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Precision Medicine in Practice

Keeping Patients Up to Date After Genetic Testing

The Evolution of Genetic Testing

There has been exponential growth in clinical genetic testing since the mapping of the human genome was completed in 2003. Originally, genetic testing was very limited and focused in scope. Most tests were for single syndromes, ranging from Huntington disease to breast and ovarian cancer susceptibility. Over the past 15 years, we have seen an evolution to widespread use of multigene panels for common indications, such as hereditary cancer or cardiac disease. Early panels analyzed only 10-25 genes, while newer multigene panels can include hundreds of genes. Whole-exome and whole-genome tests – analyzing the coding regions or complete genomes of individuals, respectively – are becoming more common, even as first-tier tests[1].

In a 2018 study that described the clinical genetic testing landscape, it was estimated that there were 75,000 genetic tests on the market, with as many as 10 new tests added each day[2]. Of these tests, 14 percent were multigene panels, whole-exome, or whole-genome tests. Health systems, employers, wellness programs, and even government-sponsored initiatives now offer genetic testing opportunities aimed at healthy populations who are curious about their disease risk or interested in preventive medicine[3,4]. Payers also increasingly recognize the health and economic benefits of personalized care based on timely genetic testing[5]. And new legislation in the **21st Century Cures Act** will give patients immediate access to their electronic health information, including genetic results[6].

5,172
Certified genetic counselors

75,000+
Genetic tests on the market

10
New genetic tests introduced each day

26,000,000+
People have had consumer DNA testing

While forward thinking, these approaches place complex genetic information in the hands of patients – few of whom have the tools or background knowledge to interpret it[7]. Seeking advice, many patients turn to their healthcare providers, who have similar discomfort and hesitation interpreting and using genetic test information[8]. Together, this produces a high rate of result misinterpretation, leading to unnecessary interventions and poor outcomes, such as inappropriate risk-reducing surgeries and late diagnoses of advanced cancers or other medical conditions[9-13].

Access to genetics professionals when they are needed is critical. However, as of January 2020, there were just 5,172 certified clinical genetic counselors in the United States to help healthcare providers and patients/consumers make sense of their genomic data[14]. And for those patients fortunate enough to speak to a certified genetic counselor, most do so only once or twice – and then never again.

Genomic Medicine: Promises and Challenges

Genetic technology has been heralded as the greatest medical breakthrough of the 21st century, yet its success in improving short- and long-term health outcomes is limited by the lack of genetic counseling tools and services to help patients understand and incorporate their results into their medical care.

A patient can have the most thorough and accurate genetic testing available, but if that information is not integrated into their health care, that testing is meaningless. Or worse, if that testing is not interpreted correctly, it can be harmful[15]. For that reason, it is critical that genetic test results are interpreted correctly and that genetic counseling resources are available to help patients, and their clinicians, incorporate critical insights about genetic risk for disease into their medical management.

These management plans are often informed by national or expert guidelines. For instance, the National Comprehensive Cancer Network ("NCCN") releases updated guidelines related to hereditary susceptibility to breast, ovarian, colorectal, and other cancers[16]. Multidisciplinary panels of experts regularly review new data, determine how genetic testing and management guidelines should be updated, and then publish updates accordingly.

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However, the NCCN does not issue guidelines related to all genes associated with inherited risk. For other genes with hereditary cancer implications and those with non-cancer health conditions, expert opinion, other guidelines, and medical literature must be used to develop and update medical management plans. Without a clear source of information and guidance, keeping up to date on genetic conditions and how to manage associated risk is challenging for providers.

As science progresses and new data emerge, the understanding of genetic variants evolves and undoubtedly has a profound impact on the health and medical care of patients. A patient who underwent testing just 10 years ago, and was found to have a genetic condition, has likely lived through dozens of updates to the management guidelines related to his or her diagnosis[17]. For example, BRCA-related hereditary breast and ovarian cancer ("HBOC") syndrome is caused by pathogenic variants in *BRCA1* or *BRCA2* and is primarily associated with increased risk for breast, ovarian, prostate, pancreatic, and skin cancers.

