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Interpretations of the Term "Actionable" when Discussing Genetic Test Results: What you Mean Is Not What I Heard

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Abstract

In genomic medicine, the familiarity and inexactness of the term "actionable" can lead to multiple interpretations and mistaken beliefs about realistic treatment options. As part of a larger study focusing on public attitudes toward policies for the return of secondary genomic results, we looked at how members of the lay public interpret the term "medically actionable" in the context of genetic testing. We also surveyed a convenience sample of oncologists as part of a separate study and asked them to define the term "medically actionable." After being provided with a definition of the term, 21 out of 60 (35%) layperson respondents wrote an additional action not specified in the provided definition (12 mentioned "cure" and 9 mentioned environment or behavioral change) and 17 (28%) indicated "something can be done" with no action specified. In contrast, 52 surveyed oncologists did not mention environment, behavioral change, or cure. Based on our findings, we propose that rather than using the term "actionable" alone, providers should also say "what they mean" to reduce miscommunication and confusion that could negatively impact medical decision-making. Lastly, to guide clinicians during patient-provider discussion about genetic test results, we provide examples of phrasing to facilitate clearer communication and understanding of the term "actionable."

KEYWORDS

Medically actionable, Genomic results, Health provider-patient communication, health literacy

1 | INTRODUCTION

The emergence of precision medicine, along with advances in genomic sequencing technology, bring new diagnostic and screening tests and new terminology (Jarvik and Evans 2016). The medical terminology used by healthcare providers and researchers is often confusing for patients and research participants, with no clear or precise meaning (Clayman et al. 2016). This lack of clarity can result in miscommunication and make it difficult for laypersons to identify, let alone understand, which aspects of genetic information are relevant for healthcare decisions (Berkman et al. 2011; Shay and Lafata 2014).

Health care providers can best communicate medical information to patients by using well-defined, plain language (i.e., wording patients can understand the first time they read or hear it) (Centers for Disease Control and Prevention 2016; Fagerlin et al. 2011; Plain Language Association International 2016; Rudd et al. 2004) so that "gist knowledge" (i.e., the essential meaning of medical information) can be achieved (Hawley et al. 2008; Tait et al. 2010). The concept of gist understanding, or the processes that form representations of an event's meaning in language or logic rather than its surface details, arises from the fuzzy-trace theory that draws upon the dual process theory of memory (Gomes and Brainerd 2012; Reyna and Brainerd 1995). However, commonly used words or phrases do not
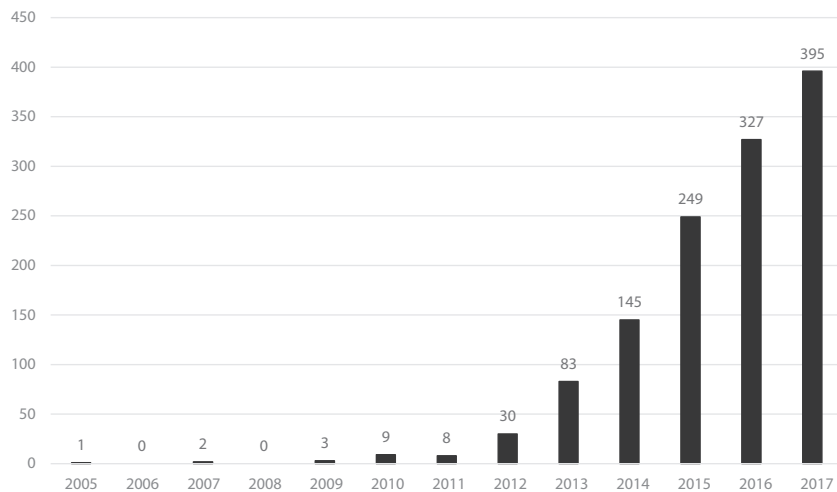
FIGURE 1 Number of journal articles that referred to actionable/actionability as it relates to human genomics/genetics (*n* = 1252). Search terms used in PubMed (through December 31, 2017) listed in supplemental table. Further exclusions: reference type: book, comment; actionable/actionability not in title/abstract; actionability not used in direct relation to genomic or genetic results, non-human genetics

always have the same core meaning for different users (Nickerson 1999). When plain language terms with different potential meanings are used as medical jargon, this may lead to imprecise or inaccurate gist understanding, undermining communication between patients and healthcare providers, and potentially impacting decision-making (Lafata et al. 2017).

