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Clinician Perspectives about Molecular Genetic Testing for Heritable Conditions and Development of a Clinician-Friendly Laboratory Report

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The use of molecular genetic tests for heritable conditions is expected to increase in medical settings, where genetic knowledge is often limited. As part of a project to improve the clarity of genetic test result reports to minimize misunderstandings that could compromise patient care, we sought input about format and content from practicing primary care clinicians. In facilitated workgroup discussions, clinicians from pediatric, obstetrics-gynecology, and family practice provided their perspectives about molecular genetic testing with a focus on the laboratory reporting of test results. Common principles for enhancing the readability and comprehension of test result reports were derived from these discussions. These principles address the presentation of patient- and test-specific information, the test result interpretation, and guidance for future steps. Model test result reports for DNA-based cystic fibrosis testing are presented that were developed based on workgroup discussions, previous studies, and professional guidelines. The format of these model test reports, which are applicable to a variety of molecular genetic tests, should be useful for communicating essential information from the laboratory to health care professionals. ***(J Mol Diagn 2009, 11:162–171; DOI: 10.2353/jmoldx.2009.080130)***

Medical test results inform clinical decision making and can influence patient and family attitudes and action. The reporting of molecular genetic tests for heritable conditions by the laboratory issuing the report to the health care provider is complex because interpretation of the test result frequently relies on patient- and family-specific information. Studies have shown that proper interpretation of test results can be compromised by practices in both laboratory and clinical settings by factors that relate to the collection and use of patient- and family-specific information, variation and format of test requisitions and result reports, and the competency of medical staff, especially those lacking specialized knowledge of genetics.[1–8]

Molecular genetic tests are being introduced into primary health care settings. In 2001, the American College of Obstetricians and Gynecologists together with the American College of Medical Genetics published a guideline for preconception and prenatal carrier screening for cystic fibrosis (CF).[9,10] Publication of this guideline was thought to have prompted a significant increase in referrals by obstetrician-gynecologists (OB-GYNs) for CF carrier testing.[11] Other genetic tests have become a part of primary care including those that identify mutations in the *FMR1* (Fragile X syndrome, premature ovarian failure, and Fragile X tremor/ataxia syndrome), *HFE* (hereditary

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hemochromatosis type 1), *BRCA 1/2* (hereditary breast and ovarian cancer), *F5* (factor V Leiden thrombophilia), and the *F2* (FII mutation thrombophilia) genes.[12,13]

Professional guidelines and policy statements have been developed to help guide practitioners in using these tests but their implementation has generally not been monitored (American College of Medical Genetics: Standards and Guidelines for Clinical Genetics Laboratories, 2007 edition, *http://www.acmg.net*, accessed October 6, 2008; College of American Pathologists: Inspection checklists for laboratory accreditation, laboratory general and molecular pathology, *http://www.cap.org*, accessed October 6, 2008).[9,10,14–17] With regards to the American College of Medical Genetics/American College of Obstetricians and Gynecologists CF guideline, in a survey of OB-GYNs, Morgan and colleagues[18] found that the majority of those surveyed thought this guideline was important; however, only 22.2% were able to correctly answer a question about residual risk and race/ethnicity, a concept essential for understanding the relevance of the test and test result for a particular patient. Other studies have reported a lack of knowledge among physicians about genetic testing, particularly with regard to risk assessment and the technical limitations of the test. In 1997, Giardiello and colleagues[1] estimated that physicians ordering genetic tests for familiar adenomatous polyposis erroneously interpreted a negative result as ruling out disease by failing to consider that the test was not able to detect the full spectrum of disease-associated mutations. In 2002, Sandhaus and colleagues[2] reported findings from a study suggesting that physicians were unprepared to interpret genetic risk information related to *BRCA1* and *BRCA2* testing. In 2003, Krousel-Wood and colleagues[6] reported that physicians wanted a report sufficiently comprehensive to be used as an aid to clinical decision making, including guidance for genetic counseling and information about implications for other family members. Considering the challenges already faced by clinicians in busy practice settings, and the evolution in the field of medical genetics, it is essential that information derived from genetic tests is effectively communicated from laboratory to clinical professionals and applied appropriately to patient care.[13,19]

