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CASE STUDY

Direct-to-Consumer Personal Genomic Testing: A Case Study and Practical Recommendations for "Genomic Counseling"

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Abstract Technological advances and information-seeking consumers have pushed forward the movement of direct-to-consumer (DTC) genetic testing. Just like with other types of testing, there are potential risks, benefits and limitations. A major limitation of DTC testing is the incomplete view it provides regarding lifetime risk for common, complex diseases, since most tests only analyze 1–2 single nucleotide polymorphisms (SNPs) and do not include evaluation of medical or family histories, which is necessary to risk assessment. Further, it is not currently well-established whether personal genomic testing results will lead toward improved health behaviors, adverse psychological effects or potential overuse of the health care system. To display these and other issues, we present an in-depth case study of an individual who ordered DTC genetic testing and subsequently sought genetic counseling. This case presents a unique learning experience for the field of genomic counseling, as the patient did not fit the typical assumptions regarding 'early adopters' of DTC testing. It also allowed the genetics health care providers involved in the case to identify gaps in current genetic counseling practice that need to be filled and approaches to employ for successful delivery of genomic counseling. Based on our experience, we developed practical recommendations for genomic counseling, which include novel approaches to case preparation, use of electronic tools during the counseling session, and focusing on education as the major component of the genomic counseling session, in order to provide patients with the knowledge necessary to independently interpret and understand large amounts of genomic testing information provided to them.

Keywords Genomic counseling · Direct-to-consumer genetic testing · Personal genomics · Family history · Risk assessment

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Introduction

A wave of direct-to-consumer (DTC) genetic testing companies has hit the market over the past several years with varied degrees of success and failure (Borry et al. 2010). DTC testing is marketed directly to consumers and in many cases, does not involve consumers' healthcare providers in the ordering or interpretation of genetic tests, but instead provides consumers the means to order their own genetic tests and then provides results directly to them. DTC companies offer genetic testing for ancestry and traits such as hair loss, and also offer tests for disease susceptibility for a large variety of conditions ranging from diabetes, cancer, mental illness and many others. Most DTC genetic testing companies offer genome-wide scans for panels of single nucleotide polymorphisms, or SNPs. Most of the genetic

variants tested for are weak predictors, accounting for only a small fraction of the overall heritability of a trait or disease, with the relative risk conferred being less than two (McCarthy et al. 2008). Also included in many testing packages are autosomal recessive carrier testing and select pharmacogenomic testing.

According to the Genetics and Public Policy Center, as of August 2011, there were at least 27 companies offering DTC genetic testing for health-related conditions ("DTC Genetic Testing" 2011). The updated list also includes information describing whether genetic counseling is offered as part of the service. Seven companies currently provide counseling by a board-certified genetic counselor included in the cost and three additional companies make counseling available at an additional cost, while the majority of companies (16/27, or 59%) do not offer counseling at this time.

A criticism of DTC genetic testing companies is that their advertisements have tended to overstate the benefits and utility of genetic tests while failing to adequately address the limitations and potential risks (Bowen et al. 2005; Gollust et al. 2002). Experts in the field of genetics and other areas of medicine have raised concerns regarding the clinical validity and utility of this type of testing (Janssens et al. 2011; Ransohoff and Khoury 2010). Multiple questions exist: Does the test add information that is clinically significant? Will the results affect medical recommendations and decision-making? Does the test improve predictive ability over simpler tests or the "gold standard" of family history? (Janssens et al. 2011) It has been shown that as new research discoveries are made regarding additional genetic risk markers, and this information is incorporated into risk prediction models, risk level may change (Mihaescu et al. 2009). There is also variance in risk prediction for the same condition depending on which DTC service a consumer might use (Ng et al. 2009; Swan 2010; Yang et al. 2009). Further research regarding complex gene-gene and gene-environment interactions will also necessitate updating of risk level information. This may produce contradictory risk information over time, which is undesirable to the consumer and their healthcare providers.

The putative "personal utility" of genomic information has also been thoroughly discussed (Foster et al. 2009) and is being measured in ongoing research studies (McBride et al. 2008; Stack et al. 2011). It has been shown that characteristics of 'early adopters' seeking personal genomic testing include reported high levels of confidence in their ability to navigate the health care system and to understand genetics, high levels of access to the Internet, and perceiving one's self as having health habits in need of improvement (McBride et al. 2009). A more recent study assessing motivations and perceptions of these early adopters, specifically, individuals attending an enrollment event for the Coriell Personalized Medicine Collaborative research study, found that 32% had misperceptions about the study or personal genomic testing, most perceived the study to have health-related benefits, and over 90% intended to share their results with physicians, mainly to request medical recommendations (Gollust et al. 2012). In this study, 40% of participants had attended graduate or professional school and 30.6% worked in the medical profession. Therefore, many participants were highly educated and medically savvy.

