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NEXT GENERATION GENETIC COUNSELING

Genomic Counseling in the Newborn Period: Experiences and Views of Genetic Counselors

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Abstract As newborn screening (NBS) technology expands, genetic counselors will become more involved in counseling for NBS results, including those potentially generated from whole exome sequencing (WES) and eventually whole genome sequencing (WGS). Members of the National Society of Genetic Counselors (NSGC) responded to an online survey (n=208) regarding genomic counseling in the context of NBS. The majority of participants (82.1 %) did not feel prepared to counsel for WGS results from NBS. Counselors with previous WES/WGS counseling experience felt more prepared (p= 0.005) to counsel for WGS results from NBS than those without WES/WGS experience. Overall, counselors expressed ethical and practical concerns regarding WGS in NBS, as well as a need for additional training regarding this application of the technology before it is implemented. Based on the results of this study, genetic counselors voice caution to the larger genetics community regarding expansion of NBS to incorporate genomic sequencing and advocate for additional education prior to initiating WGS into NBS.

Keywords Genomic counseling · Newborn screening · Whole exome sequencing · Whole genome sequencing

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Introduction

Newborn screening (NBS) is one of the nation's most successful public health programs. It has been used to detect serious and preventable health problems in the first few days of life in thousands of newborns over the past 50 years. NBS programs have significantly expanded since their inception in the early 1960s, when they only screened for PKU; they now screen for over 30 conditions in most states. The introduction of tandem mass spectrometry in the late 1990s allowed for programs to screen for multiple conditions using a single bloodspot. As NBS has expanded, a number of ethical issues have been raised; the most important issue is whether the benefits of screening outweigh the harms. This issue is especially pertinent as conditions are now included that challenge the traditional Wilson and Jungner criteria used to determine when population screening of a particular condition may be acceptable (Wilson and Jungner 1968). In particular, concerns have been raised about the addition of conditions for which there are no effective treatments available (Ross 2010) and that have phenotypic variations that include late-onset forms of a disease (Grosse et al. 2006). This shift in the types of disorders that are already included in NBS programs has raised significant ethical issues surrounding the justification for keeping NBS mandatory. Some have suggested that programs might consider making some tests compulsory and offering and obtaining consent for an expanded set of conditions. These kinds of ethical questions are becoming further complicated as NBS is once again facing the potential benefits

and challenges of a new technology—i.e., next generation genomic sequencing.

Some states have added Sanger gene sequencing technology to their diagnostic panels for NBS to screen for specific disorders such as cystic fibrosis (Comeau et al. 2004). However, there is a growing discussion nationally about the potential to utilize next generation sequencing, namely whole exome (WES) or whole genome sequencing (WGS), in an NBS setting (Clayton 2010). The integration of WES or WGS into NBS programs would allow programs to screen for a significantly wider array of genetic conditions (Goldenberg and Tarini 2012). Additionally, the use of genomic sequencing in newborns would represent a new approach to personalized medicine, with the potential to provide vast amounts of physical and psychological health information at the beginning of life. Such information could lead to disease prevention, treatment, or, at the very least, awareness.

On the other hand, genomic NBS raises challenges, especially with the identification of new variants of unknown significance; this information can potentially cause life-long stress and expose parents and their children to information they may not want to know. In addition, issues surrounding the provision of parental informed consent for their newborn will further complicate matters (Almond 2005). The amount and complexity of data that would be available though genomic screening would potentially change the focused goals of NBS, and require enhanced parental education and counseling (Goldenberg and Sharp 2012). This will likely be challenging given the compulsory nature of current NBS programs, which has been justified because true NBS positives are relatively rare, and can lead to devastating outcomes if not identified in a timely manner. More importantly, these outcomes can often be prevented. Issues arise, however, when parents lack an understanding of the NBS process, especially, regarding false positive results. Five percent of parents with children who had false positive results for Cystic Fibrosis (CF) in a Wisconsin study about NBS for CF still believed their children could be affected with CF when asked a year later (Ross 2010). Results like these reinforce the need for genetic counseling in the context of NBS, especially if the complex technology of WGS is integrated into NBS.

