EDITOR'S CHOICE

Genetic testing behavior and reporting patterns in electronic medical records for physicians trained in a primary care specialty or subspecialty

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ABSTRACT

Objective To characterize important patterns of genetic testing behavior and reporting in modern electronic medical records (EMRs) at the institutional level.

Materials and methods Retrospective observational study using EMR data of all 10 715 patients who received genetic testing by physicians trained in a primary care specialty or subspecialty at an academic medical center between January 1, 2008 and December 31, 2010.

Results Patients had a mean±SD age of 38.3±15.8 years (median 36.1, IQR 30.0—43.8). The proportion of female subjects in the study population was larger than in the general patient population (77.2% vs 55.0%, $p<0.001$) and they were younger than the male subjects in the study (36.5±13.2 vs 44.6±21.2 years, $p<0.001$). Approximately 1.1% of all patients received genetic testing. There were 942 physicians who ordered a total of 15 320 genetic tests. By volume, commonly tested genes involved mutations for cystic fibrosis (36.7%), prothrombin (13.7%), Tay—Sachs disease (6.7%), hereditary hemochromatosis (4.4%), and chronic myelogenous leukemia (4.1%). EMRs stored reports as free text with categorical descriptions of mutations and an average length of 269.4±153.2 words (median 242, IQR 146—401).

Conclusions In this study, genetic tests were often ordered by a diverse group of physicians for women of childbearing age being evaluated for diseases that may affect potential offspring. EMRs currently serve primarily as a storage warehouse for textual reports that could potentially be transformed into meaningful structured data for next-generation clinical decision support. Further studies are needed to address the design, development, and implementation of EMRs capable of managing the critical genetic health information challenges of the future.

BACKGROUND AND SIGNIFICANCE

Electronic medical records (EMRs) have enabled physicians to interact with complex medical information. The amount of genetic data will continue to grow rapidly with advances in genomic technology and for applications such as screening, diagnosis, prognostication, and prediction of response to treatment.[1–7] Physicians trained in internal medicine, pediatrics, obstetrics and gynecology, and family medicine will play a central role in applying genetic testing to clinical management.[8–10] These clinicians are expected to become major consumers of genetic and genomic data as testing becomes standard of care, and EMRs must be capable of allowing these physicians to effectively process this new type of information.[6 8 11]

Genetic results differ from traditional laboratory tests because of their persistent nature, broad scope, and complex interpretation.[12] While current EMRs present laboratory results in a structured and predictable format, genetic data are often stored as free text and presented as cumbersome, highly detailed reports.[12] This situation poses a potentially serious problem: if EMRs cannot accommodate the rapid growth of genomic data, the systems meant to improve patient outcomes could disrupt workflow and lead to suboptimal care.[8 12–14]

Building EMRs that can adapt to the genetic health needs of patients in the future requires understanding how patients and physicians consume genetic information today.[12 15 16] Studies that have addressed this issue were based on surveys or chart reviews that usually focused on a small group of genetic tests.[6 17 18] To our knowledge, a quantitative analysis of institution-wide de facto genetic test ordering and reporting in modern EMRs has not been performed, leaving a critical knowledge gap in health information system design.[8 18–21] The purpose of this study was to quantify genetic testing patterns that could lead to better ways of organizing clinically relevant genetic information in the EMR.

MATERIALS AND METHODS

Study population

The Research Patient Data Registry (RPDR) is a warehouse of patient EMR data from Massachusetts General Hospital (MGH). The RPDR stores information on patient encounters, diagnoses, demographics, medications, and diverse laboratory test information, including results from genetic testing.[22] This study focused on collecting information about patient demographics, the ordering physicians, and the types of genetic tests ordered.

We collected data on all patients at MGH who received genetic testing between January 1, 2008 and December 31, 2010 by physicians trained in a primary care specialty. Patients were of all ages, both genders, and any race/ethnic group. To avoid self-selection bias, patients satisfying the above criteria who were employees of the institution were excluded from the study.

Approval was obtained from the institutional review board of MGH, which waived the requirement for individual informed consent.

