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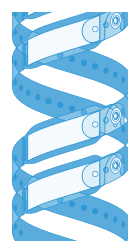
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Consent for clinical genome sequencing: considerations from the Clinical Sequencing Exploratory Research Consortium

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Implementing genome and exome sequencing in clinical practice presents challenges, including obtaining meaningful informed consent. Consent may be challenging due to test limitations such as uncertainties associated with test results and interpretation, complexity created by the potential for additional findings and high patient expectations. We drew on the experiences of research teams within the Clinical Sequencing Exploratory Research (CSER1) Consortium on informed consent for clinical genome and exome sequencing (CGES) to negotiate consensus considerations. We present six considerations for clinicians and 12 key points to communicate as they support patients in deciding whether to undergo CGES. These considerations and key points provide a helpful starting point for informed consent to CGES, grounded in the Clinical Sequencing Exploratory Research (CSER1) experience.

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Clinical genome and exome sequencing (CGES) is a powerful tool that is beginning to be used in a variety of clinical settings, most commonly as a diagnostic test for suspected genetic conditions [1–4], and increasingly, in conjunction with somatic tumor sequencing to tailor cancer treatment [5]. However, CGES may not yield clinically meaningful results because of the limited explanatory power of genetics, as well as technical and other limitations. Obtaining informed consent for CGES is challenging. Some of the challenges are familiar [6], such as conveying information about re-contacting patients, reanalysis of sequence data and long-term storage and data use. However, several properties of CGES make informed consent particularly challenging. Data from clinical sequencing may be difficult to interpret because identified variants may not be clearly linked to pathologic syndromes [7]. In addition, geneticists as well as testing laboratories may disagree on the interpretation of pathogenicity for some variants [8–10] and variant classification may change as additional data accumulate.

Another challenge of CGES is the potential to generate additional findings, also known as secondary or incidental findings, beyond those related to the indication for sequencing. The possibility of such findings has elicited both enthusiasm and trepidation: enthusiasm because such findings may inform care and treatment decisions and

prompt surveillance for disease onset or recommendations for reducing disease risk; trepidation because additional findings, if unexpected or uncertain, may overwhelm patients [11] or lead to unnecessary screening or treatment. At present, the American College of Medical Genetics and Genomics (ACMG) recommends offering patients additional findings related to the presence of pathogenic or likely pathogenic variants in 59 genes considered to be medically actionable [12]. Depending on the laboratory, additional results such as variants in genes associated with other Mendelian conditions, including those indicating recessive carrier status and gene variants affecting drug metabolism, may be offered [13]. When given the option, the majority of tested or surveyed individuals in studies that document preferences opt to learn all results offered [14–20]. Together, the ACMG's recommendation to offer additional results, coupled with patients' interest in receiving all available results, provides important context for considering informed consent for CGES.

Informed consent for CGES is complicated by the uncertainty and breadth of possible results, high patient expectations for learning useful results from sequencing [21,22] and poor genetic literacy among the general public [23,24]. The decision to undergo sequencing may be affected by an individual's assessment of the harms and benefits associated with the potential results of testing, including the possibility of uncertain information and additional findings. Furthermore, patient-specific factors such as medical and family history and the indication for and timing of testing will influence decisions about testing [22]. Given this situation, what considerations should guide the consent procedure as clinicians offer CGES to patients?

The Clinical Sequencing Exploratory Research Consortium (CSER1) experience with consent

The Clinical Sequencing Exploratory Research (CSER1) Consortium [25], comprising National Human Genome Research Institute and National Cancer Institute-funded projects conducting research on the clinical translation of genome and exome sequencing, confronted the challenge of informed consent to CGES over its 6-year lifespan (2011–2017) [26]. In Phase I of the consortium (which has now progressed to Phase II, known as 'CSER2' [27]) nine U-award CSER projects and one National Human Genomic Research Institute (NHGRI)-intramural project offered clinical sequencing in the context of research, while nine additional R-award projects focused on specific issues raised by CGES. Because CSER1 consisted of NIH-supported research projects on clinical implementation of CGES, the informed consent processes had to conform to the requirements of the pre-2019 Common Rule [28] that governed federally funded human subjects research at that time. However, the U-award projects at the heart of CSER1 were explicitly translational, studying the process of clinical integration. Applying the lessons learned from CSER1 about informed consent to CGES thus requires extrapolation from this translational context to other clinical contexts in which informed consent for CGES is not bound by the research regulatory requirements under the Common Rule. While acknowledging this limitation, most CSER1 U-award projects are engaged in sequencing that mirrors clinical testing across a range of contexts. In addition, these projects included clinicians, researchers and scholars who have considerable experience in clinical sequencing and in the evaluation of informed consent.