Proponents of DTC genetic tests have raised the issue that common genetic risk markers for diseases such as myocardial infarction and prostate cancer are independent of conventional risk factors, contending that while risk assessments will continue to evolve, we should not wait until 100% of the genetic risk for common diseases is known nor for decade-long randomized clinical trials before utilizing such genetic risk profile information for patients (Gulcher and Stefansson 2010). One reason for this stance is that personalized genetic risk information for common conditions may motivate positive lifestyle and behavior changes, though this is an area of ongoing research (McBride et al. 2010). One of the most highly-cited studies in this area, the REVEAL study, which focuses on risk information for Alzheimer disease (AD), has shown that study participants with the AD-associated risk allele APOE ε4 were significantly more likely than ε4 negative participants to report AD-specific health behavior changes 1 year after results disclosure (Chao et al. 2008). Similar studies evaluating the impact of genetic risk information related to increased lung cancer susceptibility on smoking cessation have had mixed results with some showing no effect on cessation rates (Lerman et al. 1997; McBride et al. 2002) while a more recent study found a significant increase in cessation rates among those with the highest genetic risk (Ito et al. 2006). It has also been shown that feedback including more risk variants was more likely to lead to smoking cessation compared to feedback including fewer risk variants (Hamajima et al. 2004; Hamajima et al. 2006), meaning that genetic risk information may be more likely to motivate positive health behavior changes when multiple genetic risk variants are provided to individuals and genetic risk is more appreciable.

Alternatively, concerns regarding the provision of DTC genetic risk results include the issue of potential adverse psychological effects. One study found that while magnitude of risk and disease type influenced factors such as anticipated worry and concerns about distress, they had no impact on testing interest and benefits belief (Cameron et al. 2009). The REVEAL study showed no significant differences in short-term psychological risks between groups who received APOE genotyping results compared to those who did not; however the ε4 negative group did have a significantly lower level of test-related distress compared to the ε4 positive group (Green et al. 2009). An additional concern relates to potential overuse of the health care system based on results of DTC genetic testing, and a recently published study addressed this issue as well as psychological and behavioral effects (Bloss et al.

2011). The subjects in this study were a convenience sample recruited from health and technology companies, with most subjects being Caucasian, highly educated, and of high socio-economic status, therefore not representative of the general population. The results are based on a single, short-term (3 month) follow-up assessment. Therefore, while the study found no short-term changes in use of screening tests, psychological health, or diet and exercise behavior, the authors admit a major limitation is that the results don't necessarily reflect how people in general will react to results indicating they may be genetically predisposed to certain diseases.

Another important issue that needs to be addressed is how should healthcare providers respond? Physicians may find more of their patients requesting genetic tests, and, because of the availability of DTC tests, they may also find their patients attending office visits with genetic test results already in hand. However, the primary care workforce feels inadequate to deliver genomic medicine for a variety of reasons (Scheuner et al. 2008) and it has been widely acknowledged that education in the area of genetics and genomics needs to undergo reform (Guttmacher et al. 2007; Nelson and McGuire 2010).

Multiple resources are available to both the healthcare provider and consumer, including healthcare professionals with specialized training in genetics, genomics and counseling who can serve as "genomic consultants" or "genomic counselors". The need and opportunity for genetic counselors in the area of genome-informed preventive medicine has been recognized (O'Daniel 2010), and in 2009, a group of genetic counselors who recognized the need for involvement in this burgeoning field founded a new Special Interest Group focused on Personalized Medicine within the NSGC. As of May 2011, there were 95 members in this group (personal communication with NSGC Executive Office). This group also initiated a new specialty, "Personalized Genomic Medicine", on the "Find a Genetic Counselor" search engine tool located at www.nsgc.org so that healthcare providers and consumers could more easily locate a genetic counselor specializing in this field.

The following case study discusses a genomic counseling session provided by a genetic counselor and medical geneticist to a customer of one of the most well-known DTC genetic testing companies, 23andMe. The cost of their Personal Genome Service®, requiring a 1-year commitment, was offered for $99 USD at that time. This article also provides practical recommendations for genomic counseling for DTC genetic tests to aid healthcare professionals providing such services to patients.

Case Study

The patient provided consent for his case to be published in this journal.

Clinic Background

The genetic counselor and medical geneticist staff a busy adult medical genetics clinic at a University medical center. Typical patients of the authors include those referred for cardiovascular genetics, connective tissue disorders, neurogenetics, and other adult-onset genetic conditions. The patient presented in the current case study was the first patient these genetics healthcare providers had met with in order to provide genetic counseling surrounding personal genomic testing results.

