J Genet Counsel
DOI 10.1007/s10897-014-9693-8

ORIGINAL RESEARCH

Personalized Genomic Results: Analysis of Informational Needs

Tara J. Schmidlen · Lisa Wawak · Rachel Kasper · J. Felipe García-España · Michael F. Christman · Erynn S. Gordon

Received: 2 July 2013 / Accepted: 21 January 2014

Abstract Use of genomic information in healthcare is increasing; however data on the needs of consumers of genomic information is limited. The Coriell Personalized Medicine Collaborative (CPMC) is a longitudinal study investigating the utility of personalized medicine. Participants receive results reflecting risk of common complex conditions and drug—gene pairs deemed actionable by an external review board. To explore the needs of individuals receiving genomic information we reviewed all genetic counseling sessions with CPMC participants. A retrospective qualitative review of notes from 157 genetic counseling inquiries was conducted. Notes were coded for salient themes. Five primary themes; "understanding risk", "basic genetics", "complex disease genetics", "what do I do now?" and "other" were identified. Further review revealed that participants had difficulty with basic genetic concepts, confused relative and absolute risks, and attributed too high a risk burden to individual single nucleotide polymorphisms (SNPs). Despite these hurdles, counseled participants recognized that behavior changes could potentially mitigate risk and there were few comments alluding to an overly deterministic or fatalistic interpretation of results. Participants appeared to recognize the multifactorial nature of the diseases for which results were provided; however education to understand the complexities of genomic risk information was often needed.

Keywords Genomic results · Genetic counseling · Patient needs · Personalized medicine · Complex disease

T. J. Schmidlen (✉) · L. Wawak · R. Kasper · J. F. García-España · M. F. Christman
Coriell Institute for Medical Research, 403 Haddon Avenue, Camden, NJ 08103, USA
e-mail: tschmidl@coriell.org

E. S. Gordon
Invitae, San Francisco, CA, USA

Introduction

Genomic medicine is expanding rapidly with increasing reports of the use of whole genome, exome or targeted sequencing in clinical care (Dixon-Salazar et al. 2012; Gilissen et al. 2011; Need et al. 2012) the use of next generation sequencing for multi-gene panels (Coonrod et al. 2012), tumor sequencing (Lamlertthon et al. 2011), and the use of pharmacogenomics across a variety of medical specialties (Roberts et al. 2012; Rogers et al. 2012; Walko and McLeod 2009). One burgeoning area of genomics which has attracted the most controversy but has the potential for the widest reach is the area of complex disease genomics. Genome wide association studies (GWAS) have identified thousands of variants associated with hundreds of diseases and traits (Hindorff et al. 2013); however, the clinical validity and utility of such low penetrance genetic variants as predictors of disease has been modest at best (Hirschhorn and Gajdos 2011). Given the small contribution of known genetic variants to common disease, it has been speculated that patients who are told about a genetic risk variant associated with an increased risk for a common disease such as coronary artery disease *might* overestimate the probability of developing disease, generating unnecessary worry, anxiety and possibly even depression; or conversely may underestimate risk despite the presence of legitimate risk factors (Cameron et al. 2009; McGuire and Burke 2008; Samuel et al. 2010; Wasson et al. 2006). Although some authors have shown that these fears are exaggerated (Ashida et al. 2010; Lerman et al. 2002; Meiser 2005); more data are needed to understand patient needs in the genomic era. To mitigate potential concerns associated with the delivery of genomic information, genetic counseling has been proposed to ensure that patients adequately understand the information presented (McGuire et al. 2009; O'Daniel 2010; Offit 2008; Samuel et al. 2010; Wasson et al. 2006).

Genetic counseling has historically bridged the gap in genetic knowledge among patients and non-genetics health

Published online: 03 February 2014

care professionals by helping people understand and adapt to the medical, psychological and familial implications of genetic contributions to disease (Resta et al. 2006). To date, the practice of genetic counseling has focused on chromosomal abnormalities and Mendelian (monogenic) disorders with high penetrance; however it is anticipated that the practice of genetic counseling will continue to expand and change with the evolution of genomic technology (Issa et al. 2009). Concurrent with this evolution, a greater understanding of patient needs and expectations of genomics is needed. While much has been learned about patient needs by studying individuals with Mendelian disorders, many researchers (Peacock et al. 2006; Peters and Petrill 2011a, b; Reiff et al. 2012; Salemink et al. 2013; Shiloh et al. 2006) have found that needs and expectations differ by condition. Identification of differences in patient needs and expectations of single gene disorders suggest that further differences in patient needs may exist for individuals undergoing genomic testing. These changing needs relate not only to emerging technology, expansion of the number of conditions included in a given test, and the penetrance of the conditions included in the test but also the format for result delivery.

To begin to understand the needs of individuals who have had genomic testing, we conducted a qualitative analysis of genetic counseling notes from participants in the Coriell Personalized Medicine Collaborative who had received genomic test results for common complex diseases.

Methods

Informational needs of participants in the Coriell Personalized Medicine Collaborative were assessed through retrospective review of notes from genetic counseling sessions. All sessions were conducted by two genetic counselors (authors TS and EG) between April 1st 2009 and April 30th 2011. The CPMC, described previously by Keller and colleagues (2010), is an ongoing prospective, longitudinal research study that assesses the impact of personalized disease risk information on behavior and health outcomes. The CPMC study has received human subjects approval from the Institutional Review Boards of the Coriell Institute for Medical Research and all collaborating institutions. The research activities described here are covered under the CPMC study IRB approved protocol.

