

**ARTICLE**

# Lay understandings of drug-gene interactions: The right medication, the right dose, at the right time, but what are the right words?

Karen M. Meagher  | Kelsey Stuttgart Finn | Susan H. Curtis  | Jack Borucki | Annika T. Beck | Amal W. Cheema | Richard R. Sharp 

Biomedical Ethics Research Program,  
Mayo Clinic, Rochester, Minnesota,  
USA

**Correspondence**

Richard R. Sharp, Biomedical Ethics  
Program, Mayo Clinic, 200 First St. SW,  
Rochester, MN 55905, USA.  
Email: Sharp.Richard@mayo.edu

**Present address**

Jack Borucki, University of Virginia  
School of Medicine, Charlottesville,  
Virginia, USA

Annika T. Beck, University of  
Minnesota Law School, Minneapolis,  
Minnesota, USA

Amal W. Cheema, Geisel School of  
Medicine, Dartmouth College, Hanover,  
New Hampshire, USA

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**Abstract**

As pharmacogenomic (PGx) testing increases in popularity, lay concepts of drug-gene interactions set the stage for shared decision making in precision medicine. Few studies explore what recipients of PGx results think is happening in their bodies when a drug-gene interaction is discovered. To characterize biobank participants' understanding of PGx research results, we conducted a focus group study, which took place after PGx variants conferring increased risk of dihydropyrimidine dehydrogenase (DPD) deficiency were disclosed to biobank contributors. DPD deficiency confers an increased risk of adverse reaction to commonly used cancer chemotherapeutics. Ten focus groups were conducted, ranging from two to eight participants. Fifty-four individuals participated in focus groups. A framework approach was used for descriptive and explanatory analysis. Descriptive themes included participants' efforts to make sense of PGx findings as they related to: (1) health implications, (2) drugs, and (3) genetics. Explanatory analysis supplied a functional framework of how participant word choices can perform different purposes in PGx communication. Results bear three main implications for PGx research-related disclosure. First, participants' use of various terms suggest participants generally understanding their PGx results, including how positive PGx results differ from positive disease susceptibility genetic results. Second, PGx disclosure in biobanking can involve participant conflation of drug-gene interactions with allergies or other types of medical reactions. Third, the functional framework suggests a need to move beyond a deficit model of genetic literacy in PGx communication. Together, findings provide an initial evidence base for supporting bidirectional expert-recipient PGx results communication.

**Study Highlights****WHAT IS THE CURRENT KNOWLEDGE ON THE TOPIC?**

Pharmacogenomic (PGx) testing is often the hallmark of personalized medicine, offering the ability to tailor prescriptions to specific patients. Although prior

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studies have identified PGx test result communication, few studies have explored what biorepository participants think is happening in their bodies when translating PGx research results into the clinic.

#### **WHAT QUESTION DID THIS STUDY ADDRESS?**

This study aimed to characterize biobank participants' understanding of PGx results with future clinical implications.

#### **WHAT DOES THIS STUDY ADD TO OUR KNOWLEDGE?**

This study addresses how participants' understanding of PGx results and the translational context can shape their word choices.

#### **HOW MIGHT THIS CHANGE CLINICAL PHARMACOLOGY OR TRANSLATIONAL SCIENCE?**

Patient word choices can reflect misunderstandings of drug-gene interactions and their efforts to navigate the translational context of actionable PGx research results. Findings provide clinicians and PGx researchers with a framework for identifying PGx information and communication gaps.