Data collection and definitions

Genetic testing was defined as any medical test focused on analysis and evaluation of patient DNA.[23 24] This study included information about any completed molecular genetic and cytogenetic test documented in the RPDR to investigate genetic mutations, insertions, deletions, trinucleotide repeats, rearrangements, and translocations. Genetic tests included somatic and germline tests run at laboratories within the institution as well as those sent to referral laboratories. A list of genetic tests ordered at the institution was collected from categorized laboratory test directories in the RPDR, as well as through manual search of uncategorized directories using the following keywords: gene, genetic, genotype, DNA, mutation, insertion, deletion, translocation, trinucleotide, repeat, rearrangement, panel, as well as other more focused terms (eg, warfarin, BRCA1, BRCA2, Factor V, Alzheimer's, Huntington's). The RPDR assigned a unique identifier to each patient who received genetic testing and provided additional information for each test including test name, genes tested, type of specimen collected, date the order was entered, and name of the ordering physician.

The Logical Observations Identifiers Names and Codes (LOINC) database is a standardized set of clinical and laboratory codes developed by the Regenstrief Institute in order to facilitate the exchange of clinical information between laboratories, hospitals, and other organizations.[25] The subset of the LOINC database (release version 2.34) describing the clinical components of each molecular genetic test was used to provide clinical annotation of genetic test results for patients in the study.

The National Plan & Provider Enumeration System (NPPES) is an online database developed by the Centers for Medicare & Medicaid Services to provide a standardized set of identifiers for healthcare providers.[26] Medical specialty information was collected from the NPPES to identify all physicians in the study who reported receiving training in a primary care specialty or related subspecialty.[27] A primary care specialty was defined as family medicine, internal medicine, pediatrics, and obstetrics and gynecology, consistent with the definitions described by the Institute of Medicine and the American Board of Medical Specialties.[28 29]

Statistical analysis

Summary statistics were collected for continuous demographic data as means with standard deviations and medians with IQR. Frequencies and percentages were calculated for categorical data involving patient demographics, provider specialties, and ordered genetic tests. Two-sample t tests were used for continuous variables, while differences in categorical variables (gender according to age and race/ethnic group categories) were evaluated using χ^2 tests.

A two-sided p value <0.05 was considered significant. All analyses were performed using JMP version 9.0 (SAS Institute).

RESULTS

General patient characteristics

Between 2008 and 2010, physicians ordered molecular genetic tests for a total of 10 715 unique patients seen in the inpatient or outpatient setting (table 1). Patients had a mean age of 38.3±15.8 years (median 36.1, IQR 30.0–43.8), with 1353 (8.8%) patients under the age of 18 years. Female patients made up 77.2% of the 10 715 patients who received genetic testing over the study period, a proportion higher than that seen in the general patient population (55.0%, p<0.001). The race/ethnic group distribution included white (69.4%), Hispanic (15.0%), Asian or Pacific Islander (6.7%), black (5.2%), American Indian (0.1%), other (1.0%), and unknown (2.5%), which also differed from the general patient population (p<0.001). Using the most currently available patient population totals (2008–2009), we found that ~1.13% (7450 / 659 066) of patients seen at our institution received molecular genetic testing.

The 50–59 year group made up the largest age category for male patients, while 20–29 and 30–39 years were most common female age groups, totaling ~67% of all female patients. Male patients were significantly older than female patients (p<0.001), and there was a strong association between age category and gender (p<0.001), as well as between race/ethnic group category and gender (p<0.001).

