

Genetic Counseling Following Direct-to Consumer Genetic Testing: Consumer Perspectives

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Suggested Running Head: Seeking Genetic Counseling for DTC Results

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As the use and scope of direct-to-consumer genetic testing (DTC GT), also becoming known as consumer-driven genetic testing, increases (Regalado, 2019), consumers may seek genetic counseling to understand their results and determine healthcare implications. To date, those who have studied the experience of sharing DTC GT results with genetics professionals have used survey methods (Brett et al., 2012; Darst et al., 2013; Giovanni et al., 2010), which can be limited in describing the motivations and subjective experiences of consumers. The Personal Impact of Genomics (PGen) Study (Carere et al., 2014), a longitudinal cohort study of individuals who had undergone DTC testing through 23andMe or Pathway Genomics, found that those responding to the PGen survey were more likely to seek genetic counseling for health reasons, self-reported poorer health, and uncertainty about the results (Koeller et al., 2017). 38% (390/1,026) would have sought in-person genetic counseling, had it been available, and, at 6-month follow-up, four percent (43/1,026) reported that they had discussed their DTC GT results with a genetic counselor or had a pending appointment (Koeller et al., 2017). The current study utilized qualitative interviews to provide richer descriptions of why DTC GT clients seek genetic counseling, including their motivations, expectations and experiences.

An interview guide with open-ended questions was developed by the multidisciplinary research team based on a literature review and the Coriell Institute genomic counseling interview guide (Gordon et al., 2012). An invitation letter was mailed to the 43 PGen participants who, after DTC testing, reported having genetic counseling or had an appointment pending; study participation incentive was offered. There were 24 participants who responded to our letter: 15 consented to participate, 2 declined, and 7 were excluded because, despite their reported intentions, they in fact had not actually seen a genetic counselor. The demographics of the 15 participants we interviewed June – December 2016 are presented in Table 1. The mean age of the interview participants at the time of DTC GT was 38 years (range 22-57, SD=13.16) and the population was mostly female (n=9) and mostly without children (n=9). Interviews ranged from

20 to 62 minutes (mean = 38 minutes). All interviews were transcribed and a codebook was created using an iterative process (Bryant and Charmaz, 2010). The transcripts were then excerpted and double-coded using Dedoose® software.

Generally, the participants we interviewed were “information seekers” who wanted as much information about their DTC GT results as possible. Some were seeking confirmation of conclusions they had already drawn from the report itself or their own research on test results. These participants used a variety of online resources prior to the counseling session, including resources typically used by genetics clinicians (Figure 1). The desire to have their report explained and content put into “layman’s terms” was expressed by several participants.

P7 (24-year-old male) My background is not, you know, genealogy or anything like that or whatever it is. So, it would be nice to kind of go over it with somebody who does really know what they’re talking about, kind of to get it in layman’s terms, I guess, a little bit. And just, you know, see . . . See if there was anything that I overlooked, not even realizing that I overlooked it.

P14 (57-year-old male) Not realizing that at the time that 23andMe really was pretty comprehensive in their discussion of each of the genetic findings, so I’m happy I had the appointment. It was more confirmation for me than any big epiphanies and, more discussions of the risks that were pretty consistent with what 23andMe- the narrative overview of conditions had reported out.

Interview participants generally considered their DTC GT results valid and potentially impactful for their health care. Consistent with other studies (Brett et al., 2012; Giovanni et al., 2010; Koeller et al., 2017), interview participants sought genetic counseling because they were uncertain and/or confused about their test results and concerned about healthcare implications. One of our interview participants had, in fact, misinterpreted the results as life-threatening.

P3 (30-year-old female) To be specific about why I went to the genetic counselor was I had done a through-the-mail genetic test and the results came back that I had a terminal disease [could not remember specific condition]. A terminal condition and that it was so rare that there were- and I live in [large city], there was no one- no one who had dealt with this case so finally it was recommended to me that I go speak with a genetic counselor and see what they had to say.

P5 (23-year-old male) The first reaction to results... I remember it being difficult to really understand because it popped up with several recessive alleles and... I remember age-related macular degeneration being something, and like sensitivity to caffeine and I really didn't know what to make about it.

While the PGen Study demonstrated that overall understanding of DTC GC results was relatively good (Ostergren et al., 2015), some interview participants mentioned that misunderstanding the results was very stressful.

P3 (30-year-old female) So for 9 months I had [...] my world was just spinning. And then once I knew that that particular thing [a terminal condition participant could not remember] was not likely to kill me in a slow death, then I just felt like I could breathe again. I could live again. I could... not be consumed [by fear]. And trust me, I was going to counseling weekly to try to overcome that anxiety.

As previously reported in the PGen Study (Meisel et al., 2015), we also found that some interview participants sought genetic counseling because they received DTC GT results that seemed to explain medical conditions in the participant and/or family members.

P14 (57-year-old male) And as I researched hemochromatosis symptoms and you just learn more about it... I kind of reflected on some family history. For example, my grandfather- he died pretty young and it was chalked up to kidney failure. But reading some of the symptoms like ruddy skin and things like that made me think that possibly that had been caused by hemochromatosis, or iron overload.

Poorer self-reported health has been identified by Koeller et al. (2017) as an important predictor of seeking genetic counseling. It was notable that 33% (5/15) of our interview participants had Ehlers-Danlos syndrome Type III, hypermobility type (EDS Type III). Although this high proportion likely reflects bias of ascertainment and has not been reported before in DTC studies, this is a population where DTC testing may be of particular interest given their diagnostic challenges. Of relevance, Schmidt et al. (2019) found that one-third of their clients who sought genetic counseling for consumer-driven whole exome (WES) and whole genome sequencing (WGS) were “undiagnosed and searching” and several of the symptoms they listed are seen with EDS Type III (e.g. joint pain, chronic fatigue, digestive problems).

EDS Type III is a connective tissue disorder characterized by generalized joint hypermobility and chronic pain and can be associated with other symptoms including gastrointestinal, chronic fatigue, anxiety and depression (Tinkle et al., 2017). No clinical genetic testing is currently available for this condition. There can be challenges obtaining a diagnosis, and patients may feel disbelieved (Clark and Knight, 2017). Indeed, some of our interview participants with EDS Type III, reported having health concerns that had been dismissed in the past by their doctors. Schmidt et al. (2019) also described clients feeling like physicians had “written them off.” Our participants with EDS Type III thought that their DTC GT results might offer an explanation for their difficulties with pain management and wanted test results documented so that healthcare providers would believe them.

P2 (22-year old female with EDS Type III) But I've always had problems with pain medicine because I need a lot more than other people and doctors don't really like to give out more pain medicine, obviously. So, my mom (P6, 56-year old female with EDS Type III) and I were... well my mom was really excited finding an actual reason for why that was. So, she really wanted to get it documented. That's why--so that was probably the main reason.

Turning to participants' experiences with genetic counselors and genetic counseling, the reflections were overall positive. In general, participants appreciated genetic counselors' demeanor and skills in listening and counseling. For example, genetic counselors reportedly took the time to validate concerns, explain results and check on participant understanding.

P4 (29-year-old male) ...And that's one benefit of having a person who is actually able to look at your results and have a 1-on-1 discussion with you is that they can give you that personal touch and again, not to re-tread old ground, but just the fact that she was able to give me her experience was, what her reaction was, that either validates kind of what I'm feeling or it um opens me up to the experience of kind of accepting the result...It was made much more personable, so I think that was the biggest value of being able to discuss the results with a professional.

P12 (55-year-old female) They gave me many, many times to ask questions. They asked me many times, “is this clear?” “Do you understand?” “Can I explain it in a different way?” And they did more active listening. They said, “Okay. Here's how I'm explaining this. Do you want to explain it back to me . . . and see if there's the right understanding? Is there anything that I

should clear up?” That’s really good stuff.

The participants we interviewed had high expectations for their genetic counseling visits. They were expecting the genetic counselor to be an expert in interpreting DTC GT results and to be thorough in reviewing and explaining the reports. Several interview participants mentioned statistics or hoped for a way for the genetic counselor to pool all available testing, family history, and personal health history data and come up with an overall risk for reported conditions. They wanted to know if there was other testing to be done and next steps. Participants wanted genetic counselors to lead them through “the maze” of DTC GT results and come up with a “game plan.”

P6 (56-year-old female) Well I was hoping that they would say- I would really like to go further with the testing and know exactly what type everything is and if there’s... it would be nice if they would give you a game plan, you know.

