
Genetic Services Policy Project Final Report

Chapter 6: Personal Genomics Services and Direct Access Genetic Tests

“The potential to discover what contributes to red hair, freckles, pudginess, or a love of chocolate—let alone quantifying one’s genetic risk for cancer, asthma or diabetes—is both exhilarating and terrifying. It comes not only with great promise for improving health through personalized medicine and understanding our individuality but also with risks for discrimination and loss of privacy” (Pennisi, 2007).

Context

Since 2004, the market space for retail genetics has rapidly expanded and changed. Consumer, regulatory and policy interests are increasing as powerful computational technology becomes available, private and public capital flows, and the concept of personalized medicine takes hold. All of this is happening in spite of the unimpressive clinical playbook genomic research has produced so far. This review describes the environment in which personal genomics markets evolved, the types of health-related genetic tests currently available directly to consumers, and examples of how companies market such tests. We then consider issues of regulation, clinical utility, social impacts, professional organization recommendations, and public opinion, as well as policy implications related to these issues.

To a degree, personal genomics markets grew out of rising consumer activism in health care, sometimes known as consumer-directed health care. This movement aims to increase the consumer’s commitment to healthy living and monetary investment into the health care system, the latter through steadily expanding cost-sharing by employers and payers. The long-term goal is that educated, motivated consumers investing their own money will be more parsimonious in the use of scarce health care resources.

The rise of consumer markets in genomics, however, primarily stems from increasing consumer interest in genetic information, expressed in equal measures of fear, apprehension, and fascination. The press reports discoveries of genetic health and disease associations almost daily for everything from rare to common genetic disorders (e.g., restless leg syndrome to heart disease). Entrepreneurialism is also thriving, with large companies like Microsoft, Yahoo, Google, WebMD and Revolution Health launching portal and search capabilities, and start-ups like 23andMe, Navigenics, and deCODEme promoting themselves as personal genomics companies.

The blogosphere is rife with commentary and many health care newsletters have begun to track the personal genomics market. At the same time, the rapid emergence of this field is causing concern in clinical, regulatory, and oversight circles, which are already troubled by the proliferation of consumer-oriented websites with arguably over-reaching claims (Hunter et al., 2008).

Personal Genomics Markets

Both researchers and personal genomics companies draw from the same pool of genetic data, yet they use and characterize these data differently. Researchers use aggregated genomic data from gene-wide association studies to identify single nucleotide polymorphisms (SNPs) associated with human variation in health and disease status. For example, SNPs may determine what a specific patient's response and/or susceptibility to a drug or disease might be. Personal genomics companies use these data when they provide customers with personalized SNP information from a portion of their own genome (about 1 percent, accounting for 95 percent or more of the genetic variation among us). Companies like 23andMe promote a service allowing customers to "see" their own genome, use interpretative information to infer their health status, susceptibilities to disease, and/or capabilities, and store their data securely with the company. Then customers can receive alerts as new tests become available to check their susceptibility and/or capability (23andMe website, 2008; DeCODE Genetics website, 2008). These companies specifically disclaim that they provide a health care or clinical service, advising their customers to talk to a physician before making any health-related decisions. At least four companies advertise SNP genome profiles, while a fifth company now offers full genome sequencing to a select few customers willing to pay \$350,000 for the service (Knome website, 2008).

The personal genomics market leaders deny that they are selling recreation or curiosity to the affluent and worried well. They argue that individuals informed of their personalized data will be motivated to minimize controllable risk factors, hence preventing or at least slowing the onset or progression of chronic disease. This premise sounds promising, but there is little evidence to support it to date. Researchers have not yet had enough experience with highly personalized risk information to know the likely answer (Multiplex Initiative, 2007).