Some genetic counselors are currently involved in the NBS process, either through direct involvement with state screening programs (Bach et al. 1992) or through the provision of follow-up counseling after a positive NBS result (Lang et al. 2011). In a study surveying all NBS programs in the United States, Puerto Rico, and the US Virgin Islands, 20 out of 26 respondents reported the employment of Master's-level trained genetic counselors (Farrell et al. 2001). No recent surveys have documented the number of genetic counselors currently employed by NBS programs. However, only five of the 1,232 genetic counselors who responded to the most recent National Society of Genetic Counselors' Professional Status Survey (2012) stated that newborn screening was their primary specialty. Although it is not clear how many genetic counselors are directly involved in NBS, it nevertheless appears that they provide a valuable service to families. For example, a Pittsburgh study performed over a 6-year period asked 114 parents of children who received a positive newborn screen for hemoglobinopathy traits about their experiences with genetic counselors. The authors concluded that genetic counseling was beneficial to parents; 99 % of participants said that their questions were answered, 82 % expressed feeling less anxiety after the counseling sessions, and 78 % stated they discussed the information provided to them with their partner after the session (Kladny et al. 2011).

Genetic counselors are also involved in the interpretation of genomic test results for patients in other settings. For example, they may counsel patients regarding microarray results (Schaaf et al. 2011) or provide direct-to-consumer testing counseling (Hawkins and Ho 2011). Recently, WES has also been introduced into clinical practice.

As NBS programs begin to explore the utilization of these kinds of screening platforms, either as a replacement for current screening technology or as an adjunct for secondary testing, they need to address whether health professionals, including genetic counselors, are prepared for the integration of these technologies into the newborn period and how utilization of these screening platforms might impact practice. Genetic counselors will likely have an increasing role in the follow-up of NBS results, including WES and eventually WGS, if it is introduced into NBS. Genetic counselors will likely play a major role in the communication and interpretation of results to parents if this testing is mandated. There have been studies on genetic counselors' attitudes towards expansion of NBS and counselor roles; however, there is little known regarding their preparedness to provide genomic counseling pertaining to results from a newborn screen and their opinions regarding this type of counseling. This study begins to fill this gap by exploring genetic counselors' attitudes and preparedness regarding WGS in the context of NBS.

Methods

Study Design and Participants

Members of the National Society of Genetic Counselors (NSGC) were asked to participate in an on-line survey regarding their experience with counseling for NBS and WGS. They were also asked about their preparedness to counsel for sequencing results from NBS, including current disorders on panels, WES results, and WGS results. Following approval by the University Hospitals Case Medical Center Institutional Review Board, genetic counselors who are full members of NSGC were invited to participate in this study via an e-blast

message and one follow-up reminder message sent out by NSGC. A total of 2,360 potential recipients were reached with the NSGC e-blasts. Respondents had to be full members of NSGC and currently practicing as genetic counselors in order to participate. When student and associate members of NSGC are removed from the eBlast list, there are approximately 2,270 genetic counselors on the recipient list who were eligible for this study.

Data collection was conducted from December 2012 to February 2013. Two hundred and twenty five genetic counselors participated in the study, but 17 were excluded because they did not complete the entire survey. Therefore, a total of 208 genetic counselors completed the survey (9.2 % response rate if the e-blast reached all 2,270 eligible genetic counselors).

Measures

Dr. Lainie Friedman Ross, an author of a previous study regarding genetic counselors' opinions towards the expansion of newborn screening, granted permission to utilize and adapt questions from a published survey by Hiraki et al. (2006) in order to explore genetic counselors' attitudes and preparedness regarding whole genome sequencing in the context of newborn screening. Additional questions for the current study were developed by the researchers.

The survey for the current study was divided into 11 sections, and contained 35 questions. To address content validity, three experts in NBS and/or genomic technologies reviewed the questionnaire to determine whether the survey assessed the intended information. In addition, the questionnaire was reviewed by five certified genetic counselors to assess clarity, ease of flow, and ability to address the researchers' specific study aims. Most questions were quantitative and used a five-point Likert scale (strongly disagree; disagree; neither agree nor disagree; agree; strongly agree). There were also several open-ended questions that allowed participants to add comments.

The first and second sections of the questionnaire focused on background information about the participant's career as a genetic counselor, past and current involvement with NBS results, and participants' roles in this process. These questions were modified from the questionnaire published by Hiraki et al. (2006). The third section included questions about participants' experience with WES or WGS results and their roles in these processes.

The remaining sections of the questionnaire included questions regarding participants' experience with counseling for gene sequencing results in NBS, their preparedness to counsel patients about these results, and, if they did not feel prepared, what they felt was necessary to prepare them for this type of counseling. Similar questions were asked with regard to WES and WGS in NBS using five-point Likert scale questions (strongly agree to strongly disagree) and open-ended responses.