P10 (53-year-old female) I would’ve liked for them to go through the possibilities of, “well you have a percentage of this, a percentage of that since you have all of this family history of everything.” You know just to kind of thoroughly discuss all of the things that was on the report. Or at least part of the things. And at least on the testing that they said wasn’t done... offer to do that.... It’s something that if it’s a possibility then they need to focus a little bit more on leading you through that whole maze. As far as if there’s possibility of this and at least give you a guide as to how you can go about finding out more.

P14 (57-year-old male) Well, I mean the big question is really the statistical analysis question. If you have these risk factors, and these mitigating factors, and based on your genome how do they work together? And then just sort of... and I mean are there... see I just don’t know enough about genetics to know whether that’s even valid or not. And also whether, if you have multiple risk factors is it... what is... is the impact arithmetic or exponential? I don’t know enough to really know what the next thing I want to know is.

Our results provide a unique look into the thoughts behind the reasons given in the Koeller et al. (2017) study about why DTC GT customers seek genetic counseling. Although there were study limitations (e.g. small number of interview participants who were asked to reflect on DTC GT a few years prior), findings are consistent with the prior DTC GT studies cited above, and interviewees’ key demographics are similar to more recent studies (Carroll et al., 2019). The perspectives of our interview participants contribute to the limited literature on this topic.

Participants' quotes convey their strong desire for relevant information and high expectations for genetic counseling. Motivations for seeking genetic counseling included family and personal health histories (notably one-third of participants had a personal history of EDS Type III), concern and confusion about results, and information-seeking. Participants generally saw DTC GT results as valid and wanted more thorough explanations in "layman's terms" and a "game plan." Based on our interviews, when providing genetic counseling about DTC GT results, we recommend: 1) effective contracting when starting the clinic visit, especially to determine motivations for genetic counseling; 2) ascertainment and management of expectations; and 3) listening to (not dismissing) patient concerns about their results.

Effective contracting to ascertain patients' concerns, understanding and expectations is a key component for genetic counseling and medical care in general. Our interview participants were often information-seeking, and several had already accessed online resources. Given the multiple DTC GT results to potentially discuss and based on what we learned from our interviews, we suggest that the genetic counselor ask about clients' motivations for seeking genetic counseling, their understanding of results, identification of results seen as most concerning or confusing, and resources already accessed (e.g. online resources, discussed with their healthcare providers). Genetic counselors should also elicit any remaining questions and clearly communicate if and why all results may not be reviewed. Understanding clients' motivations, what they hope to understand and learn was similarly stressed by Schmidt et al. (2019).

As with any genetic counseling session, it is important to obtain family and medical history information and to explain the results in the context of this information. Genetic counselors should recognize that consumers may have positive family and/or personal health histories that led them to seek DTC GT and could independently have warranted a genetic counseling appointment. Of note, taking the time to listen and not coming across as dismissive of DTC GT results is clearly important, especially with patients who may have used this testing because they did not feel understood or accepted by other medical professionals. Genetic counselors will need to offer a general explanation of DTC GT and its differences from clinical genetic testing and to explain why, at present, there are not statistical models for risk determination that tie together test results with family and medical history information. It is important to address why additional testing and evaluations may or may not be indicated. Additional genetic counseling

recommendations are provided in Sturm and Manickam's (2012) DTC GT case study and in the Schmidt et al. (2019) commentary on genetic counseling for consumer-driven WES and WGS.

Schmidt et al. (2019) importantly note that determining prioritization of variants to discuss and the counseling content and approach will depend on whether the client is 1) healthy and curious 2) undiagnosed and searching or 3) has interest in specific health risk or variant. They recommend that counseling include discussing genetic contributions to disease, fundamentals of human genetic variation, concepts of risk (e.g. relative, absolute) and limitations of results.

The skills a genetic counselor has in risk assessment, listening, and educating about genetic testing and results work to the benefit of DTC GT customers who are seeking genetic counseling. Providing genetic counseling about DTC GT results can be seen as an opportunity to expand provision of genetic services. However, work force issues are already limiting the number of patients who can be seen in genetics clinics (Hoskovec et al., 2018). Given limited appointment slots in genetics clinics, prioritizing and effective triaging of potential patients will be key. It will be important to identify potential patients who have DTC GT results that need to be clinically confirmed (e.g. *BRCA1*) and to efficiently determine who needs to be seen based on personal and/or family histories. Tools that allow individuals to self-identify increased risk are also needed. Directing DTC GT users to genetic counseling resources at the testing company and to telephone or telemedicine genetic counseling services will help to meet some of the demand, especially since physical exams will generally not be needed. For those patients who are seen for genetic counseling about DTC GT results, the findings from our interviews can help inform case preparation and provision of genetic counseling.