To participate in the CPMC, individuals must be at least 18 years of age, have a valid, personal email address and attend an in-person informed consent session. The informed consent session consists of a 45 min presentation which includes explanation of personalized medicine and its potential applications, study design and participation requirements; risks, benefits, and alternatives to participation; examples of "potentially actionable" health conditions and drug-gene pairs likely to be reported to participants (e.g. coronary artery disease; *CYP2C19* and Plavix); and examples of health conditions that are excluded from the study (rare/single gene Mendelian diseases or conditions for which there is no available medical or behavioral actions to reduce risk, e.g. amyotrophic lateral sclerosis). For the purposes of the CPMC, a "potentially actionable" condition is defined as a condition for which the risk is likely to be mitigated by either behavior or lifestyle modifications (diet and exercise, smoking cessation) or by medical actions like changing a drug or drug dose, increased screening, preventative treatment or early intervention.

Those who consent to participate in the study provide a saliva sample for genomic analysis and are asked to complete mandatory online questionnaires about their medical history, family history, medication use and lifestyle. Participants who complete all required questionnaires are invited to view their results through the secure web-based portal. CPMC results provide participants with estimates of their relative risk of various diseases, all of which have been deemed "potentially actionable" by an external advisory board, based on medical history, family history, lifestyle and other non-genetic contributors to risk in addition to providing relative risk due to the presence or absence of specific disease-associated genetic variants.

During the 2 year time frame captured by this study, participants received results for the following eight conditions: coronary artery disease, type 2 diabetes, iron overload/hemochromatosis, age related macular degeneration, lupus, prostate cancer, melanoma, and type 1 diabetes.

Genetic counseling is available to all CPMC participants but is not mandatory. Counseling is offered free of charge, via in-person face-to-face counseling sessions or telephone sessions. Alternatively, questions can be submitted to CPMC genetic counselors via email. Study participants may request counseling at any time (pre or post results) however, all but two requests have come after results were received. All genetic counseling was provided by the two board certified genetic counselors employed by the research study (authors TS and EG).

Participants

As of April 30th, 2011, 4,293 individuals had consented to participate, of which, 2,636 (61 %) had completed the required baseline surveys, had their sample genotyped and were provided with results of genetic analysis, family history, and lifestyle risk assessment for eight health conditions. Of those 2,636 participants to whom results were made available, 2,345 participants (89 %) chose to view at least one result. Of those who chose to view at least one result, 157 participants (6 %) submitted requests for genetic counseling to a CPMC genetic counselor. The 2,636 participants who received at least one result were primarily white (92 %) white, middle-aged, females (63 %) who had attained a Bachelor's degree or higher (71 %). Thirty-eight percent reported employment in a health

or science occupation and 52 % reported a household income greater than $100,000 per year. Additional demographic characteristics of the 2,636 participants and the subset who requested genetic counseling are provided in Table 1.

Procedures

Participants submitted requests for genetic counseling via email, by phone or through the secure web portal. All written requests for counseling (email or web portal requests) and subsequent written communications were stored verbatim, while the content of telephone or in-person counseling sessions was captured in the form of detailed session summaries which identified participant questions, issues, and information provided. Counseling notes for 50 telephone genetic counseling sessions, six in person counseling sessions and email transcripts for 101 email inquiries made by CPMC participants between April 2009 and April 2011 were included in this analysis.

This study utilized the methodology of classic grounded theory (Corbin and Strauss 1990). The first reviewer (TS) initially read all notes and email transcripts and through open coding identified main themes that emerged across the counseling notes. Subsequently the notes and email transcripts were reviewed again and closed coding was done to identify sub-themes within the main themes. Closed coding was done inclusively, including all instances which fit a theme. Five main themes emerged through this process. From the closed coding, a detailed code book was developed to code for each of the five main themes, as well as codes for narrower sub-themes. The counseling notes and email transcripts were reviewed once again and then all notes and email transcripts were imported into NVivo 9.0 (QSR International Pty Ltd., Doncaster, Victoria, Australia) where individual quotes, portions of email transcripts, and counselor notes were coded manually utilizing the detailed code book. This method often resulted in coding the same participant inquiry into multiple

Table 1 Demographics of CPMC participants requesting genetic counseling vs. participants not requesting genetic counseling

