient education, and the wide variability in prenatal health care contexts have influenced the way women learn about, receive, and experience the results of these noninvasive prenatal genetic screening. As a result, patients' experiences of being offered, undergoing, and receiving results from prenatal cfDNA screening have varied considerably.[1-2]

We compare two studies of womens' experiences in acceping cfDNA screening with starkly different results. The differences in delivery context reflected in these two groups' result in divergent experiences of prenatal cfDNA screening.

Methods

Study 1 surveyed patients in a large medical system between March 2014 and September 2015. Women in a high risk cohort, as defined by maternal age, family history, previous screening result, or previously affected pregnancy were offered a 55 minute counseling session with a certified genetic counselor. Patients in this population were offered cfDNA screening for trisomies 13, 18 and 21, and X and Y aneuploidies. Those who accepted cfDNA screening were invited to participate in a survey research study. Participants completed a mixed-method survey immediately after accepting cfDNA screening, which was returned to the clinic. After the results of cfDNA screening were reported, participants were mailed a second survey and returned it by mail. 72% of eligible patients consented; 82% completed Survey 1 and 72% of these completed Survey 2. Results were digitized and analyzed using SAS and SPSS statistical software and NVivo qualitative analysis software.

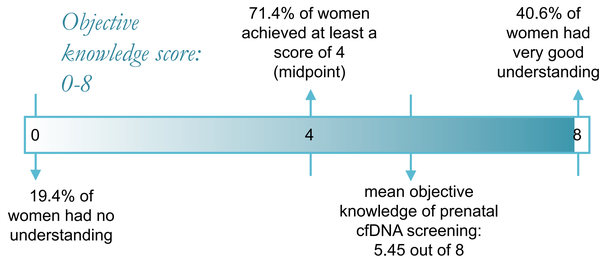
Study 2 interviewed women who had received screen-positive, incorrect, or inconclusive prenatal cfDNA screening results. Women were recruited from online pregnancy forums. Participants were consented for semi-structured interviews, conducted by telephone between September 2015 and February 2016. Interviews explores participants' experiences in accepting, undergoing, and receiving the results of cfDNA screening, their feelings about the results delivery process, the result, cfDNA screening in general and plans for follow up. Interviews were recorded, by permission of the participant, and professionally transcribed. An iterative codebook was constructed using a modified grounded theory methodology[3] and transcripts were qualitatively coded by a team of researchers using NVivo.

References

[1] Parham, L., Michie, M. & Allyse, M. Expanding use of cfDNA screening in pregnancy: Current and emerging ethical, legal, and social issues. *Curr Genet Med Rep* 2017.
[2] Minear MA, Alessi SA, Allyse MA, et al. Where are we now with non-invasive prenatal testing? A review of current and emerging ethical, legal, and social issues. *Annu Rev Genomics* 2015; 16:369–98.
[3] Charmaz K. *Constructing grounded theory: A practical guide through qualitative analysis.* Thousand Oaks, CA: Sage; 2006.

Study 1 population and results

447 women in Southern California, ages 23-44. By study design, all received screen-negative results from cfDNA. Participants reported highly positive interactions with genetic counseling and performed well on basic knowledge tests about the purpose, capabilities, and potential outcomes of cfDNA screening.



Study 1 qualitative results

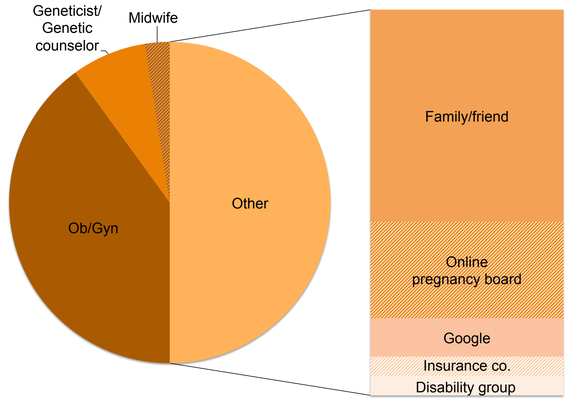
76% expressed positive feelings after learning of their cfDNA results (confidence, security, relief, calm and gratefulness).

Only 6% reported stress and anxiety while waiting to hear results.

Study 2 population and results

40 women from 19 US states, Canada, and England, ages 25-44. By study design, all received screen-positive, incorrect, or inconclusive results from cfDNA. Patients did not report receiving genetic counseling prior to screening and generally reported that they felt they has relatively low levels of knowledge prior to undergoing screening, especially about the content of cfDNA screening and its true predictive value.

"Where did you first hear about this test?"



Study 2 cfDNA Result	N(%)
False positive (T13/T18/T21)	10 (25.0)
False positive (XY/microdeletion)	9 (22.5)
High risk (T13/T18/T21)	7 (17.5)
High risk (XY/microdeletion)	4 (10.0)
True positive (T13/T18/T21)	2 (5.0)
True positive (XY/microdeletion)	2 (5.0)
False negative (T13/T18/T21)	1 (2.5)
Inconclusive	5 (12.5)

Study 2 selected quotes

"We were sort of duped by the medical industry a little bit into having a test that was really more inaccurate than accurate and left us with more questions than answers."

And the way that they represent some of the statistics, too, I think it was like, you know, 99.9 percent accuracy."

"I wouldn't eliminate the possibility [of using cfDNA again], although I think I would go into it more skeptically."

Results Comparison

Women in **Study 1** were overwhelmingly positive about cfDNA screening, understood the test and their results, and usually would recommend it to others—reporting extremely low decision regret. Women in **Study 2** largely expressed disappointment with the test, were often unaware of what was being screened (especially when the panel included microdeletions), and usually said they would not choose the same test again.

These differences in attitude reflect interrelated differences in delivery context and results received, with accompanying differences in test knowledge, counseling and support.

Study 1	Study 2
Had cfDNA because of known risk	Had cfDNA for many reasons besides risk
Had cfDNA only for trisomies	Often had expanded cfDNA (microdeletions)
Had individual GC pre-test counseling	Pre-test counseling variable
Mostly received reassuring results	Received troubling results
Had systems in place for post-test support	Post-test support variable

Discussion

The stark differences between women's experiences in **Study 1** and **Study 2** illuminate the need for consistent and strong recommendations from professional societies for best practices in offering and delivering prenatal cfDNA screening, along with improved provider education.

Knowledgeable pre- and post-test genetic counseling can increase women's understanding of the test, the screened conditions, and the results; prepare and support them in the case of positive, false, and inconclusive results; and connect them to appropriate post-test surveillance and care.

However, without clear professional recommendations, provider education, and payor coverage, many women will continue to receive inadequate counseling and education. Without support for responsible implementation, even a high-quality genetic test will have detrimental effects on many patients and families.

Limitations

- These two studies utilize very different methodologies, which may have contributed to the differences in study results.
- In addition, the recruitment periods for the two studies differed slightly, which in the context of this fast-moving technology may have affected the outcomes.
- These studies focused largely on the US context and the study populations were likely less racially, socioeconomically, and educationally than the pregnant population as a whole.
- Therefore, the generalizability of these results are limited. We suggest these findings suggest the need for further research on the delivery context of prenatal screening and testing.

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Further information

For more information about these two studies and related research, email pirc@prenatalinformation.org, visit PIRC at http://prenatalinformation.org/ or scan this QR code with your smartphone: