review

Genetics and genomics in practice: The continuum from genetic disease to genetic information in health and disease

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This article reviews how the continuum and gradual shift from genetics (study of genes) to genomics (study of the whole genome) in medicine and public health will require reassessment of the traditional approach to delivery of genetic information, namely genetic services. A more general approach is needed to assess the value-added of genetic information for promoting health and for diagnosing, treating, predicting, and preventing all diseases, not only "genetic diseases." The article also discusses how family history can serve as a bridge from genetics to genomics in practice because it reflects the presence, not only of single-gene disorders, but also of shared genes, shared environments, and complex gene-environment interactions. Because of the expected volume of new genetic information, evidence-based practice should increasingly rely on scientific data on analytic performance of such information, its validity in predicting health outcomes, and its utility in improving health and preventing disease beyond approaches that do not use genetic information. ***Genet Med* 2003:5(4):261–268.**

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We live in the "omics" era. Almost every month we hear of a new field that reminds us of an already established discipline but with an "omics" attached to it. In addition to genomics,[1] we now have pharmacogenomics,[2] nutrigenomics,[3] metabonomics,[4] transcriptomics,[5] proteomics,[6] toxicogenomics,[7] and others. Today, although we can attribute a few, if any, clinical and public health applications to genomics, we can anticipate more applications in the next decades.[1,8–11]

In preparation for the "omics" era, recent efforts have attempted to bridge existing gaps between the genetics profession and the primary-care community,[12] as well as the public health community.[13] Professional education is viewed as key for preparing healthcare and public health professionals for genomics.[14,15] Generally, these efforts have focused on integrating medical genetics and genetic services, as we know them today, into medicine and public health.[12,13]

In this article, I discuss how the continuum and gradual shift from genetics to genomics in practice will require reassessment of the traditional approach to delivery of genetic information, namely genetic services. I argue that, in addition to the traditional genetic services model, a more general approach is needed to assess the value-added of genetic information for promoting health and for diagnosing, treating, predicting, and preventing all diseases. I also discuss how family history can serve as a bridge from genetics to genomics in practice because it reflects the presence, not only of single-gene disorders, but also of shared genes, shared environments, and complex gene-environment interactions. Because of the expected volume of new genetic information, evidence-based practice should increasingly rely on scientific data on analytic performance of such information, its validity in predicting health outcomes, and its utility in improving health and preventing disease beyond approaches that do not use genetic information.

Genetics and genomics: Is there a difference?

In a primer on genomic medicine, Guttmacher and Collins[1] viewed "genetics as the study of single genes and their effects" and genomics as "the study not just of single genes, but of the functions and interactions of all the genes in the genome." This definition implies a quantitative difference between the two fields (the study of multiple genes vs. one gene, which could make genetics part of genomics). In addition, there is a qualitative shift between genetics and genomics in medical and public health applications, ranging from the concept of disease in genetics to the concept of information in genomics (Table 1). Perhaps more accurately, this shift may be best viewed as a continuum, with no clear breakpoint, from single gene disorders with high penetrance to genetic information obtained from multiple loci in somatic cells (Table 2).

The practice of medical genetics has traditionally focused on those conditions that are known to be due to mutations in single genes (e.g., Huntington disease[16]), whole chromosomes (e.g., trisomy 21 in Down syndrome[17]), or associated with

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Table 1
Genetic disease and genetic information in practice

	Genetic disease	Genetic information
Types of conditions	Single gene disorders; Chromosomal anomalies	All human diseases
Genetic involvement	Mutations with high or incomplete penetrance	Genetic variation at single and multiple loci in germ and somatic cells
Environmental involvement	Variable, many disorders have no known environmental determinants	Interactions with chemical, infectious, physical, pharmacologic agents
Medical practice	Genetic services (genetic counseling, testing, management)	Multiple health care settings: preventive medicine; pharmacogenomics; disease diagnosis; disease prognostication; may include genetic services
Public health practice	Assuring delivery of genetic services to individuals, families, and society	Developing health policy and assuring appropriate use of genetic information in population health
	Population screening (e.g., newborn screening)	Population screening

Table 2
Continuum from genetics to genomics in practice

Type of genetic variation	Examples	Practice model
Single gene disorders, High penetrance; No effective interventions	Huntington disease	Genetic services; nondirective counseling
Single gene disorders; High penetrance; Effective interventions	Phenylketonuria	Population screening (e.g., newborn screening)
Single gene disorders; Low or variable penetrance; Intervention: variable	Hereditary breast/ovarian cancer, hemochromatosis	Genetic services; counseling may or may not be directive
Genetic variation at one or multiple loci	pharmacogenetic traits; factor V Leiden, MTHFR	Communicating genetic information re future risk of disease and interventions; counseling may be directive
Genetic variation at multiple loci in somatic cells (e.g., tumors)	Gene expression profiles; serum proteomic patterns (see text for examples)	Using genetic information in early diagnosis, classification, prognosis, and treatment; genetic services/counseling model does not apply

birth defects and developmental disabilities.[18] For these conditions, a traditional genetic services model applies with its accompanying medical processes (genetic counseling/testing/management) and public health processes (assuring delivery of genetic services and newborn screening). On the other hand, the practice of genomics in medicine and public health will center on information resulting from variation at one or multiple loci and strong interactions with environmental factors (broadly defined to include diet, drugs, infectious agents, chemicals, physical agents, and behavioral factors). As will be illustrated, genetic information can come from inherited variation in germ cells or acquired variation in somatic cells (such as in cancer) or could be associated with gene products and expression. Such information can be used in diagnosis, treatment, prediction, and prevention of all diseases, not only genetic disorders. For traditional single-gene disorders, when genetic information is obtained on patients and their relatives, it is used for diagnosing or predicting a genetic disease state. For most human diseases, however, genetic information at one locus is modified by information from many other loci and their interaction with nongenetic risk factors, so much so, that the sum of such genetic information cannot be thought of as disease state but more as biological markers or disease risk factors.

Genetics in medicine and public health today

The current practice of medical genetics focuses on delivery of genetic services, as exemplified by the mission statement of the American College of Medical Genetics (ACMG): "To make genetic services available to and improve the health of the public, the ACMG promotes the development and implementation of methods to diagnose, treat, and prevent genetic disease."[19] A cornerstone of the genetic services process is genetic counseling.[20] According to the National Society for Genetic Counselors, genetic counselors "provide information and support to families who have members with birth defects or genetic disorders and to families who may be at risk for a variety of inherited conditions. They identify families at risk, investigate the problem present in the family, interpret information about the disorder, analyze inheritance patterns and risks of recurrence and review available options with the family."[21] Because of the complex nature of genetic information and the psychosocial impact of such information, genetic counseling has traditionally been founded on principles of nondirectiveness and the use of culturally appropriate educational materials.[20,21] This is especially relevant considering that, for many single-gene disorders, no or limited medical interventions

have been available. Instead, this information has been used for a variety of purposes including diagnosis and management, including reproductive planning for severe disorders affecting infants and children (e.g., Tay-Sachs disease[22]) or life planning for late-onset conditions with no treatment (e.g., Huntington disease[16]).

Although individually rare, genetic disorders tend to be collectively common, accounting for about 5% of all human diseases.[23] In addition, of the 1000 or so genetic tests available in research or practice, more than 90% are related to single-gene disorders.[24] With increasing discovery of genes for these disorders, the number of genetic tests (molecular, biochemical, physiological, and other) will rise, thereby challenging the delivery of quality genetic testing and counseling services. These challenges have called for public health action to develop partnerships with the provider and laboratory communities.[13] They also have motivated academic and government groups to develop guidelines for integrating genetic services into routine healthcare and public health programs.[13]

In public health practice, an established role for genetics starts with assessing the needs of populations in terms of the burden of these disorders, developing appropriate policies, and assuring that services are delivered to individuals, families, and communities.[13] In addition, since the 1960s, newborn screening has become a special programmatic focus for genetics and public health.[25] With the continued discovery of mostly single-gene disorders with metabolic abnormalities leading to mental retardation and other morbidities and disabilities, mandated public health screening programs flourished because of the evidence that early detection of these conditions can save lives (e.g., sickle cell disease) and prevent mental retardation (e.g., phenylketonuria) or other morbidities. Currently, the United States and many countries screen for a variable number of genetic disorders in newborns.[25] The recent emergence of tandem mass spectrometry technology has allowed the expansion of newborn screening efforts to include many more conditions in the screening panel. Ongoing discussions have emphasized the need for evidence-based criteria to determine the disorders included in the newborn screening panel, the informed consent process and parent/provider education, and assurance of systems of follow-up for medical care after screening.[25,26] For example, the current policy and program discussions on newborn screening for cystic fibrosis, a common autosomal recessive disorder among whites of European descent, have been guided by emerging and conflicting data on the clinical utility of early detection, namely its ability to lead to long-term benefits in nutritional and growth parameters and pulmonary function.[27]

Genomics in medicine and public health: The future of risk assessment

With completion of the human genome sequence in 2003, what applications should we foresee for medicine and public health and how transferable is the genetic services model to the 95% of human diseases that do not fall under the rubric of genetic disorders? First, we should expect rapid progress in the diagnosis and management of single gene disorders, through genetic testing,[20] and advances in medical interventions, including gene therapy (such as for inherited hematologic abnormalities[28]). These advances do not necessarily change the way we practice medical or public health genetics today. Similarly, advances in gene mapping and discovery will lead to the discovery of additional disorders, most likely with incomplete penetrance (e.g., hereditary hemochromatosis[29]).

Although it is not clear how many more such genetic disorders will discovered in the next few years, an important advance in human genetics will be the identification and characterization of numerous common genetic variants at multiple loci, which increase or decrease the risks for various diseases singly and in combination with other genes and with various chemical, physical, infectious, pharmacologic, and social factors.[30] This genetic information can be the basis for assessing disease susceptibility among healthy individuals, leading to personalized primary and secondary prevention strategies. Collins and McKusick[31] stated that "By the year 2010, it is expected that predictive genetic tests will be available for as many as a dozen common conditions, allowing individuals who wish to know this information to learn their individual susceptibilities and to take steps to reduce those risks for which interventions are or will be available. Such interventions could take the form of medical surveillance, lifestyle modifications, diet, or drug therapy. Identification of persons at highest risk for colon cancer, for example, could lead to targeted efforts to provide colonoscopic screening to those individuals, with the likelihood of preventing many premature deaths."

Guttmacher and Collins[1] illustrate how genomics may lead to better management of a medical condition. A 4-year-old boy has acute lymphoblastic leukemia and receives oral mercaptopurine daily. A genetic test shows that he is homozygous for a mutation in the thiopurine *S*-methyltransferase gene (TPMT), which inactivates mercaptopurine. As a result of the positive test, he receives a reduced dose and is carefully monitored for drug level in the blood, ensuring safe and effective levels (this is a classical pharmacogenetic trait at one locus, however). Pharmacogenomics could have a much larger impact in the near future.[32]

Perhaps more indicative examples along the continuum to genomics could be those that are based on genetic testing for future disease susceptibility using multiple genetic variants at several loci. This scenario was described by Collins in a fictitious clinical encounter between a 23-year-old man and his healthcare provider in 2010.[33] Because of high cholesterol level and a paternal history of early onset myocardial infarction, he undergoes a battery of genetic tests at multiple loci using many polymorphic variants, which showed he is at increased risk for heart disease, colon cancer, and lung cancer. Personalized interventions are then applied to reduce his risks for these diseases (including genotype-specific drugs to reduce cholesterol levels, annual colonoscopy starting at age 45, and behavior modification for smoking cessation[33]).

This hypothetical case raises a number of issues. For example, it is not clear whether or not genetic information is really

needed to target certain interventions, such as smoking cessation or treatment of hypercholesterolemia. In the case of smoking, testing for susceptibility may reduce the motivation for smoking cessation in those individuals who test "normal" for the genotype. Also, even when genetic information provides guidance—as is the case with early initiation of colorectal cancer screening—the need for a DNA-based or biochemical test versus the more generic information provided by a family history can be open to question. Thus, evidence-based guidelines need to be developed for using genetic information to profile disease risks. Such evidence will come from a combination of data on the analytic validity of such testing, its clinical validity and utility for improving health outcomes and preventing diseases, as well as an assessment of the ethical, legal, and social issues for using such information.[20] An important consideration for genetic testing or profiling in targeting interventions will be to evaluate the evidence for the "value-added" of interventions based on genetic risk levels (high risk approach) compared to prevention recommendations addressed toward the general population (i.e., average risk). Evidence-based medicine for the most part focuses on general practice guidelines rather than based on genetic risks.

Although premature and scientifically unjustified in 2003, testing for "genetic risk profiles" that identify individual risks for various diseases and for drug response is currently offered in the United States and England.[34,35] Such tests include oxidative stress profile, aging profile, obesity susceptibility profile, cardiogenomic profile, detoxigenomic profile, and an immunogenomic profile.[34,35] Information is generally lacking on the analytic and clinical validity of these tests, making their clinical utility impossible to assess.

An important rationale for susceptibility genetic testing is the concept of using multiple genetic variants that individually could be weak risk factors for a complex disease but together may provide a better predictive ability of future disease development.[36] Because the disease-predictive ability for testing for common variants at single loci (e.g., NAT2 and CypA2) is low, such variants seem unsuitable for clinical practice. For example, Holtzman showed that the positive predictive value for common disease genotypes tends to be low unless the genotype is rare ($< 1\%$) or the relative risks are high (20 or more) even for relatively common diseases with lifetime risks of 5%.[10] In addition, associations between a disease and a genetic variant can occur by chance, because of faulty study designs, or due to publication bias.[37] For example, in a literature review of over 600 gene-disease associations, Hirshorn et al. documented that most reported associations are not robust. Of the 166 associations studied three or more times, only 6 were consistently replicated.[38] Nevertheless, based on theoretical considerations, Yang et al.[36] showed that bundling several variants from multiple loci that interact on the same biologic pathway (e.g., folate pathways) can increase the predictive value of genetic testing for susceptibility to common disease, especially in the presence of pertinent environmental exposures (e.g., diet and folic acid intake). Such gene-nutrient interactions may be important in the etiology and prediction of numerous conditions, such as birth defects, cardiovascular disease, and several cancers.[39]

Somatic cell genetics and genomics in future practice

A promising area further along the continuum from genetics to genomics is the use of genetic information from somatic cells for the diagnosis, classification, prediction, and prognostication for numerous diseases, notably cancers. For example, van De Vijver et al.[40] used microarray analysis of gene expression profiles to evaluate 70-gene prognosis profile. They classified 295 consecutive patients with primary breast cancer as having a gene-expression signature associated with either a poor prognosis (180 cases) or a good prognosis (115 cases). The overall 10-year survival rates were 54.6% and 94.5% in the two groups, respectively. Also, the probability of remaining free of distant metastases was 50.6% in the poor prognosis group and 85.2% in the good prognosis group. The current clinical implications of an association between gene-expression profiles and outcome of disease are unclear. Several technical issues remain such as reproducibility of genomic profiling results as well as replication of the study finding in other populations. This study illustrates how work aimed to predict the behavior of cancers, combined with efforts to create targeted therapies, could provide new opportunities for reducing the burden of cancer.[41]

Another example is the use of somatic cell genetics in early detection of colorectal cancer, a major public health burden in the developed world and for which public health strategies currently exist for early detection among people over age 50 years.[42] Traverso et al.[43] purified DNA from stool samples and screened for *APC* mutations using digital protein truncation technique. APC mutations were identified in 26 of the 46 patients with colorectal cancer (57%) compared with none of the 28 control patients (0%). Although this finding needs further evaluation, especially in the potential of the digital-protein-truncation test to discriminate between small adenomas and large adenomas and colorectal cancers, the study suggests a new approach for the early detection of colorectal neoplasms that, once confirmed and refined, may be used as adjunct or replacement to the current methods of colorectal cancer screening, for which adherence has been poor in the general population.[42]

A final example is the study of Petricoin et al.,[44] which identified proteomic patterns in serum that distinguish neoplastic from nonneoplastic disease within the ovary. They generated proteomic spectra by mass spectroscopy (surface-enhanced laser desorption and ionization). Through an iterative searching algorithm, they identified a pattern that completely discriminated cancer from noncancer. The discovered pattern yielded a sensitivity of 100% and specificity of 95%. Although the finding was criticized on the basis of methodologic issues and needs further replication,[45,46] the approach further illustrates how new screening tools for early diagnosis of ovarian cancer could be discovered on the basis of the new genomic technologies. From a public health perspective, such approaches may

lead to early detection and therefore greater reduction in the population burden of morbidity and mortality from ovarian cancer. The last scenario is an example of a "proteomic" approach,[6] which, over time, could become more important in practice than genomics from which it is derived.