Table 1 Characteristics of patients receiving genetic testing from 2008 to 2010

Characteristic	Female (n=8277)	Male (n=2438)	p Value
Age group (years), No (%)			
0–9	166 (2.0)	236 (9.7)	
10–19	316 (3.8)	145 (5.9)	
20–29	1682 (20.3)	152 (6.2)	
30–39	3869 (46.7)	424 (17.4)	<0.001
40–49	1303 (15.7)	425 (17.4)	
50–59	371 (4.5)	440 (18.0)	
60–69	299 (3.6)	346 (14.2)	
70–79	166 (2.0)	190 (7.9)	
80–89	94 (1.1)	73 (3.0)	
90+	11 (0.1)	7 (0.3)	
Age (years), mean±SD	36.5±13.2	44.6±21.2	<0.001
Age (years), median (IQR)	35.0 (29.7–40.7)	45.8 (32.3–60.2)	
Race or ethnic group, No (%)			
White	5417 (65.4)	2022 (82.9)	
Black	466 (5.6)	91 (3.7)	
Hispanic	1457 (17.6)	154 (6.3)	
American Indian	7 (0.1)	5 (0.2)	<0.001
Asian or Pacific Islander	660 (8.0)	58 (2.4)	
Other	91 (1.1)	16 (0.7)	
Unknown	179 (2.2)	92 (3.8)	

Physician specialty and testing behavior

There were a total of 942 uniquely identifiable physicians, with 650 (69%) reported as being trained in internal medicine, 162 (17.2%) in pediatrics, 95 (10.1%) in obstetrics and gynecology, and 35 (3.7%) in family medicine (table 2). The number of ordering physicians in internal medicine was more than twice as large as in the other primary care specialties combined in every year studied. More specifically, the group of internal medicine physicians was 3.7–4.8 times larger than pediatric, 5.7–6.1

Table 2 Number of ordering providers and ordered genetic tests by year, stratified by medical specialty

Providers/tests	2008	2009	2010
Providers, No (%)			
Internal medicine	365 (66.7)	356 (69.1)	373 (71.2)
Pediatrics	100 (18.3)	93 (18.1)	77 (14.7)
Obstetrics and gynecology	64 (11.7)	57 (11.1)	61 (11.6)
Family medicine	18 (3.3)	9 (1.7)	13 (2.5)
Genetic tests, No (%)			
Internal medicine	1380 (26.5)	1425 (26.6)	1187 (24.9)
Pediatrics	721 (13.8)	757 (14.1)	642 (13.5)
Obstetrics and gynecology	3068 (58.9)	3159 (59.0)	2905 (61.1)
Family medicine	37 (0.7)	15 (0.3)	24 (0.5)

times larger than obstetrics and gynecology, and 20.3–39.6 times larger than family medicine each year.

There were a total of 15 320 genetic tests ordered for patients between 2008 and 2010 (table 2). While internists consistently outnumbered the other primary care specialties, obstetricians and gynecologists alone ordered roughly two-thirds of the total genetic test volume. Specifically, the number of genetic tests ordered by physicians in obstetrics and gynecology was more than two times larger than in internal medicine and four times larger than in pediatrics each year. The relative difference in volume compared with family medicine was even greater, ranging from 82.9 to 210.6 times larger per year.

Characteristics of genetic test samples

There were 236 different types of genetic tests ordered, evaluating 220 (93.2%) genetic mutations, 12 (5.1%) trinucleotide repeats, two (0.8%) translocations, one (0.4%) rearrangement, and one (0.4%) deletion. The number of genetic tests ordered by physicians in pediatrics (170) and internal medicine (150) were similar and larger than for either obstetrics and gynecology (44) or family medicine (28). By volume, patients received a total of 14 333 (93.6%) evaluations for genetic mutations, 630 (4.1%) for translocations, 305 (2.0%) for trinucleotide repeats, 50 (0.3%) for rearrangements and two (0.01%) for deletions.

Approximately 15 090 (98.5%) genetic tests were performed on blood samples, with the remainder performed on 57 (0.4%) blood/urine, 15 (0.1%) amniotic fluid, 60 (0.4%) bone marrow, two (0.0%) buccal cell swab, 37 (0.2%) cerebrospinal fluid, three (0.0%) urine, and 56 (0.4%) other/unknown samples.

Structure of genetic test reports

Genetic test reports were commonly represented as free text in the EMR. The complexity of the reported results ranged from as few as three words ('no mutation detected') to over 4300 words. The mean±SD length of all reports was 269.4±153.2 words (median 242, IQR 146–401).