Medical genetics is an area of medicine where this communication challenge is particularly acute. Not only does genetics require the communication of complex concepts, but because it is a rapidly advancing field, genetics also introduces new, unfamiliar terms, and expands and alters the meaning of existing medical jargon. The term "actionable" (as in "clinically or medically actionable"), for example, is now widely used in medical genetics. "Actionable" first gained traction in the field of medical genetics after the 2013 release of the American College of Medical Genetics and Genomics (ACMG) recommendations on how to handle disclosure of incidental findings (now known as secondary findings) from clinical genomic sequencing (American College of Medical Genetics and Genomics 2013; Green et al. 2013; Kalia et al. 2017). Following the issuance of these recommendations, there was a noticeable increase in the use of the term "actionable"in the genetics literature as a short-hand, common description of the notion that "something can be done" using results obtained from genetic testing (see Fig. 1).

The term "actionable" has been used in a variety of ways, including, but not limited to: "potentially actionable" (Bieg-Bourne et al. 2017; Damodaran et al. 2015; Ferrarotto et al. 2016), "clinically actionable" (Desmond et al. 2015; Douglas et al. 2016; Vandekerkhove et al. 2017), and "actionable mutation" (Butler et al. 2015; Schwaederle et al. 2016; Thierry et al. 2017). These articles range from guidelines, policy, and perspective pieces focusing on "actionability" (Berg et al. 2013; Carr et al. 2016; Manolio et al. 2013; Ramos et al. 2014; Sukhai et al. 2016; Vidwans et al. 2014) to empirical research that provide various, implicit, or explicit definitions of the term "actionable" (Ananda et al. 2015; Butler et al. 2015; Middha et al. 2014; Pritchard et al. 2014; Wong et al. 2015; Wyatt et al. 2016; Yuan et al. 2016). There are also differences in how geneticists define the term "actionable" as evident from the lack of full consensus over what

genes should be considered actionable and routinely disclosed when genomic sequencing is done (Green et al. 2012).

In its simplest form, actionable means "capable of being acted on" (Merriam-Webster 2018). It implies one can "do something," but gives little indication of the scope (what actions and how many?), quality (to what effect/outcome?), or availability (how likely?) of the action. Different users of the term (i.e., laboratory scientists, healthcare providers in the clinic, patients, and insurers) use it to convey a wide range of concepts. For example, in the context of genetic testing, laboratories reporting results use the term to describe a broad range of potential provider recommendations, including "referral to genetic counseling" or "genetic counseling is recommended" (O'Daniel et al. 2017). In the clinic, healthcare providers may use the term to indicate anything from the availability of screening based on a genetic test result to a newly available clinical trial to evaluate a potential therapy based on a specific gene mutation (Biesecker and Green 2014; Green et al. 2016). This expansive use of the term "actionable" in genetics can muddle the core message of this seemingly plain language term.

This combination of familiarity and lack of precision can lead to multiple interpretations, resulting in misunderstanding and miscommunication between genetics laboratories, clinicians, and patients. This disconnect can potentially increase the risk of harm to patients. Harm can occur in many ways, for example, in cases where the term "actionable" leads patients to believe that more can be done for their condition than is realistically possible (e.g., distress, depression, anxiety, disappointment, hopelessness) (Zikmund-Fisher 2017), or difficulties in trying to enumerate all possible terms in larger domains like "disease" (e.g., congestive heart failure could be considered a disease or diagnostic finding) (Cimino 1993). Given the widespread usage of this term in medicine and the potential for misunderstanding, we collected preliminary evidence regarding how the term "actionable" is defined and understood by both patients and providers, and whether different user interpretations of the term have implications for incorporating genomic information into clinical management. As part of a larger study focusing on public attitudes toward policies for the return of secondary genomic results (Gornick et al. 2017; Ryan

et al. 2017), we looked at how members of the lay public interpret the term "medically actionable" in the context of genetic testing. We also surveyed a convenience sample of oncologists as part of a separate study and asked them to define the term "medically actionable."