In an effort to explore these issues and consider means to improve communication and understanding of molecular genetic test results, a national workgroup comprised of clinical, laboratory, policy, education, information technology, and third-party payer professionals was convened in 2003 (Workgroup summary at *http://wwwn.cdc.gov/dls/genetics/comm052003.aspx*, accessed October 6, 2008). Workgroup participants concluded that limited or no data existed describing current practices in laboratory and clinical settings regarding test ordering and result reporting. As a consequence, a study was undertaken to collect these data using simulated testing scenarios for DNA-based testing for CF.[8] Significant findings from this study were: i) ~25% of test requisitions received by laboratories were missing information about the patient and/or their family deemed important by laboratories for interpreting the test result; ii) laboratories varied in how they reported residual risk and uncertainties in the interpretation of diagnostic test findings; iii) physicians were confused by the wording used in test result reports; and iv) in clinical settings, tasks related to patient care such as test ordering, reviewing results, and communicating with patients about their test results were delegated to various staff that included those lacking formal medical training, such as secretaries.[8] These findings, consistent with other published observations, suggested that in many cases test result reports are neither standardized nor contain complete interpretations.[1,3–5,7] Our findings and those reported in the literature raise concerns that benefits from genetic tests may be compromised, in some instances, as a consequence of improper test ordering, variations in the reporting of results, and the capacity of clinicians and their staff to effectively use the information contained within test result reports.

A follow-up national workgroup was convened in 2005 to review and resume efforts to improve laboratory reporting practices and aid clinicians in understanding test results. This workshop was attended by a similar mix of professionals at the 2003 meeting described above. To promote effective communication among laboratory and clinical professionals, the workgroup considered that genetic test reports can be improved by using a format that communicates clinically relevant information in a consistent manner and minimizes opportunity for misinterpretation of the results by providing a patient-specific interpretation to inform patient management decisions. It was noted that other areas of laboratory medicine were successful in applying these approaches; most notably through either of the following:

1. Adoption of a synoptic reporting framework. Synoptic reporting conveys information in a uniform manner to the clinician by making use of standardized data fields. In 1997, Hammond and Flinner[20] reported benefits to laboratory and clinical professionals through use of synoptic reporting for the laboratory assessment of breast cancer pathology. A key component in developing this synoptic reporting model was learning from the ordering clinicians how they wanted the laboratory information to be communicated. One outcome that resulted from the implementation of the synoptic reporting format was a decrease in phone calls to the laboratory from surgical oncologists requesting clarification of the test results.
2. A patient-specific narrative interpretation that explains the results and clinical implications with respect to the indication for testing for the patient tested. In 2004, Laposata and colleagues[21] reported that use of patient-specific narrative reporting for coagulation testing was perceived by physicians as more useful than other formats used to report test results.

Participants of the 2005 workgroup suggested that a combination of these approaches may provide a useful framework for reporting test results. It was envisioned that a report could be constructed with a logical flow using wording derived from commonly understood phrases that

are combined to provide a patient-specific interpretation. Because the product must serve the needs of the clinician providing health care, we adopted a strategy similar to that used by Hammond and Flinner[20] and decided to engage clinicians to obtain their input on how to construct result reports based on these principles.

In this report, we describe clinician perspectives on genetic testing, and in particular, the reporting of molecular genetic test results. Using simulated testing scenarios for CF, we have integrated the feedback from the workgroups, other studies, and professional guidelines in developing several model test result reports available online as a Supplemental Appendix (see *http://ajp.amjpathol.org*). We propose that the format and style of these reports be evaluated as models for communicating clinically relevant information on molecular genetic test results from the laboratory to clinical health care settings, and in some instances, directly to the patient.

Materials and Methods

Recruitment

Three workgroups, comprised of pediatric, OB-GYN, and family clinicians who have worked in a primary care setting for at least 3 years and used genetic testing, were convened. Each workgroup comprised physicians and other health care providers including nurses, midwives, and physician assistants. The number of participants per workgroup ranged from 10 to 13, allowing for active discussion.

The pediatric workgroup meeting was held at the National Conference and Exhibition of the American Academy of Pediatrics in October 2006, in Atlanta, Georgia. To recruit participants, we contacted each American Academy of Pediatrics chapter requesting that they contact their local membership, usually through electronic means such as E-mail, listserv, or posting on their website. The OB-GYN workgroup meeting was held at White Plains Hospital in White Plains, New York, in January 2007. We worked with an author of this article (S.J.G.) to recruit participants, all of whom worked in White Plains and the surrounding vicinities. The family practice clinician workgroup meeting was held in February 2007, at LDS Hospital in Salt Lake City, Utah, where an author of this article (M.S.W.) helped to recruit participants from the Intermountain Health Care System who practiced locally.

Workgroup participants were provided minimal information before attending the workshop. We stated the goal of the workgroup meeting was to collect their input about the use of genetic testing and more specifically, what would comprise a clinically useful laboratory report when a DNA-based test for a heritable condition was ordered. Participants were provided an incentive of $250 for their time.

