
Genetic Services Policy Project Final Report

Appendix D: The Emerging Landscape of Genetic Services

Introduction

Historically, medical genetics services focused on “genetic” diseases – diseases for which genetics is the major causal factor. Increasingly, however, genetic information is becoming relevant for common complex diseases, and provides therapeutic opportunities unrelated to inherited risk. This shift has implications for the work of genetics professionals and the knowledge needs of other health care professionals. Because many new genetic tests and technologies are already available for clinical use and many more are expected to become available in the near future, this shift also poses important challenges for health care policy-makers.

Genetic services are offered in several different locations within the health care system. For the most part, however, they are currently a component of specialty referral services. A significant portion of genetics services occur in designated medical genetics clinics, often located in academic medical centers. Major factors determining where services are provided are the clinical manifestations of the disease for which services are provided, the nature of the available treatments, current screening recommendations, and reimbursement policies.

Many early innovations resulting from genomic research will enhance currently existing genetic services, creating pressure on genetics professionals to expand their availability or delegate certain services to other health professionals. Increasingly, genomic research will also provide tests and technologies that are most appropriately integrated into primary care and other parts of the health care system. Some will challenge the current delivery of health care in fundamental ways.

Current genetic services

Services prompted by clinical presentation or the nature of treatment

Each medical specialty provides diagnosis and treatment of a subset of rare genetic diseases, based on their clinical presentation. Retinal dysplasias are seen by ophthalmologists, hereditary ataxias are seen by neurologists, porphyrias are seen by gastroenterologists and dermatologists, and so on. Because these disorders are rare, even within specialty care, specialists with the appropriate expertise are often located in academic medical centers or other sites of tertiary referral care. Many of these centers also have specialized units that provide care for genetic disorders that do not fall readily into a single specialty domain, such as metabolic disorders and congenital malformations. Some genetic diseases are both common enough and unique enough in their care requirements to have dedicated clinical units; examples include specialized clinics for patients with cystic fibrosis, sickle cell disease, hemophilia, and the muscular dystrophies.

The pathway to care is influenced by the type of symptoms and by treatment options. Some disorders are highly treatable – for example, multiple endocrine neoplasia type 2 (MEN 2) and hemophilia. For others, treatment has steadily improved but continues to fall short of definitive control – for example, cystic fibrosis. Treatment for many genetic disorders is still predominantly palliative – for example, the muscular dystrophies. Referral for discrete components of care may occur, such as surgery for MEN 2. Care may sometimes be provided through a partnership between a specialty center, genetics professionals and the primary care provider. In this model, the patient may be seen periodically – e.g., once a year – in the referral center for consultation, with day to day care provided by the primary care provider.

Services prompted by screening

- (1) *Newborn screening* Some genetic disorders require the initiation of treatment in infancy, with good prospects of a healthy outcome if treatment is started early enough. This reality led to the creation of state newborn screening programs, to identify affected infants prior to the onset of symptoms and refer them to the appropriate specialty care.
- (2) *Prenatal screening* Several genetic tests are currently recommended for routine prenatal screening, including maternal serum measures to identify increased risk for neural tube defects and Down syndrome; carrier screening for cystic fibrosis, sickle cell disease and thalassemias; and carrier screening panels for women of Ashkenazi Jewish ancestry. These tests, when positive, may be followed by prenatal diagnostic testing to determine whether the fetus is affected.

Genetic counseling

Genetic counseling is an important adjunct service in all of these clinical settings. After a diagnosis is made, whether by clinical presentation or as a result of screening, genetic counseling provides families with the opportunity to learn about the inheritance pattern of the disorder, the risk for other family members, and genetic testing options. Reproductive genetics is an important focus of genetic counseling services. For genetic disorders that are severely disabling and lack definitive treatment, some parents are interested in the use of genetic testing to prevent births of affected children. Clinical geneticists and genetic counselors assist parents to understand their reproductive options. Carrier tests for many autosomal or X-linked recessive diseases can identify couples who are at risk to have an affected child. Prenatal diagnosis is available for many of these genetic diseases, to determine whether a fetus is affected. These tests can be used to inform the use of selective abortion or assisted reproductive technologies, including pre-implantation genetic diagnosis to prevent the birth of a child with specific genetic disease. Care is provided through collaboration between clinical genetics and perinatal medicine; often genetic counselors are located in a prenatal clinic to assist in the delivery of these services.