2 | METHODS

2.1 | Lay Persons' Interpretation of the Term "Medically Actionable"

A detailed description of the study's theoretical basis, research design, and methodological procedures are described elsewhere (Gornick et al. 2017). Briefly, 66 individuals with and without a personal history of cancer were recruited through the University of Michigan Clinical Studies website, a voluntary partnership created for researchers to list studies and patients and community members to find studies that they are interested in participating [https://UMClinicalStudies.org]. This website is a secure, password-protected recruitment portal. Study teams provide basic information about their studies including, purpose, eligibility, what participation involves, and contact information. Potential volunteers visit the website and can sign up for a specific study or for a general registry. From this convenience sample, individuals who expressed interest in the study were asked a series of screening questions on age, gender, ethnicity, and personal history of cancer to ensure diversity both in sample characteristics and diversity in participant's health status. Participants had to be at least 21 years old to participate (Table 1).

Selected individuals were invited to participate in an all-day deliberative democracy (DD) session on policies for the return of secondary genomic sequencing findings. During the expert presentations at the DD session, the term "medically actionable" was defined as: "Results that show a DNA change that increases your risk for health conditions that can be prevented, screened for, reduced or treated." At the end of the DD session, participants were given a survey that included the definition of a "medically actionable" result that was expanded and listed in bullet form as follows: (1) A change in a person's DNA that increases the risk of developing a specific health condition. (2) A medical result where actions can be taken to prevent, screen, reduce, or treat symptoms of the health condition. (3) Examples: certain types of heart conditions (e.g., high risk of heart attack), cancers (e.g., colon, breast, prostate), neurological conditions (e.g., Parkinson's disease). Participants were then asked "In your own words, when you hear the term "medically actionable," what does it mean to you?" Text responses (N = 60) were analyzed using qualitative coding (i.e., content analysis) for key themes. This coding scheme was developed by study team members based on a literature review of the term "medically actionable" and refined using an iterative method (i.e., after categorical codes were developed, new codes were added as needed). Any discrepancies were resolved by group discussion. Responses were coded by types of "actions" mentioned (i.e., treatment, lifestyle change) and categorized by how closely the "actions" corresponded with the study team definition. Responses that did not include any specific, precise actions were

TABLE 1 Participant demographics

Members of the public characteristics (n = 64)[a]	n (%)[b]
Gender	
Female	45 (70.3)
Male	19 (29.7)
Age, mean (SD)	57.3 (14)
Ethnicity "mark all that apply"	
White	50 (78.1)
Black	11 (17.2)
American Indian or Alaskan Native	4 (6.3)
Asian	2 (3.1)
Hispanic	2 (3.1)
Middle Eastern/Arab	1 (1.6)
Other	1 (1.6)
Education	
High school or less	4 (6.3)
Some college/college/trade school	33 (51.6)
Graduate degree	26 (40.6)
Annual household income	
Below $40,000	16 (25.0)
$40,000–$79,999	28 (43.8)
More than $80,000	17 (27.0)
Oncologist characteristics (n = 52)	n (%)[b]
Gender	
Female	15 (28.8)
Male	37 (71.2)
Ethnicity "mark all that apply"	
White	38 (73.1)
Other	14 (26.9)
Main practice location	
Academic medical center	31 (60)
Private practice	13 (25)
Community hospital	8 (15)
Number of patients per week	
> 20 patients/week	26 (50)

[a]Included are all participants who attended DD session and responded to all three surveys [b]Some percentages do not add to 100 because not all participants answered the question

categorized as either "medical action" (e.g., rephrasing of the term "medically actionable") or "something can be done" (does not specify if it is a "medical action" or lifestyle change) responses. Finally, we had a separate category for incorrect or off-topic responses.

2.2 | Clinicians' Interpretation of the Term "Medically Actionable"

In a separate pilot study of a genomic test report prototype, a convenience sample of all medical oncologists, radiation oncologists, and hematologists practicing in the state of Michigan identified

through the Michigan Society of Hematology and Oncology mailing list was invited to participate. Oncologists were informed that the study was part of a quality assurance and improvement project of a genomic sequencing results report. Participation was voluntary, and all survey responses de-identified. A questionnaire and a postage-paid return envelope was provided. On the survey, participants were asked, "In your own words, when you hear the term "medically actionable," what does it mean to you?"

