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Clinician Perspectives on Using Pharmacogenomics in Clinical Practice

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Abstract

Aim—To describe the knowledge and attitudes of clinicians participating in a large pharmacogenomics implementation program.

Materials & methods—Semi-structured interviews with 15 physicians and nurse practitioners were conducted.

Results—Three categories of themes were identified: preparation and knowledge, pharmacogenomics usage in practice, and future management of genomic variants. Providers expressed an inability to keep up with the rapid pace of evidence generation and indicated strong support for clinical decision support to assist with genotype-tailored therapies. Concerns raised by clinicians included effectively communicating results, long-term responsibility for actionable results and hand-offs with providers outside the implementation program.

Conclusions—Clinicians identified their own knowledge deficits, workflow integration, and longitudinal responsibility as challenges to successful usage of pharmacogenomics in clinical practice.

Keywords

pharmacogenomics; attitudes; translational research; personalized medicine; qualitative research

Introduction

The use of genomic variants to tailor medical therapy is becoming increasingly relevant to routine clinical practice, as medications commonly used in primary care and cardiology practice acquire new indications for pharmacogenomics testing[1–4]. Advances in pharmacogenomics are marked by the expanding number of drug labels featuring pharmacogenomics guidance, pre-prescription testing endorsed by the Food and Drug Administration, and the growth of prescribing guidelines by the Clinical Pharmacogenomics

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Implementation Consortium (CPIC)[5–8]. Additionally, laboratory technologies to perform multiplexed genotyping are rapidly becoming more affordable and reliable [9]. Together, these developments have stimulated the funding of pharmacogenomics implementation networks within academic medical centers and integrated health systems [10–13]. Initial outreach efforts for pharmacogenomics testing typically focused on specialty care providers. As larger numbers of patients undergo testing for a wider number of drug-gene interactions, general practitioners are rapidly becoming more involved in applying this new type of data in clinical practice.

Translating research knowledge to clinical practice has historically presented multiple challenges, requiring changes to process and organizational culture[14]. Advances in the science and practice of pharmacogenomics could outpace the preparedness and receptivity of physicians and other clinical staff to effectively use the results to tailor therapy. Genomic medicine features a complex knowledgebase that is unfamiliar to both patients and physicians, many of whom have had no formal training on these concepts [15–18]. Given the complexity of the reporting and interpretation, integrating pharmacogenomics results in the electronic health record may lead to difficulty with understanding the clinical significance or problems in applying results toward individual patient cases [15–17].

The field of pharmacogenomics needs a better understanding of how clinicians are responding to genomic data in routine care activities. As part of an evaluation program for a large scale pharmacogenomics implementation, PREDICT (Pharmacogenomic Resource for Enhanced Decisions in Care and Treatment)[19, 20], we conducted a qualitative study using semi-structured interviews with healthcare practitioners. The interviews sought to answer two research questions. What are clinician attitudes towards pharmacogenomics in practice? What unanticipated barriers are clinicians encountering as they begin using drug-gene interactions in routine healthcare practice? Domains addressed by the interviews included how participants conceptualized pharmacogenomics, operationalized pharmacogenomic test ordering, interpreted results, communicated with patients, and viewed long-term responsibility for results. The interviews identified key themes that may highly influence the direction of future implementation efforts.

Materials & methods

Study setting & participant recruitment

The study was conducted at Vanderbilt University Medical Center (VUMC), which launched PREDICT in 2010[19, 20]. The program pairs a panel-based genotyping with pharmacy surveillance and clinical decision support in VUMC's electronic health record in order to facilitate genome-guided prescribing of target medications at the point of care. At initiation, PREDICT delivered CYP2C19 genetic results and clinical decision support for selection of clopidogrel or alternative antiplatelet therapy; in subsequent years, the implementation expanded to include genes and recommendations relevant to warfarin, tacrolimus and thiopurine drugs. To date, over 14,500 VUMC patients have been tested within the program, the majority of whom receive care in Internal Medicine and Cardiology clinics. We report data from clinicians practicing in these environments within 2010–2013. All of the interviews were conducted in 2013 and early 2014.

