Genetic tests are routinely ordered by health care providers (HCPs) within a wide range of medical specialties. Many providers have limited knowledge or experience with ordering and interpreting genetic tests; thus, test order errors are common. Rigorous review of genetic test orders by genetic counselors (GCs) can provide a direct financial benefit to medical institutions, patients and insurers. GCs at ARUP (Associated Regional University Pathologists) Laboratories routinely perform a pre-analytic assessment of complex molecular genetic test orders that includes reviewing clinical and family history information and considering the clinical utility and cost-effectiveness of ordered tests. GCs contact the ordering institution and/or HCP as needed to collect additional clinical information and confirm the test order or suggest alternative testing based on the provided information. A retrospective review of the GC-facilitated test changes over a 21-month period at ARUP laboratories was performed. Approximately 26% of all requests for complex genetic tests assessing germ line mutations were changed following GC review. Testing fees associated with canceled tests were summed to estimate the cost-savings resulting from GC-facilitated test reviews. The test review process resulted in an average reduction in charges to the referring institutions of $48,000.00 per month. GC review of genetic test orders for appropriateness and clinical utility reduces healthcare costs to hospitals, insurers, and patients. © 2014 Wiley Periodicals, Inc.

Key words: genetic counselors; misordered tests; molecular genetic testing; health care costs; test order review

INTRODUCTION

Genetic testing serves an increasingly important role in diagnosis and management of disease. However, genetic tests are frequently misordered, resulting in additional costs, delayed results, diagnosis, and treatment. In its 2009 recommendations for best practices in genetic testing for heritable diseases, the Centers for Disease Control and Prevention (CDC) identified that more errors occur during the pre-analytic and post-analytic phases of testing than during the analytic process itself. Many pre-analytic errors are due to inappropriate test selection [CMS, 2010]. The CDC recommends that laboratories help their clients with selection of appropriate tests and collect patient information needed for proper testing and result interpretation. In this study, we highlight how genetic counselors (GCs) in a reference laboratory decrease inappropriate healthcare expenditures by performing pre-analytic genetic test assessments.

Approximately 9% of the 3,000 GCs employed in the United States (US) work in a diagnostic laboratory [NSGC, 2010]. The remaining 91% work in a variety of settings, of which hospitals and clinics make up the majority. There are currently only 32 highly specialized masters-degree programs for training GCs in the US [ACGC, 2013]. Additionally, as of 2007, there were only 1,100 practicing M.D. clinical geneticists in the US [The Personal Genome, 2007]. Due to the small numbers of genetic health care professionals, as well as lack of patients’ proximity to tertiary care centers, many populations do not have access to genetic services; thus, genetic testing is commonly ordered by primary care providers. A recent Council of Academic Family Medicine Educational...
Research Alliance study found that 54% of academic family physicians do not feel knowledgeable about available genetic tests and 43% feel only somewhat knowledgeable [Mainous et al, 2013]. If genetic tests are ordered by health care providers (HCPs) who are not familiar with genetic testing, this may increase the chance that such tests are misordered.

A study by Giardiello et al. [1997] showed that 17% of adenomatous polyposis coli (APC) gene testing for familial adenomatous polyposis (FAP) was unnecessary. If testing is performed that is not appropriate for the patient’s clinical symptoms or family history, healthcare dollars are squandered and in many cases, the medically-indicated test(s) will still need to be performed. This results in additional testing costs as well as possible delays in diagnosis and treatment. GCs, or other health professionals with expertise in genetics, are in a unique position to be able to evaluate genetic test orders for clinical appropriateness and cost-effectiveness.

GCs employed by commercial laboratories are typically involved with both the pre- and post-analytic processes of genetic testing to support the laboratory and its clients. In the preanalytic phase, they work with the laboratory’s research and development teams in the consideration of new tests, help determine the most cost-effective and clinically useful ways to offer new tests, and develop educational materials and testing algorithms. GCs in laboratories are also involved in the post-analytic processes of testing by aiding in the interpretation of test results [Scacheri et al., 2008]. GCs contact ordering HCPs to explain complex results, answer questions for providers who contact the laboratory, and assist providers in determining when additional testing may be helpful to further clarify a patient’s diagnosis. The task of identifying genetic test errors via pre-analytic test review should not be designated only to laboratory GCs, but could also be performed by GCs at referring hospitals or payer organizations.