Direct Access Genetics

Positioned between conventional clinical genetic testing through labs and physicians and the personal genomics frontier are companies offering genetic tests marketed directly to consumers. To avoid confusion about the phrase "direct-to-consumer," often broadly used in reference to advertising for many health services and products, we instead will call these "direct access" genetic tests. Not all such tests have a medical purpose; websites for paternity and ancestry testing abound, and one can now send out for "infidelity testing" on suspicious clothing or personal items (The Genetic Testing Laboratories, Inc. website, 2008). An Internet search reveals a number of companies advertising direct access genetic tests for the purpose of providing health-related information (Genetics and Public Policy Center, 2008). The nature, complexity, and legitimacy of such tests vary. Consumers will find a bevy of tests from companies claiming to provide a beneficial, personalized product or intervention based on test results for nutrition, fitness, skin care, hair loss, smoking cessation, weight loss, and so on; so far these claims remain unproven. Some companies offer accepted tests or screens for genetic disorders, such as for BRCA1&2, cystic fibrosis, and hemochromatosis, which most patients continue to obtain via their physician or genetic counselor. These tests provide diagnostic or risk information that a qualified health care provider can interpret for patients, along with data to support the explanation and options for next steps in treatment, prevention, or other decision-

making. Newer tests for complex disease risk or other processes like drug response are also becoming available. While the latter tests are based on scientific data in most cases, the extent of the data varies, and the tests' clinical benefit remains unclear. These diseases typically involve multiple genetic, environmental, and lifestyle factors, as well as interactions between these factors. Available genetic tests may cover only a single gene or subset of genes involved in a given disease, while other genetic contributors remain undiscovered. Examples of this type of test include type II diabetes panels, pharmacogenomics tests, a soon-to-be-offered prostate cancer risk panel, and bipolar and mood disorder risk.

Business and Marketplace Issues

In new markets there are fundamental factors related to the success and prosperity of any type of business. There are a few related to the business of health care and the science of genomics that are relatively unique.

Genetic testing companies like DNA Direct serve as a virtual delivery model for a set of genetic tests that have some evidence of clinical utility. DNA Direct provides consultation with genetic counselors and focuses on developing proprietary tools to interpret genetic risk data for consumers. Though started as a pure direct access offering, DNA Direct and other companies utilize a variety of payment models, including referrals from physicians and genetic counselors, as well as third party reimbursement when available. This distinguishes these existing businesses from personal genomics companies, such as Navigenics, 23andMe, and deCODEme, though as the latter evolve, they may compete in providing testing services.

Details are not yet available to accurately describe the business model for the personal genomics market; however, it appears to be premised on securing enough subscribing customers to develop or outsource a genetic testing service, and by aggregating data, serve as a data warehouse to which access would be sold. Beyond this, these companies intend to use their customer base, presumably on an opt-in model, to create social networking relationships, with the sites supported by subscriptions, advertising, or both. These businesses have only recently been launched and they appear to be well financed by venture capital groups and, in the case of 23andMe, by Google. But to date, there is little marketplace data to support these business models (Welch and Burke, 2008).

These business models also face several criticisms as voiced by health care providers, regulatory agencies, and consumers. In the health care community, particularly researchers and providers, many express skepticism. Public oversight and regulatory agencies are also alerted and have raised concerns regarding the direct-to-consumer marketing. Many health care providers simply discount the ability of patients and consumers either to understand their health care needs or to act responsibly when they do, and a distinct business risk for these companies arises because the dim views of too many health care providers can suppress the market.

Another area of concern is the complex nature of the underlying science and technology. When selling a financial service, the complexity lies in the instruments and tools, based on tested marketplace and economic fundamentals, with the rewards going to those who execute

effectively on those fundamentals. Conversely, in health care, and especially in genomics, the complexity lies in the underlying fundamentals of the science, a fast and moving target as genomics health care further evolves. This dynamic creates at least two business risks: betting on the science to confirm the first impressions upon which the businesses depend, and understanding that good health is ultimately far more valued as a public good than financial rewards, and therefore, more protected.

Finally, there is the issue of pushback from payers and providers about driving inappropriate and unnecessary demand. Usually a solid sign of business success is the ability to prime markets and produce demand. In health care, however, driving demand is often viewed as problematic. If significant numbers of customers use personal genomics companies and start showing up with their “genome chip” or print-outs in physician offices, the cost-containing forces within health insurance may align against such companies, and pressure for regulatory oversight may increase.