Case Preparation

The genetic counselor and medical geneticist requested that the patient provide them with printed copies of his 23andMe test reports prior to his visit. A self-reported three generation family history was also provided prior to his visit. This was obtained via a five page family history collection form used regularly for all patients in our medical and cancer genetics clinics. After review of the hard copy test reports, it became clear that additional information regarding SNP tested, relative risk, etc. was most likely available within the patient's personal 23andMe web portal. Therefore, we planned to ask the patient to log in to his account during his appointment with us and made sure to have a laptop computer with wireless Internet access available to take into the counseling session.

Contracting

Our team's first question to the patient was "Why were you interested in pursuing this type of testing?" The patient indicated that in early 2011 he signed up for 23andMe testing because he was interested in ancestry testing; subsequent to this he was offered a reduced rate for the extended panel and decided to pursue this as well. After receiving test results, the patient was interested in speaking with a genetic counselor because some of the information was not clear to him. He informed us that the 23andMe website included information about genetic counseling. He subsequently located our Medical Genetics clinic after calling the Ohio State University Medical Center directly. He then self-referred for a genetic counseling appointment to discuss his personal genomic testing results.

Through interviewing the patient regarding his main questions and topics that he would like to cover during the session, we were able to determine early in the session that he seemed to have low genetic literacy as well as low overall health and medical literacy. He did not have familiarity with terms such as "gene" or "single nucleotide polymorphism". He had problems understanding the concept of autosomal dominant inheritance and the fact that he and his two sisters did

not share all of their genes in common. He also had problems with pronunciation of multiple medical conditions and tests. With additional interviewing, we also determined that the patient's main concern was his risk for cancer.

Medical History

The patient was a 55 year old, overall healthy male. His past medical history included chest pain when he was approximately 51 years of age. He indicated that his chest pain was evaluated with some type of "heart scan" that was negative and the physicians at that time felt his chest pain was heartburn related. He took Omeprazole for 1 year, which helped his symptoms. He indicated that he had high fasting triglycerides in the past that were lowered with dietary changes. He thought his lipid panel had last been checked approximately 6 years ago. His past surgical history included a hernia surgery. He was not taking any prescription medications, vitamins or supplements. He was following the U.S. Preventive Services Task Force (USPTF) guidelines for clinical preventive health care services including a colonoscopy at 51 years of age and prostate cancer screening more recently, both of which were normal. Significant to him, he had not had an upper endoscopy to date.

Family History

We obtained a four generation pedigree (Fig. 1). The patient had a significant maternal family history of heart disease with his mother dying from a myocardial infarction (MI) at 53 years of age. He indicated that she was a heavy smoker (1 pack per day for most of her adult life) and that she had hypertension (HTN). His maternal uncle died at age 56 due to heart disease; he indicated that he used tobacco and alcohol. His maternal grandmother died at age 69 due to cardiovascular disease and renal disease, according to her death certificate. His maternal grandfather died at 54 years of age from heart disease; he was unsure whether he used tobacco. His father died at age 66; he brought a letter to his genetics consultation from an oncologist where his father received care stating that his father's primary diagnosis was adenocarcinoma of the gastroesophageal junction. His 23andMe test report indicated European ancestry and he self reported the same ethnic background.

Social History

The patient lives with his wife and son. His highest level of education was a Bachelor's degree. He previously worked