This article describes the outcomes of our experience with implementing a systematic pre-analytic genetic test assessment. The objectives of this study were to quantify the volume of molecular genetic tests changed by GCs, identify which tests were most frequently misordered and estimate potential cost-savings to the health care system resulting from cancelation of misordered tests.

**MATERIALS AND METHODS**

Seven GCs employed by Associated Regional University Pathologists (ARUP) Laboratories, a national reference laboratory, performed a pre-analytic assessment of daily test orders for most complex germ line molecular genetic sequencing and deletion/duplication tests performed in-house. Cytogenetic, genomic microarray, and the majority of biochemical genetic testing were not included in this data set, as pre-analytic test review for these tests is initiated using different protocols. Because of the rapid turnaround time for the beta globin (HBB) and connexin 26 (GJB2) gene sequencing tests, these orders are not routinely reviewed prior to initiating testing; therefore, they were not included in this analysis. Upon receipt of complex molecular germ line test orders, routine ARUP procedures for sample accessioning and order processing were followed and tests were added to a laboratory work list. Laboratory technicians identified the test orders requiring pre-analytic assessment by a GC, and the sample accession numbers were entered into a case management software program for GC review.

The GCs retrieved scanned images of all paperwork submitted at the time of order. Such documents may have included a test requisition, an ARUP test-specific “Patient History Form” detailing relevant clinical and family history, family pedigrees, and/or results of previous testing performed for the patient or family members. GCs also searched, using the patient’s name and demographic information, within ARUP’s internal database of pending and completed tests to view results of testing performed previously for the patient and to attempt to identify duplicate test orders.

Clinical information submitted by the HCP, relevant patient demographics (such as age and sex), and previous test results were used to determine the clinical utility and cost-effectiveness of the test ordered. A standardized ARUP protocol with disease-specific criteria for genetic test review was used to evaluate the appropriateness of each order. This protocol was created by ARUP’s GCs using prior knowledge about common test ordering errors, clinical utility and performance characteristics of specific tests and published testing guidelines. Themes for determining the appropriateness of test orders included: selection of the most cost-effective testing methodology when multiple tests are applicable to the clinical question being posed, review of previous test results to avoid duplicate testing and to confirm that the sequence of testing is reasonable, identification of other tests that may be confused with the ordered test, confirmation that the test ordered is appropriate given the patient’s age, sex, ethnicity, clinical findings and family history, and application of professional or consensus guidelines that provide testing strategies. When new sequencing and/or deletion/duplication tests are developed in the laboratory, GCs update the protocol to include criteria for assessing the new tests. An example of disease-specific assessment criteria for hemophilia A testing is provided in Figure 1.

When additional information was required to perform an assessment of a genetic test order, GCs would contact the referring laboratory to request contact information for the ordering HCP. If the referring laboratory was able to provide the HCP’s contact information and permitted ARUP to contact their clinicians directly, the GC would then call the HCP to clarify the desired test(s) or suggest alternative testing based on the provided information. Less commonly, the referring laboratory preferred to facilitate all communication with their HCPs; thus, ARUP’s GCs would communicate the need for additional clinical information to staff at the referring laboratory. If the test order(s) appeared appropriate for the clinical scenario, the GC documented the clinical and family history information in an internal database and notified the laboratory technicians to run the testing as ordered. If the provided information suggested that the ordered testing may not be the most appropriate testing strategy for the clinical scenario, the GC would propose an alternative test choice to the HCP based on the established assessment criteria. If the HCP wished to modify the test order following consultation with the GC, the requested test change would also be approved by the referring laboratory prior to being implemented. Test change requests were documented in the ARUP’s laboratory information system (LIS) using an editable template that allowed the GC to define the specific change(s) using ARUP test codes and mnemonics, document who authorized the
change(s), categorize each change according the reason it was requested, and document which GC performed the assessment. The general categories of genetic test changes, misorder, improved, and other, along with the specific subcategories (see Table I) were defined by ARUP’s GCs prior to the initiation of this study. On average, GCs were able to assess and implement any necessary changes for three to four genetic tests per hour.

Data regarding GC-facilitated test changes were extracted from the ARUP LIS over a 21-month period between April 2010 and December 2011 using Crystal Report Designer software to identify

FIG. 1. Flow chart for assessing hemophilia A sequencing and deletion/duplication test orders.
special characters included in the GC test change template. A retrospective audit of the data was performed by a single GC to ensure consistency in categorization of the test changes according to the reason for the change, among all GC reviewers.