3 | RESULTS

3.1 | Lay Persons' Interpretation of the Term "Medically Actionable"

No respondent provided all parts of the study team definition. However, nearly all respondents (N = 58; 96.7%) provided a basic or "gist" meaning of the term "medically actionable." This included respondents who provided one or more parts of the study team definitions, used a specific, other action not mentioned in the provided definition, and/or used an imprecise definition (e.g., "something can be done"). Although the vast majority of respondents had a "gist" understanding of "medically actionable," the actual content of definitions varied. Two-thirds (N = 40; 66.7%) of respondents used at least one part of the definition we provided, e.g., "Medically actionable means that a disease or disability can be treated to the point of a positive outcome" (ID-01). One-third (N = 20; 33.3%) of respondents used two parts of the study team's definitions, e.g., "Medical diagnosis that can be treated and/or prevented" (ID-21) (Table 2).

Over one-third of the respondents (N = 21; 35%) wrote in an additional action that was not specified in the study team's definition. Nine of these participants included a non-medical (e.g., lifestyle or environmental) action in their definition. For example, one participant wrote: "I can do something to prevent/treat the disease; either by diet, environment or medicine" (ID-60). Several (N = 12; 20%)

TABLE 2 In your own words, when you hear the term "medically actionable", what does it mean to you? (N = 60)

Response code	Response code description	Responses n%
Uses complete provided definition		
Uses or rephrases definition provided by study team: "… actions can be taken to treat, prevent, delay, or reduce symptoms of the health condition" Uses all key terms, or clear synonyms of the terms: "treat," "prevent," and (delay OR reduce) in answer		0 (0.0%)
Uses 2 parts of provided definition		
Mentions two of the key terms related to treatment, prevention, or qualitative change (like "delay" or "reduce")		20 (33.3%)
Uses 1 part of provided definition		
Mentions one of the key terms related to treatment, prevention, or qualitative change (like "delay" or "reduce")		40 (66.7%)
Treatment	Treat part of definition mentioned (synonym: therapy, medication, therapeutic)	25 (41.7%)
Prevention	Prevent part of definition mentioned (synonym: avoid, screen)	19 (31.7%)
Delay or reduce	Either mentions "delay" or "reduce" (or synonyms that suggest a qualitative change: mitigate, lessen, alleviate, keep from progressing, improve, decease, slow down)	16 (26.7%)
Uses a specific action NOT mentioned in definition		21 (35.0%)
Cure	Uses term cure/curable (or synonym: eliminate, correct)	12 (20.0%)
Lifestyle change	Uses term lifestyle change of life decision, including diet, environmental, or behavior change (NOT changes medically nor non-specified types of changes)	9 (15.0%)
Uses a vague definition		17 (28.3%)
Medical action (general)	Uses or rephrases the term "medically actionable." Does not use any of the key terms (or synonyms) in provided definition. May instead use "action" synonyms: influence, intervention, effect, change, alter (not qualitative like improve, lessen)	9 (15.0%)
Something can be done	General statement that an action can be taken/something can be done, but does not specify if it is medical or lifestyle action. Does not use any of the key terms (or synonyms) in provided definition	8 (13.3%)
Gives incorrect or off-topic response	The response is either off-topic, incorrect, or unclear.	2 (3.3%)

Note. Not all participants answered the question

participants mentioned "cure" or "curable" as part of their definition, e.g., "I think it means a medical condition that can be cured or at least lessened" (ID-36).

In addition, 17 (28.3%) of participants used phrasings such as "something can be done" or "something medical can be done" but did not specify the type of action to be performed. For example, one participant stated: "Something could be done about the problem" (ID-41). Another wrote in: "Action available to medically influence a condition" (ID-03).

Finally, respondents provided different combinations of types of actions in their definitions. One participant wrote in: "Something can be done medically to reduce the risk of developing a disease, obtaining screening earlier, also a change in lifestyle choices!" (ID-11) Another wrote: "There are certain illnesses/conditions that can be treated or delayed or cured in some fashion" (ID-19).

