Motivations to learn genomic information are not exceptional:

Lessons from behavioral science

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Abstract

Whether to undergo genome sequencing in a clinical or research context is generally a voluntary choice. Individuals are often motivated to learn their results even when clinical utility—the possibility that the test result could inform medical recommendations or health outcomes—is unlikely. Motivations to seek one's genomic information can be cognitive, affective, social, or mixed (e.g., cognitive and affective) in nature. These motivations are based on perceptions of the value of the information, specifically, its *clinical* utility and *personal* utility. We suggest that motivations to learn genomic information are no different from motivations to learn other types of personal information, including one's health status and future disease risk. Here, we review behavioral science relevant to motivations that may drive engagement with genome sequencing, both in the presence and absence of clinical utility. Specifically, we elucidate ten motivations that are expected to guide decisions to undergo genome sequencing. Recognizing these motivations for learning genomic information will guide future research and ultimately help clinicians and researchers to facilitate informed decision making among individuals as genome sequencing becomes increasingly available.

Keywords: utility theory, decision making, genetic testing, social psychology, behavioral science, motivation

Introduction

Historically, genetic testing has been offered to patients primarily when clear evidence of clinical utility exists. Clinical utility can be defined as instances when genetic test results could inform medical recommendations[1] or provide a means to achieve improved health outcomes.[2] Thus, clinical utility exists when there is the promise that test results could influence one's health, but whether any individual's health is affected depends on the test result itself and the patient's response. In contrast to genetic testing, much of the genome sequence cannot yet be interpreted. Nevertheless, genome sequencing is becoming more widely available in clinical and research contexts, and studies have shown that patients and research participants (including those with rare complex conditions) desire to learn their personal genomic information *even when clinical utility is low or absent.*[3-7] Although not currently widely available, population testing of low risk individuals without a family history is being piloted and will likely increase in frequency. Individuals enrolling in this kind of testing have a low likelihood of actionable results, yet may still pursue testing.

We contend that decision making about genome sequencing is not exceptional relative to decision making in other domains and that it can be understood through the lens of behavioral and decision science. Pursuing genomic sequencing information resembles efforts to pursue any information about oneself, and thus, we consider how research on basic human motivations can be applied to understanding decision making in the novel context of genomic sequencing. We suggest that the concept of *decision utility*[8] provides a useful framework to understand patients' and research participants' decisions to undergo genome sequencing and to learn their results. In the context of pursuing genomic information, we define decision utility as encompassing expected clinical and personal utilities. Existing research on clinical and personal utilities

typically does not use the language of decision utility[9,10] (other than Smith and colleagues[11] who briefly touch on this construct), yet the construct of decision utility is directly applicable to decision making in the context of genome sequencing.

Using a decision utility framework, we identified ten common motivations for seeking personal information that may underlie decisions to undergo genome sequencing and learn one's results. Here, in order to ensure a clear and defined focus, we primarily highlight internal motivations (as opposed to external motivations such as from financial incentives) and primarily highlight motivators of testing rather than barriers, emphasizing the specific roles played by cognitive, affective, and social motivations in undergirding both clinical and personal utilities. We expect these motivations to apply in both clinical and research contexts, although empirical research is needed to confirm this. These motivations are expected to apply to adults who have their own genomes sequenced with or without diagnostic sequencing. Of note, these motivations may also be relevant to engagement with direct-to-consumer genetic tests. Interest in those tests, however, may be driven by . additional .factors including commercial influence (e.g., advertising), unrealistic expectations of clinical utility due to lack of informed genomic advice , or getting the test as a gift. It is beyond the scope of the current manuscript to consider how such factors might alter motivations to learn direct-to-consumer genetic test results as well as genomic sequencing results. Consequently, we focus specifically on research and clinical contexts and leave it to other researchers to determine to what extent this framework applies to direct-to-consumer genetic tests. Relatedly, these motivations should be relevant to genetic testing, but the focus of this framework is genome sequencing simply because clinical utility is less likely in genomic sequencing due to the sheer scope of possible test results. Thus, the range of motivations included in the framework may be more likely to have implications for

understanding genomic sequencing than genetic testing.

The ten motivations were selected based on discussion and consensus among the authorship team. We considered behavioral and decision science research as well as genetic testing research to identify motivations that were the most appropriate and applicable. The authorship team constitutes a team of investigators with expertise in social and health psychology, judgment and decision making, genomics, and genetic counseling with experience in motivations in various health contexts, including genome sequencing.

Empirical Research on Motivations to Learn Genomic Information

Before presenting the framework, it is useful to briefly review prior empirical research on motivations to learn genomic information. Understanding decision utility in the context of genome sequencing is becoming increasingly important considering rapid advances in genomics and functional genetics as well as disease risk and development of targeted treatments.[53] People may opt to learn genomic information when the test has clinical utility; that is, when it may provide information with clear implications for improving health outcomes that, in part, depends on development of evidence-based guidelines to inform health behaviors. Importantly, many participants across several large research consortia who have undergone genome sequencing and been offered the opportunity to learn their results have expressed strong preferences to learn their genomic information even in the context of limited or no clinical benefit.[3-6] These studies were designed to enroll under- represented populations and consisted of between 200-550 adults recruited from major U.S. cities (e.g., Washington, D.C., Boston) who were healthy, at risk of a heart condition, or had a heart condition.[4-6] Of note, although this is not a comprehensive review of the literature, these studies are from a large, federally funded consortium and represent the most contemporary evidence on this topic.