A cost analysis was performed for test changes resulting from GC test review. Misordered tests were defined by this study as tests that would not have answered the clinical question being posed; did not represent the most cost-effective methodology to obtain the desired information; were duplicates; or would have likely yielded inconclusive results due to the receipt of a compromised specimen. If performed, misordered tests would have resulted in wasted healthcare resources. This analysis focused exclusively on the monetary amount that would have been billed to referring laboratories had misordered tests been processed as requested. Non-monetary benefits occurring as a result of GC-facilitated test changes, such as improvements in patient care or more timely diagnoses were not considered. The cost-savings to referring laboratories was calculated by adding the testing fees associated with the misordered tests. If the test canceled would not have provided the needed information (e.g., testing for an incorrect disorder was requested) the entire fee associated with the incorrect test was included in the cost-savings calculation. If the misorder involved canceling a test because it was not the most cost-effective method to obtain the desired information (e.g., canceling full gene sequencing and ordering a familial mutation test), the cost savings was calculated by subtracting the fee of the cost-effective test from the fee of the initially requested test. Our cost analysis did not consider the monetary impact of test changes which were categorized as “improved” or “other” (see Table I), because such changes were not considered errors which would result in wasted health care resources (i.e., misorders). Thus, our cost analysis does not reflect the net financial impact of pre-analytic GC test assessment to ARUP’s referring laboratories.

This research was exempt from IRB review as defined by the University of Utah IRB committee.

RESULTS

Test Changes by Genetic Counselors

An average of 99 molecular test changes per month were facilitated by GC review during the 21-month study period. Approximately 26% of all requests for complex molecular genetic tests assessing germline mutations were changed following GC review. Test changes were categorized as misorders (61%), improvements (34%), or other types of modifications (5%) (Table I).

Misorders

We determined that misordered tests fell into eight subcategories, which are also listed with their relative frequencies in Table I. Of all misorders documented in this study, 32% resulted in the canceling of an incorrect test and the ordering of a replacement test. An example includes canceling a test order for \textit{ACVRL1} and \textit{ENG} gene sequencing for hereditary hemorrhagic telangiectasia (HHT) when the desired test was actually a mutation panel for a disorder with a similar sounding name, hereditary hemochromatosis (HH).

<table>
<thead>
<tr>
<th>Category (% of total)</th>
<th>Percentage within category(^a)</th>
<th>Subcategory</th>
<th>Percentage of all changes(^b)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Misorder [61%]</td>
<td>32</td>
<td>Canceled incorrect test, added appropriate test</td>
<td>20</td>
</tr>
<tr>
<td></td>
<td>22</td>
<td>Canceled incorrect test, no additional testing requested</td>
<td>13</td>
</tr>
<tr>
<td></td>
<td>16</td>
<td>Canceled gene sequencing, added targeted panel</td>
<td>10</td>
</tr>
<tr>
<td></td>
<td>13</td>
<td>Canceled gene sequencing, added targeted test for familial mutation</td>
<td>8</td>
</tr>
<tr>
<td></td>
<td>11</td>
<td>Canceled incorrect test, facilitated send-out for test not performed in-house</td>
<td>7</td>
</tr>
<tr>
<td></td>
<td>5</td>
<td>Canceled a previously performed test/duplicate order</td>
<td>3</td>
</tr>
<tr>
<td></td>
<td>0.8</td>
<td>Canceled test no longer necessary, based on the result of previous testing</td>
<td>0.5</td>
</tr>
<tr>
<td></td>
<td>0.2</td>
<td>Canceled test as sample was compromised or insufficient</td>
<td>0.1</td>
</tr>
<tr>
<td>Improvement [34%]</td>
<td>40</td>
<td>Canceled test and added a more comprehensive version</td>
<td>14</td>
</tr>
<tr>
<td></td>
<td>42</td>
<td>Added a test based on results of previous testing</td>
<td>14</td>
</tr>
<tr>
<td></td>
<td>18</td>
<td>Added a test requested by HCP</td>
<td>6</td>
</tr>
<tr>
<td>Other [5%]</td>
<td>30</td>
<td>Clarified patient demographics</td>
<td>1.6</td>
</tr>
<tr>
<td></td>
<td>27</td>
<td>Miscellaneous</td>
<td>1.5</td>
</tr>
<tr>
<td></td>
<td>14</td>
<td>Canceled due to lack of appropriate consent form</td>
<td>0.8</td>
</tr>
<tr>
<td></td>
<td>13</td>
<td>Test is not performed at ARUP, aided in sendout</td>
<td>0.7</td>
</tr>
<tr>
<td></td>
<td>6</td>
<td>Sample issue, aided in obtaining second sample</td>
<td>0.3</td>
</tr>
<tr>
<td></td>
<td>5</td>
<td>Test not NY approved, aided in sendout</td>
<td>0.3</td>
</tr>
<tr>
<td></td>
<td>4</td>
<td>Revised test orders to improve laboratory processing/reporting</td>
<td>0.2</td>
</tr>
</tbody>
</table>