Marketing approaches and services

The support services offered by personal genomics and direct access genetic testing companies vary greatly, as do the ways in which they portray the available tests. Below are some of the ways in which companies provide information or services, followed by specific examples.

Information formatting: Websites may provide “background info,” frequently asked questions (FAQs), tutorials, diagrams, videos, consent forms, disclaimers, reports that accompany results, phone consultations, and references to studies, scientific literature, news articles, or other websites. Some companies provide easy-to-follow, detailed information about the testing process, risks, and benefits, while others offer incomplete, misleading, vague, or hard-to-find information on their websites.

Information topics: Websites may provide basic information about genetic testing in general, why the advertised test might be helpful, potential results and meaning of results for each test offered, background information about the disorders for which they test, information about research related to the genes they test or products they offer, potential risk of genetic discrimination, implications for families, whether the customer can bill insurance for the test, and where to find additional resources.

Ordering tests: Customers may order tests online, by mail, by phone, through a participating provider (e.g., physician, dentist) or through another outlet (e.g., medical spa, pharmacy). Some require consent forms and/or pre-test counseling before purchasing a given test.

Support services: Support services may include a phone consultation with a physician, genetic counselor, nurse, or clinical geneticist; referral to a physician; online support group; in-person consult with a physician at a medical spa or with a “certified DNA fitness trainer”; and/or assistance in billing insurance (one company).

Current Examples: As stated above, no two companies take exactly the same approach in advertising their direct-to-consumer DNA tests. Some do share similar characteristics in their approach, as described below.

At least five companies have genetic counselors available in-house or through a partner company for pre-test and/or post-test counseling by phone. The tests these companies offer include more established medical genetics tests, newer complex disease tests, and genome scans, all of which consumers may purchase directly online. None of the five offer an intervention product based on test results.

DNA Direct offers a variety of tests, including single-gene disorders like cystic fibrosis and hemochromatosis, as well as newer tests like the deCODE Type II diabetes panel and drug response testing (DNA Direct website, 2008). For each test, the user-friendly website offers thorough background information about the disease and addresses such questions as how the testing works, what information it provides (including mutations for which it tests), who is an appropriate candidate for the test, pros and cons of testing, whether insurance covers the cost, and other test or condition-specific issues. The cost to order a test includes pre- and post-test counseling, or consumers can purchase counseling separately before deciding to pursue a test. DNA Direct requires pre-test counseling before ordering certain tests—breast and ovarian cancer risk, infertility, and recurrent pregnancy loss—but not for others. Consumers may also purchase post-test counseling for results not obtained through DNA Direct, such as genome scans from 23andMe and deCODE, or seek counseling to get a second opinion about whether genetic testing is appropriate for them. The website shows names, degrees, biographies, and photographs for the company’s genetic counselors and medical director. To obtain results, users log into a secure website to view a personalized report about the results and what they mean, along with information about the disease, next steps, family issues, and where to go for additional resources. Here they may also access a letter to share with their physician that explains results, genetic disease factors, limitations of genetic testing, diagnosis, patient care, treatment, population and family risks, and lists literature references.

Navigenics advertises a genome scan for SNPs related to 18 diseases or conditions listed on its website (Navigenics website, 2008). For \$2,500, consumers can purchase “Health Compass,” which includes the scan, a personalized report, genetic counseling to review results, guidance about talking to a physician about results, and a year-long subscription for online report access and updates about new genetic research and other medical studies. Consumers may renew their subscriptions for \$250 per year. The website provides information about the testing and follow-up process both in print and as a video. The scan looks for markers associated with the 18 conditions, selected on the basis of three criteria: prevalence (affects at least one per one thousand in the U.S.), ability to take preventive action (e.g., lifestyle changes, medications), and a disease-marker association study published in a peer-reviewed journal. Consumers have the option not to receive results for certain conditions if they so desire. Navigenics creates a personalized, online report that only the consumer may access and emails the consumer when the report is ready. Tools built into the report allow the viewer to compare results with the general population for each condition. The company designates a genetic counselor to review results with the consumer, who may contact the counselor as many times as needed during the membership period. The company also encourages sharing results with a physician.