3.2 | Clinicians' Interpretation of the Term "Medically Actionable"

Unlike members of the public, clinician survey respondents (N = 52; 71% male; 73% self-reported as white; 50% reported seeing ≥ 20 patients/week; 60% reported practicing at an academic medical center, 25% in private practice, 15% in a community hospital setting) almost never provided vague type "something can be done" answers, though some were vague in action, such as "It means that there is either a treatment or referral that could take place" (ID-120). Clinicians also did not give any responses that included patient behavior, environmental change, or the possibility of a cure.

Often, clinicians gave very precise or detailed definitions. For example, one clinician provided a comprehensive list of what the term includes: "(1) Known germline susceptibility, NOT [variants of unknown significance], that lead to proven strategies, (screening, prophylactic surgery, other prevention strategies), (2) Known somatic changes that lead to standard of care for THAT disease (e.g., ER+ or HER2+, mBRCA), (3) Known somatic changes that lead to standard of care with other diseases, might be considered for different disease (e.g., ER+ in lung cancer) "off label," (4) known somatic changes that make [patient] eligible for clinical trial of investigational drug (as in [Molecular Analysis for Therapy Choice]) or [standard of care] drug in different disease (as in [Targeted Agent and Profiling Utilization Registry])" (ID-114).

Another oncologist focused on the clinical indication (in this context, a patient's current cancer), "Implies there is a somatic mutation within the tumor for which there may be a drug that may affect an anti-cancer effect" (ID-116).

Several clinicians included additional types of actions that were NOT mentioned by the public, including family implications, genetic counseling, merely making decisions, or "no" action as an action. Finally, some clinicians emphasized uncertainty of benefit and a few also mentioned the challenge of access (e.g., nearness of clinical trial). For example, "That there is a clinical intervention to offer the patient, that can treat the cancer and that I can write an Rx for without having to refer every patient to a tertiary center. Many patients can't travel."

4 | DISCUSSION

4.1 | So What Does it all Mean?

As genomic medicine expands in both the research and clinical arenas, determining whether, how, and which findings to return to the clinician and patient becomes increasingly important. Several studies report the use of an a priori categorization of genes, using the concept of actionability in order to facilitate informed consent, analysis, and return of results (Berg et al. 2013; Shirts et al. 2015). Our data indicate that while laypersons generally have a good gist understanding of the term "actionable," their definition of "medically actionable" varies, even after both being provided a definition verbally in a presentation and in written form right above the question that asked for their definition. We found that clinicians also have a good understanding of the core meaning of "actionable," yet it is quite different from the understanding of the lay public. Many clinicians offered very precise and detailed definitions, and most of their definitions focused on "treatment and/or delay/reduce symptoms" through the use of medications or clinical trials. Very few clinicians used the vague type answers provided by laypersons (i.e., "something can be done"), and no clinicians mentioned cure or lifestyle change.

Overall, our preliminary data provides evidence to support the idea that when a familiar, plain language word that is also used as medical jargon has multiple gist meanings, different groups (e.g., medical professionals vs. lay members of the public) may impute their group-specific interpretations to the term, potentially without realizing that other audiences have different understandings of the same word. In this report, we provide pilot evidence suggesting that there is a lack of shared meaning of "medically actionable," which may contribute to doctor-patient miscommunication and interfere with informed medical decision-making. This creates a situation where patients could experience the disappointment of unmet expectations, confusion, and a lack of appreciation of both the range of specific actions and multiple actions that may need to be taken. For example, after diagnosis of a condition like heredity cardiomyopathy, actions might include medication for control of blood pressure, screening to monitor the heart, diet and exercise to improve heart function, or a more invasive procedure such as an implantable defibrillator.

Given that the term "medically actionable" has a range of specific and multiple meanings, as well as different gist interpretations by the various users (i.e., researchers, clinicians, and patients), we propose that rather than just using the term "actionable," health care providers should also say "what they mean" to reduce miscommunication and confusion between health care providers and patients that could negatively impact medical decision-making and trust. Discordance in interpretation can undermine patient trust. Given the longitudinal nature of the patient-provider relationship, particular challenges for facilitating trust exist since uncertainty about future related and unrelated medical interactions are unknown. Therefore, special attention should be taken to address cultural values and communication barriers, and integrate patient expectations (Kraft et al. 2018).