	Requested GC (*n*=157)		No GC (*n*=2,479)		p value
	n	%	n	%	
Gender					
Male	52	33.1	935	37.7	0.25
Female	105	66.9	1,544	62.3	
Age	Median (IQR): 57 (48–64)		Median (IQR): 51(39–60)		<0.01
Race					
Caucasian	149	94.9	2,277	91.9	0.07
African American	3	1.91	65	2.62	
Native American or Alaska Native	1	0.64	1	0.04	
Native Hawaiian or other Pacific Islander	0	0	1	0.04	
Asian	1	0.64	71	2.86	
Mixed race	3	1.91	42	1.69	
Ethnicity					
Hispanic or Latino	2	1.3	58	2.3	0.35
Education					
Some high school, HS grad	13	8.3	176	7.1	0.28
Some college	16	10.2	328	13.2	
Associates degree	20	12.7	217	8.8	
Bachelors degree	44	28.0	805	32.5	
Graduate degree	64	40.8	953	38.4	
Income					
<$25 K	6	3.8	117	4.7	0.59
$25 K–$50 K	15	9.6	269	10.9	
$50 K–$75 K	24	15.3	382	15.4	
$75 K–$100 K	35	22.3	428	17.3	
$100 K +	77	49.0	1,283	51.8	
Health/science occupation	34	21.7	651	26.3	0.20
Insured	143	95.3	2,399	95.6	0.90
Medical check-up within past year	139	88.5	1,994	80.4	0.01
Viewed at least one result	155	98.7	2,190	88.3	<0.01

main themes and/or narrower sub-themes. A second reviewer (LW) was trained to code the transcript in NVivo 9.0 using the codebook; after training, a subset of 10 transcripts was coded by the two reviewers (TS and LW) and discrepancies in coding were discussed. An additional 51 transcripts were coded by both reviewers and inter-coder reliability was 95 %. Questions from participants that were limited to study logistics, web portal technical support, or result status requests were omitted from coding and analysis and are not reflected in the 157 encounters described here. All other questions were included for analysis.

Data Analysis

Data analysis began by reviewing coded sections of transcripts for each code and analyzing them for salient attributes. Coded data was reviewed within NVivo 9.0 to determine whether or not there were any trends or relationships among coded themes according to participant socio-demographic factors (sex, age, occupation, income level, etc.) or other attributes and no significant trends were observed.

Descriptive statistics were computed for all relevant variables, using both parametric and nonparametric measures of central tendency and variability. Frequency counts were used for categorical as well as ordered categorical data. For continuous variables, between group comparisons ("requested GC" versus "No GC") was assessed by using Wilcoxon rank sum test. For categorical variables, comparisons used Chi-square or Fisher's exact test where appropriate. All computations were conducted using SAS v9.3 and the criterion for statistical significance was set at alpha=0.05.

Results

Retrospective review was completed for counseling notes and inquiries from a total of 157 participants. Ninety six participants (61 %) were counseled by TS and 61 participants (39 %) were counseled by EG. Of these requests, 50 were telephone genetic counseling sessions, six were in person counseling sessions and 101 were email inquiries. Table 1 shows the demographics of these 157 participants versus those in the study who did not request genetic counseling. Participants who requested genetic counseling were older than those who did not request counseling (median age 57 (IQR: 48–64)) versus median age 51 (IQR: 39–60). Participants requesting genetic counseling were also more likely to report having had a check up with a physician within the past year (88.5 % versus 80.4 %, $p=0.01$) than participants who did not request genetic counseling. A higher percentage of participants who requested genetic counseling had viewed at least one result (98.7 %) as compared to participants who did not request genetic counseling (88.3 %, $p<.0001$). There was no significant difference in gender, race or ethnicity, occupation, education level, income level, or health insurance status between participants that requested genetic counseling and participants who did not seek genetic counseling. In addition, all study participants completed a 15 item measure of genetic knowledge, developed for use in the CPMC study. There were no significant differences in genetic knowledge between participants who requested genetic counseling and those who did not (median score for both groups: 80 % (IQR: 66.7–86.7)).

Qualitative analysis of counseling notes and email transcripts revealed five main themes. The following themes (n = total number of questions) were identified: 1) Basic Genetics (50); 2) Complex Disease Genetics (63); 3) Understanding Risk (47); 4) What Do I Do Now? (44) and 5) Other (88). Within each main theme, sub-themes were also identified and coded. A given inquiry may have been coded under multiple themes and subthemes depending on the question(s) asked by the participant. Not all questions fit into an identified subtheme, therefore the total number of questions for a main theme may not equal the sum of the subthemes listed in Table 2. Representative quotes illustrating the variety of questions and the level of understanding of CPMC participants are provided in Table 2.

Among the CPMC research study population, we observed three levels of need for interpretation assistance: those who presumably felt that they independently understood their results and therefore did not utilize the free genetic counseling services, those who sought confirmation that their interpretation of their risk results was correct, and those who needed extensive explanation of risk results and concepts in genetics. Analysis of counseling notes identified 292 independent questions posed by 157 CPMC participants who did require some level of assistance with result interpretation. Thirty-three questions (11 %) were primarily focused on seeking confirmation of understanding of personalized genomic risk results. The remaining 259 questions were more targeted questions about terminology, inheritance, complex disease genetics, interpretation of risk, and requests for other diseases to be included in the CPMC study.

Discussion

Through requests for genetic counseling, this study identified key concepts that the lay public may struggle with when receiving personalized genomic test results. Additionally, these results highlight for genetic counselors and health care providers the differing levels of need for interpretation assistance that exists among consumers of personalized genomic testing: no perceived need, need for confirmation of understanding, and need for extensive explanation.