A few companies require that consumers order the test through a provider or affiliated partner, although they do not provide genetic counseling.

Suracell offers a DNA test reputed to relate to five cell aging processes: methylation, inflammation, glycation, oxidation, and DNA repair (Suracell website, 2008). To purchase the test, consumers complete an online consent form and use the website to locate a local affiliated medical spa, doctor's office, or wellness center where they obtain the DNA kit. A few weeks after submitting a DNA sample, the customer receives a results report with color-coded graphs indicating low, medium, or high "gene efficiency" in each of the five areas. Neither the report nor the website specify which genes the test includes. Based on the test results, the report then outlines the numbers and types of Suracell nutraceutical pills, available for purchase online, to take each day. For questions about results, Suracell recommends contacting a Suracell partner physician, or a genetic counselor; the consent form has a link to the National Society of Genetic Counselors website.

Psynomics markets two tests, one for mutations in the GRK3 gene and one for a serotonin transporter gene (Psynomics website, 2008). Studies (described, but not cited, under the "physician" tab) have associated the former with bipolar disorder and the latter with response to serotonin-based drugs. The company intends these tests for patients who already show symptoms, and therefore require physician involvement. On the consent form, customers vouch that they have been diagnosed with a psychiatric disorder and have discussed the test with their physician. After processing a customer's mail-in saliva collection kit, Psynomics sends results to the customer's physician rather than to the customer directly. In addition to the allele results, the 5-page results report includes information about DNA testing in general, the genes tested, limitations of testing, results interpretation, and what results mean for the patient's family. The consent form also notes that these particular gene tests have only been validated in populations of Caucasian, European ancestry.

Several companies provide information about the test results and may encourage consumers to consult a physician or genetic counselor, but do not provide interpretation beyond the information available on their website or in the results report.

Consumer Genetics offers two test panels related to caffeine response and asthma medication response (Consumer Genetics website, 2008). The website tells consumers that the former can affect their fertility and risk of heart attack, and that people with "a certain gene" could reduce their risk of heart attack 22 percent by drinking 2 to 3 cups of coffee per day, but stops short of actually recommending any action. For the latter test, the website quotes studies (references provided) about how patients with certain genotypes do not respond as well to particular ingredients commonly used in asthma medications. Although one could conclude that it may be beneficial to choose a medication without those ingredients, the company again stops short of recommending a specific action. The website states that results for either test, provided in a one-page, technical-sounding report, "will allow you to make a more informed decision about your health." Similar to other companies, the disclaimer states that Consumer Genetics does not intend its tests to be used for diagnosis or treatment, only for information, and that clients should consult their own physician or health care provider about the results.

CyGene suggests that taking its genetic tests will “help you take more control of your healthcare” (CyGene website, 2008). The website offers tests for glaucoma and macular degeneration, metabolic health assessment, osteoporosis, thrombosis, and athletic performance, using a mail-in cheek swab kit. Clients can log onto the website with a password to obtain a personalized report that includes results, interpretation, discussion of other risk factors, lifestyle/behavior recommendations, and more information about the disease(s) for which they obtained genetic testing. The report also recommends that clients discuss results with their physician.

As described for Suracell above, many companies sell a product or intervention tailored to consumers, based on results of genetic tests that they market online. Several companies focus on diet, either for general health or for weight-loss; other areas include skin care and smoking cessation.

Dermagenetics, a Genelink, Inc. company, advertises customized skin care products based on the results of its DNA test for “key skin aging genes” that are not specified on its website (Dermagenetics website, 2008; Genelink website, 2008). The site discusses results of a clinical trial that, according to the company, proves the effectiveness of its product, although the study has not been published in a peer-reviewed journal. Customers place an order for the personalized product online or through a participating spa, after which the company sends an at-home DNA cheek swab kit. The lab processes the kit and uses results to determine which extra ingredients to add to its basic skin crème formula, then sends the finished product to the consumer. Dermagenetics does not provide any results or interpretation of the DNA test itself.

g-Nostics, a UK-based company, offers a DNA test for genes it says affect nicotine breakdown (CYP2A6) and brain reaction to nicotine (DRD2) (g-Nostics website, 2008). In the FAQs, the website cites 14 journal articles related to the genetics of nicotine addiction. After ordering the test, available online or in UK pharmacies, g-Nostics mails clients a finger-prick/blood spot DNA kit and asks them to complete an online questionnaire. The company uses the DNA test and questionnaire results to create personalized quit programs. While waiting for results, clients begin a motivational course in preparation for the personalized program they start a few weeks later. The course also includes online peer support.