Reports were usually composed of clearly labeled sections that described multiple aspects of a test result, although no standard reporting format was used by all laboratories. A specific 'results' section appeared in most genetic reports whose exact contents depended on the type of test. Evaluations of single gene mutations presented results as binary categories (positive/negative, present/absent, detected/not detected, normal/abnormal), while reports for more complex gene sequencing were longer and more detailed. Evaluations of DNA sequence variants listed the associated nucleotide, codon and amino acid changes, and also indicated if any detected variant was heterozygous. Finally, numerical values and reference ranges were used mostly for testing for conditions related to trinucleotide repeat expansions.

The 'interpretation' section provided further clarification of results by describing the diseases, disorders, and phenotypes of positive results, and indicated whether DNA variants were 'disease-associated' or 'of unknown significance'. When a sequence variation was not found, a qualitative or quantitative assessment of the clinical implications of a negative result was often provided as well.

Other commonly provided sections of the genetic test report described the laboratory name and address, clinical indications for testing, and recommendations for genetic counseling. A 'methods' section was often used to describe how DNA was isolated and analyzed, which regions of a gene were amplified, and the technologies used to detect mutations or perform sequencing. Most genetic reports also had a detailed 'comments' section that described the limitations of the test, the sensitivity/specificity of the analysis, mutation detection rates in the population, and references to research articles for additional information.

Sub-analysis of types of genetic tests ordered

The 20 most frequently ordered tests accounted for ~88.3% of the total volume of all genetic tests (table 3). However, the relative contributions of these tests to the volume of a given specialty were not homogeneous. While the top 20 tests accounted for 83.5% and 99.5% of the total volume for internal medicine and obstetrics and gynecology, they contributed slightly smaller amounts of 50% and 67% for pediatrics and family medicine, respectively.

The genetic test for cystic fibrosis (nominal classification) was ordered most frequently, accounting for 36.7% of the overall volume as well as being more than 2.6 times larger than the second most commonly ordered genetic test for prothrombin and over 5.4 times larger than the test for Tay–Sachs disease (table 3). By specialty, physicians trained in internal medicine evaluated the prothrombin gene 2.7 and 2.8 times more often than hereditary hemochromatosis and chronic myelogenous leukemia, respectively. Cystic fibrosis (nominal classification) accounted for over half of the genetic tests in obstetrics and gynecology, and was 5.4 times larger than the next most frequently ordered test for Tay–Sachs disease. Pediatricians tested for the prothrombin mutation most often, although its relative difference in test frequency to the remaining genes was less dramatic. Family physicians ordered relatively few tests overall, with three genetic tests (hemochromatosis, prothrombin, cystic fibrosis) accounting for 60.5% of the test volume.

Stratified by age group, the most frequently ordered genetic test between 10 and 50 years of age was for cystic fibrosis, while prothrombin was the most common test for every age group after 50 years. Between 60 and 90 years, the second and third most commonly ordered tests were consistently for chronic myelogenous leukemia and hereditary hemochromatosis, respectively. Prothrombin remained in the top three most commonly ordered genetic tests for every single decade of life.

DISCUSSION

Effective genome-enabled EMRs must be designed with a strong understanding of who the target audience is and how this audience plans to use the new system.[8] To our knowledge, this is the first study to provide an extensive assessment of electronically documented genetic testing behavior on patients treated by physicians trained in a primary care specialty. Our study is timely given the increasing adoption of EMRs and the rapid advances in genomic research just a decade after the human genome was sequenced.[8]

The large proportion of young female patients in our study suggests a strong parental concern about the potential health risks to offspring and the increased visibility of genetic testing to address those risks.[30] In particular, more than half of the tests for cystic fibrosis alone were ordered within the clinical context of physicians trained in obstetrics and gynecology. Furthermore, prenatal and preconception carrier screening for conditions such as cystic fibrosis and Tay–Sachs disease, for example, are commonly accepted applications that have been recommended by medical groups for years.[30–32] In addition, most genetic tests in our study involved conditions diagnosed early in life where treatments often lead to decreased morbidity or mortality, knowledge that can strongly influence a parent's decision to be