Current research has shown limited utilization of genetic counseling services among consumers of personal genome

Table 2 Counseling themes identified

Question theme-sub-theme	Number of questions received for each sub-theme	Representative quotes
Other-confirming understanding of results	33	I'm not overly concerned about my results, but wanted confirmation that there isn't anything I should be rushing out to my doctor for.
Basic genetics-inheritance	32	I have the risk variant, what does this mean for my children?
		Do we always pass our genes on to our children? We get one gene from each of our parents-do we pass these two genes on, or just one, or maybe none?
		Can you tell whether the variants came from mom or dad?
Other-requests for conditions/traits	31	I would also like to know when you will report on the ApoE4 Alzheimer's genotype.
		Are there any plans to look for Celiac in the study? We have some diagnosed individuals in our family and I am interested in this topic.
Complex disease genetics-matching personal/family history to results	25	I have had 2 melanomas, yet my result was 2 non-risk variants.
		I have risk variants for type 2 diabetes and coronary artery disease but these are not in my family.
		I have type 2 diabetes, so I wasn't surprised at all to see that result.
		My mother had coronary artery disease, so I also was not surprised to see that risk.
What do I do now?-Prevention/reduction of risk	21	I already exercise, eat well, and do not smoke-I am at a loss as to what else to do.
		Maybe there should be recommendations as to what to do with certain (relative risk) scores.
		Type 2 diabetes is very common in my family [I] would like to know what I can do to prevent it.
Other-requests for clinical/Mendelian tests	17	I am wondering if the program was planning on testing for mutations in BRCA1 and BRCA2. As far as I am aware, Myriad Genetics currently holds the patent for the test but I was curious if the Coriell program was in contact with them to possibly provide the participants with results regarding these genes.
Complex disease genetics-diagnostic misconception	16	I have 2 copies of the risk variant; does that mean I have coronary artery disease?
		I have 2 non-risk variants, so I do not have any risk for developing the condition, right?
		My family history risk is huge and that was not news to me. And I am overweight and I always knew that was a factor. However the fact that 2 copies of the non-risk variant were detected would make me think that if I get diabetes, it would more than likely be due to my being overweight than genetic?
		I was hoping for-"you have the gene so you'll definitely get X if you don't do something to prevent it", or-"you do not have the gene that causes Y, so you do not have to worry about getting Y later in life unless you are very irresponsible with your health".
What do I do now?-Sharing with others	13	What will my doctor do with this information?
		I do not want them (doctors) to just put me on some drug because they don't understand the results.
Understanding risk-impact on family	12	I am female and carry two non risk factors for prostate cancer. Every male in my father's family died of it. Do my results mean that my son is safe?
Complex disease genetics-pleiotropy	11	I was recently informed that I have two copies of CC on Variant #1 (rs1333049) of CDKN2A/CDKN2B on chromosome 9p21.3. I understand that this means that I am 70 % more likely to develop coronary artery disease. Does this also make me more likely to develop melanoma?
Basic genetics-terminology	10	Please explain the difference between risk and non risk variant.
		I am not sure what a variant is, or what having one means.
	9	Do the risk and non-risk variant cancel each other out?

Table 2 (continued)

Question theme-sub-theme	Number of questions received for each sub-theme	Representative quotes
Understanding risk-heterozygote/ homozygote risk		Why isn't the risk due to 1 non-risk and 1 risk variant 50 % of the risk of having 2 risk variants?
		What is the difference between having 1 risk and 1 non-risk variant and having just 1 risk variant?
		Is having 2 copies of the same letter always bad?
Understanding risk-combining risks	8	My summary gave me 4 different levels of risk (1.2, 1.0, 1.0, and 1.3). I'm not sure what the aggregate risk is…an average of the 4?
		How does the risk due to this variant combine with the risk I have from BRCA1 to affect my risk of prostate cancer.
What do I do now?-Additional or follow-up testing	7	Should I get an iron overload blood test through my physician? As a vegetarian I eat a lot of spinach and broccoli…which may lead to iron overload.
Complex disease genetics-attribution of cause	6	I was shown as having 2 non-risk variant genes. However, I am currently being treated for lupus. Does this mean the cause of my lupus is environmental rather than genetic?
Complex disease genetics-sources of risk information	5	Are these results from the questionnaire, the saliva test or both?
Understanding risk-misunderstanding risk numbers	5	You saw 2 copies in my genes and it increased my risk to 70 %.
		I would like genetic counseling; I have a 30 % chance of coronary artery disease from my genetic component and a 20 % chance of coronary artery disease from my family history.
Understanding risk-protective variants	3	Can you have a risk level below 1.0? With the Diabetes type 2 results, my risk was 1.0 in all categories. Is it ever possible to have a negative score, i.e., less than a low risk?

testing, with others reporting uptake of genetic counseling services by 7.5–12.1 % of consumers (Bloss et al. 2011; Darst et al. 2013; Levin et al. 2012). Although our experience shows a slightly lower uptake rate (6 %) than published by others, survey data from 114 CPMC study participants who did not pursue genetic counseling indicated that they did not pursue counseling because they did not receive a concerning result (61 %) and/or they felt that they understood their results and therefore did not perceive a need to pursue genetic counseling (50 %) (unpublished data). Perceived understanding of genomic results has been recently reported as the most common reason consumers of direct-to-consumer genomic testing choose not to pursuing counseling and may explain the low uptake within the CPMC research study as well (Darst et al. 2013).