A few companies provide surprisingly little information about the genetic tests they sell online directly to consumers. A person could easily order a test from one of these companies without any understanding of what the results would mean.

Health Tests Direct offers over 400 types of blood tests, including a few DNA tests: cystic fibrosis carrier screen, Factor V Leiden, and MTHFR (Methylenetetrahydrofolate reductase) (Health Tests Direct website 1, 2008). The website has an alphabetical list of tests and prices, but does not provide any information about indications for obtaining a test. The company touts its service as a way to “save 40-70%” of the usual cost for blood tests by eliminating a doctor visit and insurance and billing costs (Health Tests Direct website 2, 2008). Clients pay up front, and then have blood drawn at a participating, state-certified clinic that they can find through a zip code-based search on the company’s website. It refers clients to an independent, peer-

reviewed website (not affiliated with the company) for information to interpret test results, and describes how to navigate the site to find information about the meaning of test results. Customers may purchase tests online or by phone.

Graceful Earth sells an ApoE test for Alzheimer's Disease (AD) risk (Graceful Earth website 1, 2008). A small-print, easy-to-miss link on the online order page takes the customer to a page of FAQs, which provides some information about the ApoE gene and how the company's lab processes DNA from the mail-in saliva kit. This page focuses heavily on AD risk, briefly mentioning but not explaining the connection to cardiac health. The page also contains misleading information about the meaning of results, labeling an E4/E4 genotype as "severe risk" for Alzheimer's Disease and atherosclerosis. Studies suggest that the E4/E4 genotype increases the risk of Alzheimer's Disease; however, to categorize this increase as severe may be viewed as an overstatement (National Institutes of Health, 2008). In addition, the website states that the test is an important prevention tool, because "in cases where the disease is already in progress, you can stop the disease in its early stages" (Graceful Earth website 2, 2008). In fact, nearly all peer-reviewed studies indicate that AD cannot be prevented or stopped from progressing, even with medication. The website states that several publications show that lifestyle changes reduce the risk of developing AD, but does not provide any references. It does not give an example of a results report or describe how the company makes test results available.

Clinical Issues

To health care providers, information that does not lead to known and effective treatments and good outcomes of care lacks clinical utility, and could also create problems through a mix of misleading marketing and uninformed consumers. Not all genetic disease factors have been identified. Some providers worry that if consumers' results do not show an elevated risk for a given condition at known loci, they might incorrectly assume they have no genetic risk, and hence neglect healthy behaviors. Similarly, providers are also concerned about false negative lab results, which are especially worrisome if a consumer's genetic profile inaccurately shows low risks for life-threatening and compromising conditions. This concern was recently heightened when a study of the reliability of lab results showed wide variation on reported testing results (Matthews, 2008).

Although some direct access genetic testing companies advise customers to consult a physician about their results, physicians may lack sufficient knowledge about genetics to appropriately interpret test results. In focus groups conducted in Washington State in 2002, primary care physicians reported feeling challenged in maintaining knowledge of technical and scientific advances in genetics (Gibson et al., 2003). Participants noted that "Patients are getting information and asking questions that I can't answer. It's hard to keep up with them," and "You're always concerned that there's a test you haven't heard about." As we suggest in our Chapter 8 recommendations, public programs and regulation to increase capacity for training genetic services specialties as well as increase genetics content in all medical training would help address this challenge.

Lastly, as the utility of genetic testing increases, especially with the rapid pace of diagnostic development underway, health care providers may sense competition and intensify calls for more stringent regulation. Physicians, among all health care professionals, can effectively incite regulatory action.