Facilitated Workgroup Discussions

The workgroups were designed to elicit feedback on clinician perspectives about molecular genetic testing and more specifically, how clinicians wanted test results to be reported. In addition to the workgroup participants, experts who were board-certified laboratory and/or clinical geneticists were present to answer technical questions that arose during the course of the discussion but did not otherwise participate in the discussion. All workgroups were led by a certified facilitator (L.S.). For each workgroup, a facilitator's guide was developed in collaboration with four of the authors (I.M.L., Z.G., J.R., and C.S.). At the beginning of each session, written permission was obtained from workgroup participants to record and transcribe the discussion for the purpose of verifying notes taken during the course of each workgroup meeting. Participants were also informed that their identities would not be released or equated with reporting of outcomes from workgroup discussions. Workgroup members filled out a brief questionnaire detailing their professional experience, practice setting, and experience with genetic testing.

The facilitator provided the participants with clinical scenarios in an effort to assist in focusing their comments. The pediatric and OB-GYN groups were presented with simulated CF diagnostic and carrier-testing scenarios, respectively. The family practice group was presented with CF diagnostic and factor V Leiden testing case scenarios. The facilitator guided the discussion using the following queries:

- What genetic tests are ordered in your practice?
- How are tests ordered in your practice?
- What clinical decisions are expected to be influenced by the test result?
- What information should the test report contain?
- How should this information be organized and worded?
- What educational and informational resources are used (by the participants) to understand and apply genetic tests
- What can be suggested to address shortcomings in each of these areas?

Workgroup participants were engaged using a number of tools including group discussion, two- and three-person closed discussion followed by a group discussion, and storyboarding (a technique for collecting ideas from each participant about a particular topic and using a group process to prioritize and identify those thought the most significant).

At the conclusion of each workgroup meeting, the facilitator asked participants for feedback about the discussion session including what they liked, what they learned, and what they would change in the workgroup process. From this feedback, changes in process, but not content or scope, were considered and where appropriate, implemented in successive workgroups. Based on feedback from the first workgroup comprised of pediatric clinicians, two changes were made. First, the meeting time was shortened from 3 to 2 hours. Second, we had concerns that simulated patient test result reports made available to the first workgroup may have compromised feedback by limiting the discussion to the content of those reports. We, therefore, did not provide model re-

Table 1. Composition of Clinician Workgroups

Workgroup (n = total no. of participants)	No. of physicians	No. of nonphysician clinicians	Median (range) years of experience
Pediatric (n = 10)	8	2 Nurse practitioners	12 (5.0 to 33)
OB-GYN (n = 14)	11	2 Nurse practitioners, 1 nurse midwife	16 (4.0 to 30)
Family practice (n = 11)	6	4 Physician assistants, 1 nurse midwife	11 (4.5 to 23)

ports for the latter two workgroups. The comments from the pediatric workgroup did not significantly differ from those of other workgroups so we did not think it necessary to repeat the pediatric workgroup.

Results

Each of the three workgroups was comprised of physicians and nonphysician clinicians practicing in primary care medical settings (Table 1). With exception of the pedeatric clinicians, participants were in private practice in or near the city in which the workgroup met. The median time in practice for participants was greater than 10 years with a range of 4 to 33 years of experience. Almost all physicians had a specialty certification within their specialty (eg, board certified in pediatrics, OB-GYN, or family practice). Approximately half of the pediatric and OB-GYN group participants indicated that some of their training activities included genetics. Two participants from the family practice workgroup indicated such training. None would classify their knowledge of genetics as extensive.

Use of Genetic Tests in Clinical Practice

The workgroups varied with respect to the type and number of DNA-based tests for heritable conditions ordered. Those in the pediatric workgroup indicated, on the average, ordering one genetic test per month. Those from the OB-GYN group typically reviewed genetic test results daily, whereas those from the family practice group noted that ordering such tests occurred infrequently; perhaps a few times per year.

The types of tests ordered also varied by discipline. When asked what molecular genetic tests were ordered, pediatric clinicians indicated testing was ordered for CF, fragile X syndrome, hemochromatosis type 1, Turner syndrome, and Angelman syndrome. OB-GYN clinicians indicated testing was ordered for CF (primarily carrier screening), fragile X syndrome, *BRCA1/BRCA2* hereditary breast and ovarian cancer, hemoglobinopathies (primarily sickle cell disease), thrombophilia, and conditions relevant to the Ashkenazi Jewish population. Clinicians in the family practice setting ordered tests for CF, factor V Leiden, and other thrombophilic factors, hereditary hemochromatosis type 1, *BRCA1/BRCA2* hereditary breast, ovarian, and colon cancer. Participants in all workgroups expected to order genetic testing more frequently in the near future.

Ordering Genetic Tests

Participants were queried regarding roles and responsibilities of their staff in ordering tests and reviewing result reports. Workgroup participants indicated several staff were routinely involved in various aspects of ordering genetic tests (eg, filling out the requisition form), and reviewing results (eg, identifying those results requiring immediate attention by the physician). Persons involved in these processes included the physician, physician assistant, nurse, nurse manager, midwife, and medical assistants. In assigning these tasks, it was stated that emphasis was placed on making the most efficient use of staff and time.