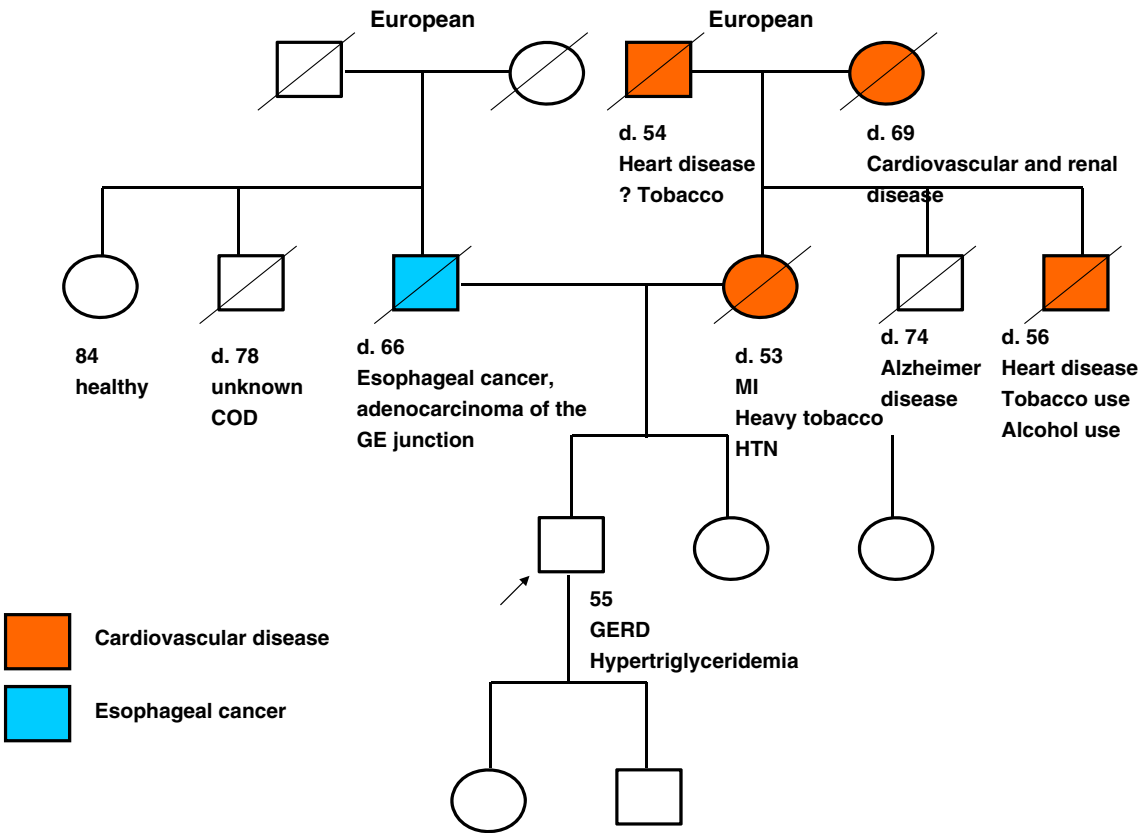

Fig. 1 Pedigree of patient seeking genetic counseling for his 23andMe personal genomic testing results. Abbreviations used: d.: died, GERD: gastroesophageal reflux disease, MI: myocardial infarction, HTN: hypertension, GE: gastroesophageal, COD: cause of death

for the United States Military and was currently retired. He had a positive history of tobacco use (10 pack years smoking 1 pack per day). There was no current use of tobacco, rare alcohol use, no history of drug use, and no regular exercise.

Review of Systems

A ten system review of systems was done with no problems noted.

Physical Examination

The patient's weight was 183 lb and his height was 72.25 in. which calculated a Body Mass Index of 24.3 kg/m^2. His physical examination was entirely within normal limits.

Risk Assessment

During our risk assessment, we focused on the patient's main concerns from his 23andMe report and then we focused on our main concerns based on his medical history, family history, and 23andMe report. These are summarized here and also listed in Table 1.

1. Esophageal cancer:
    a. Family history: According to the oncologist's letter the patient brought with him to our genetic counseling session, his father died of esophageal adenocarcinoma. He indicated that his father also worked at a wallpaper manufacturer, and asbestos exposure was likely. It is possible that asbestos exposure contributes to risk for esophageal adenocarcinoma, however the data are not conclusive(Soskolne and Sieswerda 2010). Large population-based case–control studies have shown that the occurrence of esophageal cancer among first-degree relatives did not increase the risk for any form of esophageal cancer (Dhillon et al. 2001; Lagergren et al. 2000). Therefore, the patient is at average familial risk for esophageal cancer.
    b. 23andMe test report: Based on his genetic variant result, the patient's test report indicated "Increased Risk" for esophageal squamous cell carcinoma of

Table 1 Genetic variant test results from personal genomic testing compared to family history risk assessment

Condition	Genetic variant tested	23andMe genetic variant results	Family history risk assessment
Esophageal cancer	Gene or region: *PLCE1*	Patient's test report indicated "Increased Risk" for esophageal squamous cell carcinoma of 0.6% compared to the average person's risk of 0.4% based on his genetic variant result.	Patient's father died of esophageal adenocarcinoma. Large population-based case–control studies have shown that the occurrence of esopha geal cancer among first-degree relatives did not increase the risk for any form of esophageal cancer; therefore, the patient is at AVERAGE familial risk for esophageal cancer.
	SNP: rs2274223	Patient tested positive for a risk allele in the *PLCE1* gene; this risk allele has been shown to slightly increase the risk in Han Chinese individuals for esophageal squamous cell carcinoma and stomach cancer (gastric cardia adenocarcinoma).	
Heart disease	Gene or region: 9p21 region SNP: rs10757278	Patient's test report indicated "Typical Risk" for heart attack of 20.9% compared to the average person's risk of 21.2% based on his genetic variant result.	Patient has significant maternal family history of coronary artery disease, with multiple family members affected at young ages; therefore, the patient is at HIGH familial risk for coronary artery disease.
Colorectal cancer	Gene or region: 8q24 region SNP: rs6983267	Patient's test report indicated an "Increased Risk" for colorectal cancer of 8% compared to the average person's risk of 5.6% based on his genetic variant result.	Patient does not have a family history of colorectal cancer; therefore he is at AVERAGE familial risk forcolorectal cancer.
Hemochromatosis	Gene or region: *HFE* SNPs: rs1800562 (amino acid substitution C282Y) and rs1799945 (amino acid substitution H63D)	Patient's test report indicated "Variant Present" as patient is a carrier of the H63D amino acid substitution.	Patient does not have a family history of this recessive condition; therefore he is at AVERAGE familial risk for hemochromatosis.
Warfarin sensitivity	Gene or region: *CYP2C9* and *VKORC1* *CYP2C9* SNPs: rs1799853 and rs1057910 *VKORC1* SNP: rs9923231	Patient's test report indicated "Increased Risk" status as he has slight warfarin sensitivity based on his genetic variant results.	Family history risk assessment is not applicable.