## INTRODUCTION

As pharmacogenomic (PGx) testing increases, researchers' and clinicians' will need to increase their familiarity with lay attitudes toward drug-gene interactions. However, few studies explore what recipients of PGx results think is happening in their bodies when a possible drug-gene interaction is discovered. Anticipating this possibility is especially crucial to PGx disclosure, which is adjacent to other forms of health communication, including return of disease susceptibility variants and disclosure of drug side effects. Improving understanding of lay perspectives on the body can improve health communication by addressing comparisons and analogies that can lead PGx recipients to incomplete understanding.<sup>1,2</sup>

Previous studies have pursued this evidence base by examining patient comprehension of hypothetical PGx results.<sup>3-5</sup> Others have sought to improve understanding of patient experiences receiving PGx results in clinical settings.<sup>6,7</sup> Some studies in biobanking contexts have occurred. For example, Olson et al. (2017) sought to identify predictors of patient understanding upon receipt of individual research PGx results. Prior studies have also aimed to better understand PGx communication in a research context, including investigation of aggregate PGx results disclosure<sup>8</sup> and stakeholder perspectives on laboratory reports.<sup>9,10</sup> Veilleux et al.<sup>11</sup> thoroughly reviewed different perspectives on PGx results. However, few studies have examined how impact of PGx disclosure and valuation of results shape recipients' own word choices, especially in translational contexts.

In this article, we describe the results of a focus group study conducted after PGx results conferring

increased risk of chemotherapeutic adverse events were disclosed to biobank contributors. An overview of emergent themes regarding recipients' understanding and valuation of results is described elsewhere.<sup>12</sup> Here, we provide a focused analysis explicating results specific to participants' word choices used to characterize drug-gene interactions. Specifically, we analyze how biobank contributors lacking familiarity with biomedical PGx terminology turned to more familiar health concepts to navigate subsequent clinical encounters. In sum, study findings reflect how PGx disclosure studies can improve the process of "cultural brokerage," in which biomedical and lay views of illness and medicine are co-created and negotiated by clinicians and patients.<sup>13</sup> Findings support development of bidirectional communication disclosure materials that facilitate translation of PGx testing from research to clinic. Results discussion provides PGx researchers, biorepository leadership, and clinicians with a framework for understanding how patients' views of drug-gene interactions within the body affect communication of PGx results in translational oncology settings.

## ETHICS

Approval of the study was obtained from the [Mayo Clinic] Institutional Review Board (#18-000897). Disclosure materials incorporated input from the Community Advisory Board for the [Mayo Clinic] Biobank and expert input. The membership of the Community Advisory Board reflects the sociocultural characteristics of the [Mayo Clinic] Biobank population.<sup>14</sup> In November 2017,

biobank community advisory board (CAB) members in Jacksonville, FL, and Rochester, MN, reviewed an initial draft of a proposal to disclose PGx results to CAB feedback informed revised. Revised disclosure materials are published elsewhere.<sup>12</sup>

## MATERIALS AND METHODS

### Setting

This focus group study of disclosure explored the impact of return of PGx results following an oncology study utilizing [Mayo Clinic] Biobank biospecimens to improve understanding of dihydropyrimidine dehydrogenase (DPD) deficiency. Biobank contributors included in the DPD deficiency study were not selected for prior cancer diagnosis. DPD deficiency is a metabolic condition that confers increased risk of adverse events in patients with cancer who are prescribed the common chemotherapeutic medications 5-fluorouracil (5-FU) or its pro-drug capecitabine.<sup>15</sup> Four DPD deficiency variants (\*2A, D949V, I560S, and rs75017182) were selected for disclosure due to their association with adverse events (grade 3 or higher) in clinical oncology contexts.<sup>16–18</sup> Typical adverse events include diarrhea, stomatitis, nausea, fatigue, vomiting, dehydration, anorexia, and pain.<sup>19</sup> Clinical actionability of these results is contingent upon clinical confirmation, a relevant cancer diagnosis, and relevant 5-FU or capecitabine prescription.

**TABLE 1** Focus group interview domains and example questions

Actions taken	
	What did you do with the letter?
	Did you talk with anyone about the letter or its contents?
	Did you share the letter with your doctor?
Understanding	
	What are the main points that you took away from the letter?
	What questions did you have after reading the letter?
	Based on the letter you received, how would you describe the risks that taking these medications could pose for you?
	Having read the letter, do you feel differently or the same about your health?
Value	
	Why do you think you received this letter?
	What are the good things about receiving this letter?
	What are the bad things about receiving this letter?
	What other ways could these results be shared with biobank participants like you?

