Author Manuscript

Author Manuscript

Author Manuscript

Author Manuscript

HHS Public Access

Author manuscript

J Genet Couns. Author manuscript; available in PMC 2017 August 01.

Published in final edited form as:

J Genet Couns. 2016 August ; 25(4): 691–697. doi:10.1007/s10897-015-9868-y.

Genomic Testing: A genetic counselor's personal reflection on three years of consenting and testing

Julia Wynn, MS, CGC

Columbia University Medical Center, Department of Pediatrics, Division of Genetics. New York, NY, USA

Abstract

Whole exome sequencing (WES) is increasingly used in research and clinical genetics as the cost of sequencing decreases and the interpretation improves. Genetic counselors need to be prepared to counsel a diverse patient population for this complex test. This commentary is a reflection of one genetic counselor's experiences in counseling, consenting, and returning results for clinical and research WES for over 120 participants and patients. She reflects on how she overcame the initial challenges and concerns of counseling for WES and how her counseling evolved hfrom a teaching based counseling model to an interactive patient-center counseling model. Her insights are offered to prepare other genetic counselors for the growing use of genomic testing.

Keywords

genomic testing; whole exome sequencing; research; genetic counseling; consenting

Introduction

It has been nearly 15 years since the genome was sequenced and approximately four years since technological advances enabled the use of genome-wide sequencing for clinical testing (Farwell et al., 2014; Glazov et al., 2011; Iglesias et al., 2014; Worthey et al., 2011; Yang et al., 2014). I have been involved in counseling and consenting for genomic testing in both research and clinical settings since the technology was introduced. I consented my first clinical patient for whole exome sequencing (WES) in November of 2011, and have been consenting participants in the research setting since 2012. I have now counseled over 120 individuals for genome sequencing. My counseling process has evolved over this time, and I feel that reflecting on my experiences can serve to prepare others for the expanding use of genomic testing.

Conflict of Interest Statement

Julia Wynn declares that she has no conflict of interest.

Informed Consent: For studies with human subjects

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 (5). Informed consent was obtained from all subjects for being included in the study.

Author Manuscript Author Manuscript Author Manuscript Author Manuscript

The atmosphere in these early days of genomic testing was one of excitement and trepidation. We were excited about the potential for this technology to uncover new genes and end the diagnostic odyssey for our patients (Choi et al., 2009). At the same time, we had very legitimate concerns about the volume of data that would be generated, our ability to fully interpret it, and the clinical utility of the results (Dimmock, 2013; Klee, Hoppman-Chaney, & Ferber, 2011; Majewski, Schwartzentruber, Lalonde, Montpetit, & Jabado, 2011; Thompson, Drew, & Thomas, 2012). There was concern about how to educate a patient/ subject and ensure informed consent for this complex technology. This concern and lack of consensus on best practice was reflected in the variation of the information on possible results, privacy issues and risks and benefits of testing included in the research consent forms for the some of the first studies of whole exome and genome sequencing (Henderson et al., 2014). Comprehensive genomic testing also raised the possibility of incidental results or results unrelated to why the testing was being performed. For example, genomic testing could identify a *BRCA1* mutation in research subject or patient having testing to identify the genetic cause of a congenital heart defect. There was no consensus on how to manage these types of incidental or secondary results. The genomics community did not have any guidelines on the legal and ethical obligations to identify incidental results, how to consent for them, if patient/ subject preferences about receiving incidental results should be considered and availability of resources including genetic counselors to facilitate the return of them (Appelbaum et al., 2014; Green et al., 2012).

As a genetic counselor, I was anxious conducting informed consent and pre-test counseling sessions for WES. There were early reports of the informed consent process taking many hours over multiple visits (Tabor et al., 2012). Additionally there was no framework or recommended guidelines for counseling. It seemed impossible to inform a patient in a single session of all possible results including the potential for incidental and uncertain results, the implications of the results for the participant and his/her family members and the possible psychological effects of the testing process and learning about the results. Up until this time, my counseling sessions were typically focused on a single condition and inheritance pattern. I was apprehensive about how to help a patient make an informed decision about testing when there was simultaneously a tremendous amount of information to convey and uncertainty about what the test might uncover.