Further supporting the notion that people who undergo genome sequencing might derive a range of utilities from receiving their sequencing results, studies of adults unselected for any particular trait or health condition, as well as cancer patients and their biological relatives, have shown that participants rarely regret learning their genomic information, even when the majority do not learn any actionable information for their health or their child's health.[4,5,54-56] Personal curiosity was a common motivation for learning one's sequencing results whether participants were unselected for any particular trait or health condition or they were adults with or at risk of a particular health condition.[5,16-18] Research participants have reported that all knowledge is important, which includes self-knowledge, and that "knowledge is power."[54,57,58] They often regard their genome sequencing results as worth knowing, simply because it represents information about themselves.[5] Of note, these participants have been classified by some as "early adopters;" they tend to be recruited from major U.S. cities and are primarily non-Hispanic White privileged adults with high levels of income and education. Nonetheless, people are often motivated to attain self-knowledge, and this motivation results in increased personal utility and therefore decision utility for genome sequencing results. We turn now to decision utility and link it to the ten motivations .

Ten Common Motivations to Learn Genomic Information as Informed by Behavioral Science

We next present ten salient motivations to undergo genome sequencing based on behavioral science, including research on basic human motivations and the pursuit of health risk information (Table 1). Importantly, the motivations may be relevant to tests that vary in how much clinical utility they offer, if any. The motivations to undergo testing or sequencing are often quite clear when some degree of clinical utility is present: there is the possibility to

improve one's health. The framework is necessary because it reidentifies ten salient motivations to undergo genome sequencing even in the absence of clinical utility, but the framework also includes motivations related to improving one's health.

. For the sake of parsimony, we categorize the motivations as primarily cognitive, affective, or social, but they can overlap and operate simultaneously and sometimes synergistically. For example, we categorize the motivation to reduce uncertainty as cognitive, but it also can involve the desire to minimize negative affect or anxiety, which are affective processes.

Each motivation is known to affect people's perceptions of the value of decision options (decision utility). Thus, these motivations underlie and feed into decision utility. These motivations may be independent of clinical utility but nonetheless generate value in the form of personal utility that can greatly influence choices.[9,10,11] Clinical geneticists and genetic counselors offering genome sequencing (and other health professionals such as oncologists and neurologists, as genome sequencing moves beyond specialized genetics services) can assess the role of these motivations when supporting informed decision making. We also claim that pursuit of one's genome sequence resembles motivations to seek all types of self-relevant information. Thus, clinicians can expect motivations to influence decisions in both conscious and deliberate ways, as well as through implicit mechanisms. As such, they can address motivations to pursue genome sequencing as a way to help patients weigh the utility of information in making their decisions.

Cognitive motivations form the first category of motivations posited to influence decisions to learn genome sequencing information**.** These motivations are driven by a desire to learn new information or to make sense of the world and oneself and are based on perceptions

and processes that facilitate understanding.

1. **Availability motivation**. The "availability motivation" suggests that people may desire information that is "knowable" or already known by someone else (for example, if genome sequencing had already been completed). Simply knowing that information is available tends to be motivating in and of itself. The desire to learn information because it is available—or due to the belief that more information is better—is consistent with past findings that people sometimes seek out information even when they know it is inherently useless.[12,13] This desire for knowable information is likely stronger when the information provides self-knowledge, as genomic information does. This motivation may explain the frequency of self-reported motivations to learn genomic information simply because one is "curious."[7,14-16]
2. **Self-knowledge motivation**. Starting in childhood and continuing into adulthood, people tend to display egocentric tendencies across health and other contexts.[17,18] This self-focus may explain why people are motivated to learn their genomic information. Prior research suggests that people are often more motivated to learn health information about themselves than they are to learn non-personalized health information.[19] Self-knowledge motivations may further explain desires to learn genome sequencing information about one's children (particularly in the instance of diagnostic genome sequencing for a child with symptoms), siblings, or other relatives, although this remains to be empirically tested.
3. **Motivation to reduce uncertainty**. People commonly perceive uncertainty as cognitively aversive.[20,21] Therefore, they may desire to learn their genomic

information if they perceive—perhaps inaccurately—that doing so will reduce uncertainty about their future health outcomes. For example, people who have a family history of cancer may want to learn whether they are at higher genetic risk in order to potentially take action, but also because a negative result may confer personal utility in the form of reduced uncertainty about one's risk status. Thus, people may expect that the test result will reduce uncertainty about one's risk regardless of whether the test result is positive or negative.

