



Patient re-contact after revision of genomic test results: points to consider—a statement of the American College of Medical Genetics and Genomics (ACMG)

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Clinicians are encouraged to document the reasons for the use of a particular procedure or test, whether or not it is in conformance with this points to consider document. Clinicians also are advised to take notice of the date this points to consider document was adopted, and to consider other medical and scientific information that becomes available after that date. It also would be prudent to consider whether intellectual property interests may restrict the performance of certain tests and other procedures.

Keywords: duty to re-contact; clinical genetics; medical ethics; variant reclassification; reinterpretation of genomic results

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BACKGROUND

Nearly two decades ago, the American College of Medical Genetics (now the American College of Medical Genetics and Genomics [ACMG]) Policy Statement “Duty to re-contact” was prescient in highlighting the increasingly important issue of patient re-contact.¹ Originally focused on clinical genetics practice, its importance now extends to both medical genomics and medical practice in general. Next-generation genomic testing, including multigene panels, exome sequencing (ES), and genome sequencing (GS), is permitting ever larger amounts of data to be collected on each patient sample, with a corresponding increase in the complexity of the results. These advances, barely imagined in 1999, have made the need

to revisit initial results both more frequent and more challenging.

Advances include the discovery of new relationships between a disease and a genetic variant and an expanding list of secondary variants. Many of these variants are now judged necessary to report because of their clinical implications, regardless of the findings in the original genes of interest.² Finally, and perhaps most challenging, is the reinterpretation of variants, both in the gene(s) for which the original test was ordered and potentially in other genes. Experience has shown that many results of next-generation sequencing will demonstrate one or more variants that later may need to be reevaluated.^{3,4}

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The above issues create uncertainty for the ordering physician, the clinical laboratory, and the patient. The obligations that health-care providers and clinical laboratory directors assume in terms of protecting privacy, reporting secondary findings, and updating interpretations are not clear. No definitive answers currently exist, but legal, ethical, and practical issues need to be considered.

In 2012, when the ACMG discussed the clinical application of genomic sequencing,⁵ there was no clear legal duty to re-contact patients, and that is largely the situation today. This Points to Consider document regarding the duty to re-contact is an outgrowth of prior ACMG position statements^{1,5} and the Father Robert C. Baumiller Symposium at the 2014 ACMG annual meeting entitled, “Duty to Re-contact in the Genomics Era: Interdisciplinary Perspectives and an Open Forum.”

DISCUSSION

An ethical obligation based on the principle of beneficence requires at least attempting to re-contact the patient in circumstances that may meaningfully alter medical care. Moreover, re-contacting patients may be less of a burden due to electronic communication, electronic health record (EHR) patient portals, and direct patient access to their results from testing laboratories.⁶ It is quite possible that the legal requirements for re-contact will change as the burden of re-contacting former patients is reduced and the potential resulting injury or missed opportunity for clinical benefit from failure to re-contact is better understood. It would be prudent for the provider to inform the patient prior to testing that the results have the potential to be updated and that it is important for the patient to provide up-to-date contact information.

However, many practical issues remain in re-contacting patients. Populations are mobile, and physicians and health-care networks may change. Navigating EHR systems to access patient information is often difficult as different EHR systems may not interface with each other and EHRs may not use current genetic nomenclature.

As detection of variants has increased in frequency with newer technologies, referring and treating providers are faced with the challenge of understanding the potential clinical implications if reclassification occurs. In the current US health-care system, both acute and preventive care visits are time-limited, which tends to relegate review and follow-up of inconclusive laboratory results to brief, if any, discussion. Placing primary responsibility to re-contact on the provider who ordered a genetic test or the provider who interacts with the patient may be problematic.⁷

Placing primary responsibility to re-contact on the patient or family is also problematic. Patients may lack understanding of which life circumstances should trigger an update. Patient barriers of language, culture, literacy, and lack of familiarity with the medical system complicate matters.

Finally, while the ACMG and the Association for Molecular Pathology have provided guidance for clinical laboratories on how to classify variants,⁸ there is currently no consensus for when and how often laboratories should review the

classification of a particular variant. The ACMG Laboratory Quality Assurance Committee is addressing the protocol and resources used for reclassification and other technical issues in a separate document and such issues are beyond the scope of the present document.

SUMMARY

Changes in interpretation of complex clinical genomic test results are inevitable. Ultimately, the ordering health-care provider, clinical geneticist, clinical laboratory, referring specialty and primary care physician, patient, and family each may have a role regarding re-contact. These expectations should be explicitly delineated as part of the informed consent process before the sample is obtained and reviewed again when disclosing initial results.

The following Points to Consider should be viewed as guidance for the ordering health-care provider, clinical geneticist, laboratory geneticist, and genetic counselor. They are intended to assist providers to develop policies and procedures regarding re-contact that are appropriate to their individual practice settings, and to apply them to the specific circumstances presented by each individual patient or family.

POINTS TO CONSIDER

1. Re-contact is fundamentally a shared responsibility among the ordering health-care provider, the clinical testing laboratory, and the patient.
2. As part of the informed consent process, the patient or family should be advised that:
 - a. Changes in interpretation of clinical genomic test results are possible and re-contact may be important for patient care.
 - b. If the patient’s medical history or family history changes, the patient should make the health-care provider aware.
 - c. Important times for the patient to request an update are at life cycle junctures such as preconception planning, pregnancy, and changes in family history information, including sudden unexpected death or the diagnosis of a major health issue in the person originally tested or a close relative.
 - d. When seeking an updated variant interpretation, the patient or family should contact the provider who ordered the test, the clinical geneticist who interpreted the test result with the patient, and/or the clinical testing laboratory for an update on a result with an uncertain interpretation. Alternatively, the patient can request their primary care or specialty provider to contact a genetics provider.
 - e. The patient or family has a right to decline re-contact.
 - f. The patient or family should register with the health-care facility patient portal if available.

- g. It is the patient's obligation to provide updated contact information over time.
3. The ordering provider should emphasize, through discussion and in written explanation to the patient, that the ordering provider cannot promise that re-contact regarding a revised interpretation will occur unless the patient initiates the re-contact.
4. The discussion regarding re-contact should be documented in the medical record. The patient or family ideally will be given a copy of the re-contact policy.
5. The ordering provider should inform the patient of the specific tests performed and which laboratory performed the analysis, typically by providing a copy of the test report. The patient should be encouraged to keep the report with their important health information. The test report should be entered into the EHR and should be provided to the referring physician.
6. The responsibility to inform the ordering physician of variant reclassification or discovery of a new gene-disease relationship rests with the clinical laboratory.
7. Medical geneticists need to inform referring providers that, even if the patient is referred to a medical geneticist for counseling regarding test results, the ordering physician will remain the primary contact for the laboratory.
8. If contacted by the laboratory with an updated result, the ordering physician should make reasonable efforts to re-contact the patient.

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DISCLOSURE

The authors declare no conflicts of interest.

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