My experience with genomic counseling in a research setting began in earnest when I was invited to be part of a study returning incidental findings to research participants. This study is part National Human Genome Research Institute Clinical Sequencing Exploratory Research (CSER) Consortium which was formed to develop and evaluate the best methods to integrate sequencing into clinical care and to assess the associated ethical, legal and psychosocial implications of the clinical and research applications of this technology (cser-consortium.org). In our study, led by Dr. Wendy Chung, eligible participants were identified from existing studies in which WES was used. All of these studies allowed for return of research results for the study indication but the consents did not address returning unrelated genetic results. Eligible participants were contacted by a research coordinator and consented by phone to participate in a study examining the psychological effects of returning genetic research incidental findings. As part of the consent, it was explained that they would meet with a genetic counselor to review possible results available to them and decide which

Author Manuscript Author Manuscript Author Manuscript Author Manuscript

results would like to learn about. The study population was composed of adults who have a personal history of cancer or have a child with a birth defect or suspected genetic condition. All participants had the experience of being consented for a genetic study, but experience with clinical genetic counseling varied within the cohort from those who had never had a clinical genetics evaluation to those who had multiple visits with clinical geneticists and genetic counselors. Because our clinical patients are invited to participate in any applicable research study, I had previously seen approximately 20 percent of the research population as non-research, clinical patients prior to the start of this study. While we sought to enroll a diverse population, there were some individuals who declined participation because they did not want to learn this information, despite our repeated clarification that choosing to learn about results was not obligatory. More frequently, individuals declined because of the time commitment of the counseling sessions. Ultimately, the study population was composed primarily of older, educated, white, non-Hispanic individuals, in part because this was the composition of the parent studies.

Pre-test Counseling

In an effort to prepare individuals for the wealth of information discussed in the pre-test counseling session, prospective participants were mailed a 30-minute educational video prior to their pre-test counseling session. The video introduced the study, reviewed facts about genetic information and inheritance, and discussed reproductive options. It also discussed types of possible results including pharmacogenetic results, carrier status and results for Mendelian conditions The video reviewed one or more examples for each category. Participants were also provided with vignettes of specific conditions and asked to indicate how likely they would choose to learn about the result. The video and vignettes were modeled after the bin structure in which conditions are categorized according to clinical utility and disease risk that had been developed as a framework for analyzing genomic results (Berg et al., 2013; Berg, Khoury, & Evans, 2011). For example the video discussed hemochromatosis and hereditary breast and ovarian cancer as examples of conditions varying degrees of severity with relatively effective screening and treatment and contrasted them with hereditary pancreatic cancer which has less effective screening and treatment and Alzheimer’s disease which has no known treatment.

I conducted all pre-test counseling sessions either independently or with the clinical geneticist. I was charged with reviewing the study protocol and the risks and benefits of participating, and obtaining written consent prior to beginning the pre-test counseling session. Initially, I structured my pre-test counseling sessions around the video: reviewing the different categories of results that may be identified and asking the participant to indicate their interest in receiving each type of result and exploring their decision to receive it. These pre-test sessions followed a teaching counseling model (Kessler, 1997). I provided information in an impartial manner with a goal of educating the patient to allow them to make an autonomous decision. I used the bin framework to help participants consider each option without overwhelming them with information. I also presented them with reasons why some individuals choose to receive or not receive certain results based on differences in how the results might be used for health maintenance and screening, or life and family planning.

Author Manuscript Author Manuscript Author Manuscript Author Manuscript

The initial pre-test sessions were dominated by my information giving with a few open-ended questions like, “How do you feel about receiving this type of results?” or, “Which results would you like to receive?” Despite my years of counseling experience, I asked many closed ended questions such as, “Have you thought about receiving these types of results?”; “Is this a result you want to receive?”; “Do you have any questions”; or “Have you spoken to your family about this testing?” Even when I asked open-ended questions, participants’ answers were short and did not lead to prolonged discussion. By presenting the information in this way, I had set the atmosphere of the session to be formal and didactic rather than a more casual dialog.

