Health plan considerations for growing direct-to-consumer genetic testing

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The availability of direct-to-consumer (DTC) genetic testing allows individuals to gain insight into their genetic information without involving their physicians. Initially, providers reporting genetic health risk by DTC genetic testing came under sanction by the U.S. Food and Drug Administration (FDA), but this year the agency approved genetic testing and risk reporting for 10 conditions.[1]

Growth in this area is driven by consumer awareness of the links between genetics and diseases, the evolution of patient empowerment, and precision medicine designed around individual genetic profiles. This white paper looks at the progression of DTC genetic testing and the current demand and growth, discusses industry concerns, and suggests activities for health plans to consider.

Evolving landscape

In 2003, the Human Genome Project was declared complete. This 13-year project sequenced human DNA and mapped the genes in the human genome. One outcome of the research was the development of genetic testing to identify the genetic indicators that increase the risk of developing certain diseases and identifying those who could pass genetic risks to their children.

As commercialization of genetic testing developed, the need for regulatory oversight was also recognized. Genetic tests are considered in vitro diagnostic devices (IVDs). The FDA provides oversight of medical devices, including IVDs. Therefore, genetic testing is subject to FDA oversight if the test is intended to be used for diagnosis of disease or conditions, including a "determination of the state of health, in order to cure, mitigate, treat, or prevent disease or conditions arising from a disease."[2]

The FDA puts IVDs into one of three classification levels. Levels are based on the degree of risk to the patient if inaccurate test results would not be easily detected. Class I, the lowest risk, is typically exempt from FDA premarket review. Class II is at moderate risk with most items subject to FDA premarket review. Class III, the highest risk, is subject to premarket approval. FDA oversight includes review of related advertising, evaluation of validity of the tests, assessment of consumer ease of understanding directions for use, and evaluation of consumer ability to comprehend resulting reports.[3]

As an example of regulatory oversight actions for genetic testing, in November 2013, the FDA issued a warning letter to personal genetics companies about concerns in their marketing of a personal genome service and health risk reports. This action and scrutiny resulted in removal of the personal genome service from the market.[4]

In response to the agency concerns, 23andMe, a leading provider of DTC genetic testing, provided studies to the FDA that demonstrated accuracy in detecting carrier status[5] and ease of consumer use. In February 2015, the company received FDA approval to market DTC genetic tests for Bloom syndrome and 35 other carrier status reports. Most significantly, the FDA classified carrier screening as Class II with the stated intent to exempt these tests from further premarket approval requirements after initial FDA premarket notification. The FDA additionally stated its support of direct consumer access to personal genetic information.[6]

Most recently, on April 6, 2017, 23andMe was approved for at-home testing for genetic risk of developing 10 diseases.[7] This is the first FDA-approved DTC genetic testing. Use of test results as a diagnostic basis for major treatment decisions is excluded from this approval.

1 Fox, M. (April 6, 2017). FDA approves 23andMe's at-home DNA tests for 10 diseases. NBC News. Retrieved July 16, 2017, from http://www.nbcnews.com/health/health-news/fda-approves-23andme-s-home-dna-tests-10-diseases-n743416.

2 Shuren, J., MD et al. (July 22, 2010). Direct-to-Consumer Genetic Testing and the Consequences to the Public. U.S. Food and Drug Administration. Retrieved July 16, 2017, from https://www.fda.gov/newsevents/testimony/ucm219925.htm.

3 Shuren, ibid.

4 Gutierrez, A. (November 22, 2013). Warning letter to 23andMe, Inc. U.S. Food & Drug Administration. Retrieved July 15, 2017, from https://www.fda.gov/ICECI/EnforcementActions/WarningLetters/2013/ucm376296.htm.

5 "Carrier" indicates that a person has a genetic variant that can be passed to children when both parents are carriers of the genetic abnormality.

6 FDA News Release (February 19, 2015). FDA permits marketing of first direct-to-consumer genetic carrier test for Bloom syndrome. Retrieved July 15, 2017, from https://www.fda.gov/newsevents/newsroom/pressannouncements/ucm435003.htm.

7 FDA News Release (April 6, 2017). FDA allows marketing of first direct-to-consumer tests that provide genetic risk information for certain conditions. Retrieved July 16, 2017, from https://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm551185.htm.