This paper builds on and synthesizes extensive CSER1 research on and experience with informed consent. The CSER1 Informed Consent and Governance working group reviewed informed consent documents for CGES from each CSER1 U-award study [29]. In addition, the CSER1 Genetic Counseling working group interviewed clinicians and research coordinators who conducted informed consent sessions for CSER1 projects [21,22] and several CSER1 projects have published their own experiences relevant to informed consent [14,17,21,26,30–32]. As a follow-up to these reports and given the substantial experience with informed consent for genomic sequencing within the CSER1 Consortium, the CSER1 Steering Committee tasked the Informed Consent and Governance Working Group with building on CSER1 research and experience to develop consensus guidance for clinicians about informed consent for clinical sequencing. Three writing group members (J-H Yu, BA Bernhardt and BS Wilfond) drafted an initial manuscript that was interactively revised by the writing group over a year via email, phone calls and in person at semi-annual CSER1 Consortium meetings.

As a consortium working group, our goal is to share what we have learned about consent for CGES through our respective involvement in CSER1 projects. While there is an extensive conceptual and empirical literature about consent for high-throughput genomics of condition-specific genes or gene panels, our contribution is to aggregate and emphasize consent considerations that focus on addressing the crucial features of CGES in the context of our US healthcare system.

Our considerations are meant for the range of clinicians inclusive of clinical/medical geneticists, genetic counselors and nongenetic clinicians. We think the proposed considerations are relevant for all clinical situations in which CGES may be an option, but recognize that most geneticists and genetic counselors are at a distinct advantage

due to their wealth of experience in working with patients in making testing decisions. Unfortunately, geneticists and genetic counselors are in short supply; thus, we hope these considerations are helpful to the range of clinicians who may be in a position to order CGES.

As a writing group of researchers drawn from different sequencing-related projects, we examined our initial efforts [21,22,29] along with our own respective experiences and then developed our considerations. In contrast to the article by Henderson *et al.* that focused on the content of CSER1 consent forms for research on clinical sequencing [27], we focus on the process of consent for clinical sequencing. For example, we acknowledge that clinical sequencing test results will be entered into patients' electronic medical records (EMR) and could involve research-related data-sharing but we did not develop content considerations specific to the communication of either EMR or data-sharing.

Despite the differences observed in the content of CSER projects' consent forms [29], in this manuscript, we highlight similarities in experiences and practices [21] and emphasize their importance in promoting patient autonomy. We present six considerations for clinicians and 12 key points that they should convey to patients, to guide the process and content of consent for CGES. Further, we propose sample questions to help solicit medical and personal contexts such as individual perceptions of potential harms and benefits of CGES and other patient-specific factors.

Pragmatic challenges of informed consent for clinical genome sequencing

The ACMG recommends that consent for clinical sequencing should include the opportunity to opt out of analysis for additional findings but has not provided specific recommendations on how to do this [12,23,33,34]. Uncertainty remains regarding how best to communicate benefits, limitations and risks; how the purpose of testing and the medical context in which it originates might influence the informed consent process and how the consent process can incorporate patients' and families' values that may influence their weighing of the risks and benefits of testing. Moreover, research has documented that patients and families overestimate both the likelihood of diagnostic results from CGES [21] and their clinical utility, and underestimate the limitations associated with testing. Therefore, a responsible presentation of CGES in the informed consent process will need to help patients develop a balanced assessment of benefits and risks. These challenges may be magnified by the likelihood that clinicians and specialists unfamiliar with diagnostic genetic testing and sequencing increasingly will order CGES and be responsible for obtaining informed consent. This expectation motivates and informs, in part, our proposed considerations and messages.

In addition to these challenges, commercial laboratories' policies and practices regarding CGES are heterogeneous, with implications for clinicians' approaches to informed consent [35]. For example, laboratories may differ in their policies on the scope of analysis of additional findings, reporting of uncertain findings and practices relating to future reclassification of reported variants [6,36,37]. Clinicians will need to be aware of the specific policies of their selected laboratory and discussions with patients and family members regarding the scope of testing and the handling of results will need to take those policies into account.