Table 3 Summary of the 20 most frequently ordered genetic tests according to ordering physician medical specialty

Gene evaluated (clinical component)	Total	Internal medicine	Obstetrics and gynecology	Pediatrics	Family medicine*
CFTR† (cystic fibrosis)	5625 (36.7)	250 (6.3)	5262 (57.6)	102 (4.8)	11 (14.5)
F2 (prothrombin)	2102 (13.7)	1675 (42)	194 (2.1)	218 (10.3)	15 (19.7)
HEXA (Tay–Sachs disease)	1028 (6.7)	18 (0.5)	969 (10.6)	39 (1.8)	2 (2.6)
HFE (hereditary hemochromatosis)	672 (4.4)	616 (15.4)	5 (0.1)	31 (1.5)	20 (26.3)
BCR-ABL (chronic myelogenous leukemia)	629 (4.1)	606 (15.2)	1 (0)	22 (1)	–
ASPA (Canavan disease)	470 (3.1)	14 (0.4)	416 (4.6)	39 (1.8)	1 (1.3)
DYS (familial dysautonomia)	458 (3)	8 (0.2)	408 (4.5)	41 (1.9)	1 (1.3)
GBA (Gaucher disease)	365 (2.4)	23 (0.6)	281 (3.1)	61 (2.9)	–
FMR1 (fragile X syndrome)	279 (1.8)	21 (0.5)	172 (1.9)	86 (4.1)	–
SMPD1 (Niemann–Pick disease)	271 (1.8)	7 (0.2)	226 (2.5)	38 (1.8)	–
FRAXE (fragile X syndrome)	268 (1.8)	8 (0.2)	198 (2.2)	61 (2.9)	1 (1.3)
G6PD (glucose-6-phosphate dehydrogenase deficiency)	213 (1.4)	11 (0.3)	163 (1.8)	39 (1.8)	–
MCOLN1 (mucolipidoisis IV)	208 (1.4)	5 (0.1)	165 (1.8)	38 (1.8)	–
BLM (Bloom syndrome)	206 (1.3)	5 (0.1)	164 (1.8)	37 (1.8)	–
FANCC (Fanconia anemia)	202 (1.3)	6 (0.2)	158 (1.7)	38 (1.8)	–
MTHFR C677T (vascular risk)	130 (0.9)	20 (0.5)	102 (1.1)	8 (0.4)	–
MTHFR A1298C (vascular risk)	128 (0.8)	20 (0.5)	100 (1.1)	8 (0.4)	–
CFTR‡ (cystic fibrosis)	104 (0.7)	33 (0.8)	10 (0.1)	61 (2.9)	–
HBA1 (α thalassemia)	100 (0.7)	2 (0.1)	93 (1)	5 (0.2)	–
HTC2 (hypertrichosis)	98 (0.6)	1 (0)	1 (0)	96 (4.5)	–
<top 20	1764 (11.7)	643 (16.5)	44 (0.5)	1052 (49.6)	25 (33.0)

Values are number (%).
*Empty cell indicates genetic test was not ordered.
†Nominal genetic test classification (coded report).
‡Narrative genetic test classification (text report).

tested.[7 30] Interestingly, the volume of pediatric patients who underwent genetic testing was small relative to adults, especially given the large number of childhood genetic disorders.[9] One possible explanation could be the low prevalence of many diseases of childhood; the volume of pediatric patients could then be further overshadowed by testing for adult conditions that occurred much more often in the general population.[5] By understanding the target patient population and their motivations for testing, EMR content can be organized and personalized to better address the needs of patients.