Genetic counseling can also assist in identifying affected family members so that appropriate health care can be provided. For example, if a young woman with breast cancer is determined to have a BRCA mutation, other family members can be tested to determine whether they have inherited the mutation, so that appropriate cancer screening or prophylactic surgery can be offered. Similarly, a diagnosis of hemochromatosis should prompt evaluation of other family

members at risk – in particular, siblings of the affected person – so that appropriate phlebotomy treatment can be initiated.

Evolving role of the genetics professional

The American College of Medical Genetics defines medical genetics as “a branch of biomedical science that studies the relationship between genes and health,” clinical genetics as “a primary medical specialty focused on health and illness of individuals and their families,” and a clinical geneticist as “a physician who specializes in genetic disorders and conditions”. Genetics professionals include clinical geneticists (MDs with clinical genetic training), nurse geneticists (RN), genetic counselors, who may have MS, or PhD degrees, and laboratory geneticists.

The role of the clinical geneticist has evolved over time and encompasses a range of clinical roles (Table, page 9). The typical example of a clinical geneticist is that of a dysmorphologist evaluating children with developmental delay and/or birth defects for genetic disorders. In fact, the clinical geneticist can also be involved in prenatal diagnosis, diagnosis and treatment of metabolic diseases, diagnosis of single gene disorders, evaluation of both children and adults with neurologic and neuromuscular diseases, cancer, or infertility, and evaluation of genetic traits involved in common diseases (Williams, 2001).

In the past, the focus of clinical genetics was to help establish a diagnosis for patients with rare genetic disorders and conditions. Even in the absence of treatment, a diagnosis can provide some benefits to the patient, including the elimination of unnecessary tests, risk information for reproduction and family members, and prognostic information (Williams, 2001). Except for metabolic diseases, treatment was not part of the role of the clinical geneticist. In recent years, clinical geneticists have become increasingly involved in the management of the patients they diagnose. There is also reasonable hope that the research focused on single gene diseases will bear fruit in more definitive treatments for at least some diseases. The recent publication of guidelines and monographs about the management of genetic syndromes speaks to this growing role (Cassidy and Allanson, 2004; Trotter, 2005; Kishnani, 2006). Clinical geneticists now help coordinate long-term follow-up, periodic evaluation for known complications, and supportive treatments.

Not surprisingly, the earliest clinical benefits of the Human Genome Project are in the form of more and better tests for genetic diseases. Diagnosis is becoming increasingly more accurate with the aid of DNA-based testing. The increasing availability of diagnostic tests for genetic disorders makes it increasingly impractical for the clinical geneticist to be involved in the provision of all such tests. Some of these tests have already been taken up by non-genetic specialists, like BRCA1/2 testing by oncologists or HNPCC testing by gastroenterologists. To ensure that the use of genetic tests by non-genetic specialists is successful, these providers need to be knowledgeable about the most common genetic conditions they face, about the interpretation of the genetic tests they use, and about the type of information and counseling needed when providing such tests (Greendale, 2001). Some specialty clinics have hired genetic counselors to provide counseling to patients undergoing genetic tests, although genetic counselors are not trained to diagnose conditions.

Emerging genetic tests

Clinical geneticists have not typically been involved in what is now called “genomic medicine,” i.e., the use of risk information about genetic susceptibility to disease or pharmacogenomic profiles in practice. Although these tests provide information with potential implications not only for the patient being tested but also for his/her family members, such tests are usually not accompanied by genetic counseling. Practice standards, including the evidence needed to justify test use, are not yet established, nor is the role of genetics professionals, either in setting practice standards or in assisting other clinicians by means of educational efforts, consultation, or counseling.

Pharmacogenomics

Pharmacogenomics represents one of the most promising clinical applications of genomic research. Testing for gene variants associated with drug response has the potential to improve both the safety and the efficacy of drug treatment. In the most widely anticipated use of pharmacogenomics, testing would occur before prescribing commonly used drugs to assure that the appropriate drug is chosen based on the patient’s likelihood of adverse reactions or response. The level of evidence required to justify routine use of pharmacogenomic tests is not yet established; in particular, there is controversy concerning the need for randomized controlled trials to assess the outcomes of pharmacogenomically assisted prescribing. Once this approach is determined to be useful, clinicians will need to be educated in its use.