### Data collection

Biobank contributors that tested positive for at least one of the four DPD deficiency variants received three pages of DPD deficiency disclosure materials. DPD research disclosure materials communicated three main recommendations for recipients: (1) share the result with your doctor, (2) store the result in case of a cancer diagnosis, and (3) share the result with family members. The initial letter included a disclosure study recruitment invitation. Research staff telephoned participants to confirm receipt of disclosure materials and conduct a brief survey (forthcoming). After completing this survey, select participants who received a PGx result were invited to participate in a focus group discussion. Survey respondents who resided outside driving distance (30 miles) of focus group sites were excluded.

A focus group design was used to explore the impact of returning unexpected PGx results to biobank contributors, and participant views about improving PGx communication. Between February and April 2019, focus groups were conducted within 3 to 5 weeks of the biobank mailing PGx disclosure materials. After initial focus groups, the moderator guide was refined and data collection continued until data saturation was achieved.<sup>20</sup> Interview domains included impact of PGx results on biobank contributors, including understanding, valuation of results, and actions taken (Table 1). Verbatim audio recorded and transcribed focus group discussions were analyzed using NVIVO software.<sup>21</sup>

### Participant sample

As part of a previously published research study, DPYD genotyping was performed on DNA from 3950 individuals who consented to the [Blinded for Review XXX] Biobank.<sup>22</sup> Demographics of the overall participant population and details of the methodology used for determining genotype were previously detailed by Nie et al.<sup>22</sup> In total, 236 biobank contributors received disclosure letters communicating increased DPD deficiency risk. Of 236 participants, 196 completed the telephone survey (forthcoming). One hundred sixty-one participants were eligible for focus group participation due to geographic proximity and were invited to participate. Fifty-four of 161 participants (34%) agreed to participate in focus group discussions.

Prior to the focus groups, participants completed a six-item questionnaire to collect relevant demographic and other characteristics. Questionnaire items solicited focus group participants' self-assessments of health status, prior experience with genetic and PGx testing, prior cancer

**TABLE 2** Focus group characteristics

N = 54		
	Average	Range
Age	60	35–85
Time from consent, years	8.2	5.4–10.0
		N (%)
Gender		
Female		36 (67)
Male		18 (33)
Race		
White		54 (100)
Marital Status		
Married		43 (80)
Divorced		4 (7)
Widowed		3 (6)
Single (never married)		3 (6)
Cohabiting		1 (2)
Education		
High School		3 (6)
Vocational or some college		18 (33)
College		18 (33)
Graduate		16 (30)
Self-reported health		
Excellent		4 (8)
Very good		29 (60)
Good		12 (25)
Fair		3 (6)
Previously had PGx testing		
Yes		6 (12)
No		44 (85)
Not sure		2 (4)
Previously had PGx testing		
Yes		6 (12)
No		41 (80)
Not sure		4 (8)
Ever had cancer?		
Yes		7 (13)
No		45 (87)
Have family member who had chemotherapy?		
Yes		28 (54)
No		18 (35)
Not sure		6 (12)
Heard of 5-FU before?		
Yes		11 (21)
No		40 (77)
Not sure		1 (2)

(Continues)

**TABLE 2** (Continued)

	N (%)
Worked directly with cancer patients?	
Yes	17 (33)
No	35 (67)
Confidence with medical forms	
Extremely	35 (67)
Quite a bit	13 (25)
Somewhat	3 (6)

Abbreviations: 5-FU, 5-fluorouracil; PGx, pharmacogenomic.

diagnosis, work with patients with cancer, and confidence with medical forms.