I am a veteran genetic counselor, and these sessions were not structured in the manner that I had been taught or practiced outside of the study. I was comfortable with the bin structure as it helped me to manage the possible results, but I was not considering how the participants processed the information. Outside of my normal routine, I resorted to a structured teaching model counseling session. I thought that if I could inform the participant of all possible results I would protect them from any adverse reactions or outcomes. In retrospect, the assumption that I could protect the participants by overloading them with information was unrealistic. I recognize that, after years of being a genetic counselor and mentoring genetic counseling students, this is a common defense when counseling about new information. While this approach makes us more comfortable, it may not be in our patients’ best interests and may even be doing harm.

In reflection, I had similar fears when I first began counseling for chromosome microarrays in the pediatric and then prenatal setting. Bernhardt and colleagues (2014) recently showed that many other counselors share the initial discomfort about uncertain prenatal microarray results (Bernhardt, Kellom, Barbarese, Faucett, & Wapner, 2014). I have counseled for chromosome microarrays for over eight years and while the possibility of uncertain results has decreased, it is still a possibility. Despite this possibility, I feel comfortable adapting the counseling session to each patient and engaging them in a conversation about their expectations and goals of the testing, possible test results, and possible responses to uncertain results. The difference between counseling for WES and chromosome microarrays is that I am more comfortable with the microarray technology and the spectrum of results. This comfort has come with the scientific community’s improved understanding of copy number variants and with my own experience of counseling for this test.

As part of the study, I reviewed the audio recordings of the pre-test counseling sessions. It was apparent that the bin system helped some participants to process the possible results, but for many it was not helpful. It was also obvious that the teaching model was not allowing the participants to reflect on their choices. In subsequent pre-test sessions, I made an effort to talk less and listen more. As I listened, I learned that often participants did not think about the conditions in the bin framework but rather arranged them in to own categories specific to their own health experience and knowledge. Recognizing the inadequacy of the structured discussion, I began to modify the pre-test counseling sessions to favor a counseling model approach with a more open discussion to help the patient navigate the information using their own framework and incorporating their goals and values (Kessler, 1997).

Author Manuscript Author Manuscript Author Manuscript Author Manuscript

Many individuals were concerned about specific conditions because of their own experience or that of a family member or friend. In some cases, this increased their desire to know their risk, while in other cases it was the reason they did not want to learn about their risk. One participant, who had cared for her grandmother with Alzheimer's disease, felt that this experience had led them to live a fuller life, but also taught her that she did not want to learn about her own risk. Another participant had a grandfather pass away from Alzheimer's disease and felt that it was important to know their risk in order to prepare herself and her family. A participant with a history of multiple cancers wanted to learn about her risks for all types of cancer, but she did not want to learn about her risks for other conditions as she thought it would be too overwhelming. Some participants had a strong reaction to learning about risk of disease for specific organ systems. One participant wanted to learn about risks for nearly all diseases but struggled with the idea of learning about losing her vision and felt that this would be particularly devastating.

The potential for screening and treatment of a condition was important to some participants. One participant wanted to learn only about conditions in which there was effective screening currently available. For others, the type of treatment was important. One participant elected not to learn about her risk for arrhythmias as she would never consider having an implantable cardiac defibrillator which she considered too invasive. The likelihood of developing the disease was also important. One participant decided he wanted to learn about certain conditions in which the risk was at least 50% but did not want to learn about conditions with a lower risk. Others had different thresholds of risk. Many felt that it was important to know all possible information regardless of condition, risk or certainty of the result. A few did not want to learn any specific disease risks and elected to only learn about pharmacogenetic results. Some wanted to learn about autosomal recessive conditions that they carried to inform their – or their children's – reproductive risk while others did not want to learn this information because they had completed their family and did not want to be the keeper of this information for their children and relatives.