An important question in the evaluation of pharmacogenomic testing is whether it poses significant personal or social risks. Testing is focused on informing drug prescribing, but many pharmacogenomic tests provide ancillary information, defined as information unrelated to drug response, such as predisposition to diseases for which the individual is not currently seeking treatment or does not manifest symptoms, or prognostic information that is not informative for treatment. The implications of this information for informed consent or appropriate use of pharmacogenomic tests is not yet resolved. Conceivably, some pharmacogenomic tests could pose sufficient risks to make genetic counseling a consideration.

Some pharmacogenomic tests will be introduced as a component of a new therapeutic. An example is testing *Her-2-neu* amplification in breast tumor tissue, in order to determine if the patient is a candidate for Herceptin therapy. To the extent that testing measures acquired as opposed to inherited genetic change, as in this example, the potential risks of the testing process are reduced (Haga and Burke, 2008).

Gene expression profiling

Gene expression profiling represents another new genetic testing strategy. As with testing for *Her-2-neu* amplification, this testing approach has been used to measure acquired genetic change. For example, Oncotype Dx and MammaPrint are two currently available tests that measure gene expression in breast tumor tissue, in order to predict likelihood of breast cancer recurrence. As with pharmacogenomics, the appropriate evaluation of these tests is not yet resolved. Oncotype Dx has been proposed as a means to determine which women with early stage breast cancer require chemotherapy, based on large scale retrospective analyses. The need for prospective evaluation of testing outcomes is a matter of debate. This form of testing is

presumed not to involve genetics professionals; however, it is conceivable that future gene expression profiles could measure inherited rather than acquired variation, with broader genetic implications.

Genetic susceptibility testing

Genetic susceptibility testing also raises questions regarding evaluation and appropriate use. When is genetic risk information useful and when is it harmful? Who decides? In light of the large volume of risk information that will flow from genomic research, these questions are critically important for health care policy. An important question is whether susceptibility tests should be viewed as helpful information, evaluated primarily for their predictive value, versus measures of risk that should be used only if they are proven to lead to interventions that improve health outcomes. Factor V Leiden, one of the few genetic susceptibility tests now in clinical use, illustrates the challenge: the test is widely ordered despite the fact that there is no evidence to suggest that FVL testing should routinely direct clinical management or will improve health outcome. This observation could be interpreted to mean that the test is being used inappropriately, or that it is providing information that clinicians and patients find of value. In addition, FVL testing will rarely identify individuals with very high inherited risk (e.g., FVL homozygotes), for whom specific therapy and referral to genetic counseling may be appropriate.

Consideration of genetic susceptibility testing leads to fundamental inquiries about the purpose of health care, incorporating how broadly “health” and “health outcomes” should be defined, and the limits that should be set on the use of health care resources. Genetic susceptibility testing also poses questions about delivery of care, including the degree to which current systems of primary care can be better focused on prevention. And to the extent that prevention can be made a central focus of primary care, rigorous questions will need to be asked about the value added by knowledge of genetic risk: e.g., if the health care system were already maximizing efforts to promote healthy diet, how would knowledge of genetic risk for diabetes or coronary artery disease assist patients or providers?

Storage and retrieval of genetic susceptibility information also pose challenges. The information will need to be readily accessible in all places where a patient receives health care if it is to be maximally effective. At the same time, appropriate privacy protection will be essential.

Provision of services

As discussed above, genetics professionals provide a range of services to assist families and other clinicians to care for patients with genetic diseases (Table). Patient care for rare genetic diseases is likely to be best in centers with substantial experience treating these disorders. Often the specialty center is the only source of care within a state or large geographic area. The provision of genetic services relies on appropriate referral to genetic services, effective coordination of specialty services, and interdisciplinary management of patients with genetic disorders.

Since genetics professionals are not involved in primary care, they rely on other providers for patient referral. The provider seeing the patient for an initial complaint must recognize the

possibility of a genetic disease and know where to refer the patient. For this reason, primary care providers and local specialists need sufficient background knowledge of genetics, and appropriate access to point of service information, to make appropriate and timely referrals.