Participants were also asked how WGS in NBS would affect their practices in terms of the amount of time spent performing various genetic counseling responsibilities, such as case preparation, counseling patients, and follow-up ("a lot less time; a little less time; neither less nor more time; a little more time; a lot more time") and their preparedness to counsel for WGS results in the context of NBS. Lastly, participants were asked how comfortable they felt about counseling for WGS in the context of NBS in comparison to counseling for current NBS or WES/WGS results in other contexts.

Statistical Analysis

Descriptive statistics, including means, standard deviations, frequencies, and percentages, were used to describe the study population and to quantitatively describe the area(s) of genetic counseling in which participants practiced. The frequencies of responses regarding the ways in which WGS in NBS would affect participants' counseling practices were determined. In addition, frequencies of responses regarding preparedness of counselors to counsel for sequencing results from disorders currently on NBS panels, as well as their preparedness regarding counseling for WES and WGS in the context of NBS, were also determined. This allowed for analysis of the differences between participants' preparedness to counsel for each of these described levels of sequencing technology with regard to NBS.

A Pearson's Chi-Square test was used to compare the preparedness to counsel specifically for WGS in NBS between counselors who had experience counseling for either NBS results or WES/WGS results and those who did not. This was performed to determine whether there was a correlation between preparedness and counselors' experiences. For example, those who had counseled patients regarding NBS, WES, or WGS results were hypothesized to be more likely to agree with the statements that they were prepared to counsel for WGS results in the context of NBS. All quantitative analyses were performed using SPSS for Windows version 20.0.

Analysis of Open-Ended Questions

In addition to the survey questions described above, this study also included a number of open-ended free-response questions regarding preparedness of genetic counselors. Respondents were asked, "If you do not feel prepared to counsel for gene sequencing for NBS results, what do you think is necessary to prepare you for this type of counseling?" Two other questions also asked what participants felt was necessary to prepare for counseling about "WES in NBS results" and "WGS in NBS results." Lastly, one free-response question was asked regarding how WGS in NBS would affect participants' practices. These questions were meant to allow the counselors in our study to express more detailed perspectives on genomics and NBS. However, respondents were not required to provide

answers to these open-ended questions in order to move on with the survey.

The responses to these questions were analyzed using thematic analysis (Boyatzis 1998). Two team members independently reviewed all the open-ended textual responses to look for common perspectives among respondents related to two major thematic areas: 1) preparedness for genomic counseling; 2) potential impact of genomic screening on practice. These responses were then further analyzed to identify more specific perspectives or areas of concern within these major categories. Differences between reviewers were resolved through discussions at team meetings.

Results

Participant Characteristics

Of the 208 genetic counselors who participated in this study, 96.6 % were female and seven were male (3.4 %). The majority of respondents work in the United States (93 %), with 7 % working in Canada, and reported practicing <1–5 years (54.9 %). The majority listed their primary specialty area as prenatal or pediatric genetic counseling (Table 1). There were no significant demographic differences between the 208 survey participants and the 17 counselors who did not complete the survey. These data are reflective of the demographic profiles of genetic counselors published in the Professional Status Survey (NSGC 2012).

Table 1 Demographic characteristics of sample (n=208)

Variable	n (%)
Gender (n=208)	
Male	7 (3.4)
Female	201 (96.6)
Years practicing (n=206)	
<1–5 years	113 (54.8)
5–10 years	37 (17.9)
10–15 years	24 (11.7)
15–20 years	10 (4.9)
>20 years	22 (10.7)
Specialty areas	
Pediatric	82 (39.4)
Prenatal	75 (36.1)
Cancer	60 (28.8)
Adult	44 (21.2)
NBS/Metabolic disease	37 (17.8)
Research	33 (15.9)
Laboratory	28 (13.5)
Preconception/PGD/Infertility	14 (6.7)
Education	13 (6.3)
Cardiovascular	13 (6.3)
Neurogenetics	10 (4.8)
Personal genomics	9 (4.3)
Public health	8 (3.8)
Administration	7 (3.4)
Teratogen	7 (3.4)
Support group/advocacy	5 (2.4)
Other	5 (2.4)
Ethical, legal, and social implications of human genomics	4 (1.9)
Pharmacogenetics	4 (1.9)
Population based/biobanking	3 (1.4)

Participants were able to choose more than one specialty area, so values do not add up to 100 %

NBS, WES, and WGS Counseling Experience

More counselors had experience counseling for NBS results than for WES or WGS results (NBS: n=110/207, 53.1 %; WES/WGS: n=55/198, 27.8 %). Of all of those with NBS counseling experience, 42.8 % had counseled more than 20 patients. Roles pertaining to NBS counseling included pre-test education/consent (14.5 %), confirmatory testing after a positive result (73.6 %), interpreting results (50.9 %), contacting physicians with abnormal results (33.6 %), and follow-up for patients with abnormal results (81.8 %). The number of participants who stated they performed pre-test education/consent appears higher than anticipated given the mandatory nature of NBS programs; however, this may be reflective of education about NBS that can occur during prenatal care, including genetic counseling sessions. It is also important to note that referring to "contacting physicians with abnormal results" relates to the reporting of confirmatory test results, rather than the initial abnormal NBS result that would be reported by the state.

