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ORIGINAL RESEARCH

Evaluation of Patient Education Materials: The Example of Circulating cell free DNA Testing for Aneuploidy

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Abstract Informed consent is the process by which the treating health care provider discloses appropriate information to a competent patient so that the patient may make a voluntary choice to accept or refuse treatment. When the analysis of circulating cell free DNA (ccfDNA) became commercially available in 2011 through the Prenatal Diagnostic Laboratory at Women & Infants Hospital of Providence, Rhode Island to "high-risk" women, it provided an opportunity to examine how commercial laboratories informed potential consumers. We identified, via an internet search, four laboratories offering such testing in the United States and one in Europe. We evaluated patient educational materials (PEMs) from each using the Flesch Reading Ease method and a modified version of the Suitability Assessment of Materials (SAM) criteria. Pamphlets were also reviewed for their inclusion of content recommendations from the International Society for Prenatal Diagnosis, the National Society of Genetic Counselors, the American College of Obstetricians and Gynecologists jointly with the Society of Maternal Fetal Medicine, and the American College of Genetics and Genomics. Reading levels were typically high (10th–12th grade). None of the pamphlets met all SAM criteria evaluated nor did any pamphlet include all recommended content items. To comply with readability and content recommendations more closely, Women & Infants Hospital created a new pamphlet to which it applied the same criteria, and also subjected it to focus group assessment. These types of analyses can serve as a model for future evaluations of similar patient educational materials.

Keywords Patient education materials · Focus groups · High risk

The recent introduction of circulating cell-free DNA (ccfDNA) for aneuploidy necessitated the availability of patient education materials (PEMs) that could be provided orally and/or via pamphlets or other media through the prenatal care provider's office. The source of these PEMs may be patient advocacy sites, medical professional organizations/academic institutions, or commercial laboratories.

In developing new informational materials or assessing existing ones, it is important to consider the needs of the intended audience (Deatrick et al. 2010). Factors such as content, appearance, writing style, organization of the material, and print size will impact whether the information is not only understood, but also whether it is even read. Once new materials have been developed or a decision has been made to use existing ones, it is recommended that a focus group verifies the suitability of the materials for the intended users and assures that inappropriate design and content concerns are identified and corrected (Gal and Prigat 2005).

In 1977, alpha fetoprotein (AFP) testing for neural tube defects was introduced in the United States, and patient informational materials were developed simultaneously (1978). As each advance in this screening occurred, patient materials

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were updated as well (Hall et al. 2007). In 1985, Doak and Doak published *Teaching Patients With Low Literary Skills* (Doak et al. 1996), now a classic in the field, and becoming an important resource for anyone developing PEMs.

In November 2011, the Prenatal Diagnosis Center (PDC) at Women & Infants Hospital of Rhode Island began offering the option of ccfDNA testing to women presenting with increased risk for aneuploidy (Palomaki et al. 2011). The PDC staff was concerned that adding this new choice to the other available testing options could increase a woman's difficulty in making an informed decision in the relatively short time available (BMO professional experience). To help patients make informed decisions about their health care, providers utilize PEMs which should not only include appropriate content but must also be understandable and readable. The availability of easily understandable PEM is a requirement of the Joint Commission on Accreditation of Healthcare Organization (JCAHO) (2010), which recommends that PEMS should be written at or below a 5th grade level. Healthy People 2010 (www.healthypeople.gov/2010) has defined health literacy as "the capacity to obtain, process, and understand basic health information and services needed to make appropriate health decisions."

To be sure that PEMs addressed the health literacy of women being offered the ccfDNA test, we evaluated commercially available pamphlets. Although PEMs on this subject are available through several media including the internet (Mercer et al. 2014), we limited our analysis to the preparation and evaluation of printed patient materials about ccfDNA testing provided by commercial laboratories, focusing on factors, in addition to literacy levels, that help make the material easily understandable to the average reader.