\(^a\)The subcategories describing the specific types of misorders, improvements, or other modifications are ranked by percent of test changes within each respective category.

\(^b\)Test changes in each subcategory calculated as a percent of the total volume of test changes.
In 16% of misordered tests, full gene sequencing was ordered when a mutation panel was more appropriate. The most common example of this was when cystic fibrosis transmembrane regulator (CFTR) gene sequencing was ordered erroneously on an obstetric patient for routine carrier screening. The American College of Medical Genetics recommends that a 23 mutation panel be offered to asymptomatic obstetric patients undergoing routine cystic fibrosis (CF) population screening, not full gene sequencing [Watson et al., 2004].

In 13% of misorders, full gene sequencing and/or deletion/duplication testing was ordered when the familial mutation was known. This misorder commonly occurred when a patient had a family history of a dominant disorder (e.g., multiple endocrine neoplasia type 2 (MEN2), von-Hippel Lindau (VHL) syndrome, Lynch syndrome) or was at risk to be a carrier of an X-linked disorder (e.g., hemophilia A or hemophilia B). Laboratory GCs contacted ordering HCPs to encourage them to obtain necessary documentation of the familial mutation so targeted testing could be substituted for the full gene sequencing and/or deletion/duplication test.

In 11% of misorders, an ARUP test was incorrectly ordered when the appropriate test was not performed at ARUP. In these cases a GC assisted the HCP in selecting the correct test and coordinated sending the sample to the performing laboratory. An example would include a HCP who wanted to test for Charcot–Marie– Tooth (CMT) Type 1A, which requires copy number analysis of the PMP22 gene, but instead ordered LMNA gene sequencing which detects mutations associated with CMT Type 2B1.

Finally, 5% of misorders were related to duplicate test orders. Genetic testing rarely needs to be repeated. Nearly all duplicate test orders observed were not purposeful but due to order error. An example of such was an order for ARUP’s hereditary pancreatitis panel which includes sequencing of CFTR, PRSS1, and SPINK1, when CFTR had been previously sequenced, either at ARUP or an outside laboratory. In this scenario, the panel was canceled and sequence analysis for only the two previously unanalyzed genes was ordered.

**Improvements and Other**

The 34% of test changes categorized as improvements involved the addition of tests, when the ordering HCP failed to initially order the most sensitive or cost-effective test, when previous testing failed to provide a diagnosis, or when the HCP requested additional testing. The 5% of the test modifications classified as “other” involved activities that often did not involve adding on tests or substituting one test for another, but are important to the overall testing process. These changes included: correcting patient identifiers to ensure accurate reporting, canceling requests for predictive Huntington disease testing if informed consent was not documented, and requesting additional samples if the first was suboptimal.

**Most Commonly Misordered Tests**

Table II shows the top five most frequently misordered tests ranked by number of tests canceled. The percentage of cancelations for each test category is detailed in column 3. For the purpose of this comparison, all CF tests, with the exception of the CF 32 mutation panel, were combined into a single representative test category: “cystic fibrosis”, and the five available Lynch syndrome genetic tests were combined into a group: “Lynch syndrome”. Cystic fibrosis had the largest number of misordered tests mainly due to the high volume of CF tests ordered. Alpha globin sequencing and neurofibromatosis deletion/duplication analysis had the highest proportion of test misorders.

**Cost Savings to Health Care System**

The healthcare cost-savings from the cancelation of misordered tests averaged $48,000 per month to the referring institutions, totaling almost $1.2 million over the course of the study. The average cost savings per misordered test was $792.

**DISCUSSION**

Several studies have shown that laboratory test order errors are common [Giardello et al., 1997; Riegert-Johnson et al., 2008; Mayo Clinic, 2010]. Our study supports these findings by demonstrating that approximately 26 percent of complex molecular test orders at a national reference laboratory over a 21-month period required modification.