For many years, screening for pancreatic cancer was not available. In 2019, the International Cancer of the Pancreas Screening ("CAPS") Consortium published updated screening recommendations for individuals at increased risk for pancreatic cancer due to hereditary risk[18]. For individuals with at least one first-degree relative (e.g., parent, sibling, or child) with pancreatic cancer, it was recommended that screening for pancreatic cancer begin at age 45-50 or 10 years younger than the earliest age of diagnosis in the family, whichever is earliest. The first screening should include an endoscopic ultrasound, magnetic resonance imaging/magnetic resonance cholangiopancreatography ("MRI/MRCP"), and blood tests to evaluate for new-onset diabetes mellitus, a sign of possible pancreatic cancer.

The NCCN added similar guidance in 2020. Additional instances of NCCN updates for BRCA-related breast and ovarian cancer syndrome include guidance for melanoma screening and risk reduction, as well as the inclusion of PARP inhibitors as a possible treatment option for some men with metastatic prostate cancer[19].

Other examples of frequently updating guidelines occur with Lynch syndrome, a condition caused by a pathogenic variant in one of five genes and mainly associated with colorectal, other gastrointestinal, uterine, and ovarian cancers. Aspirin use to decrease the risk of colon cancer in those with Lynch syndrome has long been discussed in medical literature. As sufficient data emerged, the NCCN updated their guidelines in 2020 to include the consideration of 600 mg of aspirin daily for at least two years to decrease the risk of colon cancer in individuals with Lynch syndrome[20].

Some of these updates are critical enough to change medical management for a patient, perhaps before they are due for a routine visit, and may alter recommendations for screening, chemoprevention, or even risk-reducing surgery scheduled within that time period. The personalized genetic management plan for a patient must be revisited as new information related to disease risk and medical management arises.

Several groups have explored recontacting patients to inform them of additional testing techniques[21] or reinterpretation of variants[22]. The American Society of Human Genetics ("ASHG") strongly recommends attempting recontact in situations in which new data are reasonably expected to affect a research participant's medical management[23]. The American College of Medical Genetics and Genomics ("ACMG") also recommends recontacting patients when the meaning of their genetic findings is reinterpreted[24]. It is possible that the trend toward recontacting will extend into medical management revisions in the future.

For the genomics industry to accomplish any one of these recontact efforts, a technical solution will be essential. The ongoing global COVID-19 pandemic has transformed the medical system, catalyzing the development and implementation of digital solutions. It has given patients a glimpse of how technology can remove barriers and improve their interactions with healthcare providers.

Not only have telehealth services surged, but patients are now accustomed to online portals, chatbots, in-home treatments, and digital medical services[25,26]. The adoption of mobile health products, combined with the rapid expansion of consumer genomics, will change the way patients and clinicians interact with genetic information as well.

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The genomics industry will need to transform to meet the expectations of patients and healthcare providers, including those providers who are not genetics experts. For consumers to fully benefit from precision medicine, it must be delivered at scale, with the ability to put the newest data and guidelines into the hands of patients and clinicians in a manner that supports shared decision-making related to personalized medical management.

The Scope of Medical Management Changes

In 2019, My Gene Counsel assessed how frequently medical management guidelines for genetic diseases were updated over a five-year period, using the American College of Medical Genetics and Genomics SFv2.0 list of 59 genes. Most of these genes are associated with hereditary cancer and cardiovascular disease and have established interventions to prevent or significantly reduce related morbidity and mortality[27]. We reviewed management guideline updates that could result in changes to the medical plans for a patient with one of these established genetic diagnoses. Over the course of five years, 623 medical management revisions were noted[17] (Table 1).

Table 1.
Total Number of Medical Management Updates per Specialty and Average Number of Updates per Gene for Each Specialty

Specialty	Guideline Updates 2014–2019	
	Total	Updates per Gene
Cancer (25 genes)	265	10.6
Cardiac (30 genes)	333	11.1
Other (4 genes)	25	6.3
TOTAL	**623**	**10.6**

Within the genes related to hereditary cancer predisposition, an average of 10.6 changes in medical management were noted over five years, or 2.1 per year. The greatest number of changes were noted for the *MSH6* gene – a gene associated with Lynch syndrome, a condition that causes increased risk of colorectal, uterine, and other cancers (26 changes in five years, or 5.2 per year).

Within the genes related to hereditary cardiac conditions, an average of 11.1 changes in medical management were noted over five years, or 2.2 per year. The greatest number of changes were noted for the GLA gene – a gene linked with cardiomyopathy (18 changes in five years, or 3.6 per year).