The majority (75.5 %) of those with WES/WGS counseling experience (in contrast to the NBS counseling experience) had experience counseling 1–5 patients, and only 5.7 % had experience counseling more than 20 patients. The roles for WES/WGS counseling included pre-test education consent (90.0 %), coordination of testing (67.3 %), interpreting results (41.8 %), contacting patients with abnormal results (49.1 %), and follow-up for patients with abnormal results (49.1 %).

Counseling for Gene Sequencing for Current Conditions on NBS Panels

Forty nine percent of respondents reported having experience counseling for gene sequencing results for individual disorders currently on NBS panels (n=97/198); 46 % did not, and 5 % were unsure. The majority of those with experience counseled either 1–5 patients (32.0 %) or more than 20 patients (29.9 %). In addition, the majority of participants, both

with and without experience with this type of counseling, felt prepared to provide this service (78.1 %).

Counseling for Whole Exome Sequencing (WES) for NBS Results

The majority of counselors (59 %) did not feel they were prepared to counsel families whose newborns currently receive WES as part of their NBS results (Table 2). Only 21.5 % of participants felt they were prepared to counsel for WES in NBS.

Preparedness to Counsel for WGS for NBS Results

Counselors felt the least prepared to counsel for WGS for NBS results, in comparison to their preparedness to counsel for gene sequencing results for current conditions on NBS panels or WES results from NBS. Only 17.9 % felt they were prepared to counsel for results from WGS in NBS (Table 2).

The preparedness of genetic counselors, both those with and without previous NBS or WES/WGS counseling experience, to counsel specifically for WGS in NBS was compared using a Pearson's Chi-Square test. Having previous NBS counseling experience did not impact preparedness for counseling for WGS in NBS; however, there was a statistically significant difference in preparedness between those with or without previous WES/WGS counseling experience (p= 0.005). In other words, having experience in NBS counseling did not impact whether counselors felt prepared to provide the service; having experience in WES/WGS counseling did have an impact (Table 3).

Secondary Analysis: Counselors with Both NBS and WES/WGS Experience

Experience with NBS and experience with WES/WGS were not mutually exclusive among our participants. Therefore, a secondary set of analyses was conducted to determine whether participants with both types of experience felt more or less prepared than those with only NBS or WES/WGS experience. Thirty-one percent (n=32/104) of those with NBS counseling experience also had WES/WGS counseling experience. There was a statistically significant difference (p=0.008) in preparedness between those who had only NBS experience and participants who had both; this supports the finding that the addition of WES/WGS counseling experience positively impacted preparedness.

Of counselors with WES/WGS counseling experience 58.2 % (n=32/55) also had NBS counseling experience, while 41.8 % did not. There was no statistically significant difference in preparedness between these two groups; this indicates that adding NBS experience to experience with WES/WGS did not change the perception of preparedness for genomic counseling in the newborn period. These analyses support the conclusion that it is the WES/WGS counseling experience that impacts counselors' preparedness for WGS in NBS, and not the NBS counseling experience.

How Counseling for Whole Genome Sequencing (WGS) in NBS Would Affect Practice

Fifty-two percent of participants felt that WGS in the context of NBS would happen in the future (n=101/195). The majority of counselors felt that counseling for WGS in NBS would result in their needing to spend a lot more time with their patients (n= 135/182, 74.2 %), preparing for counseling sessions (121/184, 65.8 %), and follow-up after appointments (130/183, 71.0 %).

Qualitative/Open-Ended Responses

To better understand the attitudes of our participants regarding the integration of genomic technologies into NBS, a series of qualitative open-ended questions were added to the survey. While these results are not meant to be representative of all genetic counselors, they do provide a more in-depth exploration of the views of counselors regarding the potential uses of genomics in newborn screening, and allowed our respondents to contextualize those views within their own practice.