4. **Motivation to obtain information that increases perceived empowerment and self-efficacy.**

People are generally motivated to be high in self-efficacy (that is, to feel that they have the ability to accomplish certain tasks), to have mastery over their lives, and to control over their life outcomes.[22-24] For example, competence—one aspect of self-efficacy—is considered a basic psychological need.[25] Learning genomic information can help people achieve self-efficacy to the extent that genomic information is perceived as empowering, regardless of whether the information is relevant to improving one's health. In general, people who expect that learning genomic information will lead to a greater sense of empowerment and control over their life and outcomes should be more likely to be interested in learning this information.

We expect that each of these cognitive motivations may be further enhanced by perceptions of genomic information as immutable. For example, unlike genetic information that does not change, health information that changes (for example, cholesterol level or blood pressure) is less likely to be perceived as reducing uncertainty or as critical self-knowledge to have.

The second category of motivations is **affective motivations**, which reflect people's desires to experience particular affective states in both the present and the future. Substantial research has shown that affect drives behavior in a variety of direct and indirect ways,[26-29] and the domain of learning genomic information is no exception.

5. People are generally motivated to **experience positive affect** (although there are cultural differences in the type of positive affect that is most desired[30])**.** More specifically, people are generally motivated to maintain current and attain future positive affective states (e.g., feeling good) and things one desires.[30,31] With respect to genome sequencing, people might be motivated to learn information if they perceive that it will maintain or lead to positive affective states, such as happiness, hope, or relief. Indeed, empirical research has shown that personalized genetic risk information can lead to positive emotion.[33,34]
6. Similarly, people are generally motivated to **minimize their experience of negative affect.** More specifically, people often seek to minimize current and future negative affective states (e.g., feeling bad) and to avoid things they dislike**.** If people believe that learning genomic information will reduce negative emotions, they may be more likely to seek out that information. For example, anticipated regret is a powerful motivator of behavior and can influence both decisions to act—"I will regret it if I do not learn this information" – and not to act – "I will regret it if I learn this information."[35] In addition, worry is a strong predictor of behavior.[36] Thus, someone who worries about diseases that could be indicated by the test (e.g., cancer) may be driven to get tested to reduce the worry and potential uncertainty, whereas someone who anticipates negative affect in

response to getting genomic test results may avoid getting the test.

The third category of motivations is **social motivations,** which refer to motivations aimed at connecting with and relating to other people. Humans are fundamentally social creatures; evolutionarily, relationships served important survival functions,[37] and the presence of high quality social relationships is a strong correlate of longevity.[38] Given this critical role of social motivations in human behavior and health, we posit that social motivations also underlie desire to learn genomic information.

7. **Social connection**. Affiliating and connecting with other people is a major component of human life, and people are generally motivated to be accepted and to belong.[39] *Relatedness* is a basic psychological need, a desire to be understood and cared for by others.[40] Similar to self-knowledge motivations, relatedness motivations may explain desires to learn genome sequencing information about one's children, siblings, or other relatives.
8. **Social norms**. Many people's behavior is strongly influenced both by what they think others are doing (descriptive social norms) and what they think others want them to do (injunctive social norms).[41,42] As such, believing that others are learning information about their own health or that others believe learning health information is the best course of action may motivate people to seek out their own genomic information. Some research has provided support for these ideas.[43,44]
9. **Social comparison.** People often naturally compare themselves to others to obtain information about themelves.[45,46] Much work suggests that people compare their health states and health risks with those of others,[47] and those comparisons can have potentially important effects on risk-related behavior irrespective of

their own health standing.[48] As such, people may be motivated to learn genomic information not only to adhere to social norms, as suggested above, but also to compare their results to those of other people.

10. **Prosocial motivation**. Prosocial behavior refers to actions aimed at improving the well-being of others.[49] Importantly, prosocial behavior can be directed towards family in addition to friends and strangers, and thus is relevant in the context of genome sequencing.[50] Learning genomic information that may be relevant to the health of one's children may be a prosocial act, and this particular motivation is commonly reported by individuals opting to learn genome sequencing information.[51] Indeed, focus groups indicated that African-American participants desired community and societal benefits related to racial justice as a result of participating in genome sequencing.[52]

Existing Models of Utility in Genome Sequencing

Stemming from empirical research indicating that people are motivated to learn genomic information when the test has low or no clinical utility, frameworks of utilities of genomic information have been developed that typically highlight constructs such as perceived utilities.[4,29] The most notable example of perceived utility is personal utility—patient-endorsed benefits that are also referred to as non-clinical outcomes.[9,10,11] Personal utility has been defined as the individual's perceived value of genomic information that is distinct from its clinical value. This construct was delineated based on findings from a systematic review,[10] a modified Delphi approach with participants enrolled in a National Institutes of Health (NIH) genome sequencing study,[9] and validation of a novel scale to assess personal utility in the NIH Clinical Sequencing Exploratory Research (CSER) Consortium,[11] and it encompasses non-clinical reasons for

undergoing genome sequencing. Examples of personal utility include concepts that are known antecedents and outcomes of the decision-making process in healthcare settings, such as informing future decisions about having children, mentally preparing for the future, and feeling more in control of one's life. The notion of personal utility describes why, when clinical utility and actionable results are unlikely, research participants and patients nonetheless seek out their genomic information.[3-7] We posit that the ten motivations in the current framework help to explain these perceptions of personal utility.