Family history as a bridge between genetics and genomics in practice

In order for the genomics scenarios depicted above to be useful, more multidisciplinary research is needed, including basic sciences, clinical, epidemiological, behavioral, economic, health services, communications, and outcome research. In the meantime, can practitioners of medicine and public health use existing tools in addition to the traditional genetic services model to find individuals and families at high risk for genetic disorders? Obviously, there are currently unmet public health needs in the assurance of genetic services for individuals and families with genetic disorders. For example, more than half of individuals with familial hypercholesterolemia, an autosomal-dominant disorder of cholesterol metabolism, associated with premature but yet preventable morbidity and mortality from coronary heart disease, may go undiagnosed.[47] Women with strong family history of breast or ovarian cancer should be counseled and evaluated for the possibility of mutations in the *BRCA1* or *BRCA2* genes, to reduce the risk for morbidity and mortality from breast and ovarian cancers in these families.[48]

In addition to the ascertainment of single-gene disorders, family history can build a bridge from genetics to genomics in practice. Family history is a risk factor for almost all diseases of public health significance, including most chromic diseases such as coronary heart disease, diabetes, cancer, osteoporosis, and asthma.[49] Family history of a specific disease reflects the consequences of genetic variation at multiple loci, shared environment, and common behaviors. Only occasionally could family history indicate single-gene disorders.[49] Yet, the collection and interpretation of family history rarely has been applied in the preventive medicine setting to assess disease risk or influence early detection and motivate prevention strategies.[49] Researchers have proposed methods for quantifying the risk associated with family history based on (1) the number of family members affected, (2) the degree of closeness of the relatives affected, and (3) early age at onset of disease.[50] As shown in Figure 1, this information could be used to stratify the population into average-risk (general population), moderate-risk (e.g., one first-degree relative affected at a late age), and high-risk groups (e.g., two or more affected first degree relatives or one affected first-degree relative with early age at onset).[50] Scheuner et al. showed that many more people in the general population fall in the moderate-risk group (30%–50%) of the population for the most common chronic diseases such as cancer, heart disease, and diabetes, compared with 10% or less who may fall in the high-risk groups (thereby meriting more extensive workup and possibly genetic evaluation for single-