Materials and Methods

We performed an internet search in January 2012 (search term: "non invasive prenatal testing Down syndrome") which identified four US companies and one located in Europe that provided, or planned to provide, ccfDNA testing for autosomal trisomies. Although several terms [e.g., non invasive prenatal screening (NIPS), non invasive prenatal diagnosis (NIPD), non invasive DNA testing (NIDT)], have evolved to describe this testing, we reasoned that the keys words used in the search were inclusive enough to identify all laboratories offering such testing. The companies, Ariosa Diagnostics, Sequenom Center for Molecular Medicine, Natera, Inc., and Verinata Health, in the US and LifeCodexx in Germany all had PEMs customized to their laboratory developed test. We limited analyses to pamphlets available in English (Table 1). Ariosa and LifeCodexx posted a patient educational pamphlet on their respective websites; Sequenom and Verinata supplied their materials upon request. The Natera pamphlet was

Table 1 Laboratory patient education materials reviewed

Laboratory	Location	Pamphlet	Source
Ariosa Diagnostics	San Jose, CA	Harmony Prenatal Test *An advance in non-invasive trisomy testing*	www.ariosadx.com/for-pregnant-women/IG_Patient_Brochure_July_2012.pdf
LifeCodexx	Konstanz, GER	PrenaTest *For non-invasive prenatal testing for fetal trisomy 21*	http://lifecodexx.com/index.php?id=24
Natera, Inc.	San Carlos, CA	Panorama prenatal test *Prenatal screening for common genetic abnormalities of the fetus*	Pamphlet provided by laboratory upon request
Sequenom CMM	San Diego, CA	*Prenatal testing Options for Trisomy 21, 18 and 13 are Evolving- What you Should Know*	Pamphlet provided by laboratory upon request
Verinata Health, Inc.	Redwood City, CA	Verifi prenatal test *Patient Guide for Non-invasive Prenatal Testing Options*	Pamphlet provided by laboratory upon request

provided by a company representative although testing itself would not be available until 2013. In 2013 we reviewed any updated patient pamphlets from the same four laboratories. To identify recommended content of patient pamphlets we conducted a separate Medline search for guidelines or recommendations published by professional organizations using [(practice guideline OR statement OR recommendation) AND Down syndrome AND DNA AND plasma], and Medline searches ((“Advisory Committees”[MeSH] OR “Position statement”[text] OR “Committee Opinion”[text] OR “guideline”[text]) AND (“prenatal diagnosis”[MeSH] OR “non-invasive prenatal”[text]) AND (“prenatal diagnosis/methods”[MeSH] OR “sequence analysis, DNA/methods”[mesh] OR “massively parallel sequencing”[text] OR “cell free DNA”[text] OR “cell free fetal DNA” [text]) AND (“aneuploidy”[mesh] OR “Down syndrome/diagnosis”[mesh]) AND (Guideline[ptyp] AND “2008/03/17”[PDat] : “2013/03/15”[PDat] AND “humans”[MeSH Terms]). Reference lists from retrieved articles were also searched. Searching identified recommendations from the International Society for Prenatal Diagnosis (ISPD) (Benn et al. 2013), National Society of Genetic Counselors (NSGC) (Devers et al. 2013), the American Congress of Obstetricians and Gynecologists (ACOG) (ACOG 2012) in conjunction with the Society for Maternal-Fetal Medicine (SMFM) and the American College of Medical Genetics and Genomics (ACMG) (Gregg et al. 2013). All contained content-specific suggestions for educational materials about ccfDNA testing. Our content assessment assumed that a woman reading the material would be aware that she is at increased risk for aneuploidy and that she has ready access to information about the clinical conditions. It also assumed that the purpose of the pamphlets is to provide information specifically about ccfDNA screening for Down syndrome and other common trisomies. One of the authors, a certified genetic counselor experienced with prenatal screening, (EMK) examined each pamphlet to determine whether each content item was present or absent.