Ethical, Legal, and Social Issues

A range of concerns arise for the bioethics community, from paternalistic (harms outweigh benefits) to dismissive (can't hurt, or buyer beware). One frequently expressed concern is that consumers at increased risk for a serious disease will either become fatalistic because they fail to recognize the probabilistic nature of genetic data (except for a few highly penetrant conditions such as Huntington Disease), or, conversely, may neglect their health if their genomic profile seems benign.

For those who worry that only the well-off will have access to genetic services, direct access tests could offer a lower-cost alternative to traditional services. Rather than having to pay for physician visits as well as a test, consumers may order a test directly online. On the other hand, these tests still often cost a few hundred dollars, a price that remains out of reach for many. Though some companies provide a phone-order option, consumers usually need Internet access and familiarity navigating websites to read the testing information. Bypassing a physician or genetic counselor visit may leave consumers confused about the meaning of their test results, unless they choose a company that provides counseling services; however, additional services add to the cost of the test. Direct access testing might improve access for some, but it remains unclear whether benefits will outweigh harms.

Legal issues include discrimination by employers and insurers on the basis of definable risk, although this concern may diminish given the passage of the Genetic Information Nondiscrimination Act (GINA) in April 2008. To date, there is very little settled law with respect to the rightful uses of genetic information because the issues had raised only marginal concerns until recently.

Genetic discrimination can be shown by communities and social systems, not just by employers and insurance companies, though its forms are different. People with presumed genetic defects and disorders have faced stigmatization. Genetic information can affect family relationships as well as personal, reproductive, and end-of-life decisions. Even with GINA in place, many consumers will remain concerned about protecting the privacy of their genetic information. People with disabilities are increasingly apprehensive about biological "stratifications". One concern is that much of the accumulation of genetic information could lead us down a slippery slope if it becomes the fodder for engineering human perfection (Sandel, 2007).

Ultimately genetic data alter our sense about our identities. These technologies are more disruptive culturally and socially than they are disruptive to business and economic models. Hence, personal genomics markets are fundamentally marked by uncertainty because of the disruptive nature of the products being offered. All the evidence points to a niche market: even

if the price point for rendering a customer's genome comes down, as predicted, to \$1,000 in ten years, personal genomics markets are indisputably elite.

On the other hand, there may be social and health benefits worth waiting for. Will providing personalized risk information be a motivational factor strong enough to cause consumers to actually reduce their risk factors through lifestyle practices? We do not have these answers yet because we have not studied the subject enough. But if positive outcomes can be achieved using specific, individualized data, it would be of even greater significance if those outcomes could counter the heavy tolls of the most common chronic diseases—diabetes, obesity, cardiovascular conditions and cancer—affecting the developed world, and increasingly, the developing world.

Regulation

Though there is ongoing debate and discussion at the federal level about strengthening the regulation of genetic testing, there is not yet a clear consensus. At root is the question of which model of oversight applies: should personal genomics markets be regulated as clinical services and hence fall under the scrutiny of the U.S. Food and Drug Administration (FDA) and state licensure requirements? Or, should they be considered a commercial concern, regulated as a consumer information business like financial services where the issues of full and fair disclosure, protections against fraud, and truth-in-advertising apply?

Two government agencies hold some authority to regulate genetic testing in the United States: the Centers for Medicare and Medicaid Services (CMS), per the Clinical Laboratory Improvement Amendments Act of 1988 (CLIA), and the FDA. The FDA reviews medical devices for safety and effectiveness; this includes test kits such as those used to collect cheek swab or saliva DNA samples, but not the in-house tests run on the samples once they reach the lab. To obtain CLIA certification, a lab must meet “standards for quality assurance, record maintenance, proficiency testing, personnel qualifications and responsibilities, and quality control” (Secretary’s Advisory Committee on Genetics, Health, and Society, 2007). With the exception of cytogenetics, however, CLIA does not recognize a specialty area for genetic tests, nor does it address the clinical validity of lab tests (Hudson et al., 2007). Thus, although the lab results may accurately report a patient’s genotype for loci tested, no federal agency has certified that these results are useful to the patient. On their websites, companies advertising direct access genetic tests typically emphasize any CLIA or FDA approvals that apply to their services and products, sometimes with wording that could mislead consumers into thinking that the approvals apply more broadly than they do.