Decision utility as an overarching framework to understand decisions to learn one's genome sequencing information

We have focused on decisions about whether to undergo genome sequencing and to learn the results in relation to both clinical and personal utility. We construe decision utility as being comprised of both clinical utility and personal utility, both of which appear to be influenced by motivations. Research on decision utility provides a useful overarching framework to understand the ten motivations and why people would seek genomic information even when the test has low or no clinical utility and is unlikely to affect one's medical recommendations or health outcomes.

Utility is not a novel concept, and, like the motivations we described, it is not specific to the context of genome sequencing and genetic testing. Utility has been described as wants and preferences, or "wantability,"[60] thus allowing for the opportunity of personal utility that we consider critical to understanding research participants' genome-sequencing decisions. We argue that by understanding the broader context of research on utility, clinicians and genome scientists will be better equipped to recognize motivations for undergoing genome sequencing as similar to motivations to learn other types of health information rather than as novel to genomics.

According to research and theories on decision utility, individuals make decisions by

determining how much they value possible outcomes, each weighted by the associated actual or perceived likelihood it will occur.[8] For example, in the domain of health, people might decide whether to exercise based on beliefs that the behavior will improve their health or will be difficult or inconvenient, and weigh the likelihood and importance of each of these possible outcomes.

In the context of genome sequencing specifically, Smith and colleagues propose a broad conceptualization of the value of genomics in translational research that builds on thinking from medicine, philosophy, decision psychology and health economics.[11] They note that when people are deciding whether to seek genome sequencing information, their decisions hinge on their expectations of the value and likelihood of the results, and values are multi-faceted. Decision utility includes clinical utility and beliefs and preferences that help to explain why people expect benefits from obtaining genome sequencing information.

We suggest that people decide whether to undergo genome sequencing and learn their results based on their perceptions of gains and losses (and their likelihoods of occurrence) within both clinical and personal utility. In other words, decisions are based in part on motivations that arise from beliefs that some valued non-clinical outcome(s) will result from the genome sequencing choice.[61,62] For example, one might be motivated to undergo sequencing because of a belief that doing so is likely to enhance social bonding with family members with similar genomic findings, and this social bonding outcome is highly desired. Using decision utility as a framework, we identified motivations known to affect decision utility that are therefore likely to affect decisions to undergo genome sequencing. Awareness of common motivations that are independent of clinical utility but can affect decision utility may facilitate appreciation of these motivations that are common in the pursuit of many types of self-relevant information.

Research Implications of this Framework

The framework presented can guide research examining decisions to undergo genome sequencing in clinical or research settings. While based on relevant existing evidence, the framework needs to be tested empirically to determine the prevalence and strength of the proposed motivations for learning genomic sequencing results. Although research supports the applicability of these motivations for learning self-relevant information more broadly, they have not all been tested in the context of genomic sequencing, and little is known about how much they differ across people and health contexts.

Here, we focused on expected utilities and the motivations that drive people to undergo genome sequencing. We expect these motivations to relate closely to the anticipated perceived utility of genomic sequencing and the utility people perceive after learning results. For example, expected utilities and motivations should influence whether people find value in receiving the information or whether they change their behavior upon learning of elevated risk. Thus, research stemming from this framework should help to predict how people will make decisions to undergo genome sequencing and how they respond to learning results. We believe it will also be important to better understand why people opt to learn genomic sequencing results as this technology becomes more widely available outside of research protocols and is used more often in clinical care.

Understanding motivations to undergo genome sequencing will also have a practical impact in that it will help researchers to recruit individuals to participate in genome sequencing research: researchers can highlight potential utilities that people may experience from learning the information. In addition, understanding the motivations will allow clinicians to walk people through the decision-making process, helping them make better decisions about whether to learn

the information. For example, a health professional might infer that a patient who mentions friends and family who have been tested is being influenced by social norms. Helping the patient understand this influence and any potential clinical relevance of genome sequencing, while treating their utility perceptions respectfully, may help the patient to balance the positive utility of the motivation with the potential clinical utility of the test.

To understand further why people may be interested in learning genome sequencing results, investigators can conduct studies and experiments using more diverse samples and with participants who are not enrolled in genome sequencing research. This would allow researchers to gain critical information about people who decline to participate in sequencing. In qualitative research, participants could be prompted regarding the specific motivations in our framework. In quantitative research, participants could be asked how much they endorse these various motivations. Additional research questions include: Which motivations are adaptive and which are not? How do these motivations map on to experienced utilities—are there some expectations that are not realized? Further, how do the motivations interact, and possibly conflict? When motivations conflict, how do people resolve the conflict to make a decision?

Future studies could assess perceived utility using measures such as willingness to pay. Another research question pertains to how much perceived utility individuals need to undergo genome sequencing. Researchers can also conduct studies to better ascertain the relationship between clinical utility and personal utility. If there is little perceived clinical utility, does that lead people to contemplate personal utility that motivates them to undergo testing? If there is sufficient clinical utility, do people even entertain personal utility? If clinical utility is low, what communication approaches should health professionals take to empower patients with knowledge of the test's limited clinical utility and an understanding of the motivations and their

influences?