These experiences helped me to change the format of the pre-test counseling session. Now in the sessions, rather than focusing on the different categories of results, I engaged the participants in a conversation about the types of results they had considered or were concerned about. I asked questions like "What are you hoping and/or expecting to receive from this testing," and "You said that you are interested in learning information about your risk for [condition], how do you think you might feel to learn that you do or do not have an identifiable genetic risk for [condition]?". I also encouraged them to, reflected on how learning these results might affect them and their family members by asking them questions such as "Tell me about how you might feel if you learned that your child/ sibling might be at risk for [condition]?" Using a counseling model approach with open-ended questions allowed me to explore the participant's understanding of the possible results and implications; rather than the participant listening to me deliver specific information, I listened to them and spoke up only to correct misunderstandings and to help them explore implications they had not considered. These misunderstandings sometimes included: how results might affect health care, life planning, reproductive options, and family dynamics. I also had a targeted discussion about their comfort with uncertain results with questions like, "Tell me about how you have experience uncertainty either in health care or some other

Author Manuscript Author Manuscript Author Manuscript Author Manuscript

aspect of your life and your reaction to it." Many people were able to reflect on an experience either in their own health care such as a biopsy result or in the health care of their child or other family member. Some even had the experience of a variant of uncertain significance in clinical genetic testing. Their reflection on this experience allowed them to better gauge their tolerance for uncertain results. While I no longer followed the strict bin framework for the session, I still referenced it during the session to be certain that we had comprehensively explored different types results and potential implications. To assess their understanding, I also asked questions like, "How will you discuss today's appointment with your spouse/sibling/friend." I became more confident that a mutual understanding was established about the types of results that participants wanted to receive and their motivation for receiving them.

Research Results Disclosure Sessions

Our experience in the initial results disclosure sessions resulted in additional modifications of our pre-test counseling session. Dr. Wendy Chung and I completed the results disclosure sessions together and we began by reviewing the types of results an individual had elected to receive and confirming that they still want to receive them. We initially disclosed results in the order that we felt might be the most comfortable for participants; starting with results that have lower impact on their health including pharmacogenetics, carrier results and then results with potential risk to the participant's health. However, after the first several sessions it was apparent that, for some, this order inadvertently created an atmosphere of suspense, so we altered the session and began by reassuring the participant about their test results. We used this approach for all participants regardless of the results. We also started asking the participant what type of results they wanted to learn about first to give them more control over the session enabling them to be more at ease and receptive to the results and information we were providing.

One notable reaction in our initial disclosure sessions was participant dissatisfaction with how few results they received. With the limitations of our current genetic technology to detect and interpret all genetic variants causing disease, we only returned disease causing mutations in known disease genes and did not return single nucleotide polymorphisms (SNPs) associated with relative risks for multifactorial conditions. Participants were often surprised and sometimes frustrated that they received no results related to specific disease risk for themselves. Not infrequently, they would refer to a specific disease in their family and ask if we had checked for it. Participants' comments and questions in the disclosure sessions indicated that the initial pre-test discussion of the limitations of the testing was not sufficient. To address this misunderstanding, I changed the pre-test counseling session to include a discussion of multifactorial inheritance using an example directly applicable to the participant. After reviewing the family history, I used a multifactorial condition present in the participant's family like diabetes, heart disease or hypercholesterolemia to discuss the likelihood of finding a genetic answer for this condition through the study. Engaging the participant in this more focused and personalized discussion of the test limitations helped them to integrate this into their understanding of the possible results. The effectiveness of this approach was demonstrated in our subsequent disclosure sessions. Subsequent participants with no results related to disease risk were not as surprised or dissatisfied and

Author Manuscript Author Manuscript Author Manuscript Author Manuscript

were able to reflect back on discussions that we had in the pre-test counseling session about their personal and family history that did not suggest a specific genetic condition.

Similar to our pre-test counseling session, we began to have a more client-centered disclosure session by engaging them in a discussion of their understanding and reactions to their results. This was especially important for our participants who received results indicating a personal disease risk such as risk for cardiomyopathy or Alzheimer disease. We discussed these results in the context of the value of this information to guide their healthcare, as well as risk assessment for family members. Participants who received these types of results expressed how they found this information helpful and empowering. While complete analysis of our qualitative and quantitative data is still pending, preliminary data analysis have demonstrated that levels of depression, anxiety, and perceptions of control over health did not change following post results disclosure. Additionally, it appears that these measures were not different between participants who did and did not receive results that incurred a personal disease risk. This suggests that the pre-test counseling session prepared our participants for these types of results.