Particularly as advances are made in diagnosis and treatment of genetic disorders, specific referral to genetic services, from both the specialty center and primary care, is also important. Clinical geneticists are most likely to know if a diagnostic test is now available for a condition previously diagnosed on a clinical basis, or if new treatments or surveillance strategies are now available for a given condition. Clinical geneticists often play a key role in diagnosis and are increasingly playing a role in guiding and coordinating patient management, as discussed above. Furthermore, a specialist may be able to provide disease management after diagnosis but may be unprepared to counsel the family about mode of inheritance, genetic testing options for family members at risk or other services, such as prenatal diagnosis and other reproductive options.

Another issue is the need for genetics professionals with the expertise to provide services to adults with rare genetic disorders. This need stems from recently improved survival rates for many genetic disorders and the greater importance placed on long-term follow-up and management, as discussed above.

One of the biggest challenges in the delivery of genetic services is effective coordination of the different components of service for patients with genetic diseases and their families. This challenge encompasses communication between different specialties to ensure effective sharing of care among primary care provider, specialty provider, and clinical genetics. It often includes the challenge of coordinating across significant distances, and taking into account different funding mechanisms for the different components of care. This challenge is often poorly addressed in the current U.S. health care system.

To address this need for effective coordination of care for patients with genetic disorders, interdisciplinary clinics organized around a specific genetic diagnosis or family of diagnoses have been developed, like specialty clinics for cystic fibrosis, neuromuscular diseases, or PKU. Other interdisciplinary clinics are organized around broader diagnostic categories, some of which may have a genetic origin. Examples include hearing loss clinics and maxillo-facial clinics. Depending on the diagnosis, the geneticist may be asked to play a coordinating role. Progress in understanding the genetic contribution to common diseases is likely to lead to a new kind of referral clinic in which a multidisciplinary team, incorporating genetics professionals, provides care. The geneticist will likely be brought in as an expert or consultant to address specific issues about diagnosis, interpretation of genetic susceptibility test results, and counseling. Such clinics already exist in cancer genetics, for example.

Location of services

Genetic services are usually provided in clinical genetics clinics based in academic medical centers or tertiary referral centers. One of the important reasons for locating clinical genetic services in academic medical centers is that they are poorly reimbursed. Often it is possible to deliver them effectively only because the salaries of the genetic counselors and clinical

geneticists are largely covered by research activities, with clinical care representing only a small fraction of their effort.

The increasing numbers of genetic tests now available will result in greater demands for the services of genetics professionals. Efficiencies may be hard to achieve in the absence of innovative approaches to support; for example, genetics professionals can often provide effective consultation to primary care providers and specialists via telephone and email, to allow them to complete the initial stages of work-up in a patient suspected of having a genetic disease. This consultation can limit inappropriate referrals and reduce time demands on genetics clinics, but is not usually reimbursed.

Barriers to integration of genetic services in practice

The evolving role of the clinical geneticist must find a balance between the trend for clinical geneticists to be increasingly involved not only in diagnosis but also in offering guidance on patient management and letting other health professionals take on the diagnosis and treatment of some genetic disorders because the clinical genetics workforce is limited in numbers. Although some common genetic disorders are already mostly under the care of other health professionals (for example, cystic fibrosis), it will be difficult to decide, among some other disorders, which ones need to be diagnosed and/or managed by clinical geneticists and which ones can be taken on by other specialties. Clinical geneticists are not the first to struggle with what should be the boundaries of their practice (Greendale and Pyeritz, 2001). This dilemma has been compared to the one faced by infectious disease specialists in the last century. As new tests and antibiotic treatments became available, infectious disease specialists started to focus on the diagnosis of complex cases and less common disorders, as well as the use of the newest therapies, while the most common diseases and their treatments were dealt with by primary care providers and other specialists (Guttmacher, 2001). The advent of new technologies led to a redefinition of the specialists' role, not their disappearance.