Views on Preparing for Genomics in NBS

Participants were first asked "If you do not feel prepared to counsel for **gene sequencing for NBS results** what do you think is necessary to prepare you for this type of counseling?" Overall, most participants who answered this question discussed the need for further education and information about the diseases on the panels, their genotypic and phenotypic variation, and the potential for receiving variants of unknown significance. One participant stated that they *"would need to feel confident in understanding the natural history of the diseases on the panel, which genes cause each disease, the detection rate of sequencing, the labs that do the testing, turnaround time, cost, etc." (Respondent 89)*. For sequencing of genes associated with current NBS disorders, there were a number of participants who describe the need for researching information on their own. One responded stated that they would want to do *" more personal research on each of the individual diseases, what is known in terms of sequencing for that disorder, which mutations have been previously described and how well one can predict protein function from the mutation."(Respondent 19)* Overall, there was a greater emphasis on the ability to prepare oneself for counseling parents regarding gene sequencing for NBS disorders.

Second, participants were asked about what they would need to be prepared for counseling about **WES in NBS**. Again, for those who were unsure or did not feel prepared, the need for education and training was the most commonly

Table 2 Preparedness for counseling for sequencing results

n (%)	Strongly disagree	Disagree	Neither agree nor disagree	Agree	Strongly agree
I feel prepared to counsel patients for sequencing of specific genes associated with current conditions on NBS panels. (n=196)	1 (.5)	16 (8.2)	26 (13.3)	106 (54.1)	47 (24.0)
I feel prepared to counsel patients for Whole Exome Sequencing (WES) for NBS results. (n=195)	30 (15.4)	85 (43.6)	38 (19.5)	35 (17.9)	7 (3.6)
I feel prepared to counsel for WGS for NBS results. (n=184)	40 (21.7)	78 (42.4)	33 (17.9)	30 (16.3)	3 (1.6)

expressed theme. However, there was less emphasis on self-education or personal research, and more discussion about outside educational opportunities to provide updated information about WES and its use in newborn screening. Respondents explained that this might be done through webinars, workshops, and guidelines on the informed consent process, covering topics such as what results to report and the frequency of incidental findings. Additional content areas identified were training in the ethical implications and psychosocial aspects of counseling for WES results in the context of NBS. One participant felt that it "*is necessary to be well versed in the ethical implications of WES for newborns. Perhaps a webinar or a class for training on WES with regard to the proper subjects to discuss may be helpful." (Respondent 78)* More generally, the focus of participant comments regarding WES focused on the need for education and training regarding the interpretation of information being generated through sequencing. One respondent describe this stating:

> "The expected number of variants that would be returned from a WES is overwhelming, especially when you have very little phenotypic information to base the interpretation on. I would need more education on how these tests would be interpreted, what type of information would be provided (medically actionable only? child onset only? all changes found?), how long the data would be stored, how frequently the data would be reanalyzed, and what the pre-test counseling would be like." (Respondent 37)

In addition to needing information regarding the interpretation of data and genomic variety, counselors also identified the need for better clinical coordination in order to integrate WES into practice and better address VUS's.

> "To feel "prepared" to counsel in these situations, I'd really need a solid clinical plan, preferably agreed-upon in advance by the clinical team, about what we'll do in these specific instances. What will we tell families? How long will we continue to follow these infants (in the absence of symptoms)? Depending on the condition, potentially contacting laboratories and having a plan in place for confirmatory assays to test these variants." (Respondent 196)

There were also a number of respondents who felt that preparedness had less to do with their own knowledge or training, and more to do with how that information gets communicated with parents. There were a number of responses that focused on the need for better parent education and consent before WES could be used in the NBS setting. One respondent stated that their main concern "*lies in the question of whether the family is being pre-counseled regarding WES with regards to their newborn screening sample. Currently limited to zero informed consent/counseling is performed 'pre' NBS." (Respondent 4).* Another worried about *"getting proper informed consent for the possibility of variants of unknown significance or incidental data (such as adult-onset conditions) that families are not expecting."(Respondent 26)*

Finally, participants were asked what they would need to feel prepared for counseling about **WGS in NBS**. Once again, the overwhelming majority of respondents expressed the need for more education. This included general information on WGS

Table 3 Preparedness regarding counseling for WGS in NBS as a function of (1) NBS experience or (2) WES/WGS experience