Limitations

In this review, we focus on clinical and research participants' motivations to learn genome sequencing information, particularly for tests that have low or no clinical utility and are thus unlikely to affect one's medical recommendations or health outcomes. These are the primary contexts in which individuals have received their genomic information; other than the availability of genome sequencing from direct-to-consumer testing companies, most opportunities to learn information about one's genomic information occur within research studies in which participants are healthy volunteers or patients with undiagnosed, rare, or complex conditions. The motivations described in the proposed framework are intended to apply across clinical scenarios, and as such are described broadly. For example, within any specific clinical context there may be specific types of uncertainty that individuals want to resolve—e.g., the cause of a child's symptoms—but the overarching motive to reduce uncertainty is shared. Importantly, empirical research is needed to test the extent to which various motivations apply across different clinical contexts. Empirical research is also needed to determine the extent to which motivations apply across different health contexts. For example, we expect the motivations to carry less weight when the likelihood of clinical utility is higher. In addition, motivations to learn genomic information in research settings may differ from motivations among people undergoing clinical or commercial testing. For example, research participants may be more motivated by curiosity than participants undergoing clinical genome sequencing in pursuit of the underlying cause of a rare disease. These questions can be empirically assessed once genome sequencing is more widely available outside of research settings.

Another limitation of the current commentary pertains to limitations of the research on

which this commentary is based. Behavioral science research has been criticized for being conducted with what is known as "WEIRD" samples—samples in which people are recruited from societies that are Western, Educated, Industrialized, Rich, and Democratic.[63] Many of the initial studies of participants enrolled in genome sequencing research included primarily White adults with high socioeconomic status who can be considered "early adopters" of this technology.[64] Notably, efforts are underway to increase the socioeconomic and racial diversity of people who participate in genome sequencing research.[65] Further efforts to increase dissemination of genomic sequencing to members of historically underrepresented groups, including people with lower socioeconomic status, should pay careful attention to additional barriers that may be stronger among members of these groups, such as medical mistrust,[64] genomic knowledge, and access to and resources needed to undergo genome sequencing. Clinical utility is objectively lower for individuals who are not of European descent because these individuals have been underrepresented in genome sequencing research.[66] Finally, we note that although the authorship team of this commentary is multi-disciplinary, we are approaching this topic primarily from a social psychology lens and that has likely influenced the claims made and examples provided.

Discussion

We have provided a review of motivations that influence decision utility and thereby drive decisions to undergo genome sequencing. These motivations are not specific to learning genomic information; they underlie human behavior regardless of context or domain and are therefore not exceptional and thus likely to apply to genome sequencing—they are relevant to healthy adults deciding whether to undergo genome sequencing when clinical utility is low or absent. Knowledge about and understanding of these motivations may give genome scientists a

fuller picture of the reasons for participants' choices and may help clinical geneticists understand how participants may perceive utility in genomic information with limited clinical utility. We suggest that benefits falling in the domain of personal utility—such as increased positive affect or adherence to perceived norms—can be as important as more (seemingly) concrete clinical utility benefits of learning that one should undergo accelerated screening due to elevated disease risk. An understanding of a full range of human motivations for learning genomic information will allow clinicians to facilitate informed decision making among individuals as genome sequencing becomes increasingly available. It may also help to increase understanding of why patients and participants value information that genome scientists may view as benign.

Conclusions and Ways Forward

The motivations underlying people's ability to perceive utility in their genome information are not exceptional and can be understood based on the study of motivations in the behavioral and decision sciences. Motivations for seeking out genome sequencing information can be categorized as cognitive, affective, and/or social, with these motives exerting influence beyond conscious awareness. We contend that considering these motivations in the clinical context of genome sequencing builds on the case for personal utility championed by others[9,10,11] and also introduces several promising areas of future research.

References

1. Shickh S, Mighton C, Uleryk E, Pechlivanoglou P, Bombard Y. The clinical utility of exome and genome sequencing across clinical indications: a systematic review. *Hum Genet.* 2021;140(10):1403-1416. doi: 10.1007/s00439-021-02331-x

2. Retterer K, Juusola J, Cho MT, et al. Clinical application of whole-exome sequencing across clinical indications. *Genet Med.* 2016;18(7):696-704. doi: 10.1038/gim.2015.148

3. Lewis KL, Heidlebaugh AR, Epps S, et al. Knowledge, motivations, expectations, and traits of an African, African-American, and Afro-Caribbean sequencing cohort and comparisons to the original ClinSeq® cohort. *Genet Med.* 2019;21(6):1355-1362. doi: 10.1038/s41436-018-0341-9

4. Roberts JS, Robinson JO, Diamond PM, et al. Patient understanding of, satisfaction with, and perceived utility of whole-genome sequencing: findings from the MedSeq Project. *Genet Med.* 2018;20(9):1069-1076. doi: 10.1038/gim.2017.223

5. Zoltick ES, Linderman MD, McGinniss MA, et al. Predispositional genome sequencing in healthy adults: design, participant characteristics, and early outcomes of the PeopleSeq Consortium. *Genome Med.* 2019;11(1):10. doi: 10.1186/s13073-019-0619-9