The Federal Trade Commission administers a variety of consumer protection laws. Its Division of Advertising Practices enforces federal truth-in-advertising laws, including such areas as “claims for foods, drugs, dietary supplements, and other products promising health benefits” (Federal Trade Commission website, 2008). In July 2006, the FTC issued a consumer warning about at-home genetic tests, based on a Government Accountability Office (GAO) study of nutrigenomics tests from four companies (Federal Trade Commission, 2006; U.S. Government Accountability Office, 2006). The report found that “the results from all the tests GAO

purchased mislead consumers by making predictions that are medically unproven and so ambiguous that they do not provide meaningful information to consumers.”

New York State requires companies offering personal genomics services and direct access genetic tests to obtain a permit. In April 2008, the New York State Department of Health sent letters to 23 companies to notify them of the state’s permit requirement (Winnick, 2008). Taking matters into their own hands, parents filed a class-action lawsuit against a company for refusing to give promised refunds after providing incorrect baby gender results from their DNA test on mothers’ blood (Lawyers and Settlements website, 2008). It will be interesting to see whether additional lawsuits involving similar or other aspects of direct access tests arise.

In Chapter 8, we recommend several policy steps to help address the issues above. The government could assure that the FTC, FDA, and state attorneys general achieve their mission of preventing harm and fraud, and monitor the accuracy of lab results by regulating “home brew” genetic tests. They could consider licensing retail genetics companies and regulating direct-to-consumer advertising for genetic services to gain more control over the information companies provide to consumers. The government could also facilitate federal interagency discussions about additional policy actions.

Evidence and Utility

A Centers for Disease Control and Prevention (CDC) pilot project, “Evaluation of Genomic Applications in Practice and Prevention” (EGAPP), aims to assess the evidence for and utility of specific genetic tests for clinical practice (National Office of Public Health Genomics website, 2008; EGAPP website 1, 2008). The project’s recommendations may help guide consumers who consider ordering direct access genetic tests. The working group issued its first recommendation in December 2007 regarding cytochrome P450 polymorphism testing to inform treatment for adult depression using selective serotonin reuptake inhibitors (SSRIs) (EGAPP Working Group, 2007). The group did not find enough evidence linking CYP450 testing to clinical outcomes for adults treated with SSRIs to recommend for or against using the test to inform treatment initiation. Taking into consideration other factors suggesting potential benefit or harm of testing, the group felt the potential for harm was greater and discouraged using the test until more clinical data becomes available. The working group has pending recommendations for several other tests they have reviewed: gene expression profiling tests for breast cancer treatment, mismatch repair gene testing for Hereditary Nonpolyposis Colorectal Cancer, and genomic tests for ovarian cancer detection and management (EGAPP website 2, 2008). The group is currently reviewing a multi-gene cardiovascular disease panel for risk assessment and lifestyle management, as well as a gene test to predict colorectal cancer patient response to irinotecan therapy (EGAPP website 3, 2008). Tests under consideration for future workgroup review include several currently being offered direct to consumer, such as ApoE for Alzheimer’s Disease risk assessment, MTHFR for cardiovascular disease prevention and management, and two genes related to type II diabetes risk (EGAPP website 4, 2008).

In a recent article, researchers reviewed evidence of gene-disease associations for the genes tested by seven companies offering predictive genetic profiling and personalized interventions or

products online (Janssens et al, 2008). Of the 56 genes (69 variants), they found meta-analyses for 32 genes; only 38 percent of these meta-analyses showed a statistically significant association. The researchers noted that these associations were mostly modest, and were often tied to a different disease from those for which the companies advertised online as the purpose of testing. For some of the 56 genes, the authors found a single study showing gene-disease association, but no replicated findings to show sufficient evidence of the association. The researchers believe that a meaningful genetic risk profile would require an understanding of gene-gene interactions beyond current knowledge, and found current evidence “insufficient to support useful applications.”