Authors Contributions

Tessa Marzulla, J. Scott Roberts, Raymond DeVries, Diane R. Koeller and Wendy R. Uhlmann all significantly contributed to the conception and design of the work, analysis and interpretation of data, drafting and revising the paper, and final approval of the version to be published. All interviews were conducted and transcribed by Tessa Marzulla, with the first interview conducted by Raymond DeVries for demonstration. Robert C. Green conceived of the PGEN Study and also significantly contributed to revising the paper and final approval of the version to be

published. All agree to be accountable for all aspects of the paper.

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Conflict of Interest

Tessa Marzulla, Scott Roberts, Raymond De Vries, and Diane Koeller declare that they have no conflict of interest.

Dr. Green receives compensation for advising the following companies: AIA, Humanity, United Health Group, Wamberg Genomic Advisors and Verily; and is co-founder and advisor to Genome Medical, Inc., a technology and services company providing genetics expertise to patients, providers, employers and care systems.

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Human Studies and Informed Consent

The study was approved by the University of Michigan Institutional Review Board (HUM00102970). 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 participants for being included in the study.

References

Brett, G.R., Metcalfe, S.A., Amor, D.J., & Halliday, J.L. (2012). An exploration of genetic health professionals' experience with direct-to-consumer genetic testing in their clinical

practice. *European Journal of Human Genetics*, 20(8), 825–30.
<https://doi.org/10.1038/ejhg.2012.13>

Bryant A & Charmaz K editors (2010). *The SAGE Handbook of Grounded Theory*. London, UK and Thousand Oaks, CA: SAGE Publications, Inc.

Carere, D.A., Couper, M.P., Crawford, S.D., Kalia, S.S., Duggan, J.R., Moreno, T.A., ...Green, R.C. (2014). Design, methods, and participant characteristics of the Impact of Personal Genomics (PGen) Study, a prospective cohort study of direct-to-consumer personal genomic testing customers. *Genome Medicine*, 6(12), 96.
<https://doi.org/10.1186/s13073-014-0096-0>

Carroll, N.M, Blum-Barnett, E., Madrid, S.D., Jonas, C., Janes, K., Alvarado, M., ...Burnett-Hartman, A.N. (2019). Demographic differences in the utilization of clinical and direct-to-consumer genetic testing. *Journal of Genetic Counseling*. Epub 2019 Nov 20. doi: 10.1002/jgc4.1193

Clark, C.J. & Knight, I. (2017). A humanisation approach for the management of Joint Hypermobility Syndrome/Ehlers-Danlos Syndrome-Hypermobility Type (JHS/EDS-HT). *International Journal of Qualitative Studies on Health and Well-Being*, 12(1), 1371993.
<https://doi.org/10.1080/17482631.2017.1371993>

Darst, B.F., Madlensky, L, Schork, N.J., Topol, E.J., & Bloss, C.S. (2013). Perceptions of genetic counseling services in direct-to-consumer personal genomic testing. *Clinical Genetics*, 84(4), 335-339. <https://doi.org/10.1111/cge.12166>

Giovanni, M.A., Fickie, M.R., Lehmann, L.S., Green, R.C., Meckley, L.M., Veenstra, D., & Murray, M.F. (2010). Health-care referrals from direct-to-consumer genetic testing. *Genetic Testing and Molecular Biomarkers*, 14(6), 817-819.
<https://doi.org/10.1089/gtmb.2010.0051>

Gordon, E.S., Griffin, G., Wawak, L., Pang, H., Gollust, S.E., & Bernhardt, B.A. (2012). “It’s not like judgment day”: Public understanding of and reactions to personalized genomic risk information. *Journal of Genetic Counseling*, 21(3), 423–432.
<https://doi.org/10.1007/s10897-011-9476-4>