A survey of physicians in the USA revealed that ~60% of primary care providers practicing more than half-time have ordered at least one genetic test.[6] A diverse group of physicians at our institution were similarly involved with genetic testing, with our study further describing the relative contributions of each primary care specialty. While internal medicine was the largest group, obstetrics and gynecology ordered the largest volume of tests. Furthermore, despite a clear disparity in size between internal medicine and pediatrics, the number of unique tests ordered by each group was remarkably similar. Interestingly, several important tests ranked outside of the 'top 20' ordered at our institution, including genetic evaluations for breast cancer and Factor V Leiden.[17 18] In the case of breast cancer, it is possible that physicians referred patients to specialists outside the scope of our analysis who may have ordered BRCA testing instead of the physicians in our study.[6] In practice, clinicians also commonly order prothrombin testing together with, or as a reflex to, Factor V Leiden, making the discrepancy between the ordered volumes of these two tests potentially concerning.[33] Future studies will be needed to explore these findings in greater depth, particularly how testing behavior may be influenced by physician differences in genetics expertise, clinical reasoning, and workflow.[19 30] As the clinical utility of genetic testing improves, EMRs must provide an efficient, intuitive and comprehensive information interface at the point of care in order to gain widespread acceptance and adoption.[34]

The nature of patient genomic data distinguishes genetic results from laboratory tests and presents an unprecedented challenge for physicians managing patient information in the future.[12] The clinical value of traditional laboratory results is transient and degrades with time, while the meaning of findings in other results (eg, radiology reports) remains static after being interpreted. In contrast, genetic information persists over a patient's lifetime but must be reinterpreted as new research and disease correlations are discovered over time.[12] Furthermore, the large variation in the length, structure, and content of genetic test reports highlights a critical shortcoming in the ability of current EMRs to store genetic information. The absence of a structured and standardized reporting format could obscure important results and increase the risk of misinterpreting information communicated to patients or used in clinical decision-making.[19] The current generation of EMRs will need to make significant changes to allow this constantly evolving form of information to be ready for widespread physician consumption.[12] An informatics approach using natural language processing or other techniques could possibly be used to transform genetic reports into meaningful structured data.[21 35–37] This information could then potentially be utilized for more effective genetic results navigation, quality improvement studies, and clinical decision support capable of dynamic reinterpretation of genomic data.[21 35 38 39] While the complexity of genetic results may increase the information that physicians must integrate into their practices, EMRs could serve as a bridge to better organizing, understanding, and using these new data to improve patient health.[8]

Our study had several limitations. First, potentially useful physician information was not available for analysis, including years of formal training, duration of practice, and additional genetics instruction; data on total physician volume would have also provided a more complete view of the contributions of each medical specialty. Second, since the NPPES required physicians to select only one specialty as their primary field of practice, misclassification of physicians trained in multiple fields and an

underestimation or overestimation of the test count was possible. However, the data suggest this applied to only a small number of physicians in our study and we believe it is unlikely any misclassifications would have dramatically changed our conclusions. Third, the findings may not be generalizable and we acknowledge that attempting to classify genetic testing data from the EMR of a single institution will be imperfect and give patient, provider, and genetic test characteristics that will likely differ across organizations.[40] Finally, the LOINC coding system, in its current form, limited our ability to accurately classify every genetic test result in the EMR. Although widely adopted and capable of describing most laboratory results, the LOINC system currently has gaps for cytogenetic results that may lead to potential under-representation of such tests in our analysis.[40] As laboratory coding standards continue to improve in their ability to describe the rapidly growing body of genetic test categories, more comprehensive evaluations will likely become possible over time. Regardless, we believe our study provides critical insight as an assessment of institutional molecular genetic testing behavior, highlights the importance of more structured and standardized genetic data in EMRs, and lays the groundwork for more comprehensive studies in the future.

CONCLUSION

In our study, genetic tests were often ordered by a diverse group of physicians for women of childbearing age being evaluated for diseases that may affect potential offspring. EMRs currently serve primarily as a storage warehouse for textual reports that could potentially be transformed into meaningful structured data for next-generation clinical decision support. Further studies are needed to address the design, development, and implementation of EMRs capable of managing the critical genetic health information challenges of the future.

Contributors All authors included in the manuscript provided substantial contribution to (1) conception and design, acquisition of data or analysis and interpretation of data, (2) drafting the article or revising it critically for important intellectual content, and (3) final approval of the completed manuscript.

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