READ MORE:
How Often Do Medical Management Guidelines Change for People with Germline Genetic Findings? A Solution for Keeping Patients and Providers Updated

Bridging Genetic Testing and Precision Medicine

Given the growth in genetic testing, the frequency of medical guideline revisions, and the expanding volume of patients and clinicians that need to be recontacted, My Gene Counsel created a scalable model to return genetic test results alongside updating digital genetic counseling information. The technical solution – developed by certified genetic counselors, medical experts, and patient advocates – tracks, collates, and delivers updates via a Living Lab Report® when new disease risk information and/or medical management guidelines change to inform the downstream decision-making for patients and their healthcare providers. With this tool, entire health systems can keep pace with rapid movements in the genomics field in a timely and responsible manner.

A Scalable Solution for Updating Patients

In 2020, My Gene Counsel tracked the delivery of updates to patients for the ACMG SFv2.0 list of 59 genes[27]. Over the course of one year, 400 notifications were delivered across five categories: Medical Management, Risks, Family Information, General Information, and Resources/Support (Table 2). Per gene, an average of 6.8 notifications were sent.

Table 2.

Notification Categories

Category	Description	Example
Medical Management	Updates related to new evidence or guidelines that could change a patient's health care plan	Consideration of a new medical screening or intervention
Risks	Updates related to changes in the risks of a particular condition	A variant that increases cardiomyopathy risk found to also increase risk of inflammation and arrhythmia
Family Information	Updates that directly impact the risks of other family members	A change in understanding of an inheritance pattern
General Information	Updates related to a gene or condition that do not directly impact disease risk or management	Information related to somatic testing
Resources/Support	Updated materials and information services relevant to a patient's hereditary condition	Webinars, conferences, and online groups

The most frequent type of update was related to the Medical Management category with 111 notifications (28%). Resources/Support updates consisted of 93 notifications (23%), followed by General Information with 71 notifications (18%), Risks with 66 notifications (16%), and Family Information with 59 notifications (15%) (Table 3).

Table 3.

Total Number of 2020 Patient Notifications per Category

Category	Number of Notifications
Medical Management	111
Risks	66
Family Information	59
General Information	71
Resources/Support	93
TOTAL	**400**

Within the 25 genes related to hereditary cancer predisposition, there were 233 notifications, with an average of 9.3 notifications per gene. Updates related to Medical Management were most numerous at 75 notifications (32%), with an average of 3.0 per gene. Resources/Support updates consisted of 61 notifications (26%), averaging 2.4 per gene. Updates related to General Information and Risks had 35 notifications each (15%), with an average of 1.4 per gene. And updates pertaining to Family Information had 27 notifications (12%), averaging 1.1 per gene (Table 4). The greatest number of updates for a hereditary cancer gene was noted for *BRCA1* with 21 notifications (Figure 1).

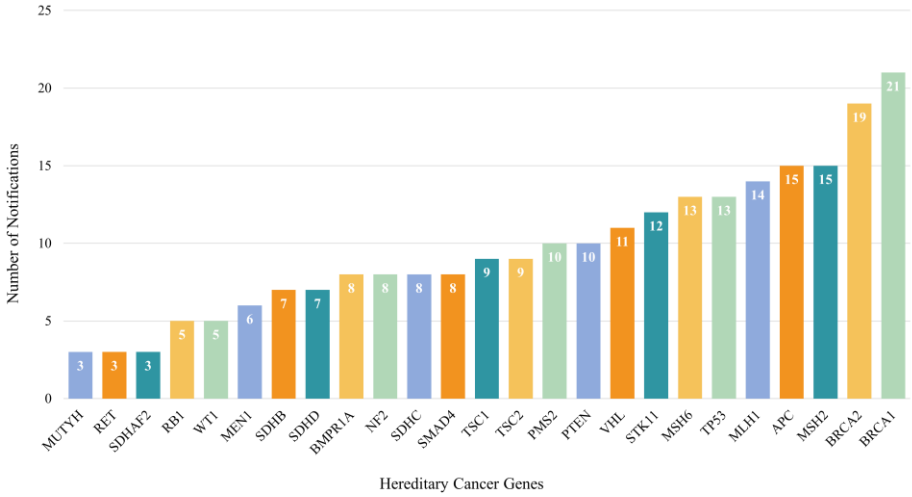
Table 4.