## Analysis

A framework analysis approach was used. Deductive codes were derived from interview domains and inductive codes from emergent themes.<sup>23</sup> Data were coded by two primary coders, using codes, which were conceptually refined through consensus-based and iterative codebook development within the multidisciplinary bioethics research team.<sup>24</sup> Framework analysis proceeded via five stages: (1) familiarization with the data, (2) creating a thematic framework, (3) indexing, (4) charting, and (5) mapping and interpretation.<sup>25–27</sup> The indexing stage included in vivo coding via the constant comparative method<sup>28</sup> and also incorporates deductive codes identified in research design. Although the processes of charting and mapping/interpretation are iterative, charting consisted of identifying themes that were primarily descriptive (e.g., patient word choice, or “labeling,” which led to the themes of health implications, drugs, or genetics).<sup>25</sup> Mapping and interpretation used insights from discourse analysis to develop a functional explanatory account of *why* patients were making these word choices (including utterances reflecting confusion, requesting clarification, and conveying pragmatic action).<sup>26,29</sup>

## RESULTS

Focus group demographics and additional details are described in Table 2. A total of 54 participants attended a focus group. Ten focus groups were conducted, ranging in size from two to eight participants. Participants ranged from 35 to 85 years old. DPD deficiency results were often not expected by participants, as an average of 8.2 years had passed from time of biobank consent to when participants received the disclosure letter (range of

5.4–10.0 years). One hundred percent of participants identified as White. Most focus group participants (68%) self-reported excellent or very good health status. Ninety-six percent reported higher levels of education (ranging from some vocational school to graduate school). A majority (67%) indicated high confidence with medical forms, as indicated by a survey question used to assess health literacy.<sup>30</sup> Most reported no prior experience with genetic or PGx testing (80%). The majority (77%) reported no familiarity with the cancer drug 5-FU.

Emergent themes related to the body reflected participants' uses of different health concepts. Participants turned to consequences and other more familiar health terminology regarding genes and medications, but almost never used the terms “pharmacogenetics,” or “drug-gene interactions.” Emergent themes relevant to understanding of the body include PGx recipient efforts to make sense of PGx findings in terms of:

1. health implications
2. drugs, and
3. genetics

### **Theme (1): Participant understanding of health implications**

Focus group participants articulated the meaning of results in terms of health, including avoiding harm when receiving chemotherapy. Some participants mentioned their take-away as needing to avoid the mentioned medications and often placed these consequences in relationship to their current health status, especially if they were struggling with other conditions. This theme captures participant understandings of results as assimilation of new health information:

FG5-5: “I think it’s very much like when you’re diagnosed with diabetes, and all of a sudden you find out you shouldn’t do this or this or this, and if you do, there’s a price to pay. Well in this case, we shouldn’t have this [chemotherapy] because there’s a price to pay. Doesn’t say you’re gonna die, but you may have severe reactions. I think it’s basically a very similar situation.”

Many other participants emphasized that the disclosure letter mentioned the possibility of death. The following exchange with some participants expressing sincere existential concern and others using gallows humor to relieve tension was common:

Moderator “What would you say would be the risks to you if you did take 5FU or Capecitabine?”

FG2-2 “Sounds like we’d be dead.” [Laughter.]

FG2-4 “Yeah. It said life-threatening. Not good.”

FG 2-5: “Because we’re in this group, we are all highly susceptible to having a high reaction to it. Yes. I mean - Life or death.”

Many other participants were less certain about the health consequences and asked questions about what would happen if they took 5-FU. For participants in many focus groups (7 of 10), family history of cancer often informed the sense of importance, or value, participants attributed to their PGx results.<sup>12</sup> Other health outcome questions covered whether negative consequences of 5-FU exposure were reversible, how to clinically confirm test results, and how much DPD deficiency variants increased their risk. The few participants with more proximate possibilities of exposure described specific actions that they were able to take in relation to their health:

FG2-5: “But then my husband looked at it, and he says, ‘Oh, that’s the drug that I’ve been using,’ ‘cause he has a precancerous disposition to his face, and he has done, several times, these face washes with fluorouracil. ‘I’ve thought, ‘we’ve had this in our house.’ He has used it. He’s filled the bathroom sink with it, sharing the same towels or whatever. I thought, ‘wow.’ At first, I thought it didn’t apply to me at all, but I realized we’ve had it in the house a couple times now.”