Further, prior familiarity and personal knowledge have been shown to elevate patient's comfort with disease information. Peters and Petrill (2011b) found that patients seeking cancer genetic counseling reported the least amount of uncertainty about their condition and the most favorable beliefs about available treatment when compared to individuals pursuing reproductive, pediatric or adult genetic counseling. The authors attribute this difference to the fact that many cancer genetic counseling patients have a lived experience with the condition for which they are seeking counseling and are often already familiar with or participating in increased disease surveillance options, whereas patients seeking counseling for a reproductive, pediatric or adult genetics indication are less likely to be familiar with the diseases discussed or their associated treatments. Similarly it could be argued that CPMC participants may have less uncertainty about receiving risk information for common, complex diseases because the diseases are familiar and many participants may have either personal experience or the experience of a close family member contributing to their background level of understanding of the condition. Additionally, CPMC participants may already be familiar with or engaging in general risk reduction behaviors typically recommended for the prevention of common, complex diseases, such as getting regular exercise and making healthier diet choices. Our data, in combination with previous studies suggests that the majority of consumers of genomic information will not need or perceive a need for counseling or additional explanation of their results, beyond that provided as part of the test report.

Familiarity with the common complex diseases included in the CPMC in combination with a perceived confidence in handling genetic information created a small population that falls between those needing and wanting counseling and those who perceive no need for counseling. This intermediate group is comprised of those who believed they understood their results but requested genetic counseling, seeking confirmation of their interpretation of their genetic results. This population

may truly be a subset of those who do not believe they need counseling, but lack a feeling of complete confidence in their independent interpretation of their results, leading them to contact a genetic counselor for reassurance.

The third level of interpretation assistance need observed in this study, "extensive explanation", was represented by the more targeted participant inquiries about specific concepts like inheritance, complex disease genetics, and risk. Many of the questions posed by CPMC participants mirrored gaps in genetic literacy previously identified among the lay public.

While some participants indicated awareness that their personal results may have some impact on other family members, others questioned whether or not genetic variants are passed on from parents to offspring. Similarly, previous researchers have found that the lay public inconsistently recognizes that children receive 50 % of their genes from each parent (Molster et al. 2009; de Vries et al. 2005). A very common sentiment expressed by participants was the expectation that their genetic variant results should mirror their personal or family history experience with disease, which reflects the observations of Chapple et al. (1995), who found that people did not understand how risk for a condition can be inherited, yet never before seen in their family. Similar to previous observations of how the general public understands genetics concepts (Lanie et al. 2004), the majority of participants articulated some understanding of the multifactorial nature of the conditions for which reports were provided; however some were disappointed in the lack of certainty that accompanies multifactorial risk estimates.

The personalized risk reports that CPMC study participants receive provide relative risk data for a genetic risk variant, family history and non-genetic risk factors like body mass index or cigarette smoking. Although the reports explicitly state that risk estimates across these risk factors cannot be combined due to their overlap, a few participants (n=8) were trying to determine an "overall" or combined risk based on all of the risk factors provided in their reports. Participants are reminded both in the study consent and in counseling that "family history and medical history are still the best predictors of risk of complex diseases".

Despite previous speculation that individuals who are told about a genetic risk variant associated with an increased risk for a common disease *might* overestimate the probability of developing disease possibly resulting in unnecessary worry, anxiety and even depression, our results suggest that the majority of individuals who sought genetic counseling were not grossly over or underestimating their risk of disease. Of 291 total questions raised by 157 participants, only 16 questions (5 %) were coded as "diagnostic misconception" (Samuel et al. 2010; Wasson et al. 2006). This misconception was anticipated and the informed consent document and enrollment presentation both highlighted that "participants may over estimate or under estimate risk of a particular condition based on the results of this study". Both the study consent form and the limitations section of each result report inform participants that "it is not possible to rule out your risk of diseases by participating in this study" and "it is also not possible to diagnose a condition by participating in this study". While these misconceptions are extremely important to correct, they affect a minority of participants in this study who sought genetic counseling. It is possible that participants who did not seek counseling have similar misconceptions; however, based on our experience with the participants who did seek counseling, this is not anticipated to be a widespread problem.

Practice Implications

Genetic counseling strives to meet patient educational and psychosocial needs; however patients' needs vary depending on the information they are seeking, the level of detail and what they find relevant (Pieterse et al. 2005a, b, 2006). Review of genetic counseling inquiries made by participants in the CPMC revealed that differing levels of assistance and education are needed, lending further support to the idea that genetic counseling goals should take into account the background needs of patients and counseling sessions should maintain the flexibility to address different levels of patient education and experience (Peters and Petrill 2011b). Some participants sought genetic counseling to confirm their understanding of their personalized genomic risk results, while other participants who sought genetic counseling struggled with understanding basic concepts in genetics, confused relative risks with absolute risks, and mistakenly attributed greater role and risk burden to individual genetic variants in the etiology of a common complex disease than is warranted.

As genomic testing continues to expand beyond Mendelian diseases and chromosomal abnormalities, the demand for genetic counseling will also grow. The low uptake of genetic counseling (6 %) and the varying needs of participants requesting counseling in this study suggest that new mechanisms may need to be developed in order to identify those patients who need counseling as opposed to assuming that all patients undergoing genomic testing require counseling. Identifying those who actually need counseling for genomic testing will allow genetic counselors to better manage increasing demand.