"There are time constraints, we have busy offices. We are seeing the next patient while the nurse fills the form out."

Differences were voiced among participants with regard to how tests are ordered within their practices. Several of the physicians stated that they completed laboratory requisition forms themselves, whereas others delegated this task and acknowledged not being familiar with the laboratory forms. Several clinicians in the family practice group noted it was common to order tests by writing the request in the patient's medical record. We did not explore the process by which such written orders are translated to laboratory requisition forms. For those workgroup participants familiar with the laboratory forms and protocols, there was consensus that requisition forms were typically complex and challenging; sometimes leading to confusion about which tests to order.

"Well, we don't usually use order forms, we write out test orders on patient charts, so there's no standardized form."

Participants were asked about their willingness to provide ancillary information (eg, clinical, family history, race/ethnicity, and so forth) requested on requisition forms. A number of clinicians within each workgroup stated that they failed to see the relevance of taking time to provide such information because it seemed to have little bearing on the care of their patient. Some suggested their beliefs that the requests were to provide data only of interest to the laboratory. On the other hand, there was general agreement among participants to provide such information when its relevance to patient care was apparent. The clinicians also pointed out that another cause for failure to provide requested information was the possibility that persons delegated to fill out the requisition forms might not be sufficiently trained or have the necessary information available to complete the requisition forms.

Table 2. Challenges with Genetic Test Result Reports

Terminology
Ambiguous (eg, what is normal versus abnormal?)
Definitions for genetic-specific terms not known or provided (eg, detection rate)
Content and organization
Complexity of result and interpretation not clearly communicated
Too long
Clinical relevance of result not clearly stated
Recommendations for follow-up not provided in a useful format
Positioning and wording of disclaimers raise concern about test validity
Other
Information technology systems not user friendly

"They have a lot of information on the forms; most of us have medical assistants and secretaries filling them out and they may not know what it's for. The forms can be very confusing and are not easy to navigate."

Genetic Test Result Reports

Workgroup participants were asked about challenges regarding using genetic test results in their practice (Table 2). These encompassed a broad array of issues that included the use of ambiguous terminology, a lack of clarity about the clinical relevance of the test result, and difficulties associated with the use of information technology systems. In reviewing test results, clinicians stated they first read the result and generally do not read further if they conclude the clinical question has been answered. Thus, they acknowledged that if important information were presented elsewhere in the report, it is likely to be missed. The clinicians further stated that these challenges are not unique to genetic test result reports but for many medical test reports the organization of information, the information provided, and terminology used can lead to misunderstanding of the test result when sufficient knowledge about the test ordered is lacking.

"If the neonatologist is having trouble deciphering what it means, how do you explain it to the parents when you have to give them a diagnosis?"

"Something about a 5T allele comes back in some of my reports; I don't have any idea what to tell patients when I see that."

Clinicians identified the results and interpretation sections of test result reports as sections most in need of improvement. Participants from all three workgroups wanted the clinical section of a test result report to: i) clearly state the result, ii) clearly state the significance of the result, and iii) provide guidance for the next steps. Participants generally preferred a shorter rather than longer report. When important commentary about the test result is provided, participants stated this should be made clear to the reader. Clinicians, particularly from the OB-GYN and family practice workgroups, expressed a preference for having graphic representations associated with the interpretations in lieu of descriptive wording, when possible. For example, a table of residual risk assessments for various racial/ethnic groups was thought useful for conveying essential information.

"We want to see clearly things that we need to react to or not react to, then the information for the specialists goes at the end of the report."

Participants from all workgroups wanted the report to provide guidance for informing their clinical decision-making and to serve as an aid when conveying the results to patients, particularly regarding residual risk, need for additional testing, and implications for other family members. Several clinicians, however, emphasized that the guidance offered should assist and not prescribe clinical decision-making. It was suggested that guidance to clinicians occupy its own section of the report.

"Since we're not geneticists, it would be helpful to have a synopsis of the consequences and ramifications so that when we're explaining results to our patients, we can be more informed."

"Sometimes the interpretations can go on forever. It's really nice if there's a clear cut test result, but usually there's a positive range, negative range, and a gray area. It would be nice to have recommendations for retests or confirmatory tests, but I don't want the report to be five pages long."