Transitioning from Research to Clinical

At the same time we started our study, clinical WES was being used more frequently in our clinic. Eighteen months into our study, the ACMG published its guidelines for returning incidental/secondary results for 56 genes (American College of Medical & Genomics, 2013; Green, Berg, et al., 2013). While there was considerable debate about these guidelines within the genomics community, our clinical lab joined many others in following the guidelines of returning secondary results for the 56 genes to patients, with the option to opt out of receiving them (Green, Lupski, & Biesecker, 2013; Klitzman, Appelbaum, & Chung, 2013; Klitzman, Appelbaum, Fyer, et al., 2013; McGuire et al., 2013; Wynn et al., 2015). Counseling for clinical WES prior to the ACMG guidelines was similar to counseling for panel gene testing for which uncertain results were a possibility but the results were specific to the disease of concern. Additionally, the initial patients and families I counseled and consented for WES were established patients – some of whom had been followed by us for over a decade. They were familiar with genetic testing, had experience receiving uninformative negative results and sometimes uncertain results. They were also highly motivated to have the test, sometimes paying thousands of dollars out of pocket, as labs initially did not accept insurance payment. The introduction of the secondary findings changed this dynamic.

Previous experience in the research setting had prepared me for many aspects of counseling for clinical WES with secondary findings, but there were some differences between research participants and clinical patients that necessitated adaptation in the clinical setting. All of our study participants already had genetic knowledge from their experience in the parent study and many had had genetic counseling in the clinical setting and/or sought information about genetics from online or media sources. Some had even participated in direct-to-consumer genetic testing. Their previous experience in genetics helped them to integrate the new information about genomic sequencing. Additionally, their experience with a possible

Author Manuscript Author Manuscript Author Manuscript Author Manuscript

genetic condition in themselves or their family members provided a basis for understanding the other types of genetic conditions and the related risks.

By comparison, the clinical patients had greater variability in their levels of genetic knowledge and experience with genetic testing. Sometimes I was introducing patients to genes and inheritance in the same session in which I was discussing the option of WES. I had to be more careful to assess their knowledge and often, take more time to explain the concepts of genes and inheritance. The patients were also more diverse in age and, unlike the most of our research study participants, many were still planning and growing their families. Therefore, I had to spend more time discussing possible reproductive implications. In the clinical setting, many patients offered WES were children, and we therefore had to discuss the implications of secondary findings in a minor. It was important to incorporate a discussion of the risk for symptoms of these conditions in a child, the value of a child's autonomy, guidelines regarding genetic testing in children for adult-onset conditions and the potential risks of the testing including genetic discrimination and adverse psychosocial response (Committee On et al., 2013). These were complex discussions to have with families who were focused on finding a diagnosis for themselves or their child.

In the first several months of counseling for clinical WES, I once again felt intimidated by the amount of information to be discussed. I was falling back into the habit of overloading the patients with information. Reflecting back on the lessons learned in the research consenting process helped me to become more comfortable listening to the families and personalizing the counseling. Initially, I was concerned about the educational differences among the research participants and clinical patients; however, as I learned from years of genetic counseling experience, ultimately patients do not need a detailed discussion of complex genetic terms and inheritance patterns to understand that a genetic mutation can cause disease or that a disease can be passed down through generations. Rather, like all my other patients and study participants, I simply needed to gauge their understanding of genetics, correct misunderstandings and then engage in a conversation to understand their concerns, expectations and goals of the test.

Recognizing that learning about genetics and WES in the same session was overwhelming for some patients, I, with the guidance of our geneticist, Dr. Chung, and the help of a medical student, created an educational video that we used to supplement the counseling. The experience with the informational video we created for the pre-test counseling portion of our research study guided us in developing a video for secondary findings in the clinical setting. For our clinical patients, we abandoned the long video that used complex language and presented results in bins and replaced it with several short videos, all less than 5 minutes that explained genes and inheritance and genomic sequencing using simple terms with approachable examples and analogies (www.learninggenetics.org). We also made videos explaining the benefits and drawbacks of learning secondary findings, as well as factors to consider when deciding whether to receive them. Offering individual videos allowed patients to skip over information they already knew and to focus on issues that were new and/or of interest to them. We have found these videos to be helpful in the clinical setting to augment rather than replace our counseling sessions. We plan to conduct a study to formally test the utility of these videos in the coming year.