This study found that the majority of participants interpret genomic test results on their own and that participants are not overwhelmed by multiplex testing. Approximately one-fifth of participants (n=31) contacted Coriell to request that the study provide genetic risk results for other health conditions such as Celiac disease or Alzheimer's disease. This interest in receiving additional personalized genetic results suggests that participants are interested in continuing to learn more about their future health risks, even for conditions like Alzheimer's disease where risk reduction options may be more limited. These requests for additional results is encouraging as whole genome sequencing

technologies yielding a multitude of results, are becoming increasingly accessible tools in clinical care.

Limitations

The CPMC research study has several limitations. The cohort is predominantly Caucasian, with a high level of education and income, therefore this population is not representative of the general public; however it is believed to be representative of current consumers of personalized genomic testing. In this study, there were several ways of delivering genetic counseling—by telephone, in-person, and via e-mail, which may have influenced the number and type of questions asked by participants. Analysis was conducted on written exchanges between the participant and the genetic counselors when possible but, in part, relied on session notes taken by the CPMC genetic counselors. While every effort was made to accurately capture the questions, needs and concerns expressed by participants, session notes are not able to capture the interactions verbatim. The framing and content of session notes may also have been biased toward topics that genetic counselors are trained to focus on, such as family history and risk comprehension. Ideally, transcripts of phone and in-person counseling sessions would have been available for study. An additional limitation of this study is that it only examines the needs and misconceptions of the individuals who contacted us for genetic counseling.

Research Recommendations

Further research should be performed to understand the reasons participants choose not to seek genetic counseling as well as to determine the needs and potential misconceptions among this population. More investigation is also needed to determine the genomic informational needs of patients of more diverse racial, ethnic, educational and socioeconomic status.

In addition, further work to create an assessment tool which can be used to identify those at risk for misunderstanding and those who require counseling will help the profession appropriately plan for genomic counseling sessions (time per session, staffing needed) as well as to triage questions and concerns of patients seeking genomic testing.

Conclusions

Among participants in the Coriell Personalized Medicine Collaborative only 6 % sought genetic counseling. Those who did seek counseling could be divided into two groups, those seeking confirmation of their own interpretation of their results and those who had more questions and needed more extensive genetic counseling. The groups identified through this study suggest that the majority of individuals undergoing genomic testing are comfortable interpreting their test results independently. However, the majority of the study population that these conclusions are based on is highly educated and therefore not representative of the general public. Counseling approaches must be flexible to accommodate those who simply need confirmation of their understanding versus those who need more detailed education regarding their test results and result implications.

Acknowledgments The CPMC would not be possible without the efforts of a team of scientists and staff including: Neda Gharani, Margaret Keller, Catherine Stack, Joseph Jarvis, Daniel Lynch, Norman Gerry, Courtney Kronenthal, Susan Delaney, Mark Bellafante, Leo Lnu, and Corey Zuares. We are extremely grateful for the participants of the Coriell Personalized Medicine Collaborative for their continued participation in the study. We owe many thanks to the staff of the Coriell Genotyping and Microarray Center and of the Coriell Information Systems Department for their significant and ongoing work on the study. We acknowledge the physicians of Cooper University Hospital (NJ, USA) and Virtua Health System (NJ, USA) for their assistance in reviewing educational web pages and surveys on health conditions included in the study and we thank Christa Sherburne-Law for her work on the survey of participants who did not seek genetic counseling (unpublished data). Finally, we acknowledge the members of the Informed Cohort Oversight Board (David Pellman [current Chair], Erin O'Shea [past chair], Jennifer Hoheisel, Marc Lenburg, Steve Murphy, Kenneth Offit, Robert Green, Michael Grinkemeyer, Charles Rotimi, Reverend Floyd White and Ellis Neufeld), for their advice and suggestions concerning the project. This research was supported by grants from the William G. Rohrer Foundation, the RNR Foundation, and a generous grant from the endowment of the Coriell Institute for Medical Research.

Informed consent All procedures followed were in accordance with the ethical standards of the responsible committee on human experimentation (institutional and national) and with the Helsinki Declaration of 1975, as revised in 2000 (5). Informed consent was obtained from all participants for being included in the study.

Conflict of Interest Tara J. Schmidlen declares that she has no conflict of interest. Lisa Wawak declares that she has no conflict of interest. Rachel Kasper declares that she has no conflict of interest. J. Felipe García-España declares that he has no conflict of interest. Michael F. Christman declares that he has no conflict of interest. Erynn S. Gordon declares that she has no conflict of interest.

References

Ashida, S., Koehly, L. M., Roberts, J. S., Chen, C. A., Hiraki, S., & Green, R. C. (2010). The role of disease perceptions and results sharing in psychological adaptation after genetic susceptibility testing: the REVEAL Study. *European Journal of Human Genetics, 18*(12), 1296–1301. doi:10.1038/ejhg.2010.119.

Bloss, C. S., Schork, N. J., & Topol, E. J. (2011). Effect of direct-to-consumer genomewide profiling to assess disease risk. *New England Journal of Medicine, 364*(6), 524–534. doi:10.1056/NEJMoa1011893.