Current market and growth

DTC genetic testing is typically accomplished with a saliva test kit purchased online with little or no physician involvement. The test kit is sent to the consumer's home where the sample is self-collected and mailed to the DTC provider for processing. In some cases, the consumer's primary care physician writes the order for the test or a physician working for the testing company orders the test. Kit availability has expanded to retail stores.

A press release on a recent market growth report from Credence Research, Inc.[8] indicates that the DTC market is expected to grow by 25.1% compound annual growth rate from 2016 to 2022. This translates to a projected annual revenue growth from $70.2 million in 2015 to $340 million in 2022.

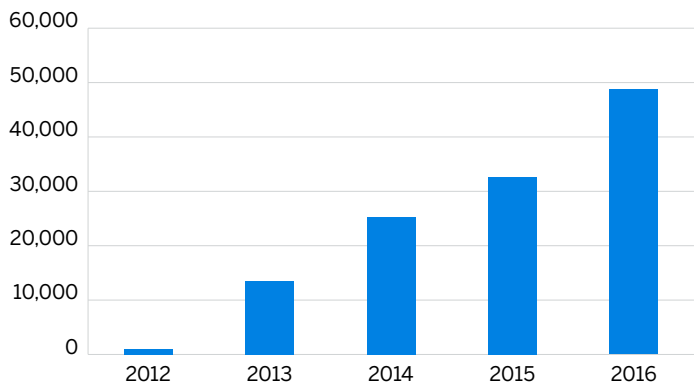
Using 23andMe as an example of the revenue progression in this space:

- The company was founded in 2006 with financial backing by Google.
- In 2015, news reports indicated that more than 850,000 people have used the service at a cost of $99 per test.[9]
- In 2017, the CEO reported that 23andMe has more than 2 million customers.[10]
- Annual revenue is estimated at $15.2 million.[11]

The Genetic Testing Registry (GTR)[12] of the National Institutes for Health (NIH) provides publicly available information about genetic testing voluntarily submitted by test providers. The graphic in Figure 1 illustrates the increasing volume in genetic testing based on this data.

Consumer volume, significant revenue, and the increasing amount of genetic testing indicates strong market interest and likely continued expansion. In response to the evolution of DTC genetic testing, healthcare industry groups have responded with varied perspectives.

FIGURE 1: GENETIC TEST VOLUME



The volume of testing has grown significantly over time.

Note that the NIH does not independently verify information submitted to the GTR, but relies on submitters to provide information that is accurate and not misleading.

Industry concerns

Providers and regulators have expressed concerns about the DTC process, including the absence of healthcare providers from it, concerns for unnecessary testing, patient anxiety, erroneous test results, and misinterpretation of test results by untrained consumers. Insurers have concerns about the possibility of adverse selection. If a person knows they have a positive indicator for a disease, will those people seek insurance in greater numbers than those without any genetic concerns?

One key factor driving concerns is that not all persons with a positive genetic test will develop the indicated disease. Many variables, including environment, personal lifestyle choices, and other genetic factors, have a significant impact on health. Concern exists that genetic test results may lead to unnecessary treatment. In the case of false positive and false negative outcomes, the added concern is that treatment choices may be made in error. In a 2012 study[13] of 179 people from four countries, the average person was found to have about 400 defects in their genes, some associated with disease. However, these people were well. Even if results cause people to seek insurance or care, they may never develop the disease indicated by genetic testing.

Concerns have been raised about the potential for DTC testing to create added costs and consume resources in the healthcare system with little value. For example, positive DTC genetic testing results may lead consumers to follow up with their physicians for treatment based on a test result that may not indicate a genuine health issue.

8 AB Newswire (May 11, 2017). Direct-to-consumer genetic testing market is expected to reach USD 340 mn by 2022, Credence Research. Retrieved July 16, 2017, from http://www.abnewswire.com/pressreleases/directtoconsumer-genetic-testing-market-is-expected-to-reach-usd-340-mn-by-2022-credence-research_115696.html.

9 Pollack, A. (February 19, 2015). F.D.A. reverses course on 23andMe DNA test in move to ease restrictions. New York Times. Retrieved July 16, 2017, from https://www.nytimes.com/2015/02/20/business/fda-eases-access-to-dna-tests-of-rare-disorders.html?mcubz=0&_r=0.