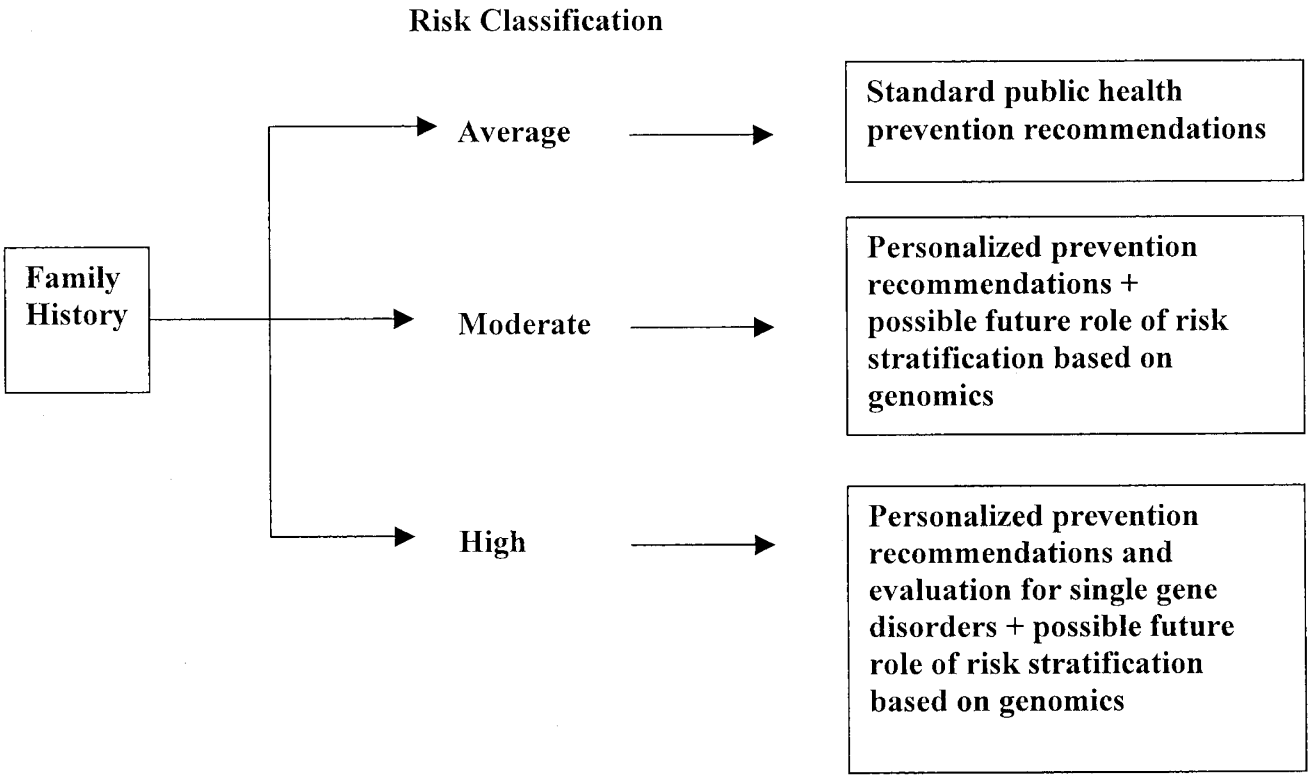

Fig. 1 Family history as a potential bridge between genetics and genomics in practice (adapted from Yoon et al.[52]).

gene disorders[50]). Interestingly, people with moderate family history risk for a certain disease have relative risks for the same disease that range from 1.5 to 10 (depending on the disease[49]), which is in the same range of many associations between common genetic polymorphisms and risks for various diseases, as illustrated in the hypothetical 2010 case scenario.[33] In addition, although there may be an unknown subset of the population with less than average risk of disease based on family history, that group would receive the same prevention recommendation targeted to the general population to avoid confusing public health messages.

To assess current evidence on utility of family history for disease prevention, CDC convened a multidisciplinary workshop in 2002 to discuss the use of family medical history for identifying persons at increased risk for common chronic diseases.[51] A research agenda emerged to assess the validity and utility of using family history to prevent common chronic diseases and for describing specifications of a family history tool that could be evaluated in different public health and clinical settings.[52] In the next few years, a family history risk-stratification tool will be tested as a guide to prevention activities (Fig. 1). Persons at average risk could be encouraged to adhere to standard public health prevention recommendations. Persons with increased risk (i.e., those classified as being at high and moderate risk) could be given personalized recommendations specific to their familial risk that might include assessment and modification of risk factors, lifestyle changes, alternative early detection strategies, and chemoprevention. Persons at high-risk may need a genetic assessment for possible single gene disorder that could include counseling, education, and possible genetic testing. Such persons also may benefit from receiving recommendations regarding screening and prevention appropriate for their risk. Perhaps, in the future, individuals at moderate or high-risk could be even further stratified for disease risks depending on the results of testing for multiple gene variants, or biochemical tests[33] (Such tests could also be used in the absence of family history as part of population-wide testing under specific circumstances[25]). It is noteworthy that the value of personalized prevention based on family history is likely to be highly variable depending on the particular condition and availability of prevention strategies. Therefore, conditions included in the initial family history public health research agenda will be those with existing prevention recommendations that could vary according to family history risk levels, as well as the relative accuracy of family history recall.[52]