Considerations for informed consent for clinical genome & exome sequencing

The broad goal of the CGES consent process, grounded in respect for persons, should be to promote patient autonomy in the context of deciding what tests to perform by facilitating patient control and choice over test-related decisions. Equally important, clinicians should seek to locate the potential results of testing within the patient's medical and personal contexts and to address the limitations of testing. Therefore, the practical function of informed consent discussions for CGES should be to convey the information needed for making testing decisions and to promote reasonable expectations about CGES. We present six considerations intended to advance these goals. [Table 1](#) provides a summary of the considerations, [Table 2](#) provides sample questions to aid in eliciting the patient's medical and personal context and [Table 3](#) provides key points for each consideration. These six considerations are organized into two categories: the first three focus on the personal and clinical context of testing and the latter three focus on the results and their implications.

Consideration 1: Decisions about CGES occur in the context of ongoing clinical decision-making

The decision to undergo CGES may be one in a series of decisions patients are asked to make about diagnostic testing and follow-up. For example, a patient may need to make decisions about ongoing symptomatic treatment, multiple diagnostic tests and procedures, clinical or behavioral follow-up for specific findings, sharing results

Table 1. Considerations for informed consent for clinical genome and exome sequencing (CGES).

Personal and clinical contextual considerations
1. Decisions about CGES occur in the context of ongoing clinical decision-making
2. The consent process should be succinct and responsive to the patient's personal situation and context
3. Information about basic genetics and technical descriptions of sequencing is often unnecessary
Results and implications
4. Focusing on the range of possible results including the limitations of current interpretations can promote reasonable expectations
5. Clinicians can facilitate decision-making and prepare patients for testing by discussing the potential clinical and emotional implications of results
6. Considering the implications of results for the patient's family is an important part of the process

CGES: Clinical genome and exome sequencing.

Table 2. Sample questions to aid elicitation of medical and personal context.

1. What has been your experience with genetic testing?
2. What would the benefits of this genetic test (genome sequencing) be for you?
3. What questions do you have about this genetic test?
4. What are your concerns about this genetic test?
5. Have you already made a decision about having the test? How can I help you to decide? What additional information would help you make a decision?
6. How might you react to different kinds of results, for example, if you got a result indicating that the cause of your child's condition wasn't identified?

Table 3. Key points to improve decision-making and facilitate realistic expectations for clinical genome and exome sequencing.

The range and the limitations of CGES results
<i>Types of results available</i>
1. Results might identify the cause of your condition
2. Additional (secondary) results might explain or predict other conditions
<i>Limitations of testing</i>
3. Genome sequencing may not report all variants in a person's entire genome and will not identify all disease risks
4. The interpretation of results can involve uncertainty, due to variants of uncertain significance, variable penetrance and other factors
5. Interpretation of findings can change over time
Implications of CGES results
<i>Clinical implications of results for tested individual</i>
6. Your healthcare may not change, even if the cause of your condition is identified
7. You may need to see other doctors
8. You may need additional testing
<i>Emotional implications</i>
9. Results can be reassuring or emotionally distressing
<i>Implications of results for family members</i>
10. Results could have implications for your children and other family members and could influence your reproductive plans
11. Your test results may suggest that other family members are also at risk
12. Sharing results with family members can be challenging in some families

CGES: Clinical Genome and Exome Sequencing.

with family members, testing other family members, learning additional findings and so on. Equally important is recognizing that this clinical context may hold different meanings or significance for different patients. For instance, the prospect of CGES testing following a long diagnostic odyssey may be qualitatively different than in the case of a recent-onset condition. As such, the clinician should ascertain the patient's particular context and understanding of CGES testing. Table 2 provides sample questions generated by experienced CSER1 genetic counselors to aid in eliciting a patient's personal and medical context. While these questions and patients' responses in themselves may not yield a clear testing decision, starting the discussion in this way can help patients identify and prioritize their informational needs.