70.6% compared to the average person's risk of 0.4%. This is based on the patient testing positive for a risk allele in a gene called *PLCE1*, which has been shown to slightly increases the risk in Han Chinese individuals for esophageal squamous cell carcinoma and stomach cancer (gastric cardia adenocarcinoma) (Abnet et al. 2010; Wang et al. 2010). Because this genetic variant has only been studied in Chinese individuals to date, we explained that we aren't able to determine whether this genetic variant will also cause an increased risk in individuals of European ancestry. Of note, on the web page where a 23andMe consumer is able to review their genetic data, there is a dropdown on the page where they can choose their proper ethnicity. However, when we reviewed the *PLCE1* result with this patient, he was only able to choose "Asian" ethnicity, and therefore, was not able to apply the result to him. We also explained to the patient that esophageal squamous cell carcinoma is a different pathological type of esophageal cancer from what his father reportedly had.

c. Personal medical history: Our patient had long term gastroesophageal reflux, which is a risk factor for the development of esophageal carcinoma because of prolonged esophageal exposure to gastric acid.

2. Heart disease:

a. Family history: The patient had a significant maternal family history of coronary artery disease, with multiple family members affected at young ages. This placed the patient and his family into the high familial risk category for coronary artery disease (Scheuner 2003; Scheuner et al. 2006).

b. 23andMe test report: The patient's 23andMe test report indicated a "Typical Risk" for heart attack of 20.9% compared to the average person's risk of 21.2% based on his genetic variant result. We explained the limitations of this result to the patient, as it only evaluated variation in one genetic region, and heart disease likely has hundreds of genes associated with its risk as well as epigenetic, behavioral, environmental, and family history risk factors.

c. Personal medical history: The patient did not exercise regularly but did have an appropriate body mass index. He reportedly had hypertriglyceridemia, but this was not recently checked and he was not on medical management for this at the time of our visit. He did not appear to have any other co-morbid medical conditions which would predispose to coronary artery disease.

3. Colorectal cancer:

a. Family history: The patient did not have a family history of colorectal cancer; therefore he is at average familial risk for colorectal cancer.

b. 23andMe test report: His 23andMe test report indicated an "Increased Risk" for colorectal cancer of 8% compared to the average person's risk of 5.6% based on his genetic variant result.

c. Personal medical history: He had a normal colonoscopy at age 51.

4. Hereditary Hemochromatosis:

a. Family history: He did not have a family history of this recessive condition and therefore is at average familial risk for hemochromatosis.

b. 23andMe test report: His test report indicated "Variant Present" as he is a carrier of the H63D mutation, one of the two common mutations in the *HFE* gene leading to a risk for hereditary hemochromatosis (HHC). We explained to the patient that individuals only have a risk for the development of this low-penetrant disease if they have two predisposing mutations.

5. Warfarin sensitivity:

a. Family history: Not applicable to the patient's risk assessment for warfarin sensitivity.

b. 23andMe test report: His test report indicated "Increased Risk" status as he has a "slight" warfarin sensitivity, meaning he may require a slightly decreased dose of this medication should he ever be prescribed it.

Recommendations

After our risk assessment discussion, we provided the patient with recommendations. We provided a written summary of our consultation, along with a copy of his pedigree, to him via mail approximately 1 week after his in-person appointment. We also obtained written permission from him during his visit to share the written summary with his family physician. He also gave us permission to share the information from his consultation with his two sisters. The recommendations we provided to the patient and his physician are summarized below.

1. The patient inquired whether we would recommend an upper endoscopy to screen for esophageal cancer. We did not recommend screening endoscopy because we were not able to apply the 23andMe esophageal cancer genetic variant result to him since the risk allele association had only been studied in Chinese individuals and because the type of cancer his father had does not typically run in families and the patient had no other family history of esophageal adenocarcinoma or the precursor disease Barrett's esophagus. However, since he did report a previous history of heartburn causing chest pain, we did recommend that he start taking Omeprazole again.
2. Regarding heart disease risk, our message to the patient was that his genomic testing results provided a very limited evaluation as it only evaluated two SNPs in one

genetic region, and heart disease has hundreds of genes associated with its risk as well as behavioral, environmental, and family history risk factors. Since he had a high familial risk for coronary artery disease, we recommended that he have a fasting lipid panel ordered by his family physician since it had been approximately 5–6 years since his last screening test. We also recommended that he monitor his blood pressure closely. He informed us that his family physician previously recommended that he take a baby aspirin daily. We agreed with this recommendation and suggested that he discuss this option in more detail again with his family physician. We also provided him with brochures for his sisters for a preventive cardiovascular genetics clinic at our institution (the High Risk Family Heart Clinic at Ohio State's Ross Heart Hospital) in case they were concerned about their risk for heart disease and would like to meet with a cardiovascular genetic counselor and cardiologist for prevention.