Building a Useful Report

In each workgroup discussion, participants offered their opinions on broad categories of information elements useful to have in a report and the organization of the report. Interestingly, a common structure emerged among the three workgroups, with minimal differences in opinion, that included the following ordered elements:

1. Laboratory contact information
2. Patient identification and demographics (including patient and family health information)
3. Test ordered
4. Indication for testing/specimen sent
5. Test results and a brief interpretation (grouped within the report)
6. Guidance for next steps
7. Ancillary information/information for specialists (supplemental information)

Patient Identification and Demographics (Including Patient and Family Health Information)

Participants suggested that test result reports present information in blocks organized in a logical manner. There were some differences of opinion noted for the proposed report formats. Several participants from the family practice workgroup, but not those from other groups, suggested that the patient's race/ethnicity and family history should be placed later in the report because in their opinion that information does not contribute to understanding of the test result.

Indication for Testing/Specimen that Was Sent

Several of the clinicians from the OB-GYN workgroup suggested it is not necessary to have the indication for testing on the result report because it should be obvious from the patient's medical record, whereas others countered that the inclusion of the indication for testing on the report is important because the medical record may not be readily available, especially if the patient is being seen by a health care provider different from the one who ordered the test.

"Why do we really need the reason for testing on the report; it's either a prenatal patient or a gyn patient?"

"I think the reason for testing is on the sheet sent to the laboratory. All of these test results are interpreted in view of the patient's history. You have the chart so you know why the patient was sent for the test."

"I still think it's important to have the reason for testing; especially in a group practice. Sometimes one patient is better known to one doctor than the other and it's just a reminder to the person reviewing the result."

Test Results and a Brief Interpretation in Close Proximity

Constraints on time did not permit a detailed discussion of the terminology used to describe the genotypic result of a DNA-based test. The subject was briefly addressed during the family practice workgroup in which participants voiced an understanding of certain genetic terms including homozygosity, heterozygosity, and allele. Clinicians stated a strong tendency to interpret the result of a DNA-based test in terms of a positive or negative finding; for instance, interpreting a negative finding for a carrier test as meaning the patient has no risk for harboring a disease-associated mutation. Participants suggested this type of misinterpretation may be minimized by closely linking a concise informative interpretation in close proximity to the genotypic result within the same section of the report. Also, if additional information is required to further clarify the test result, those reading the report should be directed to a section later in the report where additional details are provided.

"If it just says negative, I would actually stop reading at that point."

"It should be clear that negative doesn't mean never, never, never; we need . . . negative, but . . ."

Guidance for Next Steps

Workgroup participants discussed the type of guidance they thought should be included in reports. Suggestions were fairly uniform among the three workgroups although the OB-GYN workgroup felt strongly about having information to help explain the test result to the patient. Among the workgroups, the following information elements were suggested for inclusion in the guidance section:

- Additional testing that may be useful for clarifying the test result
- Testing of other family members, where relevant, for the purpose of identifying those at risk for a clinical condition or reproductive planning
- Genetic counseling
- Resources for additional information about the test (including where to find credible information about the test and availability of practice guidelines)
- Resources for additional information about the test useful for patients and their family

The value placed on a recommendation for genetic counseling varied among workgroups. The pediatric and OB-GYN groups felt it was important to include a recommendation for genetic counseling, when appropriate, for example as in the simulated CF case. On the other hand, some family practice clinicians suggested that a recommendation for genetic counseling not be included because they felt that the necessary information about the test and the test result is provided to the patient as a part of routine medical practice.

"We're going to get the result to the patient in the best way possible anyway, so you don't have to put that recommendation (for genetic counseling) on the report."

Several clinicians in the pediatric workgroup noted the usefulness of ACTion sheets, which are concise written summaries that provide guidance for immediate follow-up when a newborn screening result indicates that a child is at higher risk for disease. ACTion sheets were developed under the direction of the American College of Medical Genetics with funding provided by the Maternal and Child Health Bureau of the Health Resources and Services Administration of the U.S. Department of Health and Human Services. ACTion sheets are endorsed by the American Academy of Pediatrics (see *http://www.acmg.net/AM/Template.cfm?Section=Act_Sheet&Template=/CM/HTMLDisplay.cfm&ContentID=1858*, accessed October 6, 2008). It was suggested that a similar approach may be useful for providing essential information to clinicians when molecular genetic test results are reported.

Another topic raised only in the family practice workgroup was that of direct patient access to test results and in particular, increasing use of electronic patient portals that enhance such access. The concern raised was that the patient might not understand the report and as a consequence be misinformed and unduly alarmed. Members of the workgroup suggested that individuals who are designing reports may wish to consult with their clients to develop language and a test result format to reduce the potential for misunderstanding by the patient of the information presented in the report.