We assessed readability using published criteria (Doak et al. 1996). This formal Suitability Assessment of Materials or SAM analysis (which encompassed the Flesch Reading Ease score (Flesch 1948)) takes into account content, literacy demand, and use of graphics, layout, and typography in assessing readability. One of the authors (PKH), a professional educator familiar with the methodology, scored each pamphlet against four of the six SAM criteria on a scale of 0–2 where “not suitable” was rated 0, “adequate” earned 1 point, and “superior” was rated 2 points. “Learning Stimulation & Motivation” was not scored because the pamphlets were designed to inform rather than influence behavior change (i.e., understanding ccfDNA testing rather than choosing ccfDNA testing was the goal). Neither was “Cultural Appropriateness” scored since only English-language versions were reviewed, and the target audience was self-selected as women interested in prenatal testing following high-risk designation. Once the pamphlets were rated against the four remaining criteria (and their sub-criteria), scores were tallied and converted to percentages based on maximum possible score. Scores of 70–100 % were classified “superior,” those with a score of 40–69 % “adequate,” and less than 40 % were deemed “not suitable”, per SAM standards.

If our analyses of commercially available pamphlets identified shortcomings, we considered developing our own generic pamphlet unconstrained by proprietary bias and including all recommended content elements.

Results

Content Recommendations from Professional Organizations

A summary of recommended content items from each professional organization is shown in Table 2. All organizations recommended inclusion of information about results, available follow up, the implications of a positive result, confirmatory testing following positive results, very high risk associated with positive results, consideration of an invasive procedure in lieu of screening, and the possibility of false negative results. All groups except the NSGC suggested the inclusion of a statement that ccfDNA testing may not be informative for some patients. Only ACOG and the ACMG included the caution that structural abnormalities such as open neural tube defects were not detectable by ccfDNA screening and only the ISPD and ACMG recommended that patients consider the possibility of stress related to waiting for final results.

Assessment of Patient Pamphlets for Recommended Content

Results of the pamphlet review for recommended content items are shown in Table 3. None of the pamphlets included possible stress associated with the wait for results; two labs also neglected to mention the need to screen for structural abnormalities but otherwise included all eight of the remaining content items. Two other labs included seven of the 10 content recommendations, one failing to reference an invasive diagnostic procedure as an alternative to screening, and another excluding the possibility that the test may be uninformative. The remaining lab’s pamphlet only included three recommended content items: the implications of a positive test result, its associated high risk, and the alternative of an invasive procedure as an option.

Assessment of Patient Pamphlets for Readability

Results of the readability assessment, the most important of the suitability criteria, are shown in Table 4 for the five

Table 2 Recommended content for patient pamphlets regarding ccfDNA testing

Recommended Content	Professional Organization			
	ACOG	ISPD	NSGC	ACMG
Information about results	√	√	√	√
Information about available follow-up	√	√	√	√
Implications of a positive ccfDNA test result	√	√	√	√
False positive results and need for further testing	√	√	√	√
High DS risk associated with positive ccfDNA test results	√	√	√	√
Amnio/CVS may be indicated instead of screening	√	√	√	√
Possibility of false negative results	√	√	√	√
Test may not be informative for some patients	√	√		√
Screen for structural abnormalities, e.g., ONTD	√			√
Potential stress in wait for final results		√		√

commercial pamphlets (first five columns of results). Each pamphlet was classified as "superior," "adequate" or "not suitable" based on scores obtained using specific SAM criteria (Doak et al. 1996). Below is the summary assessment in each of the assessment areas.

Content This assessment relates to *how* the content is presented and not to the *recommended* content discussed earlier. All pamphlets reviewed provided "superior" or "adequate" *statements of purpose* and all rated "superior" for providing content *aimed at health behaviors*. Three had "superior" ratings for *limited scope* (i.e., addressing essential information specifically related to the purpose), while two were "adequate." Two pamphlets provided "superior" material for a *summary/review*, while the remaining three included no summary or review.