6. Facio FM, Eidem H, Fisher T, et al. Intentions to receive individual results from whole-genome sequencing among participants in the ClinSeq study. *Eur J Hum Genet.* 2013;21(3):261-265. doi: 10.1038/ejhg.2012.179

7. Sanderson SC, Linderman MD, Suckiel SA, et al. Motivations, concerns and preferences of personal genome sequencing research participants: Baseline findings from the HealthSeq project. *Eur J Hum Genet.* 2016;24(1):14-20. doi: 10.1038/ejhg.2015.179

8. Kahneman D, Tversky A. Prospect Theory: An Analysis of Decision under Risk. *Econometrica.* 1979;47(2):263-291.

9. Kohler JN, Turbitt E, Lewis KL, et al. Defining personal utility in genomics: A Delphi study. *Clin Genet.* 2017;92(3):290-297. doi: 10.1111/cge.12998

10. Kohler JN, Turbitt E, Biesecker BB. Personal utility in genomic testing: a systematic literature review. *Eur J Hum Genet.* 2017;25(6):662-668. doi: 10.1038/ejhg.2017.10

11. Smith HS, Brothers KB, Knight SJ, et al. Conceptualization of utility in translational clinical genomics research. *Am J Hum Genet.* 2021;108(11):2027-2036. doi: 10.1016/j.ajhg.2021.08.013

12. Peters E, Klein W, Kaufman A, Meilleur L, Dixon A. More Is Not Always Better: Intuitions About Effective Public Policy Can Lead to Unintended Consequences. *Soc Issues Policy Rev.* 2013;7(1):114-148. doi: 10.1111/j.1751-2409.2012.01045.x

13. Bastardi A, Shafir E. On the pursuit and misuse of useless information. *J Pers Soc Psychol.* 1998;75(1):19-32. doi.org/10.1037/0022-3514.75.1.19

14. Facio FM, Brooks S, Loewenstein J, Green S, Biesecker LG, Biesecker BB. Motivators for participation in a whole-genome sequencing study: implications for translational genomics research. *Eur J Hum Genet.* 2011;19(12):1213-1217. doi: 10.1038/ejhg.2011.123

15. Rego S, Dagan-Rosenfeld O, Bivona SA, Snyder MP, Ormond KE. Much ado about nothing: A qualitative study of the experiences of an average-risk population receiving results of exome sequencing. *J Genet Couns.* 2019;28(2):428-437. doi: 10.1002/jgc4.1096

16. Gollust S, Gordon E, Zayac C, et al. Motivations and perceptions of early adopters of personalized genomics: perspectives from research participants. *Public Health Genomics.* 2012;15(1):22-30. doi: 10.1159/000327296

17. Bocian K, Baryla W, Wojciszke B. Egocentrism shapes moral judgements. *Soc Pers Psychol Compass.* 2020;14(12):1-14. doi: 10.1111/spc3.12572

18. Gilovich T, Savitsky K. The spotlight effect and the illusion of transparency: Egocentric

assessments of how we are seen by others. *Curr Dir Psychol Sci.* 1999;8(6):165-168. doi.org/10.1111/1467-8721.00039

19. Kreuter MW, Bull FC, Clark EM, Oswald DL. Understanding how people process health information: a comparison of tailored and nontailored weight-loss materials. *Health Psychol.*

20. Han PK, Reeve BB, Moser RP, Klein WM. Aversion to ambiguity regarding medical tests and treatments: measurement, prevalence, and relationship to sociodemographic factors. *J Health Commun.* 2009;14(6):556-572. doi: 10.1080/10810730903089630

21. Anderson EC, Carleton RN, Diefenbach M, Han PK. The relationship between uncertainty and affect. *Front Psychol.* 2019;10:2504. doi: 10.3389/fpsyg.2019.02504

22. Harter S. Effectance Motivation Reconsidered. Toward a Developmental Model. *Hum Devel.* 1978;21(1):34-64. doi.org/10.1159/000271574

23. White RW. Motivation reconsidered: the concept of competence. *Psychol Rev.* 1959;66(5):297. doi.org/10.1037/h0040934

24. Bandura A. Human agency in social cognitive theory. *Am Psychol.* 1989;44(9):1175-1184. doi.org/10.1037/0003-066X.44.9.1175

25. Deci EL, Ryan RM. The" what" and" why" of goal pursuits: Human needs and the self-determination of behavior. *Psychol Inquiry.* 2000;11(4):227-268. doi.org/10.1207/S15327965PLI1104_01

26. Peters SA, Laham SM, Pachter N, Winship IM. The future in clinical genetics: affective forecasting biases in patient and clinician decision making. *Clin Genet.* 2014;85(4):312-317. doi: 10.1111/cge.12255

27. Peters E, Lipkus I, Diefenbach MA. The functions of affect in health communications and in the construction of health preferences. *J Commun.* 2006;56:S140-S162. doi.org/10.1111/j.1460-

2466.2006.00287.x

28. Rivis A, Sheeran P, Armitage CJ. Expanding the affective and normative components of the theory of planned behavior: A meta-analysis of anticipated affect and moral norms. *J Appl Soc Psychol.* 2009;39(12):2985-3019. doi.org/10.1111/j.1559-1816.2009.00558.x

29. Damasio AR. *Descartes' error: Emotion, rationality and the human brain.* Putnam; 1994.

30. Tsai JL. Ideal affect in daily life: Implications for affective experience, health, and social behavior. *Curr Opin Psychol.* 2017;17:118-128.