I am prepared to counsel for WGS for NBS results.	Strongly disagree /disagree n (%)	Neither agree nor disagree n (%)	Strongly agree/agree n (%)	Pearson chi-square	p-value
NBS counseling experience				1.598	.450
Yes	60 (63.2)	20 (21.1)	15 (15.8)		
No	58 (65.2)	13 (14.6)	18 (20.2)		
WES/WGS counseling experience				10.749	.005
Yes	27 (51.9)	8 (15.4)	17 (32.7)		
No	91 (68.9)	25 (18.9)	16 (12.1)		

technology in the context of NBS as well as information on how to consent parents, interpret test results, and counsel families. Counselors also felt they would need to learn how to counsel for the large number of variants of unknown significance. General guidelines for this type of counseling as well as protocols for opting in or out of receiving certain results were also listed as areas that would be beneficial. For example, one respondent noted that she would need *"some sort of guidelines about what to report back, how to come to an agreement about what to report back (with family, etc.), and how to handle variants of unknown significance and adult onset disorders. I think there is still a lot that needs to be sorted out in the consenting process for WES/WGS before we start testing asymptomatic newborns." (Respondent 76*). Another respondent provided a list of what counselors would need to have before WGS could be integrated into newborn screening, including:

> "Counseling aids for explaining the WGS process and results / An easily accessible resource to turn to for accurate updated information about VUSs identified on NBS / A plan in place (nationally) to handle updated testing techniques and updated VUS information / More results from research studies currently examining the most effective way to consent for and disclose this type of testing information (such as the ClinSeq study at the NIH)." (Respondent 121)

Lastly, when discussing the use of WGS in NBS, there were also a number of counselors that cautioned the use of this technology in the newborn setting altogether. These concerns centered on the ability to get proper consent, interpret findings, and communicate those results effectively to patients. One counselor described this concern stating that:

> "The field of genetics itself needs to evolve into an era of interpretation, not just technical advancement- just because we can DO the sequencing, does not mean we can interpret what the heck it means. Until that is worked out, it doesn't matter how much time you can spend with a patient, or how "prepared" you FEEL you are… the data just aren't there to interpret what most of the genome (and variation within it) means. This isn't just a matter of having counselors attend a session to "learn how to counsel for this"." (Respondent 148)

Views on the Impact of Genomics in NBS on Practice

In addition to open-ended questions regarding what might be necessary to prepare for the integration of genomics into NBS, participants were also asked to list additional ways this type of counseling would impact their practice. Common themes noted were a higher patient load and having to see more "urgent" clinic patients who may be concerned or confused by complex genomic results. One counselor stated that they think *"it will impact the number of patients that I am capable of seeing each week, therefore impacting both reimbursement and wait times for future patients. As hospital billing and payors are only slightly recognizing the time and effort of genetic counselors, I think it would be difficult to justify the time spent on each case."* (Respondent 41) There were also concerns that unlike current NBS practices, WES or WGS would identify "abnormal" results in most newborns. One participant worried that this form of screening would result in *"A lot more highly distressed patients. Right now most babies have a normal NBS. Presumably there would something abnormal (carrier status etc.) for everyone."(Respondent 34)*

Other areas listed included having more long-term relationships with patients and less satisfaction for parents, most often due to confusion from results of unclear significance. One participant explained: "*Our role is increasingly to do damage control when test results return that are unclear or uncertain. We will spend less and less time giving patients meaningful results that they actively elected to pursue" (Respondent 105).* Similarly, another participant wrote:

> "I think counseling for WGS would impact the structure of the session. For example, if a child was coming in because they were found to have CF or sickle cell disease by NBS—that the main issue that the parents are concerned about, but now there may be a whole other plethora of information that needs to be relayed to the parents as well. So either that session turns into a marathon (which the parents will most likely not remember most of the information) or it turns into multiple sessions counseling about the various results. I think it will require a lot more time for little reimbursement" (Respondent 130).

Finally, there were also concerns that adding WES or WGS to newborn screening would add a significant amount of time to prepare for each patient in order to better understanding their results. One counselor worried that *"It would be difficult to work through the amount of information generated through WES in a NBS setting—determining which information is the most appropriate at the time and what would be given at a later time, assuming there will be follow up time. This is made more difficult by patients potentially being lost to follow up."(Respondent 6)*

Discussion

Implications for Genetic Counselors

Discussion of the potential to initiate WGS into the context of NBS has accompanied the expansion of NBS and rapidly advancing genomic technologies. If this technology were to

be implemented into clinical practice, it would have many potential implications for genetic counselors. Such implications include a substantial increase in patient referrals, as well as the need for additional training regarding the interpretation of and counseling for test results from WGS. While genetic counselors are involved in NBS and WES/WGS counseling (as noted in previous work as well as this study), more participants had NBS experience, as these programs are older. Moreover, while previous research has focused on counselors' roles in the NBS process (Farrell et al. 2001) or explored genetic counselors' opinions regarding the expansion of NBS (Hiraki et al. 2006), the current study was unique in that it focused on genetic counselors' experiences and, more importantly, on the impact that these experiences have on their preparedness for counseling for WGS results from NBS. In addition, this study's respondents expressed concerns about the implementation of WGS in NBS. Thus, it will be important for genetic counselors to be involved in discussions regarding such implementation as they are the ones who will be involved in providing this type of counseling.