3. The patient stated that he thought he would require more frequent colonoscopy screening based on his 23andMe test report for colorectal cancer. We advised that he continue with the colonoscopy screening plan recommended by his gastroenterologist and explained that he most likely did not require more frequent screenings.
4. Because the patient had tested positive for one of the two common mutations in the *HFE* gene, we also needed to discuss his children's possible risk for having two *HFE* gene mutations associated with an increased risk for HHC, or iron overload, if his wife is also a carrier. This risk assessment necessitated a discussion regarding autosomal recessive inheritance and the high carrier frequency of HHC in Caucasian individuals. Our patient had never heard of HHC, so the information was completely novel to him. We explained that his wife could have genetic testing to determine if she is also a carrier, and then their children could have genetic testing if she is a carrier. Our discussion also included the concept of reduced penetrance, since the presence of two predisposing mutations for HHC does not guarantee that an individual will develop symptoms of this disease (Watkins et al. 2008). However, we did discuss screening and management of HHC, since individuals at risk should be screened with iron studies to determine whether they are starting to develop iron overload, which is easily treated with phlebotomy (Alexander and Kowdley 2009).
5. Finally, we also discussed the concept of pharmacogenomics with the patient since his genetic variant result showed a slight sensitivity to warfarin. Pharmacogenomics was also a novel concept to the patient, and he was not familiar with the medication warfarin or its indication for use. We recommended that the patient make his physicians aware of his warfarin sensitivity result in case he is ever prescribed this medication. We also explained the possible indications for warfarin to the patient.

Additional Questions and Follow-up

Toward the end of the counseling session, the patient asked whether we could provide long term follow-up to him as he continues to receive new results from 23andMe. He explained that he signed up for continued results release through a monthly subscription fee. For example, he described to us that his most recently released results included a result for elevated risk of kidney stones. We reviewed this result with him on his web portal during the session, which showed he had a relative risk of 1.14 for the development of kidney stones. We also explained that our goal was to help him understand the concepts of relative risk, SNPs, risk and non-risk alleles, heritability, as well as the information the test provides but also its limitations, so that he could better interpret new test results as they are provided. We also offered to answer future questions by telephone and offered follow-up in-person consultation if needed.

In the written summary we sent the patient and his family physician, we also included information on additional genetics educational tools that could assist him as he continues to receive risk reports from 23andMe. We included information from the following reputable websites:

1. The Genetic Science Learning Center: http://learn.genetics.utah.edu/
2. "DNA From the Beginning", funded by the Josiah Macy, Jr. Foundation and developed by the Dolan DNA Learning Center: http://www.dnaftb.org/
3. Additional materials from the Dolan DNA Learning Center: http://www.dnalc.org/
4. Comprehensive list of resources hosted by the University of Kansas Medical Center Genetics Education Center: http://www.kumc.edu/gec/

Since his in-person counseling session, the patient has called our office two times. The first time was to again inquire about screening endoscopy and his risk for esophageal cancer. During the second phone call conversation, the patient informed the genetic counselor that he had been doing more research and reading on the Internet, and wanted to talk with her about the total number of genes humans have. He went on to make the point: "If we have at least 20,000 total genes, and my test only looked at parts of a couple hundred genes, this assessment really isn't complete, is it?"

Practical Recommendations for Genomic Counseling

This was the first "genomic counseling" session this genetic counselor and medical geneticist had provided. We had

preconceived notions about 'early adopters' of personalized medicine (Gollust et al. 2012; McBride et al. 2009) that our patient did not fit, especially with regard to reported high levels of confidence in their ability to navigate the health care system and to understand genetics, as well as being highly educated and medically savvy. As a result of these preconceived notions, we were caught somewhat off guard and underprepared. For example, during the session itself, we were not prepared with educational visual aids to help explain genomics concepts and this patient's personal genomic testing results.

A previous article in this journal provides a detailed summary on genomic medicine (O'Daniel 2010), with information on Web-based resources for genomic variants, the need for genetic counselors in the area of genomic medicine including potential roles for genetic counselors, background information on genomic risk testing and interpretation of results present on DTC genetic testing panels, and initial guidance for "genomic counseling" and genomic medicine service delivery models.

Here, we present practical recommendations for successful genomic counseling sessions in order to assist genetic counselors, medical geneticists, and other healthcare providers who may find themselves providing "genomic counseling" to patients based on their DTC personal genomic testing results.