Literacy Demand None of the pamphlets had suitable *reading grade level.* One had a 10th grade reading level, and four were at 12th grade reading levels. Two pamphlets used the *active voice* more than 50 % of the time, earning them a "superior" rating while the remaining three were rated "adequate." Three of the pamphlets were rated "not suitable" for *use of common words*, and two were rated "adequate." Because of the topic being presented, medical terminology has to be used to some extent. For the materials that were rated "not suitable," there were few if any explanations of the technical terms in language that an average reader could understand. Three pamphlets were rated "superior" in providing an *early context* for subsequent material and two were rated "adequate." All pamphlets received a rating of "superior" in providing *headers or captions* (so-called "road signs") to introduce upcoming content.

Use of Graphics Two pamphlets were rated "superior" in having a *cover graphic* showing the purpose, one was rated "adequate," and two were rated "not suitable." Two pamphlets received "superior" ratings for inclusion of *simple line drawings* representing key messages, one was rated "adequate," and two were rated "not suitable." For using *on-topic, relevant illustrations,* the ratings were the same as for inclusion of graphics. Four of the pamphlets had no *captions for*

Table 3 Presence (+) or absence (−) of recommended content in each reviewed patient pamphlet

Content suggested by Professional Organizations	Source of Patient Pamphlets				
	Lab A	Lab B	Lab C	Lab D	Lab E
Information about results	+	+	+	−	+
Information about available follow-up	+	+	+	−	+
Implications of a positive ccfDNA test result	+	+	+	+	+
False positive results and need for further testing	+	+	+	−	+
High DS risk associated with positive ccfDNA results	+	+	+	+	+
Amnio/CVS may be indicated instead of screening	−	+	+	+	+
Possibility of false negative results	+	+	+	−	+
Test may not be informative for some patients	−	+	+	−	−
Screen for structural abnormalities, e.g., ONTD	+	−	−	−	−
Potential stress in wait for results	−	−	−	−	−

Table 4 Results of formal Suitability Assessment of Materials (SAM) readability assessment of patient pamphlets

SAM Criterion[a]	Lab A	Lab B	Lab C	Lab D	Lab E	WIH
Content						
Purpose is evident	2	2	2	1	2	2
Addresses health behavior	2	2	2	2	2	2
Scope is limited	1	1	2	2	2	2
Summary/review is included	2	0	0	2	0	1
Literacy/Demand						
Flesch Reading Ease (grade)	0 (12+)	0 (12+)	0 (10)	0 (12+)	0 (12+)	1 (8–9)
Active voice is used primarily	1	1	2	2	1	2
Vocabulary uses common words	1	0	1	0	0	2
Context is given first	2	2	2	1	1	2
'road signs' are used	2	2	2	2	2	2
Graphics						
Cover graphics shows purpose	0	0	2	1	2	2
Simple/familiar line drawings used	0	0	2	1	2	1
Illustrations are relevant to text	0	0	2	1	2	2
Captions are used for graphics	0	0	1	0	0	0
Layout[b] and typography[c]						
At least 5 layout factors are present	–	–	2	–	–	2
At least 3 layout factors are present	–	1	–	1	1	–
2 or fewer layout factors are present	–	–	–	–	–	–
4 typography factors are present	–	–	–	–	–	2
2 typography factors are present	1	1	1	1	1	–
1 or no typography factors is present	–	–	–	–	–	–
Subheads are used	2	2	2	2	2	2
Raw Score out of 34 (%)	**16 (47 %)**	**14 (41 %)**	**25 (74 %)**	**19 (56 %)**	**20 (59 %)**	**27 (80 %)**
Overall SAM rating	**Adequate**	**Adequate**	**Superior**	**Adequate**	**Adequate**	**Superior**

WIH Women & Infants Hospital of Rhode Island

[a] Scoring: 2=superior, 1=adequate, 0=not suitable, '–'=not applicable

[b] The eight layout factors include: illustrations on the same page, adjacent to the related test; layout and sequence of information are consistent, making it easy for the reader to predict the flow of information; visual cluing devices (shading, boxes, arrows) are used to direct attention to specific points or key content; adequate white space is used to reduce the appearance of clutter; use of color supports and is not distracting to the message; line length is 30–60 characters and spaces; there is high contrast between type and paper; paper has non-gloss or low gloss finish

[c] The five typography factors include: type is serif, sans-serif or similar; type size is at least 12 point; typographic cues emphasize key points; there are no "all caps" for long headers

graphics and therefore were rated "not suitable," while the fifth received a rating of "adequate." *Explanation of lists and tables* is an additional consideration in the SAM but is not applicable to any of the reviewed pamphlets.