Preparedness

Overall, counselors who participated in this study felt more prepared to counsel for sequencing results from current conditions on NBS panels, than for results associated with either WES or WGS in NBS. These results were not surprising as the use of WES and WGS in the context of NBS is currently hypothetical, and neither screening platform is widely utilized clinically at this time.

However, the finding that counselors who reported having WES/WGS experience felt more prepared to counsel for WGS in the context of NBS than those without it suggests that WES/WGS experience is necessary to move towards incorporating this type of counseling into NBS. Moreover, the finding that this was not true for participants with or without NBS experience supports the conclusion that it is the interpretation of WES/WGS sequencing results that concerns counselors. This was confirmed by the open-ended responses regarding preparedness, in which counselors frequently mentioned their concerns regarding counseling for variants of unknown significance found in WES or WGS. In this study, genetic counselors did not express the need for education about NBS, but rather about the interpretation of sequencing results. It is crucial that the concerns raised by these participants regarding WGS in NBS be given serious consideration; genetic counselors will be key stakeholders in the implementation of this technology because of their past and current involvement with NBS and genomics. Regardless of whether genetic counselors have had experience counseling for WES or WGS results, they are still the group of health care professionals who, along with geneticists, are frequently involved in discussing genetic testing results. More importantly, genetic counselors are the professionals who are trained to explain these results to patients.

Ethical and Practical Concerns

Genetic counselors who participated in this study expressed many concerns about WGS in the context of NBS. These included the potential for this technology to overwhelm their practices with increased patient referrals and decreased satisfaction of parents of newborns with a "positive" NBS result. This lack of parental satisfaction would stem from the counselors' practical inability to interpret all of the WGS data in a clinically useful manner. This may be frustrating to parents, counselors, and other medical professionals. If WGS is integrated into NBS, clinicians may look to genetic counselors to explain these results to families because of their expertise in interpreting genetic testing results. Parents also look to trained genetics professionals to be able to helpfully interpret this information. The results of this technology provide a great volume of information, including information that is not or may not be clinically useful. Despite these issues, WGS technology is moving forward, and there is ongoing discussion of its integration into NBS. This study found that genetic counselors may not feel prepared to counsel for WGS results from NBS. We hope that results from this study will inform the NBS community in its discussions of the integration of WGS into NBS, and highlight the importance of having a well-prepared workforce—i.e., genetic counselors, prior to such a change.

Educational Recommendations

The majority of genetic counselors responding to this study did not feel prepared to counsel families about WES or WGS results obtained as part of NBS at this time. In addition, they clearly articulated several critical concerns and needs that are also being discussed by the NBS community before considering the incorporation of WES or WGS into NBS programs—e.g., questions regarding appropriateness, information to be returned, and informed consent issues. Based on study data we believe the following educational recommendations should be addressed prior to implementation of genomic sequencing strategies into NBS:

1. Incorporating education about WES and WGS sequencing technologies as early as possible into genetic counseling training programs.
2. Providing peer mentorship by genetic counselors who are experienced with WES/WGS counseling—including how to interpret and counsel for these results.
3. Making training sessions and educational seminars on WGS in NBS available to all genetic counselors through conferences, webinars, etc.

As with any recommendations, challenges can arise. There is a potential concern as to how the integration of genomic education into genetic counseling programs can be accomplished, especially in light of the already "packed" curricula. In addition, there may be issues with counselors who have years of experience but do not have enough time to pursue education specifically covering this technology. These are concerns that need to be considered before WGS in NBS is implemented.

Limitations

Limitations of this study include the sample size. Two hundred and eight genetic counselors participated, out of approximately 3,000 genetic counselors who are members of NSGC. In addition, study results are based on a hypothetical situation and not actual practice, as WGS is not currently included in the context of NBS. Because opinions of genetic counselors may change in the future, it may be beneficial to repeat a similar study to determine whether more exposure to sequencing technologies affects preparedness.

Another topic that was not addressed in this study was why participants who felt prepared to counsel for WES/WGS in the context of NBS felt that way. The current study only asked those who were not prepared what they believed was necessary to prepare them for WGS counseling in NBS.

This study addressed some of the ethical and practical challenges of WGS currently being debated within the genetics and bioethics communities, including questions regarding appropriate consent for WGS, interpretation and management of results, and decisions about what types of data and results should be returned to families. As a result, there may have been an ascertainment bias–i.e., counselors may have been more likely to participate because they had strong opinions regarding these issues. This could have skewed the data because most participants were not in favor of implementing WGS into NBS.