31. Isen AM, Simmonds SF. The effect of feeling good on a helping task that is incompatible with good mood. *Soc Psychol.* 1978:346-349. doi.org/10.2307/3033588

32. Isen AM, Shalker TE, Clark M, Karp L. Affect, accessibility of material in memory, and behavior: A cognitive loop? *J Pers Soc Psychol.* 1978;36(1):1-12. doi.org/10.1037/0022-3514.36.1.1

33. Aspinwall LG, Taber JM, Leaf SL, Kohlmann W, Leachman SA. Genetic testing for hereditary melanoma and pancreatic cancer: a longitudinal study of psychological outcome. *Psychooncology.* 2013;22(2):276-289. doi: 10.1002/pon.2080

34. Aspinwall LG, Taber JM, Kohlmann W, Leachman SA. Psychological aspects of hereditary cancer risk counseling and genetic testing. In: Carr B, Steel J, eds. Psychological aspects of cancer. Springer; 2013:31-64.

35. Brewer NT, DeFrank JT, Gilkey MB. Anticipated regret and health behavior: A meta-analysis. *Health Psychol.* 2016;35(11):1264. doi: 10.1037/hea0000294

36. Hay JL, McCaul KD, Magnan RE. Does worry about breast cancer predict screening behaviors? A meta-analysis of the prospective evidence. *Prev Med.* 2006;42(6):401-408. doi: 10.1016/j.ypmed.2006.03.002

37. Taylor SE, Klein LC, Lewis BP, Gruenewald TL, Gurung RA, Updegraff JA. Biobehavioral responses to stress in females: tend-and-befriend, not fight-or-flight. *Psychol Rev.* 2000;107(3):411-429. doi.org/10.1037/0033-295X.107.3.411

38. Holt-Lunstad J, Smith TB, Layton JB. Social relationships and mortality risk: a meta-analytic review. *PLoS Med.* 2010;7(7):e1000316. doi: 10.1371/journal.pmed.1000316.

39. Leary MR. Affiliation, acceptance, and belonging: The pursuit of interpersonal connection. In: Fiske ST, Gilbert DT, Lindzey G, eds. Handbook of social psychology, Vol. 2, 5th ed. John Wiley & Sons, Inc.; 2010:864-897.

40. Deci EL, Ryan RM. The" what" and" why" of goal pursuits: Human needs and the self-determination of behavior. *Psychol Inquiry.* 2000;11(4):227-268. doi.org/10.1207/S15327965PLI1104_01

41. Sheeran P, Maki A, Montanaro E, et al. The impact of changing attitudes, norms, and self-efficacy on health-related intentions and behavior: A meta-analysis. *Health Psychol.* 2016;35(11):1178. doi: 10.1037/hea0000387

42. Cialdini RB, Trost MR. Social influence: Social norms, conformity and compliance. In: Gilbert DT, Fiske ST, Lindzey G, eds. The handbook of social psychology, Vols. 1-2, 4th ed.. McGraw-Hill; 1998;151-192.

43. Reid AE, Taber JM, Ferrer RA, et al. Associations of perceived norms with intentions to learn genomic sequencing results: Roles for attitudes and ambivalence. *Health Psychol.* 2018;37(6):553-561. doi: 10.1037/hea0000579

44. Heck PR, Meyer MN. Information avoidance in genetic health: Perceptions, norms, and preferences. *Soc Cog.* 2019;37(3):266-293. https://doi.org/10.1521/soco.2019.37.3.266

45. Festinger L. (1954b). A theory of social comparison processes. *Hum Relations*, 7, 117-140.

1954.

46. Gilbert DT, Giesler RB, Morris KA. When comparisons arise. *J Pers Soc Psychol.* 1995;69(2):227-236. doi.org/10.1037/0022-3514.69.2.227

47. Buunk BP, Gibbons FX, Buunk A. Health, coping, and well-being: Perspectives from social comparison theory. Psychology Press; 2013.

48. Klein WM. Objective standards are not enough: affective, self-evaluative, and behavioral responses to social comparison information. *J Pers Soc Psychol.* 1997;72(4):763. doi: 10.1037//0022-3514.72.4.763

49. Dovidio JF, Piliavin JA, Schroeder DA, Penner LA. The social psychology of prosocial behavior. Psychology Press; 2017.