- Hoskovec, J.M., Bennett, R.L., Carey, M.E., DaVanzo, J.E., Dougherty, M., Hahn, S.E., ...Wicklund, C.A. (2018). Projecting the supply and demand for certified genetic counselors: a workforce study. *Journal of Genetic Counseling*, 27(1), 16-20. doi: 10.1007/s10897-017-0158-8
- Koeller, D.R., Uhlmann, W.R., Carere, D.A., Green, R.C., Roberts, J.S. & PGen Study Group (2017). Utilization of genetic counseling after direct-to-consumer genetic testing: findings from the Impact of Personal Genomics (PGen) Study. *Journal of Genetic Counseling*, 26(6), 1270-1279. <https://doi.org/10.1007/s10897-017-0106-7>
- Meisel, S.F., Carere, D.A., Wardle, J. Kalia, S.S., Moreno, T.A., Mountain, J.L., et al. (2015). Explaining, not just predicting, drives interest in personal genomics. *Genome Medicine*, 7(1), 74. <https://doi.org/10.1186/s13073-015-0188-5>
- Ostergren, J.E., Gornick, M.C., Carere, D.A., Kalia, S.S., Uhlmann, W.R., Ruffin, M.T., ...Roberts, J.S. (2015). How well do customers of direct-to-consumer personal genomic testing services comprehend genetic test results? Findings from the Impact of Personal Genomics Study. *Public Health Genomics* 18(4), 216-224. <https://doi.org/10.1159/000431250>
- Regalado, A. (2019, January 3). More than 26 million have taken an at-home ancestry test. *MIT Technology Review*. Retrieved January 20, 2020 from <https://www.technologyreview.com/s/612880/more-than-26-million-people-have-taken-an-at-home-ancestry-test/>
- Schmidt, J.L., Mass, R., & Altmeyer, S.R. (2019). Genetic counseling for consumer-driven whole exome and whole genome sequencing: A commentary on early experiences. *Journal of Genetic Counseling* 28(2), 449-455. <https://doi.org/10.1002/jgc4.1109>.
- Sturm, A.C., Manickam, K. (2012) Direct-to-consumer personal genomic testing: a case study and practical recommendations for “genomic counseling.” *Journal of Genetic Counseling*, 21(3): 402-412. <https://doi.org/10.1007/s10897-012-9489-7>
- Tinkle, B., Castori, M., Berglund, B., Cohen, H., Grahame, R., Kazkaz, H., & Levy, H. (2017). Hypermobility Ehlers-Danlos Syndrome (a.k.a. Ehlers-Danlos Syndrome Type III and

Ehlers-Danlos Syndrome Hypermobility Type): clinical Description and natural history.
American Journal of Medical Genetics. Part C, Seminars in Medical Genetics,
175(1),48-69. <https://doi.org/10.1002/ajmg.c.31538>

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Table I. Demographics of participants.

Participant (P#)	Sex	Age at Testing	Participant had children at time of study?	Company	Sought Genetic Counseling (GC)?	Genetics Appointment for Other Indication(s)?
P1	F	33	No	Pathway Genomics	Phone GC ¹	No
P2	F	22	No	Pathway Genomics	In-Person GC	EDS III ²
P3	F	30	Yes	Unknown	In-Person GC	No
P4	M	29	No	Pathway Genomics	In-Person GC ¹	No
P5	M	23	No	23andMe	No	No
P6	F	56	Yes	Pathway Genomics	In-Person GC	Infertility, EDS III ²
P7	M	24	No	23andMe	No	No
P8	M	45	Yes	23andMe	No	Son with CHARGE Syndrome
P9	M	51	No	23andMe	No	HCM ³
P10	F	53	Yes	23andMe	Geneticist Only	EDS III ²
P11	F	34	Yes	Pathway Genomics	No	No
P12	F	55	Yes	Pathway Genomics	Phone ¹ and In-Person GC	Lynch Syndrome evaluation
P13	F	33	No	Pathway Genomics	In-Person GC	EDS III ²

P14	M	57	No	23andMe	Phone GC	No
P15	F	27	No	Pathway Genomics	In-Person GC	EDS III ²

¹Genetic Counseling through Pathway Genomics; ²Ehlers-Danlos Syndrome Type III (Hypermobility Type); ³Hypertrophic Cardiomyopathy
P2 is the daughter of P6

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Figure 1. Resources used by participants who sought genetic counseling about their DTC GT results. Participants could select multiple resources. Specific website answers: PubMed, 23andMe, GeneticGenie, GEDmatch, RegulomeDB, SNPedia, Promethease, OpenSNP, Wikipedia, WebMD. Talked to other healthcare professional answer: Cardiologist. Other (please specify): Patients Like Me, email lists, specific condition sites, called 23andMe.