Layout and Typography One pamphlet was rated "not suitable" by including two or fewer of the layout factors listed in footnote b to Table 4. Three pamphlets were rated "adequate" by including three or four layout factors. One was scored as "superior" by including at least five layout factors. All pamphlets were rated "adequate" on typography factors by having two or three of the factors present. None of the pamphlets used itemized lists, so use of *subheads* was not rated.

Overall Assessment of Readability Out of 34 possible points, four pamphlets earned at least 14 (40 %) but less than 24 points (70 %) and received an "adequate" rating (Lab A - 47 %, Lab B - 41 %, Lab D – 56 % and Lab E – 59 %). The pamphlet from Lab C received a "superior" assessment with a score of 74 % by earning 25 points.

Development of a New Patient Pamphlet

Because none of the existing pamphlets included all recommended content items as suggested by the professional societies, we drafted a new pamphlet. Revisions to that pamphlet were made based on specific patient recommendations (e.g.,

the inclusion of a graphic representing amniocentesis, more information about trisomies18 and 13, a realistic appraisal of the procedure-related risk of miscarriage, and more information about out-of-pocket costs and/or insurance coverage).

With approval from the Women & Infants Hospital Institutional Review Board we convened two focus groups of pregnant women to review the materials, facilitated and recorded by one of the authors (PKH or EMK). A total of six pregnant Rhode Island women selected by the authors affiliated with the Division of Maternal-Fetal Medicine were invited to read the draft pamphlet and then were asked open-ended questions regarding content, format and vocabulary. The pregnant women (four in the 1st group and two in the 2nd) were from varied socio-economic backgrounds and were not themselves candidates for ccfDNA testing. Women from the second group raised many of the same issues and offered suggestions similar to those from the first group but added little new information, indicating that most issues had been addressed. We modified the pamphlet based on the focus group responses then subjected it to the same evaluation of readability and content as materials from the commercial laboratories.

The new Women & Infants Hospital pamphlet that we developed as a result of professional and focus group recommendations included all recommended content items except advice to screen for ONTD. Regarding its readability (Table 4 column 6), it received ratings of "superior" for purpose, content about behaviors, and limited scope, and "adequate" for summary included, in the *content* category. In *literacy demand*, this pamphlet was rated "superior" in every category except reading grade level (grade 8–9) which was "adequate." In the *graphics* category, the ratings were "superior" for cover graphic and relevance of illustrations, "adequate" for simplicity, and "not suitable" for captions. For *layout and typography*, the Women & Infants Hospital pamphlet received "superior" ratings in all sub-categories. As an example of "superior" versus "not suitable" writing in the areas of reading ease score and vocabulary, the implications of a negative result were presented in one commercial pamphlet as:

> "A negative test result means that the existence of trisomy 21 in the unborn child can be excluded with a high degree of certainty. Depending on the medical reason which caused the [commercial name] test to be performed, your responsible physician will nevertheless track the course of your pregnancy with special attention and advise further examinations, if necessary."

That same information in the new Women & Infants Hospital pamphlet reads:

> "A negative test means that the chance that your baby has Down syndrome, trisomy 18, or trisomy 13 is less than 1 in 2000. You would no longer be considered at 'high risk'."

The WIH pamphlet earned 27 out of 34 possible points (80 %), consistent with a "superior" overall rating.

Discussion

Patient education materials (PEMs) are often used to initiate positive health behaviors in patients lacking essential health knowledge or skill sets. PEMs however will not be effective if written at a grade level that surpasses the comprehension of the target audience (Taylor-Clarke et al. 2012). Although it may be difficult to write PEMs at the 5th grade reading level as recommended by the Joint Commission, many PEMs are written at such a high level as to be unhelpful (Schloman 2004).