It is important to "say what you mean" (Astor 2011; Cimino 1993; Fantry 2016). In order to guide clinicians during patient-provider discussion about genetic test results, we have set out a list of suggested phrases (see Table 3).

We also believe that there are also situations where the term "medically actionable" needs additional clarification. For example, referring to the availability of a clinical trial or off-label use of an FDA-approved drug as "medically actionable" may lead to patient misunderstandings about distinctions between research and clinical care.

Clarity in "what you mean" is essential in the "no stone unturned"/"there is nothing we can do" category. This describes the situation when genetic testing may be done, even though the anticipated yield of a positive result is low, in order to not miss a potential diagnosis for which there could be a treatment. In this context, testing is being used to determine that nothing more can be done, and it needs to be made clear to the patient that doing this testing might be a "last resort" option. For example, clinicians may order whole exome sequencing when all previous genetic testing, including panel testing, has been negative.

This report has some limitations. First, due to the convenience sample recruitment strategy, both clinician and lay person respondents were necessarily self-selected and thus unrepresentative of the general population. Also, clinician and citizen responses were gathered as part of separate surveys in which a study team definition of medically actionable was provided to lay persons but not clinicians, which may in turn have had a differential impact on responses to the "medical actionability" question. Despite these limitations, we feel that our findings are suggestive of a communication challenge that merits consideration and that caution should be taken with phrasing when "actionable" is used in laboratories reporting clinical results and in healthcare.

The lack of shared meaning of "medically actionable,"—which may contribute to doctor-patient miscommunication and interfere with informed medical decision-making—is a resolvable challenge. Confusion regarding medical terminology and challenges in relaying risk information can be addressed through both patient and clinician education. When conveying medically actionable information, asking the patient or research participant to state back their understanding can help the healthcare provider or researcher determine whether the information

TABLE 3 Suggested phrasing for clinicians to use with the term "medically actionable"

Type of action	Description	Suggested language
Screening		By "medically actionable," I mean that…
Patient screening	Imaging or screening of patient for a disease or disorder	…you should get regular screening (e.g., imaging of your heart to screen for hypertrophic cardiomyopathy).
Family screening	Genetic testing of relatives (cascade screening) for a disease or disorder	…your at-risk family members (e.g. siblings) can be tested to see if the gene change for [specify name of condition] has been inherited (e.g. patient with a family history of malignant hyperthermia).
Treatment		
Treatment avoidance	Not having a treatment or therapy that may be potentially harmful	…you should avoid… (e.g., certain types of anesthesia and instead use safer alternatives during surgery [patients with malignant hyperthermia]).
Additional treatment	Having an additional therapy or treatment that may be potentially helpful	…you could… (e.g., take a beta-blocker medication, which will reduce your risk for heart problems [patients with hypertrophic cardiomyopathy]).
Surgical options		
Insertion	Having surgery to insert/implant something that may be potentially helpful	…you could have surgery to insert… (e.g., a defibrillator in or near your heart to reduce your risk of a heart attack [patients with hypertrophic cardiomyopathy]).
Removal	Having procedure/surgery to remove something that may be potentially affected	…you could have surgery to remove… (e.g., the colon to significantly reduce your risk for colon cancer [patients with familial adenomatous polyposis]).
Behavior		
Diet	Changing diet to reduce health risks or symptoms	…you could change your diet by… (e.g., eating less fatty food and eating more foods with fiber to reduce your risk for heart problems [patients with familial hypercholesterolemia]).
Activities/exercise	Doing activities to reduce health risks or symptoms	…you should exercise regularly… (e.g., to lower your cholesterol levels and reduce your risk for heart problems [patients with familial hypercholesterolemia]).
Avoiding activities	Avoid certain types of activities/exercise to reduce health risks or symptoms	…you should avoid… (e.g., contact sports and choose safer alternatives such as swimming to reduce your risk for heart problems [patients with Marfan syndrome]).

has been effectively conveyed or when additional explanation is needed. Further studies are necessary to examine patient reactions to a clinician using the phrasing "By medically actionable, I mean…" and assess changes in comprehension. Many of the challenges discussed here can be resolved by taking the time to communicate medically actionable information in a deliberate, direct, clear, and concise way.

5 | COMPLIANCE WITH ETHICAL STANDARDS

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SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section at the end of the article.