Professional Organization Statements

The American Society of Human Genetics (ASHG), the American College of Medical Genetics (ACMG), and the National Society of Genetic Counselors (NSGC) have all issued statements about direct access genetic testing. ASHG’s statement makes specific recommendations about the type of information companies should provide about their tests, how professional organizations should educate their members about direct access tests, and changes that CMS, the FTC, and the FDA should make to improve regulation (Hudson et al., 2007). The ACMG statement lists minimum requirements it believes should be in place for any genetic testing protocol, including direct access tests. It recommends involvement of a genetics expert to order and interpret the test, a clear statement of scientific evidence for a test, and lab accreditation by CLIA, but also calls on consumers to fully inform themselves about the meaning of test results and the security measures in place to protect the privacy of their results (American College of Medical Genetics, 2008). The NSGC statement expresses concern that consumers may not receive appropriate input from a knowledgeable health care provider when ordering a direct access genetic test, though acknowledges that this model of testing may increase access for some people. The statement lists nine issues that NSGC urges consumers to review prior to ordering a test, including topics of materials and information, informed consent, referrals to genetics professionals, privacy safeguards, and laboratory credentialing (National Society of Genetic Counselors, 2007).

Consumer opinions

In 2003-2004, the Washington State Department of Health conducted a series of 15 community focus groups to discuss genetic discrimination, equity of genetic services, and newborn screening. In the course of discussions, the topic of at-home genetic tests and related issues arose several times (Washington State Department of Health, 2005). On the positive side, participants thought that direct access tests could help improve access to genetic testing, ensure privacy of results, provide useful information, and perhaps be affordable and easy to use. “I like it,” one respondent commented. “There’s privacy. I can do it right there and then.” Another participant drew a comparison to at-home HIV testing, a model for assuring confidentiality. Concerns about at-home kits included licensing, regulation, test accuracy, and availability of help to interpret results. The latter was their primary concern; some participants worried that they might panic without counseling. They also wanted to know if the FDA approved the tests,

asked if results would be accurate, and expressed worry about contamination. One participant said that if she received positive results, she would go see her physician because she would not trust the information.

One scenario that participants specifically considered in some of the forums involved testing for a gene variant that would confer higher risk of developing Alzheimer's Disease (AD). Although the test scenario described to participants was not direct access, the information they requested and their comments about different possible results could easily apply to the ApoE AD risk tests currently offered online. Their discussion highlights the importance of providing accurate information. Participants requested additional information about 1) the accuracy of the test; 2) who is available to interpret the results and what their qualifications are; 3) who has access to test results (e.g. insurance companies); 4) whether insurance companies can deny coverage after a positive result; 5) the cost of the test; and 6) if AD can be cured or effectively treated. Some participants felt that there was no benefit in getting tested if one could not take any action in the case of a positive result. If people who feel that way read the misinformation on one company's website, claiming that "you can stop the disease in its early stages," they might reach a different decision about testing. Others in the focus groups thought that since the genetic test lacked predictive certainty, a positive result would be equivalent to a positive family history. Those who favored taking the test thought it could help someone emotionally and financially prepare for the future. They also felt that a support system to help understand and deal with results would be critical.

Conclusion

The prospect for genomics technologies illustrates why genomics has been called a "terrible gift" (Carlson and Stimeling, 2003). The potential benefits are exciting and profound, but along the way, society will have to deal with social, cultural, and economic uncertainties. Thus far, companies offering direct access genetic tests or personal genomics services have faced little regulatory oversight. Consumer and professional organization opinions about such services agree about the importance of regulation, accurate and complete information, and counseling by qualified providers to explain results. While a few companies provide sufficient information and support to satisfy these needs, the majority fall short in one or more areas. For now, it appears that consumers are on their own to navigate the many genetic testing options available to them on the Internet. The opportunities to improve public health are increasingly evident, but our social uncertainties are deep and linked to a fear of excessive entrepreneurialism in the health care setting. Our economic uncertainties, on the other hand, arise out of the complexity of the underlying science and how to scale demand for first generation genetic service technologies that are limited to those who can afford them for now, but, guided by cogent public policy, could eventually be more accessible and far reaching.

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