Educational and Informational Resources

Clinicians were asked to share their thoughts regarding their educational needs and information resources help-

ful for using DNA-based genetic tests in clinical practice. Workgroup participants were aware that educational opportunities existed but could not specify a particular venue. Clinicians reiterated that their time was limited. As such, it was voiced that participation in course work outside their normal routine was unlikely. However, workgroup participants did indicate that they were more likely to participate in educational efforts if they were part of a CME, CNE, or similar program and fit into their schedule for meeting their professional educational requirements. When questions arise regarding genetics, workgroup participants indicated that they typically seek answers from other clinicians within their practice, specialists outside their practice, textbooks, and journal articles. The laboratory was considered a resource by a few of the participants who also stated that finding the right person to speak with can be problematic in that contact information provided on the test result report often connects one to a switchboard. In terms of electronic resources, the OMIM (Online Mendalian Inheritance in Man) database was familiar to many of the clinicians (see *http://www.ncbi.nlm.nih.gov/omim*, accessed October 6, 2008). However, it was interesting to note that only one or two clinicians per workgroup were familiar with GeneTests (see *http://www.genetests.or*g, accessed October 6, 2008), a publicly funded database designed to provide credible information about clinical genetic tests.[22] Further, none of the participants identified as resources the professional organizations relevant to their respective disciplines (eg, American Academy of Pediatrics, American College of Obstetricians and Gynecologists, or the American Academy of Family Physicians) or those primarily associated with genetics (eg, the American College of Medical Genetics, the National Society of Genetic Counselors).

"We need CMEs; we've got high CME requirements."

"GeneTests was very helpful. You can go to laboratory sites; you can get interpretive data, information on what's needed to run the test."

"It would be helpful to see online resources listed at the bottom of laboratory result reports."

Discussion

Clinicians want to provide the best medical care for their patients within the constraints of a busy clinical practice. From this perspective, clinicians want test results that can inform their clinical decision-making by: i) providing the molecular genetic test result, ii) indicating its relevance to the patient in the context of the indication for testing, and, iii) providing guidance for integrating the findings into patient care. The concern raised was that patient care may be compromised if test results are misinterpreted as a consequence of reports that do not provide sufficient or useful information about the test result and its clinical relevance. Workgroup participants were enthusiastic about being engaged in an effort to address these issues and contribute to improving the process of reporting molecular genetic test results.

Participants indicated that medical genetics has become a component of medical practice and conveyed their belief that genetic testing will become a more prominent part of their practice. This is consistent with a 2005 study by Acheson and colleagues[13] that showed physicians are already addressing a range of genetic issues. Among workgroup participants, OB-GYNs appeared to order the greatest number of tests, with carrier screening for CF being the most common. By comparison, those within the family practice workgroup ordered far fewer DNA-based genetic tests. In considering what drives utilization of medical tests, Whitting and colleagues[23] identified five key factors that included: diagnostic factors, therapeutic and prognostic factors, patient-related factors, doctor-related factors, and policy- and organization-related factors. For instance, policy-related factors, ie, the American College of Obstetricians and Gynecologists/American College of Medical Genetics guideline on CF screening, appeared to be key in driving the increased utilization of CF testing by OB-GYNs.[11] Other factors such as increased public awareness, perceived usefulness for diagnosis, and capacity to be reimbursed have and will continue to influence the uptake of genetic testing in practice.[11,12,24]

The provision of clinician education is intended to promote appropriate use of genetic testing. Workgroup participants conveyed a willingness to participate in continuing education offerings relevant to improving their knowledge of genetics but noted such offerings needed to be convenient and fit into their scheduling for fulfillment of CME professional requirements. This need is being addressed by private and public sector entities that include the National Coalition for Health Professional Education in Genetics; an organization of organizations that facilitates collaboration and cooperation to promote health professional education and access to information about advances in human genetics (see *http://www.nchpeg.org*, accessed October 6, 2008). Also many groups have developed and made available education and information resources useful to clinicians, laboratory professionals, patients, and others are available through the Internet.[25]

Workgroup participants stated that various members of their staff make use of the information on the genetic test report in providing patient care functions. In a previous study, findings from a pilot survey of OB-GYNs showed that personnel included secretaries who were tasked with responsibilities that included reviewing test results and communicating results to patients by phone.[8] These findings suggest that test result reports need to be formatted and use language that provide for understanding of the result among persons having varying medical knowledge and expertise; or alternatively, promote referral to persons having expertise in the use of genetic testing, ie, medical geneticists.

Professional guidelines describe the essential elements that should be incorporated into test result reports, such as patient identifiers, description of the test method, detection rate, and relevant family-specific information (College of American Pathologists: Inspection checklists for laboratory accreditation, laboratory general and molecular pathology, *http://www.cap.org*, accessed Octo-

ber 6, 2008).[9,10,14–17] Although a few guidelines do provide model language or result reports, most usually do not comment on the means by which these elements are combined to communicate clinically relevant concepts, such as the clinical implications for a carrier test result when no mutations are detected by test methods that cannot detect all possible mutations.[9,10,16,26] A simple but elegant structure for reports was proposed in an international guideline developed under the auspices of the Organization for Economic Cooperation and Development that divided information provided in test result reports into three categories: i) basic, but essential information (eg, unique identifiers and the genotypic result); ii) specific information (eg, date of birth and reason for testing); and iii) other useful information (eg, suggestions for further testing).[7] Such a tiered approach is consistent with that suggested by our workgroups who desired a logical and efficient structure to effectively communicate clinically relevant information.