Test changes were classified as misorders (61%), improvements (34%), or other (5%). Misordered tests are those that would not have answered the clinical question being posed, would have answered the question but not in the most cost-effective manner, or were duplicate orders. Because molecular germ line sequencing and deletion/duplication tests are generally expensive compared to other types of laboratory testing, processes to identify errors in genetic test selection and ordering result in significant cost-savings even when overall test volumes are comparatively low.

**Tests Commonly Misordered**

As shown in Table II, the most commonly misordered test group was cystic fibrosis. The typical error was a request for CFTR gene sequencing, with or without deletion/duplication analysis, when a mutation panel for routine carrier screening in an obstetric patient was the more appropriate test. In our experience, the cause of this misorder was usually a miscommunication between the HCP and
the referring laboratory. Use of preprinted requisition forms and specific test codes by ordering HCPs might improve this communication and reduce these errors.

Alpha globin gene sequencing was the second most commonly misordered test. In the case of alpha globin, approximately 90% of mutations are due to seven common large deletions that are not detectable by sequencing Galanello et al. [2011]. The best first line molecular test for alpha thalassemia is most often analysis for large alpha globin gene deletions. However, alpha globin gene sequencing was often mistakenly requested (58% of alpha globin orders) when the provider desired analysis for the common alpha globin gene deletions. The very high rate of order errors involving alpha globin gene sequencing likely involved two factors: (1) HCP’s impression that “sequencing” is always the most sensitive and informative methodology and (2) the test name included “alpha thalassemia,” which caused staff at the referring laboratory to instinctively select it as the best match when the HCP did not provide a specific test code.

Deletion/duplication analysis for neurofibromatosis type I (NF1) was the third most commonly misordered test and had the highest percentage of cancelations (87%). We believe that this error was caused by ARUP, due to the way in which the test was offered. Only NF1 deletion/duplication analysis was available at ARUP Laboratories during the time frame of this study, but GC review determined that practitioners usually desired NF1 gene sequencing which has a higher clinical sensitivity than deletion/duplication analysis. In these cases, NF1 deletion/duplication testing was canceled and the sample was forwarded to an outside laboratory for NF1 sequencing.

Lynch syndrome testing was the fourth most commonly misordered test. HCPs often order testing of all four genes when immunohistochemistry/microsatellite instability tumor testing could have been performed as an initial screen. We also observed HCPs mistakenly order testing of a Lynch-associated gene other than the one shown to be mutated in the family or erroneously request full gene analysis when targeted testing for the familial mutation is needed. The majority of order errors appear to be due to HCP’s lack of familiarity with the testing guidelines for Lynch syndrome. Additionally, there is significant similarity in the gene names involved in Lynch syndrome testing which may foreseeably cause confusion for providers who do not routinely deal with this testing and are not familiar with the genes.

The fifth most commonly misordered test was targeted sequencing for a familial mutation. This test was often incorrectly requested for patients who had a reported family history of a genetic disorder even when the molecular etiology had not been identified. A causative mutation must be detected in an affected family member before targeted sequencing can be performed for at-risk relatives.

Laboratories should consider identifying which of their tests are most commonly misordered. This would enable them to re-evaluate test ordering processes and information on their website and implement changes. The following examples illustrate changes implemented by ARUP as a result of this study.

- As mentioned above, many HCPs simply requested “alpha thalassemia” when writing test orders; therefore, ARUP changed the test name from “alpha thalassemia (HBA1 and HBA2) sequencing” to “alpha globin (HBA1 and HBA2) sequencing.” Now, the word “thalassemia” is only used in the name of what should generally be the first line test, “alpha thalassemia (HBA1 & HBA2) 7 deletions,” which may encourage more appropriate orders of both tests.
- The second modification implemented by ARUP was the addition of a statement to the online test directory stating that clients must contact an ARUP GC before ordering either alpha globin gene sequencing or sequencing for a familial mutation (5th most commonly misordered test). This allowed the GC to obtain critical clinical and family history information, request records when needed, and provide advice regarding which test(s) would be most appropriate. Sample requirements were also removed from the online directory for these tests, which provided further incentive for the collection facility to contact a GC before drawing a sample from the patient.
- Since GCs were actively reviewing each NF1 deletion/duplication test order (3rd most commonly misordered test), they were able to identify and communicate the need for developing an in-house NF1 sequencing assay. Once the NF1 sequencing assay was available at ARUP, the erroneous NF1 deletion/duplication test orders were virtually eliminated.