50. Padilla-Walker LM, Carlo G, Memmott-Elison MK. Longitudinal change in adolescents' prosocial behavior toward strangers, friends, and family. *J Res Adolesc.* 2018;28(3):698-710. doi: 1111/jora.12362

51. Biesecker BB, Lewis KL, Umstead KL, et al. Web platform vs in-person genetic counselor for return of carrier results from exome sequencing: a randomized clinical trial. *JAMA Intern Med.* 2018;178(3):338-346. doi: 10.1001/jamainternmed.2017.8049

52. Yu JH, Crouch J, Jamal SM, Tabor HK, Bamshad MJ. Attitudes of African Americans toward return of results from exome and whole genome sequencing. *Am J Med Genet A.* 2013;161a(5):1064-1072. doi: 10.1002/ajmg.a.35914

53. Prokop JW, May T, Strong K, et al. Genome sequencing in the clinic: the past, present, and future of genomic medicine. *Physiol Genomics.* 2018;50(8):563-579. doi: 10.1152/physiolgenomics.00046.2018

54. Hoell C, Aufox S, Nashawaty N, Myers MF, Smith ME. Comprehension and personal value of negative non-diagnostic genetic panel testing. *J Genet Couns.* 2021;30(2):418-427. doi: 10.1002/jgc4.1327

55. Taber JM, Klein WMP, Lewis KL, Johnston JJ, Biesecker LG, Biesecker BB. Reactions to clinical reinterpretation of a gene variant by participants in a sequencing study. *Genet Med.* 2018;20(3):337-345. doi: 10.1038/gim.2017.88

56. Napier CE, Davies G, Butow PN, et al. Cancer patient knowledge about and behavioral intentions after germline genome sequencing. *Patient Educ Couns.* 2022;105(3):707-718. doi: 10.1016/j.pec.2021.07.004

57. Kauffman TL, Irving SA, Leo MC, et al. The NextGen Study: patient motivation for participation in genome sequencing for carrier status. *Mol Genet Genomic Med.* 2017;5(5):508-515. doi: 10.1002/mgg3.306

58. Mighton C, Carlsson L, Clausen M, et al. Quality of life drives patients' preferences for secondary findings from genomic sequencing. *Eur J Hum Genet.* 2020;28(9):1178-1186. doi: 10.1038/s41431-020-0640-x.

59. Smith HS, Morain SR, Robinson JO, et al. Perceived Utility of Genomic Sequencing: Qualitative Analysis and Synthesis of a Conceptual Model to Inform Patient-Centered Instrument Development. *Patient.* 2022;15(3):317-328. doi: 10.1007/s40271-021-00558-4

60. Kahneman D. New Challenges to the Rationality Assumption. *J Institut Theor Econ.* 1994;150(1):18-36.

61. Hallowell N, Cooke S, Crawford G, Lucassen A, Parker M, Snowdon C. An investigation of patients' motivations for their participation in genetics-related research. *J Med Ethics.*

2010;36(1):37-45. doi: 10.1136/jme.2009.029264.

62. Lewis C, Sanderson S, Hill M, et al. Parents' motivations, concerns and understanding of genome sequencing: a qualitative interview study. *Eur J Hum Genet.* 2020;28(7):874-884. doi: 10.1038/s41431-020-0575-2

63. Henrich J, Heine SJ, Norenzayan A. The weirdest people in the world? *Behav Brain Scis.* 2010;33(2-3):61-83. doi: 10.1017/S0140525X0999152X

64. Hull LE, Vassy JL. Toward greater understanding of patient decision-making around genome sequencing. *Per Med.* 2018;15(1):57-66. doi: 10.2217/pme-2017-0037

65. Amendola LM, Berg JS, Horowitz CR, et al. The Clinical Sequencing Evidence-Generating Research Consortium: Integrating Genomic Sequencing in Diverse and Medically Underserved Populations. *Am J Hum Genet.* 2018;103(3):319-327. doi: 10.1016/j.ajhg.2018.08.007

66. Gutierrez AM, Robinson JO, Outram SM, et al. Examining access to care in clinical genomic research and medicine: Experiences from the CSER Consortium. *J Clin Transl Sci.* 2021;5(1):e193. doi: 10.1017/cts.2021.855

Table 1: Motivations to undergo genome sequencing

Name of motivation	**Description of motivation**
Cognitive motivations	**Driven by a desire to learn new information or to make sense of the world and oneself**
1. Availability motivation	People desire available and "knowable" information
2. Self-knowledge motivation	People desire to learn about themselves
3. Motivation to reduce uncertainty	People desire to minimize uncertainty and to obtain accuracy and predictability
4. Motivation to obtain information that increases perceived empowerment and self-efficacy	People desire to feel empowered and to experience self-efficacy, which can be increased by personally relevant information irrespective of its clinical utility
Affective motivations	**Driven by a desire to experience positive affect and avoid negative affect**
5. Maximize current and future positive affect	People desire to increase or enhance positive emotion, such as happiness, hope, or relief, now and in the future
6. Minimize current and future negative affect	People desire to decrease or prevent negative emotion, such as sadness, disappointment, fear, worry, or regret, now and in the future
Social motivations	**Driven by a desire to connect with or relate to others**
7. Social connection	People desire to affiliate with and connect to other people
8. Social norms	People tend to adhere to social norms indicating what others are doing or expect others to do
9. Social comparison	People tend to compare themselves to other people, allowing them to better understand the self or to feel better about the self
10. Prosocial motivation	People desire to engage in actions that improve the well-being of others