Cameron, L. D., Sherman, K. A., Marteau, T. M., & Brown, P. M. (2009). Impact of genetic risk information and type of disease on perceived risk, anticipated affect, and expected consequences of genetic tests. *Health Psychology, 28*(3), 307–316. doi:10.1037/a0013947.

Chapple, A., May, C., & Campion, P. (1995). Lay understanding of genetic disease: a British study of families attending a genetic counseling service. *Journal of Genetic Counseling, 4*(4), 281–300.

Coonrod, E. M., Durtschi, J. D., Margraf, R. L., & Voelkerding, K. V. (2012). Developing genome and exome sequencing for candidate gene identification in inherited disorders. *Archives of Pathology and Laboratory Medicine*. doi:10.5858/arpa.2012-0107-RA.

Corbin, J., & Strauss, A. (1990). Grounded theory research: procedures, canons and evaluative criteria. *Qualitative Sociology, 13*(1), 3–20.

Darst, B., Madlensky, L., Schork, N., Topol, E., & Bloss, C. (2013). Perceptions of genetic counseling services in direct-to-consumer personal genomic testing. *Clinical Genetics*. doi:10.1111/cge.12166.

de Vries, H., Mesters, I., van de Steeg, H., & Honing, C. (2005). The general public's information needs and perceptions regarding hereditary cancer: an application of the Integrated Change Model. *Patient Education and Counseling, 56*(2), 154–165. doi:10.1016/j.pec.2004.01.002.

Dixon-Salazar, T. J., Silhavy, J. L., Udpa, N., Schroth, J., Bielas, S., Schaffer, A. E., et al. (2012). Exome sequencing can improve diagnosis and alter patient management. *Science Translational Medicine, 4*(138), 138ra178. doi:10.1126/scitranslmed.3003544.

Gilissen, C., Hoischen, A., Brunner, H. G., & Veltman, J. A. (2011). Unlocking Mendelian disease using exome sequencing. *Genome Biology, 12*(9), 228. doi:10.1186/gb-2011-12-9-228.

Hindorff, L. A., MacArthur, J., Morales, J., Junkins, H. A., Hall, P. N., Klemm, A. K., & Manolio, T. A. (2013). A catalog of published genome-wide association studies. Available at: www.genome.gov/gwastudies. Accessed 1 May 2013.

Hirschhorn, J. N., & Gajdos, Z. K. (2011). Genome-wide association studies: results from the first few years and potential implications for clinical medicine. [Review]. *Annual Review of Medicine, 62*, 11–24. doi:10.1146/annurev.med.091708.162036.

Issa, A. M., Tufail, W., Hutchinson, J., Tenorio, J., & Baliga, M. P. (2009). Assessing patient readiness for the clinical adoption of personalized medicine. [Research Support, Non-U.S. Gov't]. *Public Health Genomics, 12*(3), 163–169. doi:10.1159/000189629.

Keller, M., Gordon, E., Stack, C. B., Gharani, N., Schmidlen, T. J., Mintzer, J., et al. (2010). The Coriell personalized medicine collaborative: a prospective study of the utility of personalized medicine. *Personalized Medicine, 7*(3), 301–317.

Lamlertthon, W., Hayward, M. C., & Hayes, D. N. (2011). Emerging technologies for improved stratification of cancer patients: a review of opportunities, challenges, and tools. [Review]. *Cancer Journal, 17*(6), 451–464. doi:10.1097/PPO.0b013e31823bd1f8.

Lanie, A. D., Jayaratne, T. E., Sheldon, J. P., Kardia, S. L., Anderson, E. S., Feldbaum, M., et al. (2004). Exploring the public understanding of basic genetic concepts. *Journal of Genetic Counseling, 13*(4), 305–320.

Lerman, C., Croyle, R. T., Tercyak, K. P., & Hamann, H. (2002). Genetic testing: psychological aspects and implications. [Research Support, U.S. Gov't, P.H.S.]. *Journal of Consulting and Clinical Psychology, 70*(3), 784–797.

Levin, E., Riordan, S., Klein, J., & Kieran, S. (2012). Genetic counseling for personal genomic testing: optimizing client uptake of post-test telephonic counseling services. *Journal of Genetic Counseling, 21*(3), 462–468. doi:10.1007/s10897-012-9496-8.

McGuire, A. L., & Burke, W. (2008). An unwelcome side effect of direct-to-consumer personal genome testing: raiding the medical commons. *JAMA, 300*(22), 2669–2671. doi:10.1001/jama.2008.803.

McGuire, A. L., Diaz, C. M., Wang, T., & Hilsenbeck, S. G. (2009). Social networkers' attitudes toward direct-to-consumer personal genome testing. *The American Journal of Bioethics, 9*(6–7), 3–10. doi:10.1080/15265160902928209.

Meiser, B. (2005). Psychological impact of genetic testing for cancer susceptibility: an update of the literature. *Psychooncology, 14*(12), 1060–1074. doi:10.1002/pon.933.

Molster, C., Charles, T., Samanek, A., & O'Leary, P. (2009). Australian study on public knowledge of human genetics and health. *Public Health Genomics, 12*(2), 84–91. doi:10.1159/000164684.

Need, A. C., Shashi, V., Hitomi, Y., Schoch, K., Shianna, K. V., McDonald, M. T., et al. (2012). Clinical application of exome sequencing in undiagnosed genetic conditions. *Journal of Medical Genetics, 49*(6), 353–361. doi:10.1136/jmedgenet-2012-100819.