### **Theme (2): Participant understanding of the “drug interaction” in drug-gene interactions**

Participants understood the drug or medication aspect of DPD PGx results in different ways, predominantly in terms of other types of reactions to medications. These include “allergies,” “side-effects,” or “adverse reactions/effects.” Some referred to their PGx results directly with these alternative terms, while others used the terms by way of comparison.

Some participants understood their result in comparison to their experience with drug side effects. The most often expressed their appreciation of DPD PGx results as facilitating avoidance of negative experiences. Participants sometimes described their own or others’ negative experiences with medications:

FG3-5 “It made me think that if I do get cancer, I’m not going to be cursing people that I’m going down because of a cancer treatment drug, and if I could’ve known that before they gave me [acetaminophen

hydrocodone], I definitely would've liked to know that. That was terrifying.

Moderator You've had strong adverse reactions or allergies to meds in the past?

FG3-5: Yeah, at least three different ones. I would really not like to ever put myself or my family through that ever again. If I can know this stuff ahead of time, that makes me feel a little bit safer, actually. A little bit more secure."

Most commonly (7 of 10 focus groups), participants discussed their results as akin to an allergy. Whereas many participants even used the term "allergy," to describe PGx findings, some participants wanted to refer to their result as an allergy for pragmatic reasons. Some participants invoked the comparison to allergies as a way of trying to gain clarity about the consequences of 5-FU exposure.

FG3-8: "What is the saving point for this? How do you reverse this? Is there a reversal for it? That would be my—because even [diphenhydramine] doesn't work for everything."

It was often difficult to disentangle whether participants' use of the term "allergy" reflected underlying confusion, their more pragmatic desires to gain clinical action on research results, or both. At least one participant in all 10 focus groups wanted to place their result in their electronic health record and ensure their healthcare team was informed about the information. Allergy language was viewed by this participant as a signifier of the medical importance of the result:

FG1-8: "It was more about the fact that I was trying to defend the fact that I wanted something listed as an allergy when, to me, it looks plain as day that this needs to be an allergy. I read the letter, and I think some of you did too, as, 'Oh, my gosh. Take this seriously.' I didn't feel that it was fair to have to defend that. I felt like this [letter] should have been enough."

The second most common way participants understood their results was a "reaction" to the provided list of chemotherapeutics, sometimes using the term "adverse reaction" used in the disclosure materials. Usage of the term "reaction" also reflected ambiguity of the term, as it can be shorthand for both "adverse reaction" and "allergic reaction." The notion of reaction did help some participants connect what was happening in their bodies concerning PGx result implications for drug dosage, for example:

FG4-3: "Well, you know, you wonder how—you-you hear people say—getting their blood pressure—getting it

regulated, you know, so this must go on all the time. People have to take medicine er—take more, take less. 'We'll figure out how it works,' you know. I don't, you know, take medic—yeah, anything. So, you know, I haven't experienced it yet, but I suppose it's with any medicine. Everybody reacts to it differently. So, you know, man, it's-it's, you know—years back, everybody took the same thing and either died or lived. And, now, it's, you know [different]."

### Theme (3): Participant understanding of the "gene" in drug-gene interactions

Notably, whereas the medication aspect of 5-FU PGx results was driven home by a list that comprised part of the disclosure materials, genetics figured slightly less predominantly in discussions of participant understanding. However, genetics was raised by at least one participant in all focus groups. Many participants were often interested in heritability and implications for family members. Those participants understood their result as having a genetic basis and used a variety of terminology, including "susceptibility," "mutation," or "defect" to describe their understanding:

FG4-11 "I would explain it as a susceptibility as-as looks like based on this—these studies—because I'm suspecting there's a sequence of studies. And then, based on these studies, that I have a genetic susceptibility to this specific kinda medication."