These three examples demonstrate the ability of laboratories to modify their test menus, test names or user’s guide instructions to reduce genetic test order errors. However, such changes can only be implemented after a laboratory has identified a specific pattern of ordering errors.

Monetary Consequences

GC assessment of complex molecular test orders resulted in a net savings of almost 1.2 million dollars to ARUP’s clients over 21 months, and through them, to insurance carriers and ultimately to patients. The average cost-savings per misordered test was $792. GCs at ARUP were able to perform three to four pre-analytic test assessments per hour. This included reviewing the test order and all accompanying clinical information, communicating with ordering facility and HCPs if additional clinical or family history information was needed, assessing test appropriateness, communicating any relevant information to the laboratory, and implementing any requested test change. Employing GCs to review genetic test orders comes at some expense and may best be performed by those benefiting financially from such a review. Hospital laboratory send out departments and insurance companies would benefit directly by the employment of GCs to review genetic test orders and to proactively assist HCPs in genetic test selection. For laboratories in university medical centers or other large private or public health centers, the most practical approach may be to collaborate with departments such as pediatrics, obstetrics, and oncology, which already employ GCs and who may be able to spend part of their day reviewing genetic test orders. Kim et al. [2011] reported a 20% reduction in pediatric genetic reference laboratory expenses at their institution using a collaborative approach with their medical geneticists in developing practice standards for ordering costly genetic tests. In September 2013, Cigna indicated that GCs or geneticists are the only providers from whom they will consider reimbursing for genetic test orders for breast cancer, colon cancer and long QT syndrome.
Clinical Consequences

Although the monetary impact of identifying and correcting molecular genetic test misorders can be quantified, it is more difficult to assess the clinical consequences resulting from such misorders. The following two examples, identified during the course of our study, illustrate the potential for adverse clinical outcomes resulting from misordered tests.

A test request for MSH6 full gene sequencing and deletion/duplication analysis for Lynch syndrome was received without clinical information. An ARUP GC contacted the HCP and learned there was a positive family history of Lynch syndrome. A copy of the relative’s test result was requested to document the familial mutation, which revealed that the mutation resided in the MSH2 gene, not the MSH6 gene. Targeted sequencing for the familial MSH2 mutation was ultimately performed. Had the initially ordered MSH6 test been performed without the HCP recognizing the wrong gene was analyzed, the patient would have likely been informed she did not have Lynch syndrome when in reality she remained at 50% risk. In addition, she would not have been offered the intensive screening recommended for high-risk patients and may have been misinformed about risks of transmitting the mutation to offspring.

A test request for CFTR gene sequencing was received for a newborn whose sibling had CF; however, the sibling’s mutations were not provided. An ARUP GC contacted the HCP emphasizing the improvement in test interpretation and reduction in cost of analysis if the sibling’s specific CFTR mutations could be documented. The sibling’s results showed one copy of the F508del mutation and one multi-exon CFTR deletion. Although the F508del mutation would have been detected by CFTR gene sequencing, the large deletion would have been missed. This illustrates how even when the correct gene is being tested, the appropriate methodology must be used to ensure the mutations of interest are assessed. This order error would have failed to identify that the infant was actually affected with CF which might have prevented this newborn from receiving early, specialized care to maximize his long-term health.

Such cases exemplify the importance of obtaining medical records from previously tested family members before ordering testing on relatives and confirming that the test selected will detect the mutation(s) of interest.

Specialized Knowledge Needed

During pre-analytic specimen processing, laboratory technicians identify and correct many common order errors including duplicate tests ordered on the same sample, submission of inappropriate sample types, missing patient identifiers, or clarification of testing when the test name and test number do not match. These errors are largely clerical in nature and their identification does not require indepth knowledge about the specific test or its intended applications in clinical practice. Our study has found, however, that despite correction of order errors during pre-analytic specimen processing, GC review still resulted in test modification for 26% of complex genetic test orders. This is likely because genetic test review requires specialized knowledge of, and training in, clinical genetics.