For clinical geneticists to continue providing services, reimbursement issues must be resolved. Current reimbursement practices do not cover the costs associated with the provision of genetic services (Pletcher, 2002). The majority of clinical geneticists receive at least part of their income as a salary, and only 6% receive most of their income from traditional fee for service (Pletcher, 2002). In clinical genetics, patient evaluation, counseling, and education require more time than in other specialties, but reimbursement does not reflect this (Howell, 2002). Furthermore, counseling services provided by genetic counselors are often not reimbursed. Genetic counselors must be paid out of other sources of income. Academic clinical genetic laboratories used to be an important source of income for clinical genetics services, but competition from commercial laboratories has made them less profitable. Clinical genetic services cannot be maintained in the long run using the current reimbursement practices.

Because clinical genetics services are located in tertiary care centers, they rely entirely on referral from other providers for their practice. Primary care providers and other specialists need to be aware of the availability of genetic services in their area. They also need to be better educated about appropriate use of genetic services and indications for referral to a clinical

geneticist (Taylor, 2003). Clinical geneticists might need to come up with new ways to provide services to increase their visibility and availability; the use of phone or telemedicine consultations with providers and/or patients could reduce the number of unnecessary referrals while increasing the number of cases addressed by the clinical geneticist.

Because the number of clinical geneticists and other genetics health professionals is limited, some areas have little or no access to genetic services. Incentives must be in place to attract more qualified individuals into the field of clinical genetics and more genetic professionals to underserved areas. The use of telemedicine could also increase access to genetic services in underserved areas, but assumes that there are genetic professionals elsewhere who have the time and resources to offer telemedicine consultations. It must also take into consideration that not all services can be provided using telemedicine, and that a subset of patients will still have to travel to see the genetics specialist at a tertiary care center. In considering these challenges, however, the emerging uses of genetics testing and technology need to be considered. Some are readily integrated into existing health care while others may require specific efforts to define appropriate use and the role of genetics professionals.

Other innovative uses of genomic technology

Genetic technology has also entered the health care system in a different way, as the source of improved health care tools for various health care problems, often based on genomics analysis of pathogens. The most obvious example is the use of DNA-based tests to identify microbial pathogens, providing more accurate and rapid means to determine the cause of many infectious diseases. Typically, the testing process itself is simple, requiring no specialized expertise.

Innovative genome-based therapeutics are also part of this trend. For example, fomiversen, an antisense oligonucleotide that binds to the messenger RNA of an essential protein of cytomegalovirus, can inhibit protein expression. It has proved to be an effective therapy for cytomegalovirus infections of the eye in AIDS patients. More innovations of this kind are likely; in general, they will be integrated into health care by the same route as non-genetic technical innovation, generally by direct comparison to the technology they are replacing, and will not necessarily change the structure or process of health care delivery.

Conclusions

Although clinical geneticists still “specialize in genetic disorders and conditions,” there have been tremendous improvements in their knowledge about these disorders and the tools at their disposal to diagnose and treat them. As the role of the clinical geneticist evolves to integrate these advances into clinical services, their relationship with other providers will change.

Primary care providers and other specialists need to be aware of the availability of genetic services, learning how and who to refer for genetic evaluation. In addition, clinicians not trained in genetics will need to develop the skills to use certain genetic services independently – notably pharmacogenomics and genetic susceptibility testing.

Clinical geneticists have to develop new ways to increase access to their services in a context of limited resources, and also participate in the development of robust practice standards for the use of genetic tests and technologies in other clinical settings, in partnership with the appropriate medical specialties. Interdisciplinary collaborations will become more common.

Reimbursement practices will have to change to reflect these new developments to sustain the provision of genetic services.

Table: Roles of Genetics Professionals

| | Clinical roles | Usual site of practice |
|--|--|--|
| Clinical Geneticists | <ul style="list-style-type: none"> • Diagnosis of genetic disease • Consultation regarding clinical management • (Rarely) primary care of patients with genetic disease • Supervision of genetic counselors (not required in all states) | <ul style="list-style-type: none"> • Academic medical centers |
| Genetic counselors and nurse geneticists | <ul style="list-style-type: none"> • Evaluation and counseling of patients related to risk for genetic disease in themselves or family members • Counseling before and after genetic testing | <ul style="list-style-type: none"> • Academic medical centers • Specialty referral clinics • State-supported genetics clinics |
| Genetics laboratory professionals | <ul style="list-style-type: none"> • Perform or supervise laboratory procedures for genetic tests • Interpret test results | <ul style="list-style-type: none"> • Academic medical centers • State laboratories • Commercial laboratories |

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