1. Review genomic testing results prior to the genomic counseling session if at all possible. Our patient's DTC genetic testing included almost 200 tests for disease risk, carrier status, drug response, and traits. Having print-outs of the testing before the consultation allowed us to see that the test results were organized in a user-friendly fashion with categories including Elevated Risk, Decreased Risk, Typical Risk, Carrier Status, and Pharmacogenomics. Our team was able to easily focus in on the 8–10 results that showed an elevated disease risk, positive carrier status or altered sensitivity to medications. Preparing for a discussion surrounding these 8–10 test results was much more manageable than preparing for the entire repertoire of tests a DTC company offers.
2. Use the primary literature and other online tools to evaluate genetic variants and their associations with disease risk. Our patient's main concern was his risk for cancer. This concern was heightened because he tested positive for a risk allele associated with esophageal squamous cell carcinoma and he knew his father died from "esophageal cancer." We suspected that the patient might be concerned about his family history of cancer since we had his pedigree information prior to the in-person session and were able to review the two articles published in *Nature Genetics* in 2010 regarding the association of the *PLCE1* risk allele with esophageal squamous cell carcinoma (Abnet et al. 2010; Wang et al. 2010). We were quickly able to determine that these two studies had been performed in Han Chinese subjects, and therefore were not applicable to our patient. Without this information regarding the specific population in which the risk allele had been studied, we may have counseled the patient completely differently and concluded that he was at increased risk for esophageal cancer. Individuals providing genomic counseling should also refer to web-based resources for genomic variants, including dbSNP (http://www.ncbi.nlm.nih.gov/projects/SNP/) and SNPedia (http://www.snpedia.com), among others cited in the journal article mentioned above (O'Daniel 2010).
3. Use electronic tools during the counseling session. The paper reports the patient was able to print from his web portal and provide to us prior to his in-person session were incomplete and did not include important information from the 23andMe website including the actual SNP tested, the patient's genotype, odds ratio or relative risk provided, or citations. Upon review of the 23andMe website prior to his consultation, we were able to learn some of this information, including the SNP(s) tested and the citations used. However, because we did not have the patient's genotype or specific risk information, our team decided we wanted to have the capability to enter the patient's web portal with him in real time during the consultation, as long as we received his permission. Our patient was happy to allow us to view his web portal, which allowed us to view much more information regarding his results that was imperative for our analysis and risk assessment.
4. Identify and/or develop new types of educational visual aids to facilitate discussion of genomics concepts. Our team was definitely underprepared in this area, as many of the visual aids we had available to us in our clinic did not include terms (i.e. genomic testing, SNP) and concepts (i.e. heritability) that we needed to explain during this session. We anticipated that our patient would have a better understanding of genetics and genomics than he did, one reason being that 23andMe's website includes a section on "Genetics 101", which is a collection of education materials on genes, SNPs, and other genomics topics. During the counseling session, however, it was our collective assessment that this patient's health, genetics, and genomics literacy was low, as he had difficulty with multiple terms and concepts including Mendelian inheritance patterns. For this patient to understand his personal genomic testing results, it was necessary that our education and risk assessment discussions include descriptions of the following terms and concepts in detail for which visual aids would have been very helpful. For many genetics health care providers, some of these concepts may be novel and therefore not currently part of their collection of visual aids.

    a. Genomic testing
    b. Single nucleotide polymorphism

   c. Mendel's Law of Segregation
   d. Inheritance patterns
   e. Common, complex disease
   f. Heritability
   g. Relative risk
   h. Lifetime risk
5. Education should be a major component of genomic counseling sessions, including the provision of additional educational resources for the patient to use after the session. Much of the time spent during a genomic counseling session should be focused on genomics education that will provide the patient with a foundation of knowledge necessary to understand all of the different types of test results provided by personal genomic testing services. For example, education regarding complex concepts such as relative risk and lifetime risk will help patients understand their SNP-based results for common, complex disease risk. However, patients will also need education on Mendelian concepts to understand their carrier testing results for recessive diseases as well as educational information on pharmacogenomic testing. One strategy to employ is to review a handful of SNP-based results for common, complex diseases with the patient during the genomic counseling session. A representative mix of results that shows increased, typical, or decreased risks should be included in order for the patient to understand how to interpret each type of result. This discussion can include the SNP tested, the patient's genotype, what risk their result confers, as well as relative and lifetime risk information. In addition, the genomic counseling session will also need to include review of a subset of carrier and pharmacogenomic testing results. By working through a collection of representative results of each type of testing included on personal genomic testing panels, patients will hopefully obtain the "toolkit" they need for their own independent interpretation of additional and future results of all types.