Author Manuscript Author Manuscript Author Manuscript Author Manuscript

Practice Implications

Many of my experiences of counseling, consenting and returning results from WES are similar to those of other counselors pioneering in this field. The CSER Genetic Counseling working group has recently published several manuscripts illustrating the unique challenges of WES counseling (Amendola et al., 2015; Tomlinson et al., 2015). Tomlinson and colleagues (2015) surveyed genetic counselors and healthcare providers in the CSER consortium about their experience of obtaining informed consent for WES. Some of the challenges experienced included: varying levels of genetic literacy, managing expectations, the importance of context (sick versus health subject), impact of family dynamics and counselor discomfort with patient decisions. While many of these challenges are not unique to WES, the cases presented by Tomlinson and colleagues (2015) illustrate how the breadth of information, the variety and uncertainty of possible results and potential broad implications of the results from WES create new dimensions to these challenges (Tomlinson et al., 2015). Amendola and colleagues (2015) recently published a collection of cases of returning results from WES from CSER studies highlighting some recurring themes including returning multiple complex results, addressing misconceptions of negative results and navigating atypical presentations of well-known conditions (Amendola et al., 2015). These publications provide important insight for genetic counselors as they prepare to counsel for WES and may help counselors avoid some of the anxiety and uncertainty that I faced when I began counseling for WES. The experiences of the CSER consortium will create an invaluable resource in this new era of genomic testing.

It is also important to look further into the future and the possibilities of this technology. Many of the lessons learned about counseling for secondary results are applicable to the next wave of genetics – personalized genomics/precision medicine. Like counseling for secondary findings, personalized genomic counseling involves discussions about genetic risk and implications of results for conditions about which the patient has little existing knowledge. The initial population seeking personalized genomics will be similar to our study population (older and well educated), but if this testing is demonstrated to be beneficial to the health of patients and cost effective, it will become more mainstream and the population of consumers will grow. We, as counselors, need to be prepared to educate this increasingly diverse population that will have different knowledge of genetics and genetic testing and different goals and expectations of the testing.

Conclusion

Genomic technology has the potential to lead to a better understanding of genetic conditions, treatment and prevention. While the information we need to convey in a genetic counseling session is seemingly endless, we cannot lose sight of our obligations as genetic counselors. We are not simply keepers of complex information but rather interpreters of genetic information who must engage a patient in an interactive discussion to help them to be both informed and satisfied with their decisions. Technologies can also be helpful to augment our counseling sessions. Educational web videos and interactive tools that allow patients to pick and choose the information that is relevant to them will likely have an important role as genomic technology has increasingly broader applications.

Author Manuscript Author Manuscript Author Manuscript Author Manuscript

Given the tremendous technological advances in genetics, genetic counselors are increasingly reminded about the importance of the psychosocial aspects of the profession. Studies have shown that meeting the emotional needs of a patient are associated with better psychological results, which in turn facilitates their cognitive processing of complex medical information (Austin, Semaka, & Hadjipavlou, 2014). As counselors, we must not only provide information but also, and arguably more importantly, engage the patient in a discussion about their response to this information. The history of our profession does not allow us to hide behind complex medical information and jargon. Rather we are the liaisons between the science and the patient, and we are responsible for making complex information accessible to everyone. We cannot forget the valuable counseling skills that we have developed which are applicable to current and future genetic testing. Additionally it is critical, that we continue to conduct research informed by psychological science to understand psychological impacts of genomic testing and the effectiveness of our counseling in this era of genomic testing (Khan et al., 2015).