As an example, the identification of duplicate germ line genetic test orders, which seemingly does not necessitate in-depth knowledge about genetic testing, was improved by GC test review. At the time of specimen receipt at ARUP, laboratory staff assess for duplicate requests for the same test on the current specimen. Prior to testing, ARUP’s GCs also perform a patient name search in ARUP’s internal database of pending and completed tests to determine if the ordered test, or any of its individual components, was performed on a previous sample or may be concurrently ordered. Without an appreciation of clinical sensitivity of or the types of genetic mutations detected by certain tests, duplicate orders represented by overlapping test components would likely not be identified. An example would include concurrent orders for beta globin (HBB) gene sequencing and a common mutation panel to detect the Hbs, Hbc, and HBe mutations (all of which are also identifiable by HBB sequencing). Although a cursory review of molecular genetic sequencing and deletion/duplication test orders detects some errors, review by GCs was ultimately needed to identify many misorders.

GCs are aptly trained to engage in pre-analytic review of complex genetic tests because of their specialized knowledge of the complexities of such tests, including available genetic testing methodologies, current clinical guidelines and recommendations, medical implications of test results and test limitations. The benefits of GC test order review are likely to extend beyond the individual patient by providing an opportunity for HCP education, alerting HCPs to better ordering practices, and encouraging HCPs to communicate with a GC prior to ordering a genetic test.

Limitations

Limitations of the study’s data include that only germ line molecular sequencing and deletion/duplication test misorders were analyzed. Although review of biochemical and cytogenetic tests also occurred during this time period, and likely saved hundreds of thousands of additional healthcare dollars, these tests were not included in this study. Furthermore, many clients and ordering HCPs contact the laboratory GCs to discuss test selection prior to sample collection. Therefore, one can assume that if such consultation had not occurred prior to test submission, the rate of test order errors would be even higher than observed. There were also limitations associated with the data extraction. The data extracted from the LIS were determined to underestimate the GC-facilitated test changes that occurred during the study period. For example, if a GC initiated a conversation with a HCP that ultimately resulted in the referring laboratory contacting ARUP Client Services (instead of contacting the GC directly) to request cancelation of a genetic test order, the GC would not have completed the template in the LIS, and thus, such data would not have been included in the data extracted. In addition, some GC-facilitated test changes were not included in the dataset because the software used was not able to distinguish them from test changes initiated by clients or other ARUP employees.
The financial impact of test improvement by adding additional testing or more comprehensive testing following GC review with the HCP was not included in this analysis. While recommending additional testing or more comprehensive testing may increase costs, these test additions do not take away from the cost-savings resulting from the cancelation of misordered tests. For the purpose of this study, only the cancelation of misordered tests was considered in the cost analysis.

This study did not attempt to quantify the monetary impact of this genetic test review to ARUP. The overall monetary impact of GC test review would include GC salary and benefits, ARUP’s potential loss of revenue due to the cancelation of test orders that would have otherwise been processed, and the cost-savings resulting from increased laboratory efficiencies by ensuring that only correctly ordered tests were performed.

Efforts were made to ensure consistency in the methodology of test review among GCs using a standardized internal protocol with disease-specific criteria for assessment of clinical utility. However, this study did not examine possible differences in the types and frequency of test changes among the GCs and how this may have biased study results. It is possible that rates of test modifications vary from one GC to another, due in part to differences in how individual GCs assess appropriateness of testing and explain the rational for test modification to the ordering HCP. It would be important for facilities implementing GC test review to attempt to minimize this variability by developing standardized protocols and guidelines within their institution for assessment of clinical utility and discussion of potential test modifications with HCPs.

Because ARUP is a reference laboratory, the source of order errors is not always identifiable and may stem from either the requesting HCP or the referring institution. Given this limitation, we did not attempt to stratify the misordered tests by practice specialty of the ordering HCP, although determining the source of the order errors may help direct education efforts and changes to test ordering practices in a more efficient manner.

CONCLUSION

Despite their highly specialized knowledge, GCs are an underutilized resource within the healthcare system. It is critical to have personnel who understand the complexities of genetic testing evaluate genetic test orders. GCs are well-qualified for this role, and by reviewing genetic test orders can help to reduce unnecessary costs to hospitals, laboratories, insurers and patients, thereby improving patient care and reducing waste of healthcare resources. Given these data, hospital laboratories and third party payers would be predicted to benefit by employing the service of a GC to review genetic test orders. Based on ARUP Laboratories’ experience, there is a high likelihood that a GC pre-analytic test review program would pay for itself by reducing costly order errors. Additionally, from a quality of care perspective, fewer patients would receive genetic test results that may have limited clinical utility or may be erroneously interpreted with possibly life-threatening consequences.

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