Based on simulated indications for testing for CF, the authors developed five model test result reports intended to be consistent with existing guidelines and published finding and to encompass the principles identified by the workgroup participants (College of American Pathologists: Inspection checklists for laboratory accreditation, laboratory general and molecular pathology, *http://www.cap.org*, accessed October 6, 2008).[6,8,9,10,14–17,26] Model reports are available online as a Supplemental Appendix at *http://ajp.amjpathol.org*. In the model reports, information is presented in discrete blocks with brief, but informative content. Although the wording chosen for each section of the model reports was adapted from guideline recommendations and feedback from the clinician workgroups, readers should not consider the wording to be a standard, but rather a suggested means for conveying relevant information amenable to evaluation. In the model reports, bolding, italics, and underlining are used to emphasize key information for the purpose of this publication; however, we realize that electronic information systems used in many laboratories and clinical settings cannot preserve formatting when transmitting or receiving information. In adapting the model reports to such electronic information systems, designers may need to consider other options such as separation of sections in the report by highlighting key information through use of spacing, capitalization, and special characters (eg, * and #).

The patient identification/information field is important for matching the test result with the patient for which the test was ordered. Despite differences in opinion among some of the clinicians about placing information on race/ethnicity and family history in this section rather than later in the report, we opted to include it in this section. Having this information relatively close to the beginning of the report provides an opportunity to inform the reader of the importance of this information, particularly when it is missing (see online Supplemental Appendix: Model Report 3 at *http://ajp.amjpathol.org*).

Information about the test ordered, indication for testing, and specimen type provides necessary information for both the clinician ordering the test and others who may use the report in the future. As discussed during the course of the workgroup meetings, the test name should reflect what is measured and should be selected to minimize ambiguity. For the model reports, we used "*CFTR* mutation panel analysis" as the test name to signify both the analytes and the fact that a panel of mutations is queried to minimize the presumption of broader evaluation of the *CFTR* gene such as by sequence analysis. Some OB-GYNs suggested that it is not necessary to include the indication for testing on the result report because this is provided in the patient's medical record; however, others disagreed and pointed out that the medical record may not be available or consulted, especially if the report is reviewed at a later time by a clinician who did not order the test or have access to the patient's medical record. The inclusion of both the test name and indication for testing can orient the clinical end user to the reason the test was ordered; which is particularly important when a given test can be ordered for different reasons. For instance, *CFTR* mutation analysis may be ordered to diagnose CF in a person with symptoms of CF, to determine a carrier status in a relative of a person with CF, or to establish the etiology of pancreatitis or male infertility of unknown cause. Limitations are also inherent in the use of electronic laboratory information systems (LIS), many of which have difficulty in recording the name of the laboratory test and/or indication for testing (personal communication from co-authors M.M.M., E.L., V.M.P., and J.A.W.). In practice, the LIS may truncate or abbreviate the name of the test and only allow entry of the indication for testing in free text.

The greatest interest to the clinician reviewing a result report is the relevance of the test result to the patient; thus, there was strong support for placing the genotypic result in close proximity to a brief, but informative interpretation. The interpretation should: i) describe succinctly the clinical relevance of the result such as its association with diagnosis, likelihood of disease in the future, carrier status, or residual risk for having a disease-associated mutation; ii) limitations inherent in the analytic procedure or laboratory interpretation that may affect clinical decision making; and iii) when appropriate, refer to additional information provided later in the report. For example, when a family history of a disorder is noted but the family-specific mutation is not provided or not known, the interpretation of the test result should note this but also refer the reader to a section later in the report that explains how the family-specific mutation may be determined and its relevance to the patient's residual risk (see online Supplemental Appendix: Model Report 2 at *http://ajp.amjpathol.org*). Also important is the need for the report to specify that a second mutation may be present but not detected by the current panel when this can affect interpretation of the test result (see online Supplemental Appendix: Model Report 4 at *http://ajp.amjpathol.org*).