Consideration 2: The consent process should be succinct & responsive to the patient's personal situation & context

The experience of CSER1 projects suggests that individuals conducting informed consent need to support patients in making CGES decisions in the context of their lives, health and values. Diversity in cognitive processing and differences in decision-making styles mean that patients' informational needs and general concerns about a particular decision vary greatly. Therefore, it is unsurprising that comprehensive disclosure of test-related information during

genetic counseling has been found, in general, not to be useful [38,39] (see Consideration 3 below). The consent process should begin by exploring what types of information patients think will be most important to their decision-making regarding issues such as treatment decisions or symptom management [39]. With the patient's input, information that is not vital to informed decision-making may be mentioned briefly or held for future discussion. The clinician could present an overview of topics from which a patient may seek more in-depth descriptions if desired. Detailed discussion of these topics may best be deferred to avoid burdening the patient with information not directly relevant to the immediate decision of whether or not to undergo CGES [39]. This 'menu' approach allows patients to be made aware of possible issues but does not force them to receive information they believe is not important to their decision. In the research setting, Sage Bionetworks is developing an analogous 'headlines' approach in the Precision Medicine Initiative's All of Us program [40,41]. While such approaches are promising, future study is needed to learn if such 'menus' or 'headers' affect the duration of the consent process, whether they convey sufficient notice to patients of their underlying content and how effectively they balance the need for parsimony with the obligation to communicate essential information to patients.

Consideration 3: Information about basic genetics & technical descriptions of sequencing is often unnecessary

Consistent with Consideration 2, we recommend avoiding detailed description of genetics (e.g., genetics 101) and technical details of exome or genome sequencing and analysis. To facilitate the ethical commitment to obtain meaningful consent, it is not necessary to provide extensive technical information; rather, patients may be better served by focusing on the primary purpose of the tests and the risks, benefits and implications of CGES for themselves and their families. Individuals conducting pretest informed consent sessions in CSER1 projects considered a number of contextual factors such as medical background, time available for consent and prior experience with genetic testing in determining how much basic genetic information to relay [21]. Over time, individuals seeking consent in CSER1 projects focused less on relaying technical information and more on helping families appreciate the limitations and implications of results. While the approach taken should be tailored to the context of particular patients and families, the discussion of science should generally be limited [39].

Consideration 4: Focusing on the range of possible results including the limitations of current interpretations can promote reasonable expectations

The purpose for ordering CGES and the range of potential primary findings is an important part of the consent disclosure, including the realistic likelihood of informative findings with regard to diagnosis, treatment or prevention (Key point 1). When CGES is undertaken for diagnosis, clinicians should make clear to patients that although a test result may provide a diagnosis, that diagnosis might not alter clinical management. Nonetheless, even in the absence of medical actionability, a diagnosis may be valuable to many patients. In addition, the discussion should acknowledge the limits of CGES analysis and interpretation. Various types of uncertainty should be conveyed (Key point 4). These include: Some people, including family members, may not experience the condition even if they have the particular variant; the implications of a negative result may be uncertain either because of technical limitations or because some causes of a condition remain unknown [42] and it may not be known whether a variant is truly associated with a condition (variants of uncertain significance) (Key point 3). Further, clinicians should convey the fact that the interpretation of results can change over time (Key point 5). In addition to discussing the range and potential limitations of primary results, the range of possible additional results should be presented, as well as options to decline analysis and return of additional findings [12,43]. Although limitations and uncertainties will have been introduced in the discussion about primary CGES results, it should be made clear to patients that the same issues extend to additional results – indeed, the uncertainties may be even greater (Key point 2).

Consideration 5: Clinicians can facilitate decision-making & prepare patients for testing by discussing the potential clinical & emotional implications of results

As noted above, the clinical implications of CGES test results may be uncertain. Even if a genetic cause of a patient's condition is identified, the patient's healthcare may not change (Key point 6). Conversely, identification of a genetic variant may require additional testing and follow-up with their associated costs (Key points 7 and 8). Similar to the clinical implications, the emotional impact of CGES results may vary. Depending on the context of testing, results may be reassuring or distressing (Key point 9). For instance, an unanticipated result may cause distress by alerting a patient to a potential new risk to her health. On the other hand, genetic results may confirm suspected health risks

based on family history and may provide desired clarity [44]. Such clarity may not only offer the end of a diagnostic odyssey but also provide relief from guilt or blame for causing the condition [45].