In this paper, I present a discussion based on reflection of my experience with anecdotal evidence as support. As part of our research study, we are in the process of analyzing both qualitative data including recorded transcripts of counseling sessions and follow up in depth interviews with participants and quantitative data including participants' levels of depression, anxiety, genetic stigma, secrecy, coping behavior, health behavior, and social behavior over the course of the study. This analysis, as well as the results of the other CESR studies examining the experience of genomic sequencing in the prenatal, cancer and pediatric setting, will provide important information about best practices for counseling for genomic sequencing.

Acknowledgments

I am greatly appreciative of Barbara Bernhardt's guidance and encouragement in the preparation of this manuscript and Dr. Wendy Chung's mentorship and to Kevin Lynch for his careful edits.

I am appreciative of all the individuals who have participated in our study and my clinical patients.

The research presented in this work was funded by a grant from the National Human Genome Research Institute: R01 HG006600 (Dr. Chung).

References

Amendola L, Dautenbach D, Scollon S, Bernhardt B, Biswas S, East K, et al. Illustrative Case Studies in the Return of Exome and Genome Sequencing Results. Personalized Medicine. 2015

American College of Medical, G., & Genomics. Incidental findings in clinical genomics: a clarification. Genet Med. 2013; 15(8):664–666. [PubMed: 23828017]

Appelbaum PS, Fyer A, Klitzman RL, Martinez J, Parens E, Zhang Y, et al. Researchers' views on informed consent for return of secondary results in genomic research. Genet Med. 2014

Austin J, Semaka A, Hadjipavlou G. Conceptualizing genetic counseling as psychotherapy in the era of genomic medicine. J Genet Couns. 2014; 23(6):903–909. [PubMed: 24841456]

Berg JS, Adams M, Nassar N, Bizon C, Lee K, Schmitt CP, et al. An informatics approach to analyzing the incidentalome. Genet Med. 2013; 15(1):36–44. [PubMed: 22995991]

Berg JS, Khoury MJ, Evans JP. Deploying whole genome sequencing in clinical practice and public health: meeting the challenge one bin at a time. Genet Med. 2011; 13(6):499–504. [PubMed: 21558861]

Author Manuscript Author Manuscript Author Manuscript Author Manuscript

Bernhardt BA, Kellom K, Barbarese A, Faucett WA, Wapner RJ. An exploration of genetic counselors' needs and experiences with prenatal chromosomal microarray testing. J Genet Couns. 2014; 23(6): 938–947. [PubMed: 24569858]

Choi M, Scholl UI, Ji W, Liu T, Tikhonova IR, Zumbo P, et al. Genetic diagnosis by whole exome capture and massively parallel DNA sequencing. Proc Natl Acad Sci U S A. 2009; 106(45):19096–19101. [PubMed: 19861545]

Committee On, B., Committee On Genetics, A. N. D., American College Of Medical Genetics, A. N. D., Genomics, S., Ethical, & Legal Issues, C. Ethical and policy issues in genetic testing and screening of children. Pediatrics. 2013; 131(3):620–622. [PubMed: 23428972]

Dimmock D. Whole genome sequencing: a considered approach to clinical implementation. Curr Protoc Hum Genet. 2013; Chapter 9(Unit9):22. [PubMed: 23595600]

Farwell KD, Shahmirzadi L, El-Khechen D, Powis Z, Chao EC, Davis BT, et al. Enhanced utility of family-centered diagnostic exome sequencing with inheritance model-based analysis: results from 500 unselected families with undiagnosed genetic conditions. Genet Med. 2014

Glazov EA, Zankl A, Donskoi M, Kenna TJ, Thomas GP, Clark GR, et al. Whole-exome re-sequencing in a family quartet identifies POP1 mutations as the cause of a novel skeletal dysplasia. PLoS Genet. 2011; 7(3):e1002027. [PubMed: 21455487]

Green RC, Berg JS, Berry GT, Biesecker LG, Dimmock DP, Evans JP, et al. Exploring concordance and discordance for return of incidental findings from clinical sequencing. Genet Med. 2012; 14(4):405–410. [PubMed: 22422049]

Green RC, Berg JS, Grody WW, Kalia SS, Korf BR, Martin CL, et al. ACMG recommendations for reporting of incidental findings in clinical exome and genome sequencing. Genet Med. 2013; 15(7):565–574. [PubMed: 23788249]