10 PRNewswire (April 6, 2017). 23andMe, Inc. granted first FDA authorization to market direct-to-consumer genetic health risk reports. Retrieved July 16, 2017, from http://www.prnewswire.com/news-releases/23andme-inc-granted-first-fda-authorization-to-market-direct-to-consumer-genetic-health-risk-reports-300436028.html.

11 *San Francisco Business Times*. Top Private Companies: 23andMe, Inc. Retrieved July 16, 2017, from http://companies.bizjournals.com/profile/23andme/100222/?mkt=sanfrancisco.

12 National Center for Biotechnology Information. GTR: Genetic Testing Registry. Retrieved July 16, 2017, from http://www.ncbi.nlm.nih.gov/gtr/.

13 Stein, Rob (December 6, 2012). Perfection is Skin Deep: Everyone Has Flawed Genes. NPR. Retrieved July 27, 2017, from http://www.npr.org/sections/health-shots/2012/12/06/166648187/perfection-is-skin-deep-everyone-has-flawed-genes.

Another example of added costs with unclear value is hereditary thrombophilia testing, which indicates an increased chance of a person developing blood clots. A study from the University of Michigan[14] examined the use of genetic testing for thrombophilia. The study noted that whether or not a person has this genetic indicator, treatment for a blood clot is the same. Persons with this gene would not be given medications in advance of developing a clot as there is no evidence of a preventive effect of the drug. This raises the discussion of the value of doing genetic testing for this condition. The study estimated the annual cost of the tests between $300 million and $670 million. Some limited, specific clinical circumstances were noted to support use of the tests.

A review of 2014 Milliman data for three of the codes used for thrombophilia genetic test billing provides an example of the impact to the U.S. healthcare system. Nearly 80,000 tests were done for this genetic condition that physicians have identified as typically unnecessary in the study from the University of Michigan. Figure 1 above shows the significant growth of genetic testing since 2012. There are 47,240 genetic tests currently available, according to the GTR. Considerable industry impact can be inferred from growth and volume of available tests as compared with the limited sample represented. The per member per month (PMPM) paid for this sample is $.02, with the University of Michigan study noting approximately a half billion dollars in cost for this condition nationally.

FIGURE 2: THROMBOPHILIA GENETIC TEST CLAIMS EXAMPLE

PROCEDURE CODE	UTILIZATION	BILLED	ALLOWED	PAID
81240 - F2 GENE	45,298	$11,134,722	$4,922,362	$3,279,766
81241 - F5 GENE	21,196	$7,072,756	$2,307,883	$1,640,282
81291 - Mthfr GENE	13,141	$5,783,372	$1,164,784	$762,619
GRAND TOTAL	**79,635**	**$23,990,850**	**$8,395,029**	**$5,682,668**

2014 claims data—23.7 million total members

Confidentiality of genetic data is another concern that is being raised in this evolving market. As a direct seller to consumers, typically without physician involvement, these services do not fall under HIPAA privacy requirements. Privacy policies are posted on company websites with the option for consumers to opt in or out of inclusion in research data. 23andMe cites that about 80% of its consumers agree to be included in the databank. Testing results used for research are de-identified and generally aggregated.

The growing genetic databank has created another revenue stream for DTC companies. 23andMe charges a fee for access to data for use in pharmaceutical research. In 2015, the company CEO stated it had 14 partnerships signed, including with major pharmaceutical companies and universities.[15] Agreements may include shared revenue from the sale of drugs developed using the genetic data.

With the growing volume, consumer interest, and industry concerns, what actions might health plans contemplate in response?

Health plan considerations

Health plans have several opportunities to engage the issues raised by DTC genetic testing, including:

- **Provider education**
  Research showed that, of 1,026 patients, 27% took their genetic testing results to their providers, with 18% unsatisfied with the interaction.[16] In a provider survey, 53% of providers stated that they do not see the value of DTC genetic testing and question the validity of the results; 37% of providers stated they would not assist patients in interpreting data.[17]

  Providers also indicated concern about their ability to provide genetic test interpretation. These findings highlight an opportunity to assist providers with tools to aid in interactions with their patients on DTC testing results. Examples include:

  - Educate on plan medical policy related to genetic testing requirements and benefits.
  - Provide patient educational tools to assist providers in guiding their patients in the appropriate use and interpretation of DTC results, and clinical indications for treatment based on results of genetic testing.
  - Provide evidence-based materials on genetic testing as research evolves.