The provision of additional educational resources, like the examples listed above, for patients to use after the session can also aid in continued learning about genomics in general, as well as how this information relates to their specific personal genomic testing results. By providing these educational resources to our patient, we feel that, based on a follow-up discussion with the patient, we helped him further understand the information provided to him by 23andMe, the limitations of this testing, and the complexity of the human genome and his risk for common, complex diseases.

Conclusions

This case, which reports the experience of providing genomic counseling to a user of an online DTC personal genomic testing service, highlights unique issues for consideration regarding the approach to genomic counseling. Multiple aspects of this case provided novel challenges to the genetics health care providers involved. Firstly, case preparation for genomic counseling requires a much different approach compared to genetic counseling for one specific Mendelian condition where a genetics team may only need to discuss one, or a few, genetic tests or potential differential diagnoses. In this case of genomic counseling, the genetics team included as part of their case preparation a cursory review of over 200 results in order to focus in on those most pertinent to the care of the patient. Having the genomic testing results ahead of time did allow the genetics team to fully prepare for a discussion of those genetic variants that placed the patient at elevated risk, or for which he was a carrier or may have an altered response to certain medications.

In addition, it was imperative for our team to, similar to standard genetic counseling sessions, collect detailed medical and family history information from the patient in order to discuss his personal genomic testing results in the context of his own personal and family health history. In order to allow for the most efficient use of time, we collected detailed family history information from the patient prior to his scheduled appointment to assess his family history for potential Mendelian and/or other actionable conditions. However, in spite of having this information ahead of time, our genomic counseling session still lasted approximately three hours. Therefore, because of the vast, and potentially overwhelming, amount of information provided via DTC personal genomic testing, a recommended strategy is to thoroughly review a smaller number of results with the patient during their genomic counseling session that includes a discussion of applicable terms and concepts such as SNP, the patient's specific genotype and associated relative risk, and lifetime risk for disease. The goal is that this new knowledge gained by the patient can then be used for future, independent review and understanding of additional results.

Unlike most standard genetic counseling sessions, with genomic counseling sessions for personal genomic testing results, patients are walking in to their appointment with results already in hand. As with our patient, it may be difficult to dispel inaccurate interpretations of these results, particularly when they relate to a disease or condition that is present in their family history. It has been discussed that one of the downsides to DTC genetic testing is that users of these tests may ask for screening and other types of tests that they don't necessarily need. This did happen in our case, where the patient's own personal beliefs, fear due to his family history of cancer, and interpretation of his genetic variant results led him to ask both during and after the session for a screening endoscopy that he did not require. Consumers requesting unneeded screenings may be a common theme that is observed in other genomic

counseling sessions, too, and genetics and other health care providers must be prepared to continue to provide evidence-based medical recommendations based on accurate interpretations of medical and family histories and genetic test results.

The volume of patients requesting genomic counseling for personal genomic testing results has been low at our institution thus far. To date, the patient presented in this case study continues to be the only individual to seek our services in order to help him interpret his genomic testing results. However, as prices for personal genomic testing, including whole-genome sequencing, continue to drop, genetics and other health care providers may indeed see their volume of these types of patients increase and the definition of 'early adopters' of personal genomic testing services may change over time. Indeed, while our patient did not fit some of the characteristics of reported 'early adopters', previously discussed above, he did fit others, such as having Internet access, having misperceptions about personal genomic testing, and sharing results with physicians in order to request medical recommendations. If more individuals request genomic counseling appointments, this model of genomic counseling may not remain practical or sustainable. Instead, novel and scalable models and approaches may be necessary that incorporate methods such as group counseling on genomics concepts and/or the use of web-based modules for genomics education. Further, automated, patient-directed collection of as much personal and family health information as possible prior to the genomic counseling session would remain applicable and a priority for personalized application of identified risk factors and preventive recommendations.

In conclusion, genetic testing, when paired with appropriate informed consent, risk assessment, education and support, can be a very powerful tool in providing essential information regarding health risks to patients, their family members and the physicians who care for them. The role of the genomic counselor is to keep abreast of new developments in the fields of personalized genomic testing, pharmacogenomics, complex risk assessment methods, and the science of epigenetics and complex gene-gene and gene-environment interactions. The skills of genomic counselors should be utilized and applied in the translation of clinically applicable genome-informed medicine for personalized prevention plans for consumers and their families. Certain components of the genomic counseling process may be able to be automated and therefore made scalable, such as the development of online educational modules and family history risk assessment tools. Still, the need for integration of all this information, including patients' medical and family histories, behaviors, exposures, and personal genomic testing results, in order to provide an accurate and complete risk assessment upon which preventive medical recommendations can be made, offers a continued role for genomic counseling experts in the care of patients who seek DTC genomic testing. Through genomic counseling, we hope the patient presented in this case study was able to learn, and that others will learn, what information personal genomic testing results can provide, what these results may exclude, and the additional imperative information provided by a complete risk assessment.

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