Total Number of 2020 Patient Notifications per Category for Each Specialty and Average Number of Notifications per Gene

	Cancer (25 Genes)		Cardiac (30 Genes)		Other (4 Genes)	
Category	Total	Notifications per Gene	Total	Notifications per Gene	Total	Notifications per Gene
Medical Management	75	3.0	36	1.2	0	0.0
Risks	35	1.4	31	1.0	0	0.0
Family Information	27	1.1	30	1.0	2	0.5
General Information	35	1.4	36	1.2	0	0.0
Resources/Support	61	2.4	32	1.1	0	0.0
Total	**233**	**9.3**	**165**	**5.5**	**2**	**0.5**

Figure 1.

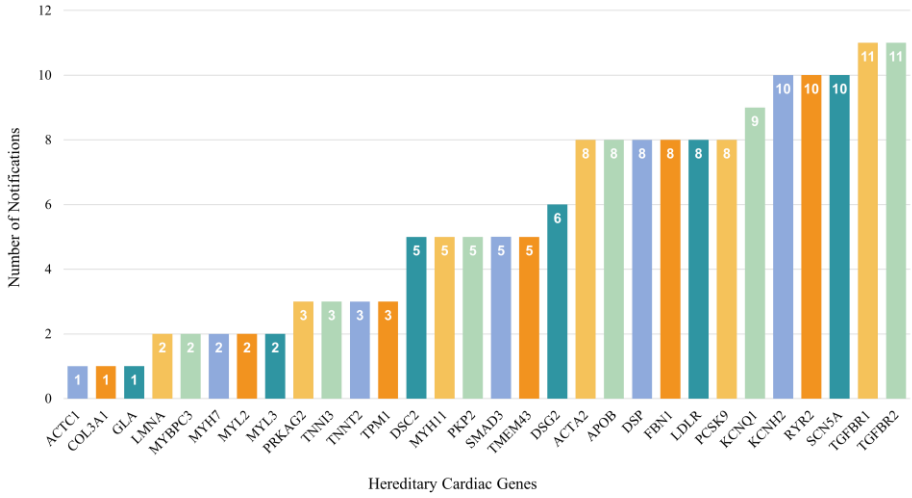
Hereditary Cancer Notifications by Gene



Within the 30 genes linked to hereditary cardiac conditions, there were 165 notifications, with an average of 5.5 notifications per gene. Updates related to General Information and Medical Management were most numerous at 36 notifications each (22%), with an average of 1.2 per gene. Resources/Support updates had 32 notifications (19%), averaging 1.1 per gene. Updates related to Risks had 31 notifications (19%), with an average of 1.0 per gene. Updates pertaining to Family Information had 30 notifications (18%), averaging 1.0 per gene (Table 4). The greatest number of updates for hereditary cardiac genes was noted for *TGFBR1* and *TGFBR2* with 11 notifications each (Figure 2). Both genes are associated with hereditary aneurysm conditions.

Figure 2.

Hereditary Cardiac Notifications by Gene



Within the remaining four genes that are part of the ACMG list of returnable findings, there were two notifications, with an average of 0.5 notifications per gene in one year. Both of these updates which were related to Family Information.

Driving Precision Medicine Forward

Layering the responsibility of monitoring research and recontacting patients onto healthcare providers, who are already stretched thin, is insurmountable[28] and only expected to get more challenging. In May 2021, the scope of the ACMG 59 increased to 73 genes, and leaders in the field predict this number will grow to over 200 within the next 10 years[29]. As the list of actionable genes grows, so too does the number of people impacted, further increasing the pressure to return results, monitor, and recontact.

It is unreasonable to expect providers to track and update the litany of advances that occur in genetics every year. With new tests, expanding gene panels, variant reclassifications, new clinical risk information, and medical management changes, the scope is enormous. Each medical management change alone would require identifying the relevant patients and recontacting them, potentially multiple times per year. The problem of recontacting is further magnified when it is extended beyond the initial provider-patient relationship to the other clinicians who follow a high-risk patient and also need accurate, updating information.

My Gene Counsel is dedicated to helping individuals fully benefit from precision medicine by keeping patients and their clinicians connected to the latest information related to their genetic test results. We leverage state-of-the-art genomics tools and the necessary infrastructure to extract and deliver the most recent data and guidelines to patients and providers.

The connection that My Gene Counsel forms between the genetic test result, the latest genomics research, the patient, and their clinicians facilitates informed decision-making, thus providing opportunities for risk reduction, early detection, and tailored treatment related to hereditary conditions. It is this informed, long-term medical management that delivers the value of genetic testing. We must think beyond the one-time return of results to the integration of continuously updating genetic counseling information in order to bring the genomics revolution to fruition.

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