The "guidance for next steps" section recommended by workgroup participants was developed to aid the clinician with medical decision-making and identifying resources helpful for understanding of the test and the result. Suggested elements were: i) recommendations, if any, for follow-up testing to clarify the interpretation of the test result; ii) recommendations to identify and counsel

other family members at risk for having a disease-associated mutation; iii) information resources to better understand the test, the test result, and their implications for the person tested; iv) information resources for professional referrals (ie, the GeneTests Clinic Directory); v) consumer health-oriented information resources. The OB-GYN workgroup was particularly interested in having a link on the report to consumer health-oriented resources. One such resource is the Genetics Home Reference that is supported by the National Library of Medicine (see *http://ghr.nlm.nih.gov/*, accessed October 6, 2008).[27] Although these Internet-based references strive to present credible information, some laboratories may be concerned about recommending resources that they neither maintain nor monitor. In such cases, laboratories should consider other means to satisfy a client's desire for credible information about genetic tests. Several laboratories make available written and/or electronic information about the tests they offer. A previous study showed variability in the provision of recommendations for genetic counseling among the DNA-based CF test reports.[8] Workgroup participants shared differing views of genetic counseling, including a few that saw this service as duplicative for what is normally provided in a primary care setting. These findings suggest it useful for laboratory reports to define genetic counseling. In further consideration of this issue, we propose it may be useful to use the term "genetic consultation" rather than "genetic counseling" which may be more meaningful to some clinicians and able to convey a broader range of options available to the patient, such as referral to a clinical geneticist or other professional, as warranted. For example, with reference to the recommendations provided in the model reports detailed in this article, referral to a genetic counselor is an appropriate option for counseling regarding the risk for having an affected child. In a different scenario requiring establishment of a diagnosis or ruling out a genetic condition, referral to an medical doctor clinical geneticist or other medical doctor with the requisite expertise would be appropriate. The term "genetic consultation" is applicable to both situations. For the model reports, we derived a definition for "genetic consultation" from elements taken from the definition for genetic consultation provided on the GeneTests website (see *http://www.genetests.org*, accessed October 6, 2008) and that for "genetic counseling" developed by the National Society of Genetic Counselors.[22,28] If the broader term consultation is used, it may be helpful to also include resources for identifying genetic counselors, clinical geneticists, or other professionals, as appropriate. Within the model reports, we provide website links to directories of M.D. and Ph.D. certified geneticists and certified genetic counselors. It would be informative to test the acceptance and usefulness of this language among users of test reports to determine whether it enhances an understanding of the genetic consultation process and influences referral patterns.

Participants in the family practice clinician workgroup noted that in some settings patients have direct access to medical records through electronic portals independent of a visit to their health care provider.[29] A concern was raised that genetic test results appearing in the medical record in the absence of a carefully constructed interpretation have the potential for being misinterpreted resulting in undue alarm to and/or faulty decision-making by patients and their families. To minimize the potential for misunderstanding and promote patient understanding, workgroup participants suggested that patients or patient groups be consulted in developing or improving the format and wording of the result report and its presentation in the medical record. It has also been proposed that direct patient access to the test result report may enhance patient communication with their health care providers about the test and ensure that important results are not missed by their clinician.[30]

We propose that wording used in result reports should be based on standardized phrases that can be combined to provide a patient-specific interpretive component. This is the essence of synoptic reporting and is amenable to rules-based electronic systems. For instance, taking an example from the model report based on the testing scenario for CF carrier testing in which neither race/ethnicity nor family history was provided to the laboratory, several important concepts are combined in the interpretive component (see online Supplemental Appendix: Model Report 3 at *http://ajp.amjpathol.org*): These include: "(1) *These results do not rule out..;* (2*) The magnitude of the risk cannot be determined because.. and,* (3) *This interpretation is based on the assumption that this individual is not clinically affected."* This approach is similar to that used by Qu and colleagues[31] in which process improvement was realized after implementation of a web-based synoptic system for reporting tumor pathology that integrated the College of American Pathology template for tumor pathology into a dynamic format. It is important to note that although process improvement is important, we also want to achieve measurable benefits to patient outcomes. In looking at the implementation of clinical decision support systems, Garg and colleagues[32] performed a systematic review and found evidence for process improvement (ie, workflow) but also noted the effects on patient outcomes were inconclusive. This argues that in evaluating changes in practices relevant to the reporting of genetic test results, the delivery of clinical services and the benefits sought for the patient and their family must be considered.

Although our findings are based on feedback from a limited number of participants and cannot be assumed to be generalizable to all clinical settings, there was a high level of consensus within and among workgroups, and conclusions voiced were consistent with previous studies and professional guidelines.[8,9,10,16,33] Based on these findings, we constructed a reporting format and model test result reports potentially applicable to a broad range of molecular genetic tests. To test whether the model reports we prepared meet expectations for their usefulness to clinical and laboratory professionals, we propose these be evaluated against reports in use for their capacity to effectively communicate clinically relevant information, ensure appropriate clinical decision making, and promote desirable patient outcomes such as realizing reduced time to diagnosis, timely referrals to appropriate

specialists, and improving on the capacity of individuals and their families for making informed decisions.

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