Our review of five commercially available PEMs for ccfDNA testing revealed that pamphlets regarding ccfDNA testing for aneuploidy left room for improvement in meeting the health literacy needs of high risk patients. While all were at least adequate according to SAM criteria (none were superior), all were written at a reading level of 10th grade or higher. The vocabulary and the spacing and size of the text of some commercial pamphlets were also inadequate. The ISPD (Benn et al. 2013), the NSGC (Devers et al. 2013), the ACMG (Gregg et al. 2013), and the ACOG/SMFM (ACOG 2012) have promulgated policy statements outlining key content issues. The content assessment revealed that the PEMs we evaluated lacked basic information crucial to patients in making an informed choice about acceptance or interpretation of ccfDNA testing. This is especially concerning since, unlike health messages designed to encourage nutrition or increase exercise, information about ccfDNA testing has only recently been in the public eye. Furthermore, health care providers themselves may be unfamiliar with the unique features of ccfDNA testing and can offer limited reinforcement (Musci et al. 2013).

The resources that we accessed to gauge the commercial pamphlets (and our own) are readily available to commercial PEM developers, though it is not known whether they were utilized. Gal and Prigat (2005), through a series of semi structured interviews of PEM developers in Israel, identified four key mistakes which can lead to readability and usability problems:

- Organizational pressures caused by inappropriate people (technicians, legal consultants, etc.) influencing content
- Mistaken assumptions about how the PEMs would be used
- Mistaken assumptions about literacy, numeracy, or educational achievement of end users
- Lack of adequate pilot testing

The extent to which any of these issues influenced the preparation of the five pamphlets evaluated is unknown.

Our response to the identification of unsatisfactory PEMs was the creation, validation and evaluation of an improved new pamphlet that met most standards for professionally-approved content and had a marginally adequate reading grade level score. This highlighted for us the challenge of creating a readable educational pamphlet even when focusing on readability as a primary goal. Terms such as "chromosome," "ultrasound," and "amniocentesis" do little to lower reading grade level, and opportunities to make the pamphlet more understandable must be found elsewhere.

Study Limitations

There are limitations to the current study. We evaluated PEMs prepared by commercial laboratories when they introduced ccfDNA testing for the common trisomies, 21, 18, and 13. All of the US commercial companies now include select sex chromosome abnormalities, and some laboratories are now targeting other less common trisomies as well as micro deletions (Vora and O'Brien 2014). Additionally, incidental reports have emerged of maternal neoplasm being identified through ccfDNA testing (Osborne et al. 2013). As PEMs are updated to reflect these changes, laboratories will likely take the opportunity to better tailor these materials to their audiences and include recommended content previously omitted, while proactively including the updated information.

Although assessment of reading level is well defined, the SAM criteria used to assess other aspects of these PEMs are not the only ones available. Our focus groups were smaller than intended, but their responsiveness was important to the improvement of the Women & Infants Hospital pamphlet.

Implications for Patient Education

The commercial laboratories located in the US all highlight or at least mention one or more of the professional guidelines on their websites, but none followed all of the content recommendations contained in those guidelines. Laboratories should consider promptly modifying patient pamphlets to meet new content recommended by professional organizations and/or changes in their tests. In the future, ccfDNA testing is likely to expand routinely into the general pregnancy population. In this scenario, informing women of the benefits and limitations of ccfDNA testing will rest heavily on PEMs since individualized education provided by genetic counselors, routinely available in high-risk centers, will likely not be available in primary care prenatal offices.

Lastly, academic and non-profit institutions can obtain an editable generic copy of the validated Women & Infants Hospital pamphlet online (www.ipmms.org).

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Conflict of interest Paula Haddow declares that she has no conflict of interest.

Jacquelyn Halliday declares that she has no conflict of interest.

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Human Studies and Informed Consent All procedures followed were in accordance with the ethical standards of the responsible committee on human experimentation (institutional and national) and with the Helsinki Declaration of 1975, as revised in 2000. Informed consent was obtained from all patients for being included in the study.

Animal Studies No animal studies were carried out by the authors for this article.

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