Consideration 6: Considering the implications of results for the patient's family is an important part of the process

Although there is no single approach to exploring the implications of results for family members, we describe a general approach and context-specific applications. In general, clinicians should tell patients that results may have implications for certain biological family members (Key point 10), and that the patient, with the help of the clinician if desired, should consider informing potentially affected relatives about findings and their implications (Key point 11). The importance of addressing implications for family members, including the potential identification of misattributed parentage, will be particularly salient when samples from family members, such as parents or siblings, are obtained for testing at the same time as the patient's sample. Specifically, we recommend informing family members who are providing blood samples whether they will have the option to learn each other's findings, and if so, the kinds of results they might receive. A potentially sensitive consideration for clinicians and their patients is access to the patient's findings after death or loss of decisional capacity. For example, if a patient has a short life expectancy, he or she may want to consider whether to authorize sharing of CGES data and results with family members [44]. Finally, sharing CGES results may be challenging in some families, perhaps even generating conflict among family members (Key point 12).

Applying the considerations: the case of developmental delay

We have emphasized the importance of tailoring the approach to consent to both the clinical context and the patient's family and social context. Below we illustrate the application of these considerations using an increasingly common clinical scenario for CGES. Consider a 4-year-old child with developmental delay. For the past year-and-a-half, his parents have searched unsuccessfully for a diagnosis. Their provider recommends exome sequencing in an effort to uncover the source of the child's symptoms.

As the clinician discusses the recommendation with the parents, the six considerations and 12 key points (Tables 1 & 3) can guide the content of the discussion. First, she should solicit information about the family's past experiences so the discussion can be contextualized to their needs (Consideration 1). For example, the clinician may engage the family to set their goals or agenda by asking questions such as "*What are your concerns today? What do you want to find out? How would the results of a DNA test be important to you?*" Then, the recommendation about sequencing should be placed in the context of prior clinical studies and the rationale for sequencing at this time (Consideration 2). The family should be told about the potential benefits of receiving a diagnosis, including possible implications for clinical care, establishing recurrence risk with future children, creating an opportunity to participate in research and even connecting with other families with the same condition (Consideration 4) [45]. The limitations of clinical CGES should be discussed, including the possibility that CGES will not lead to a genetic diagnosis. Recognizing that this family may expect a genetic diagnosis to inform their child's management and educational needs, the clinician should emphasize that a genetic diagnosis may not alter treatment and that additional testing or follow-up decisions may be required after CGES (Consideration 5). She should highlight that CGES may generate additional results that might have implications for the child, his parents and other family members (Consideration 6), but also acknowledge that they may neither be prepared for nor interested in additional findings, and that they may opt out of analysis and disclosure of such findings (Consideration 4). In the case where the child and parents undergo sequencing (i.e., trio sequencing), she should make clear that parents may receive their own results including additional findings, depending on the laboratory's or institution's disclosure policy (Consideration 6). It is important to note that the key considerations and points do not require detailed discussions of DNA and genetics (Consideration 3).

Implementation challenges & future considerations

In this paper, we propose a minimum or floor rather than a maximum or ceiling of important considerations that arise when communicating with patients about CGES. Indeed, there may be other considerations and key messages that may be relevant to a patient's decision-making in some clinical or social contexts, such as the potential for insurance discrimination, out-of-pocket costs and secondary research uses of patient's data that a clinician and patient may wish to discuss. Further, insurance coverage and out-of-pocket costs associated with CGES and follow-up testing and medical care based on results may be particularly important to some patients. On the other

hand, extrapolation to a primarily clinical context may be less complex and require less of the consent process than the translational context of the CSER1 program.

Another important point to consider is whether CGES-acquired data will be used for research. This might range from condition or phenotype-specific genetic discovery research that may directly inform affected patients and families to health systems research, such as assessing the cost-effectiveness of implementing CGES in different clinical settings. Also, research uses may not be fully anticipated at the time of testing. Clinicians, clinician-researchers and their institutions need to consider these potential uses in formulating the consent process for CGES. For further consideration of consent and governance as clinical and research boundaries blur, we refer readers to additional resources [46,47].

Consent and clinical decision-making can be enhanced by incorporating innovations in patient education, communication and decision support. Novel approaches to providing educational information and increasingly self-directed platforms for receiving and managing personal genomic health information hold promise [48,49]. Such innovations may address the structure of consent processes, tailoring the consent approach and the informational content. Tailoring consent might include directing patients to different consent modes (e.g., single session vs multiple sessions, in-person vs phone, etc.), educational content (e.g., web-based introduction to genetics) and timing (e.g., some patients may need more time than others to decide about additional findings). However, as innovations are developed and used in the process of consent, they must be evaluated to ensure that they enhance patients' abilities to learn about CGES and its implications and to make informed decisions.