FG6-3: "They had identified a DNA mutation that could leave me susceptible to a severe reaction or death in, um—if I was treated with particular chemotherapies."

Although many participants emphasized the worrisome aspects of inherited results, some participants framed the PGx result by identifying the value of individualized care:

FG7-2: "I guess I've had other conversations about it since then, because I have a friend whose husband has mental health issues, and it's dealt with the whole—it's common I think, with mental illness, the whole trial and error of medication and trying to pinpoint what works and what doesn't work. I know that that's another area that they are targeting or trying to target medication to specific people in genetics, and it's just interesting. I think it's fascinating to learn more about how certain medications can work for some people and not for others, and so that's just how conversations have gone about this too."

The genetic context and associated terminology caused confusion. Although some participants connected the genetic nature of their result with heritability, and realized their family members could be at risk, others did not.

FG6-4: “I must say that, when I first talked to this one lady whoever she was, [referring to the phone survey], she said, ‘Are you gonna share this information with your children?’ And, at first, my reaction was, ‘Why?’ Not thinking it’s the blood, it’s in the family. Then, well, yeah, of course, but I didn’t tell her that. I told her, ‘Well, I don’t know why I would.’”

Both patterns of inheritance and how genetic variation comes about generated many questions and other expressions of uncertainty:

FG5-1 [Reading from disclosure letter] ‘Specific genetic changes RS75.’ “I thought ‘what does that mean? that mean my DNA changed, did I have a mutation?’”

FG1-2: “The questions [I had] were: ‘Was the change something I did, something that my parents had done? What creates that change?’”

Less frequently, the perception that deleterious DPD deficiency variants were uncommon lent the genetic aspect of results a sense of distinction:

FG2-3: “I don’t know how many people were in the entire study, but I do know that it’s considered a rare genetic variant. It’s not common at all. So, yeah. We’re special.” [Boisterous laughter and crosstalk.]

## FUNCTIONAL FRAMEWORK

Although descriptive themes around PGx comprehension emerged during the charting stage of analysis, it was subsequently necessary to move beyond description to seek an explanation of participants’ word choices. Critical discourse analysis is an analytic lens that seeks to illuminate and critique structures of power. Given participants’ frustration with the translational nature of research results, we considered their interactions with care providers. We also assessed their interactions with other focus group participants: these frequently featured a process of shared “meaning-making” or affirmation of emotional reactions to DPD deficiency results and confirmation of both confusion and initial understanding of results. Interactions with focus group study staff also indicated that the social context of PGx receipt affected the psychosocial impact of results in ways that a deficit model of genetic literacy did not adequately explain.

During mapping and interpretation, critical discourse analysis led to articulation of four functions of participants’ use of terminology: reflects confusion, requests clarification, conveys pragmatic action, and indicates value or import (Table 3). Many patient utterances can perform multiple functions or be ambiguous.

## DISCUSSION

Our aim in this study was to explore participants’ understanding and valuation of PGx research results, with a focus on how participants understood drug-gene interactions in relation to the body. First, participants’ use of various terms suggest patients generally understand their PGx results, including how they differ from disease susceptibility genetic results. Second, PGx disclosure in biobanking can involve participant conflation of drug-gene interactions with allergies or other types of medical reactions. Third, a functional framework provides a complementary analysis of how PGx recipients communicate back to experts. Together, findings provide an initial evidence base for supporting bidirectional expert-recipient PGx results communication.

First, study results document recipients’ basic understanding of PGx results, concurring with similar findings on comprehension.<sup>7,31</sup> Other studies have also described participants’ valuation of PGx results as possibilities to avoid side effects.<sup>32,33</sup> In particular, these DPD deficiency focus group results align well with Trinidad et al.<sup>34</sup> *HLA-B* focus group findings, especially discussions of side effects and a desire to avoid therapeutic trial-and-error. Participants’ reliance on more familiar health concepts is also similar to findings that patients in clinical contexts often situate PGx results as validating their experiences of whether a medication or dosage works for them.<sup>35</sup> These results identify an additional area of good comprehension, given that study participants explicitly did not confuse DPD deficiency PGx variants with genetic variants conferring a greater risk of cancer diagnosis.