In addition, a small proportion of respondents reported that they were involved in the interpretation of WES/WGS results during their counseling (about 23 people, or 11.6 % of the sample). However, the majority of genetic counselors who reported having experience with WES/WGS were involved in pre-test education consent and coordination of testing. This may have impacted the overall views of genetic counselors on preparedness to counsel for WGS results in the context of NBS. It also raises the question of whether genetic counselors feel unprepared to counsel for WES/WGS results outside of the NBS context. This was not addressed in the current study.

Questions may have been misinterpreted or interpreted differently among participants due to the wording. As previously mentioned, the reference to contacting physicians with abnormal results in the context of NBS was intended to relate to one's involvement in reporting confirmatory test results. It is possible, however, that participants thought this wording referred to reporting an initial abnormal NBS result. This would change the meaning of these data. In addition, preparedness refers to one's knowledge or experience. This definition was not provided in the survey, thus allowing for potential differences in interpretation. Lastly, the similarity in the abbreviations (WES and WGS) may have been confusing, especially if one read through the survey quickly. This may have affected the responses that were given.

Future Directions

As newborn screening programs consider the potential uses of WGS, there will be a need for more guidance on issues related to data management, consent, and interpretation of results. For example, programs may need to consider whether the utilization of WGS is more useful as a replacement for current screening technologies or as an optional adjunct or follow-up service. Future research is necessary to address these issues appropriately and develop recommendations based on the findings. In fact, research efforts on the integration and effectiveness of WGS into NBS were recently initiated. Earlier this year, the National Institutes of Health (NIH) awarded up to $25 million in funding for four pilot projects that will involve WES and WGS of newborns (National Institutes of Health 2013). These projects plan to address whether WES/WGS allows for health information that would provide a greater benefit than what is gathered from current NBS technology, both with the advancement in sequencing technology and the ability to identify disorders that have not previously been included in screening. They also plan to explore the ethical, legal, and social implications of WES and WGS of newborns and the impact it will have on clinical care (National Institutes of Health 2013).

If WGS is integrated into NBS, recommendations for genetic counselors on consenting parents, interpreting test results, determining which results to report, and appropriate follow-up guidance after an "abnormal" result will be necessary. It would be beneficial for genetic counselors to take a lead role in evaluating the utility and effectiveness of such recommendations.

Conclusions

While there has been a study to assess genetic counselors' attitudes towards expanding NBS (Hiraki et al. 2006), there is little data available regarding the preparedness of counselors to provide genomic counseling for test results from WGS in the context of NBS, or their opinions regarding the challenges of this type of counseling. This study explored the preparedness of genetic counselors regarding counseling related to WGS results in NBS.

Overall, counselors who participated in this study felt *less* prepared to counsel for WES or WGS results from NBS than to provide counseling for sequencing results pertaining to current conditions on NBS panels. This was expected as the former (WGS) is a newer technology that is not clinically available yet; thus, applying it to the newborn period is a hypothetical situation. It was found, however, that counselors with previous WES/WGS counseling experience felt more prepared to counsel for WGS in NBS than those without this experience. Previous NBS experience did not have the same effect on preparedness. Because the majority of genetic counselors who participated in this study did not feel prepared for this type of counseling, it is hoped that this study's results will provide empirical data to argue the importance of genetic counselors being integral stakeholders in the discussions of integrating WGS into NBS.

Moving forward, genetic counselors stated that education and experience with WGS in NBS would be needed before they would feel adequately prepared for this type of counseling. Their concerns included the high volume of referred patients, inability to interpret results, and the question of how to explain uncertain results to parents. Based on these concerns, we have recommended that educational programs on WGS in the context of NBS, such as training through genetic counseling programs, peer mentorship, and conferences, be implemented.

In conclusion, this study provided information regarding genetic counselors' opinions on genomic counseling in the newborn period. Genetic counselors will play a major role in this type of counseling if WGS is integrated into NBS in the future; therefore, it is essential to understand their current level of preparedness. Genetic counselors have experience with interpreting and explaining genetic testing results to patients; this experience would be relevant to counseling parents in the context of WGS results from NBS as well. It is hoped that the ethical issues, concerns, and recommendations for additional educational experiences gathered from these data will provide the necessary background to inform the NBS and genetics community at large.

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Conflict of Interest Monica Nardini declares that she has no conflict of interest.

Anne Matthews declares that she has no conflict of interest.

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