Whereas targeting the general population with prevention efforts could be cost-prohibitive, targeting higher-risk individuals with these same efforts could prove to be cost-effective.[53] Certainly, one could argue that current public health approaches that promote healthy lifestyles and target the population-at-large have not been entirely successful. Recent studies reveal that more than 60% of people do not get enough physical activity,[54] 23% of the US population still smokes cigarettes,[55] 21% of people are obese,[56] and 44% adhere to recommendations related to colorectal cancer screening.[57] If people could be convinced on a more personal level of their need to improve their health based on a family history of chronic disease (and almost all of us have some family history of disease), they may be more likely to engage in healthy behaviors, although changing behavior as a result of genetic information has proved to be challenging,[58] and there may be concern that people at "average" risk may become more complacent in engaging in healthy behavior. Because of the relatively large fraction of people in the population with moderate family history risk, family-centered interventions that complement, but do not replace, existing prevention strategies could have a large public health impact on the burden of various diseases.[52,53,59] Family history can begin to build a genomic bridge between a public health approach to prevention (one size fits all) and a clinical genetic approach (one at a time).[59]

Can the current genetic services model apply to genomics?

Given the qualitative shift expected to occur between the concept of genetic disease to the concept of genetic information in all diseases, how much of our current genetic services model can still hold in the "omics" era under the various scenarios discussed above? Certainly, genetic information will become more complex and more difficult to interpret than a traditional single gene setting with known Mendelian expectations. Also, the probabilistic nature of disease prediction depends on the presence or absence of other genetic variation and a host of environmental, personal, and behavioral factors (such as age, ethnic group, use of drugs and medications, smoking, etc.). Today, we see the complexities of communicating probabilistic epidemiologic information in the context of *BRCA1/2* genetic testing for breast and ovarian cancer, with widely variable estimates of penetrance.[60] The complex nature of this information and its potential ethical, legal, and psychosocial implications make a strong case for genetic counseling in these instances. Nevertheless, the example of BRCA1 still represents an application of the classical paradigm of a "genetic disorder" albeit with incomplete penetrance of the genotype.

So how will "genetic services" look further along the continuum to genomics discussed above? How will communication of "genetic information" occur in the context of pharmacogenomics, for example, in using different medications, or adjusting the dose of a medication for the treatment or prevention of a condition we do not think of as genetic (e.g., the example of 6MP in the treatment of ALL discussed above)? How will we communicate disease risk information to individuals with moderate family history of disease, which constitute a substantial fraction of the general population (eventually all of us)? How will communication of genetic information occur in the context of interpreting complex gene expression profiles that may be associated with increased risk of future disease or prognosis from existing disease or response to therapy? Are the ethical, legal, and social implications of information on genetic disorders different from those for genetic information at multiple loci, gene expression profiles, and so on? What is the role of public health in assuring the use of genetic information in

the prevention of disease outside the traditional purview of newborn screening and delivery of genetic services?

The answers to such question are not quick or easy and do require further evaluation. If, in fact, genetic information will become a routine component of the practice of every day health care and disease prevention, health care providers and public health professionals will need to be equipped with the tools of evaluating and communicating complex genomic (and family history) information. The expected increasing uncertainty of the implications of genetic information in the "omics" era will necessitate a true integration of the fields of genetic counseling with health education and communication sciences.[61] The paradigm of genetic services will always apply for a small proportion of individuals and families that will need support and services for the management and understanding of specific disorders. However, a threshold between delivery of genetic services for "genetic disorders" and communication of "genetic information" as a routine component of practice will have to be delineated and established.

Concluding remarks

This article presented the continuum from genetics to genomics in the practice of medicine and public health in the post- Human Genome Project era. Genomics will challenge us with the necessity of using and communicating genetic information outside the existing paradigm of genetic services. Even today, family history illustrates how the traditional approach of finding and managing high-risk families will not address the much larger fraction of the population with moderately increased risk for various diseases, as a result of genetic variation at multiple loci, gene-environment interaction, and shared environments. As more multidisciplinary research delineates the value added of using genetic information in improving health outcomes and preventing human diseases, training the workforce in genomics should be a high priority in medicine and public health. Practitioners need to become more savvy in interpreting probabilistic genetic information that could be used in developing medical and behavioral interventions, health policy and financing, and occasionally population screening. In order to truly use genetic information in practice, creative processes for communicating complex genetic information need to be established. Government, academia, professional organizations, community groups, and the private sector should collaborate to conduct the necessary research, and to promote consensus on thresholds for using genomics and family history in practice, including testing, referral, and reimbursement. Only then, can we achieve a true integration of genetic information in the practice of medicine and public health in the 21st century.

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