Second, gaps in patients’ genetic literacy have been well-documented more generally, but less thoroughly for PGx specifically testing.<sup>36–39</sup> Study findings documenting remaining questions about PGx results are also consistent with Haga et al.’s<sup>38</sup> survey results capturing patient lack of familiarity with how genes can affect their response to a medication, including dosage or drug selection. In addition, these study results confirm a relatively limited understanding of underlying scientific and genetic concepts encountered elsewhere in the general public.<sup>36,40</sup> Especially notable in these results is the absence of the phrase “drug-gene interaction,” which was almost never used by study participants. This finding reinforces prior documentation of persistent genetic knowledge gaps, including in those with higher education levels or health

**TABLE 3** Functional framework for focus group participant word choice

Function	Definition	Example
Reflects confusion	A PGx recipient's use of terms reveals a knowledge gap in their understanding of the test result and/or its related underlying physiological process.	Here, the participants' use of the terms "susceptibility," "predisposition," and "genetics" reflect partial comprehension, but s/he wants to better understand the scope of the DPD result: "If we had this <b>genetic predisposition</b> for problems with this [cancer drug], <b>does that mean we're more susceptible to others?</b> "
Requests clarification	Occurring in both statement and question form, a PGx recipient's use of a health concept can seek to confirm or revise their understanding of the result.	This participant refers to all focus group members' health implications (death and sickness) to gain clarity on the magnitude and likelihood of genetic risk upon exposure: "If 100 percent of us were hooked up to an IV and fed this medicine, <b>are all of us dying? Are we getting sick?</b> "
Conveys pragmatic action	A PGx recipient's use of terms relies on more familiar health concepts to communicate what they expect clinicians to do in reaction to a PGx result.	This participant uses the "allergy" section of the EHR to describe her experience requesting a pediatric chart note for her child based on her own DPD result: "Not [entering the result in the EHR] as an allergy, but <b>we can put in?</b> Because I have a significant medical condition that does affect them [my kids], there are ways that their pediatrician is able to word— <b>she words things in such a way where, "Talk to Mom. Please review Mom's history with X."</b>
Indicates value or import	A PGx recipient's use of terms reveals the value or sense of urgency concerning result, which they might want a provider to validate, especially if (un) concerned.	Similarly, this participant wants EHR documentation (conveys pragmatic action) but also uses the term "allergy" to communicate discordant patient-provider valuation of the DPD result: "I have an allergy to sulfa drugs from a baby, when I was a baby. I report that. That's self-reported. This [DPD test result] is a documented allergy, and <b>they're not treating it with the same weight</b> as they are the sulfa that I had as a baby. It's like, this is documented."

Abbreviations: DPD, dihydropyrimidine dehydrogenase; EHR, electronic health record; PGx, pharmacogenomic.

literacy.<sup>40,41</sup> In contrast to prior studies, these results raise the possibility of mistaken self-report of PGx results as an allergy or other medical condition during a medical history, although further study is needed to determine the likelihood of such self-reports.

Third, this study reports findings in the reverse direction of communication. Recipients' word choices can perform different communicative functions to experts.

Functions of biobank recipients' efforts to communicate what their results mean to them reflect the limitations of a traditional deficit model of science communication. The deficit model has been critiqued in health literacy literature for failing to capture what the public already knows.<sup>42,43</sup> Crucially, the pragmatic and value functions of patient communication are likely to be overlooked if pharmacists, geneticists, or clinicians solely interpret lay word choice as reflections of underlying genetic illiteracy. This framing is similar to prior research pointing to a mismatch in the amount of information PGx recipients are given and what they want.<sup>44</sup> This framework also adds to this finding by identifying how recipients can respond to PGx disclosure with their own communication efforts.