Green RC, Lupski JR, Biesecker LG. Reporting genomic sequencing results to ordering clinicians: incidental, but not exceptional. JAMA. 2013; 310(4):365–366. [PubMed: 23917280]

Henderson GE, Wolf SM, Kuczynski KJ, Joffe S, Sharp RR, Parsons DW, et al. The challenge of informed consent and return of results in translational genomics: empirical analysis and recommendations. J Law Med Ethics. 2014; 42(3):344–355. [PubMed: 25264092]

Iglesias A, Anyane-Yeboa K, Wynn J, Wilson A, Truitt Cho M, Guzman E, et al. The usefulness of whole-exome sequencing in routine clinical practice. Genet Med. 2014; 16(12):922–931. [PubMed: 24901346]

Kessler S. Psychological Aspects of Genetic Counseling IX. Teaching and Counseling. J of Genet Couns. 1997; 6(3):287. [PubMed: 26142236]

Khan CM, Rini C, Bernhardt BA, Roberts JS, Christensen KD, Evans JP, et al. How can psychological science inform research about genetic counseling for clinical genomic sequencing? J Genet Couns. 2015; 24(2):193–204. [PubMed: 25488723]

Klee EW, Hoppman-Chaney NL, Ferber MJ. Expanding DNA diagnostic panel testing: is more better? Expert Rev Mol Diagn. 2011; 11(7):703–709. [PubMed: 21902532]

Klitzman R, Appelbaum PS, Chung W. Return of secondary genomic findings vs patient autonomy: implications for medical care. JAMA. 2013; 310(4):369–370. [PubMed: 23917282]

Klitzman R, Appelbaum PS, Fyer A, Martinez J, Buquez B, Wynn J, et al. Researchers' views on return of incidental genomic research results: qualitative and quantitative findings. Genet Med. 2013; 15(11):888–895. [PubMed: 23807616]

Majewski J, Schwartzentruber J, Lalonde E, Montpetit A, Jabado N. What can exome sequencing do for you? J Med Genet. 2011; 48(9):580–589. [PubMed: 21730106]

McGuire AL, Joffe S, Koenig BA, Biesecker BB, McCullough LB, Blumenthal-Barby JS, et al. Point-counterpoint. Ethics and genomic incidental findings. Science. 2013; 340(6136):1047–1048. [PubMed: 23686340]

Tabor HK, Stock J, Brazg T, McMillin MJ, Dent KM, Yu JH, et al. Informed consent for whole genome sequencing: a qualitative analysis of participant expectations and perceptions of risks, benefits, and harms. Am J Med Genet A. 2012; 158A(6):1310–1319. [PubMed: 22532433]

Thompson R, Drew CJ, Thomas RH. Next generation sequencing in the clinical domain: clinical advantages, practical, and ethical challenges. Adv Protein Chem Struct Biol. 2012; 89:27–63. [PubMed: 23046881]

Author Manuscript Author Manuscript Author Manuscript Author Manuscript

Tomlinson A, Skinner D, Perry D, Scollon S, Roche M, Bernhardt B. “Not Tied Up Neatly with a Bow”: Professionals’ Challenging Cases in Informed Consent for Genomic Sequencing. Journal of Genetic Counseling. 2015:1–11. [PubMed: 25432783]

Worthey EA, Mayer AN, Syverson GD, Helbling D, Bonacci BB, Decker B, et al. Making a definitive diagnosis: successful clinical application of whole exome sequencing in a child with intractable inflammatory bowel disease. Genet Med. 2011; 13(3):255–262. [PubMed: 21173700]

Wynn J, Martinez J, Duong J, Zhang Y, Phelan J, Fyer A, et al. Association of Researcher Characteristics with Views on Return of Incidental Findings from Genomic Research. J Genet Couns. 2015

Yang Y, Muzny DM, Xia F, Niu Z, Person R, Ding Y, et al. Molecular findings among patients referred for clinical whole-exome sequencing. JAMA. 2014; 312(18):1870–1879. [PubMed: 25326635]