O'Daniel, J. M. (2010). The prospect of genome-guided preventive medicine: a need and opportunity for genetic counselors. *Journal of Genetic Counseling, 19*(4), 315–327. doi:10.1007/s10897-010-9302-4.

Offit, K. (2008). Genomic profiles for disease risk: predictive or premature? *JAMA, 299*(11), 1353–1355. doi:10.1001/jama.299.11.1353.

Peacock, S., Apicella, C., Andrews, L., Tucker, K., Bankier, A., Daly, M. B., et al. (2006). A discrete choice experiment of preferences for genetic counselling among Jewish women seeking cancer genetics services. *British Journal of Cancer, 95*(10), 1448–1453. doi:10.1038/sj.bjc.6603451.

Peters, K. F., & Petrill, S. A. (2011a). Comparison of the background, needs, and expectations for genetic counseling of adults with experience with Down syndrome, Marfan syndrome, and neurofibromatosis. *American Journal of Medical Genetics Part A, 155A*(4), 684–696. doi:10.1002/ajmg.a.33863.

Peters, K. F., & Petrill, S. A. (2011b). A comparison of the background, needs, and expectations of patients seeking genetic counseling services. *American Journal of Medical Genetics Part A, 155A*(4), 697–705. doi:10.1002/ajmg.a.33979.

Pieterse, A. H., Ausems, M. G., Van Dulmen, A. M., Beemer, F. A., & Bensing, J. M. (2005a). Initial cancer genetic counseling consultation: change in counselees' cognitions and anxiety, and association with addressing their needs and preferences. *American Journal of Medical Genetics Part A, 137*(1), 27–35. doi:10.1002/ajmg.a.30839.

Pieterse, A. H., van Dulmen, A. M., Ausems, M. G., Beemer, F. A., & Bensing, J. M. (2005b). Communication in cancer genetic counselling: does it reflect counselees' previsit needs and preferences? *British Journal of Cancer, 92*(9), 1671–1678. doi:10.1038/sj.bjc.6602570.

Pieterse, A. H., van Dulmen, A. M., Beemer, F. A., Ausems, M. G., & Bensing, J. M. (2006). Tailoring communication in cancer genetic counseling through individual video-supported feedback: a controlled pretest-posttest design. *Patient Education and Counseling, 60*(3), 326–335. doi:10.1016/j.pec.2005.06.009.

Reiff, M., Bernhardt, B. A., Mulchandani, S., Soucier, D., Cornell, D., Pyeritz, R. E., et al. (2012). "What does it mean?": uncertainties in understanding results of chromosomal microarray testing. *Genetics in Medicine, 14*(2), 250–258. doi:10.1038/gim.2011.52.

Resta, R., Biesecker, B. B., Bennett, R. L., Blum, S., Hahn, S. E., Strecker, M. N., et al. (2006). A new definition of Genetic Counseling: National Society of Genetic Counselors' Task Force report. *Journal of Genetic Counseling, 15*(2), 77–83. doi:10.1007/s10897-005-9014-3.

Roberts, J. D., Wells, G. A., Le May, M. R., Labinaz, M., Glover, C., Froeschl, M., et al. (2012). Point-of-care genetic testing for personalisation of antiplatelet treatment (RAPID GENE): a prospective, randomised, proof-of-concept trial. *Lancet, 379*(9827), 1705–1711. doi:10.1016/S0140-6736(12)60161-5.

Rogers, H. L., Bhattaram, A., Zineh, I., Gobburu, J., Mathis, M., Laughren, T. P., et al. (2012). CYP2D6 genotype information to guide pimozide treatment in adult and pediatric patients: basis for the U.S. Food and Drug Administration's new dosing recommendations. *Journal of Clinical Psychiatry, 73*(9), 1187–1190. doi:10.4088/JCP.11m07572.

Salemink, S., Dekker, N., Kets, C. M., van der Looij, E., van Zelst-Stams, W. A., & Hoogerbrugge, N. (2013). Focusing on patient needs and preferences may improve genetic counseling for colorectal cancer. *Journal of Genetic Counseling, 22*(1), 118–124. doi:10.1007/s10897-012-9519-5.

Samuel, G. N., Jordens, C. F., & Kerridge, I. (2010). Direct-to-consumer personal genome testing: ethical and regulatory issues that arise from wanting to 'know' your DNA. *Internal Medicine Journal, 40*(3), 220–224. doi:10.1111/j.1445-5994.2010.02190.x.

Shiloh, S., Gerad, L., & Goldman, B. (2006). Patients' information needs and decision-making processes: what can be learned from genetic counselees? *Health Psychology, 25*(2), 211–219. doi:10.1037/0278-6133.25.2.211.

Walko, C. M., & McLeod, H. (2009). Pharmacogenomic progress in individualized dosing of key drugs for cancer patients. *Nature Clinical Practice Oncology, 6*(3), 153–162. doi:10.1038/ncponc1303.

Wasson, K., Cook, E. D., & Helzlsouer, K. (2006). Direct-to-consumer online genetic testing and the four principles: an analysis of the ethical issues. *Ethics and Medicine, 22*(2), 83–91.