  Data indicates growing use of DTC testing despite healthcare community concerns about validity, potential for misinterpretation of results, and some provider reluctance to address DTC genetic testing. This testing can be of particular interest where there is a history of a disease frequently occurring in a family. Health plan proactive education and support can assist providers with evolving consumer use of DTC testing for prevention and early detection.

14 University of Michigan Institute for Healthcare Policy and Innovation (November 2, 2016). A lot of blood, for no reason? U-M team concludes that common, costly clot test has few benefits. Retrieved July 16, 2017, from **http://ihpi.umich.edu/news/lot-blood-no-reason-u-m-team-concludes-common-costly-clot-test-has-few-benefits/**.

15 Sullivan, M. (January 14, 2015). 23andMe has signed 12 other genetic data partnerships beyond Pfizer and Genentech. VentureBeat. Retrieved July 16, 2017, from **https://venturebeat.com/2015/01/14/23andme-has-signed-12-other-genetic-data-partnerships-beyond-pfizer-and-genentech/**.

16 van der Wouden, C.H. et al. (April 19, 2016). Consumer perceptions of interactions with primary care providers after direct-to-consumer personal genomic testing. Annals of Internal Medicine. Retrieved July 16, 2017, from **http://annals.org/aim/article/2498491/**.

17 Begley, S. (February 12, 2016). Consumers aren't wild about genetic testing – nor are doctors. STAT. Retrieved July 16, 2017, from **https://www.statnews.com/2016/02/12/consumers-arent-wild-genetic-testing-doctors/**.

- **Member education**
  In a January 2016 poll[18] of over 1,000 randomly selected, representative adults, 50% stated they know something about genetic testing, and 57% believe tests are typically accurate and reliable. While few have had genetic testing (6%), 81% of those who had testing believe the results were helpful. The majority of those polled (56%) indicated an interest in genetic testing to know if they have predispositions for cancer or Alzheimer's disease.

  There is consumer interest and a growing market for DTC testing. Health plans have the opportunity to provide meaningful information to help their members understand the benefits and potential risks of DTC genetic testing. Evidence-based information provided in consumable form for laypersons can help plan members make informed decisions. Tools can help members use DTC genetic testing information to engage in meaningful dialogue with their healthcare providers. Resources for genetic counselling may be appropriate for those who find test results confusing or experience anxiety over potential disease development. Helping members understand their personal health information privacy protections and limits can help the member evaluate privacy policies and practices. The health plan can serve as a supportive partner in its members' health self-management.

- **Medical policy**
  Insurance plans are hesitant to provide benefits for tests if there is no treatment. For example, if the genetic indicator for Huntington's disease is present, patients will eventually develop the disease, but there is no cure for it. This raises the question of the usefulness of the testing, which can be incorporated into policy criteria and decisions. Health plan access and/or limits to genetic test results raises industry policy and principle issues, meriting continued attention and thought.

  Recent FDA approval for DTC genetic testing for 10 indicators of possible disease development can be used to inform health plan policy. As an example, genetic testing for hereditary thrombophilia is one of the FDA-approved tests. Review of online health plan medical policies indicates that this test is categorized as not medically necessary as it is deemed "investigational." As previously noted, the value of this testing is an important consideration for policy development.

  Some DTC genetic testing companies list their insurance network connections on their websites and offer to assist with preauthorization and bill the insurance. As health plans extend coverage to DTC testing, review of medical policy to keep current with industry trends is practical.

Conclusion

DTC genetic testing provides individuals with information about genetic indicators for disease in a way that is convenient and removes traditional barriers of the healthcare system. Continued growth in the marketplace is probable with the recent FTC approvals for DTC genetic testing and health risk reporting for diseases. Growing consumer use and subsequent follow-up with healthcare providers and insurers can be anticipated.

Data trends indicate consumers are likely to seek information perceived as helpful in self-management of health. Health plans may wish to consider how to best respond to the evolving impact of DTC genetic testing and subsequent member expectations with education, tools, and medical policy that optimize the use of these tests and support member engagement in their health.

18 Harvard T.H. Chan School of Public Health and STAT (January 2016). The Public and Genetic Editing, Testing, and Therapy. Retrieved July 16, 2017, from https://cdn1.sph.harvard.edu/wp-content/uploads/sites/94/2016/01/STAT-Harvard-Poll-Jan-2016-Genetic-Technology.pdf.

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