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Pediatric clinical exome/genome sequencing and the engagement process: encouraging active conversation with the older child and adolescent: points to consider—a statement of the American College of Medical Genetics and Genomics (ACMG)

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As exome and genome sequencing become more widely incorporated into clinical pediatric care, it becomes increasingly important to encourage a robust engagement process with the mature older child and adolescent patient to facilitate meaningful conversation that can aid in the complex decision-making and return of findings process around genomic testing. A dialogue that promotes this engagement process is best attained when the clinician shares salient information, including the relatively distinct implications of the test, while listening and responding to the child's evolving perspectives as well as the parent(s)' concerns ("parent" used broadly throughout to include guardians and others who act in this capacity for the genetics encounter). The American College of Medical Genetics and Genomics considers such an active conversation among the child, parent, and clinician(s) fundamental to the application of sequencing technology with children, regardless of the decision-making outcome and potential situational dilemmas presented.

With this goal in mind, we present several considerations for the genetics professional or other ordering clinicians when engaging children both before and after sequencing.

- The purpose of the engagement process is to ensure that the mature older child is actively involved in conversation to understand the goals and implications of genomic testing and potential findings and to consider its personal benefits and limitations while having the opportunity to express their feelings and opinions.
- Optimal engagement is aspirational rather than a blueprint; we acknowledge that it is not always feasible despite best efforts. However, we caution that limiting the conversation risks eroding the child's trust in the genetics professional and parent if the child later discovers that he or she was not adequately informed and/or did not have an opportunity to voice opinions in the decision-making process.

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- It is critical to engage the child as much as possible in this process, which includes the assent of the child whenever reasonable.[1–3] The aim of this document is to emphasize encouraging conversation and active engagement of the child together with parent and clinician when clinical exome/genome sequencing involves children.
- Children as young as 8 years of age should be part of an active engagement process to the extent that they are considered by the clinician and parent to be psychologically and cognitively capable.[1–3] These conversations should begin prior to testing and continue in the disclosure of results. Often, preparatory discussion with the parent before discussion with the child is useful to learn more about the child's capacity and the parent's goals and concerns.
- It is essential that the clinician clearly articulate to the child whether their parent already decided what testing is to be performed or whether assent is being requested from the child and will be honored if the child decides to decline testing, with the understanding that their parent may later decide to override the child's preference.
- Strong consideration should be given to encouraging the family to weigh and respect the child's preferences whenever reasonable, with even greater consideration given if the child is already experienced with medical choices due to the course of their condition or if an adolescent.
- Ideally, the clinician will engage the child in a conversation together with the family to facilitate expression of preferences and potential concerns while providing developmentally appropriate information before sequencing and during or after results disclosure. During the conversation(s), the clinician should also foster an open dialogue regarding psychosocial issues and understanding of key concepts surrounding the genomic test.
- Recognizing that challenges to implementation may be encountered, it remains important to encourage some degree of an engagement process with the older child and adolescent along with the parent, while being sensitive to different individual and family cultural, religious, and personal values. At times this may require flexibility in expectation on the clinician's part and necessitate further conversations over time.
- Continued discussion over time is also optimal in some cases as the child grows and the relevance and significance of the genomic information potentially change with life stage and as new data/recommendations may emerge.
- Developmentally appropriate communications with children regarding testing will ideally be documented in their medical record, along with any potential recommendations for the family to recontact the clinician.

While the concept of a pediatric engaged-assent process with parental permission was first presented in 1985 by Bill Bartholomew,[1] and has been supported by the American Academy of Pediatrics Policy statements since 1995,[2] only limited data about engagement have been incorporated within pediatric practice.[3] We believe that for genomic sequencing it is important that children over the age of 8 at the appropriate neurocognitive developmental level and of appropriate psychological maturity clearly understand the key, relatively unique, features of this type of test, at a minimum:

- Sequencing is a test that may not find the answer related to the indication for testing at this point in time.
- Some test results may be more important to learn about as an adult or closer to the time an individual is thinking of having children.
- New information may be generated over time.
- The test might uncover unexpected information unrelated to the indication for the testing and may lead to additional tests.

As with other medical tests and procedures, the level of information presented will be optimal when developmentally appropriate and individualized for the child, with clear communication and education prior to both genome sequencing and results disclosure.[4–6] A nuanced assent process is particularly important in light of several distinct implications of pediatric sequencing. Key informational elements for the ordering professional to elaborate for the child *prior to testing* that differentiates this test from others they may have undergone include:

- While this test is being requested now, and some information may be reported back to a child now, other information may be disclosed in the future. For example, some conditions are not recognizable until past childhood and have no recommended screening, monitoring technology, or preventative interventions until adulthood, while others may currently have no available treatment.
- Information that is not relevant at this age might not be told to a child by their health-care provider at this time but might be told to their parents, who may share that information with their child now or at a later date. When a child becomes an adult, they may have the opportunity, if they wish, to obtain their pediatric sequencing report from their health-care provider or the laboratory, provided the results are in a medical record to which they have access. However, as time passes and scientific knowledge/technology advance, clinical interpretation may change and retesting may be necessary.
- Genome-sequencing results are often complicated. While a specific result may be found, the answer may not provide useful information related to the reason that testing was performed (the child's condition), or it might provide information completely unrelated to their

condition. Sometimes a test such as this reveals information that science may not yet understand completely (of "unknown" or "uncertain" significance) and may raise the possibility of further testing or reanalysis of the results at a later time.

A fully informative "adult-type consent" discussion is not needed when engaging a child in the conversation and the assent process. However, parents must give permission for the child or adolescent to be engaged in the process and, irrespective of whether the child or adolescent participates, fully informed consent must be obtained from the parents before any testing is begun.

Efforts should be made to keep in mind that the process of comprehensive genomic testing is complex; however, many children and adolescents are capable of participating in engaged conversations that promote expression of feelings and decision-making preferences.

While the focus in this document is on comprehensive sequencing in the clinical domain, we concur with Wilfond and Diekema[7] that the need for engagement with older children also exists in the research setting, where different regulations and varying IRBs must be taken into account. Accordingly, we recommend that clinicians and researchers strive to facilitate active engagement of the child together with the parent whenever possible, being sensitive to the child's developmental constructs, psychological maturity, and cognitive capacity, as well as family dynamics and cultural-religious norms.

Enhancing these conversations is a timely and critical issue for pediatric patients for whom genome sequencing is recommended. It is essential for clinicians to encourage an active informed-engagement process from assent to result disclosure, demonstrating respect for the child in the context of individualized developmental levels and family dynamics.

DISCLOSURE

The content of this article is solely the responsibility of the authors and does not necessarily represent the official views of the authors' affiliated institutions. No conflicts of interest were reported.

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