Another key challenge for implementation, which requires additional evidence and debate, is the timing of analysis for additional findings and its implications for consent. The ACMG recommends that a minimum set of additional results be evaluated and offered for disclosure based on expected medical benefit and clinical utility, with the option for patients to opt out [12,43]. Overall, our recommendations are consistent with those of the ACMG and others: informed consent for sequencing should include discussion of the types of results available and their implications for probands and families; consent conversations should address the likelihood of obtaining certain results and the limitations of the testing [23,50], and perhaps most important, clinicians should communicate to patients that they can opt out of additional findings [43]. Others have also emphasized the need for confirming preferences for additional results on disclosure of primary results [51] and have advocated for more dynamic approaches to consent [52]. Where we depart is in how patients' decisions concerning additional findings should be operationalized during consent; specifically, we point to the advantages of deferring decisions about additional findings until after receipt of primary results. Informed consent for sequencing, including analysis for additional results and disclosure, is often conducted as part of the consent process for primary results. This consent is usually conducted before a sample is collected and sent to the laboratory for sequencing and analysis. Although there is significant variation in the policies and practices of commercial sequencing laboratories, most follow this testing procedure [53]. Yet individuals who express the need for more time to decide about additional findings may benefit from deferred analysis of – and staged consent [54] for – secondary findings for a number of reasons. First, patients may experience a high cognitive burden if required to consider both primary and secondary results at the same time. Second, individuals may often change their preferences for information upon further reflection [19,55]. Third, it is plausible that an individual or family's experiences with genetic testing and genetic conditions may influence future testing and responses to results. Finally, staged consent may offer patients the opportunity to make use of additional resources to inform their decisions.

We suggest that genetics professionals and clinical genetics laboratories consider implementing a modified workflow to allow for the possibility of staged consent and rigorously evaluate the impact of such modifications as compared to current workflows. With this modified workflow, a sample from a patient who has consented to sequencing is sent to a laboratory and sequenced. The laboratory conducts an initial bioinformatic analysis that is narrowly tailored to answer the diagnostic question that motivated the test, and the result is disclosed as appropriate. At this point, a second consent conversation occurs to learn if the patient desires that the sequence data be reanalyzed for additional results. If so, the laboratory is informed that it should proceed with the additional analysis.

Although this potential workflow for staged consent may offer some advantages to patients and providers, we recognize that a number of practical challenges exist and that separating the consent procedure may not always be feasible. These challenges include potential modification of laboratory procedures, additional costs for analysis, the need for a second consent discussion and the possibility of an additional office visit for results disclosure. At a minimum, this staged consent approach requires future empirical studies on patients' interest in and response to

such a consent process, whether there is any added value in practice and the costs or savings associated with such a workflow.

Future perspective

These considerations for clinical sequencing are based on the experiences of the CSER1 Informed Consent and Governance work group and Genetic Counseling work group and are limited by the experiences of these groups and by the published literature to date. Variation in other national and international contexts with respect to guidelines for return of additional findings, consent for additional findings and resource constraints, may limit the utility of our considerations. We appreciate that our recommendation to individualize the informed consent process may challenge attempts to standardize consent language and content for CGES [56]. However, the 12 key points can serve as a foundation for individualized consent. Indeed, we expect a variation that is responsive to the context of consent to enhance decision-making. More research is needed to understand how individuals and families decide to undergo sequencing and how their values influence these decisions. In addition, more research is required to determine which approaches to consent are associated with better comprehension and downstream responses to results. Overall, based on the experiences from the CSER1 Consortium, we believe that these six considerations and 12 key points provide a helpful starting point for informed consent to CGES in clinical care.

Executive summary

- Clinical Genome and Exome Sequencing (CGES) is increasingly used in a wide range of clinical settings.
- Informed consent for CGES is a challenge because of the potential for additional or incidental findings; complexity, uncertainty and heterogeneity in interpreting variants; and high patient expectations.
- We describe six considerations and 12 key points to communicate including the need to ascertain the patient's medical and personal contexts, tailoring information to the patient's contexts, limiting basic genetic and technical information, promoting reasonable patient expectations by focusing on the range of expected results and test limitations, facilitating decisions by discussing potential clinical and emotional implications of results and considering implications for the patient's family.
- Additional consent issues include the value of maximizing CGES data for research purposes, the potential role of innovation in patient education and the timing of consent and analysis for additional results.
- We propose that a model of staged consent may be optimal.

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