A functional framework can be useful to facilitate bidirectional PGx results communication, especially in

translational settings. Developing PGx communication based on how patients view their own bodies can support a patient's involvement in diagnostic events.<sup>45</sup> Research findings on patient word choices in response to PGx disclosure can add to prior efforts, such as stakeholder informed laboratory reports.<sup>9,46</sup> The requests clarification function is especially relevant to PGx communication, where recipients often appear to grasp half of the compound concept of drug-gene interactions, but not always both. Although a deficit model emphasizes the aspect lay recipients miss, the functional approach emphasizes how disclosure materials or clinical interactions can affirm and build off what recipients already know.

In addition to increasing PGx recipient familiarity with biomedical vocabulary to improve genetic literacy, the functional framework suggestions that PGx communication should clarify how PGx results will be recorded in the patients' medical record. Recipient talk of allergies, for example, sometimes conveys pragmatic action, indicating how recipients expected clinicians or health systems to act reliably by tracking their results over time. PGx disclosure can set shared expectations for practical action. In a research context, disclosure materials can clarify that research results might not be fully transferable directly



to clinical care without clinical confirmation. DPD deficiency focus group findings demonstrated the need to distribute the burden of remembering across health systems and recipients, especially when PGx clinical actionability is contingent upon a future diagnosis.

## Strength, limitations, and future directions

This study has several limitations. Focus group discussions likely influenced perceptions, as participants reviewed disclosure materials prior to attending and reported the recruiting telephone call increased their perception of the result's importance. Eligibility for focus groups was limited by proximity to the study site, which might have influenced focus group discussions. Some of the 11 participants who reported familiarity with 5-FU were clinicians whose work with patients with cancer is unlikely to re-occur in other populations. Biobank contributor demographics include higher educational attainment and less ethnic diversity than the population in the surrounding upper Midwest community.<sup>14</sup> Cohorts with greater racial, ethnic, educational, and socioeconomic diversity might reveal other comprehension findings, including use of different terminology to make sense of their PGx results. Participation in the [Mayo Clinic] biobank might have given focus group participants greater familiarity with genetic research, affecting valuations. The functional framework for recipient communication to experts is limited by recollected, as opposed to real-time, clinical interactions. Exploration of reactions to non-cancer related PGx results is needed, especially to determine whether patients conflate PGx results with disease susceptibility information in other contexts.

Our findings reflect the importance of including but also moving beyond a deficit model of science communication. A variety of health professions are likely to be involved in PGx disclosures.<sup>47</sup> Future research is needed to build the evidence base for effective PGx health communication, anticipating and bridging the terminology disconnect likely to occur in clinical encounters. For example, the proposed functional framework needs validation in other contexts. Study findings suggest an avenue of research for ethical and social researchers to further explicate patient attitudes toward PGx tests results in relation to what is happening in their bodies.

## Conclusion

As PGx testing increases, it will become increasingly important to document and address lay gaps in understanding in parallel to what has occurred in disease

susceptibility genetics. PGx recipients used existing health constructs within their experience to fill in for unfamiliarity with PGx information. Whereas much attention has been directed at genetic literacy, study findings reflect that a functional framework of PGx recipient communication to experts can be complementary in identifying communication gaps.

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## CONFLICT OF INTEREST

The views expressed here are those of the authors and not of Mayo Clinic. The authors have no conflicts of interest to declare.

## AUTHOR CONTRIBUTIONS

K.M.M., K.S.F., S.H.C., and R.R.S wrote the manuscript. K.M.M. and R.R.S. designed the research. K.M.M, K.S.F., S.H.C., J.B., A.T.B., and A.W.C. performed the research. K.M.M., K.S.F., S.H.C., and J.B. analyzed the data.

## ORCID

Karen M. Meagher  <https://orcid.org/0000-0002-1055-6091>

Susan H. Curtis  <https://orcid.org/0000-0001-6317-1577>

Richard R. Sharp  <https://orcid.org/0000-0001-5441-2084>

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