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We developed a purposive sampling plan for interviews along two axes: usage patterns and practice domain. The sampling plan solicited users from two types of practice, primary care and cardiology, selected because of the indications for the commonly used medications targeted by the program. Usage patterns were quantified by the number of orders for the PREDICT test. Low usage pattern was defined as < 10 orders summarized over the prior year, medium usage was defined as between 10 and 99 orders, and high usage patterns defined as > 100 orders for pharmacogenomics testing. We recruited subjects along the two sampling axes, contacting potential subjects directly by email or in person and requesting their interview participation. Interview subjects were compensated for their time. We continued with interviews within each subgroup until we reached a point of data saturation, where additional interviews did not yield significant additional knowledge.

Data collection

Semi-structured interviews were selected to assess clinician attitudes and knowledge based on prior experience evaluating health information technology and program evaluations[21]. Interviews were selected over other approaches such as observation due to the limited number of times on any day that a specific clinician might interact with pharmacogenomics testing or clinical decision support. Qualitative methods such as interviews are commonly used in social science research, and increasingly applied to healthcare research. The methods are well-suited to understanding the rationale behind technology usage patterns and underlying aspects of clinical decision-making.

Interview questions were developed based on the research questions motivating the study. We developed the interview instrument through discussion and iterative refinement by the research team, including experts in qualitative research approaches. Research questions were divided into categories: role and computer use, meaning and use of pharmacogenomics, experiences with PREDICT, pharmacogenomics nomenclature and open-ended feedback. Each question category sought to elicit specific feedback regarding pharmacogneomic use in practice. Subsequently, we pilot tested the instrument with two interview subjects. Pilot testing led to minor changes to the instrument to clarify the phrasing and content of the questions. Finally, we arranged interviews in locations convenient to our interview subjects. Each semi-structured interview used the same interview script (appendix A), but allowed the flexibility to add clarifying questions or to modify questions based on subject responses.

Each interview was conducted by one or two researchers with experience in qualitative methods. All interviews were either audio or video recorded, with interview subjects allowed to choose between the two options. Interview subjects reviewed a written informed consent document prior to the interview beginning, and all interview subjects provided signed consent.

Data Analysis

After interviews were completed, the audio or video files were transcribed. Transcribed files were then uploaded to Dedoose, a cloud-based data analysis package, specifically developed to support analysis of qualitative and mixed methods data. Users are able to upload files to Dedoose in a variety of formats, including text files containing, for example, transcribed

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content of audio- or video-recorded data. Once uploaded to Dedoose, the tool allows users to review file contents, tagging text elements and applying codes to them. Dedoose organizes the qualitative data throughout analysis and supplies aggregate views of codes and text excerpts coded by researchers.

Using Dedoose, we analyzed the data, applying a grounded theory approach to data analysis. Grounded theory approaches allow theory to emerge from the data, rather than applying existing theoretical frameworks to data analysis [22]. During an initial open coding phase of analysis by two separate researchers, data were analyzed to identify and code key concepts in the data[23]. A second phase of data analysis involved review of all codes to identify common patterns and recurrent themes across interviews. We examined the patterns and themes to identify elements and concepts that connected the initially identified themes together. Initial patterns and themes that shared common elements (i.e., were similar in content and meaning) were aggregated into the themes presented in the results, all grounded in the initial interview data [24].

Two researchers working independently reviewed each transcript in Dedoose and applied codes to the data to identify elements of interest through an open coding process. Working collaboratively, researchers then identified the main themes, looking for recurrent patterns and key themes in the assigned codes [25]. The Vanderbilt University Institutional Research Board approved the study.

Results

We recruited 15 clinicians from both internal medicine and cardiology and from each of the three usage categories. Nine cardiology and six primary care providers were interviewed representing four low usage, four medium usage, and seven high usage clinicians. More high usage clinicians were interviewed as they expressed a greater diversity of opinions regarding the testing and more interviews were required to achieve data saturation. The majority of interviewees (13) were attending physicians, as the majority of PREDICT users had this role. We also interviewed two nurse practitioners who actively prescribed medications targeted by PREDICT and interacted with clinical decision support.

Based on analysis of interview data, we identified three high-level theme categories in the data: preparation and knowledge, pharmacogenomics usage in practice, and future implementation challenges. Each category consisted of multiple themes incorporating related concepts.

Preparation and knowledge

None of the clinicians in our sample had specific coursework or other training in pharmacogenomics prior to the program implementation, an expected outcome given the early stages of translating pharmacogenomics to practice. Despite the lack of formal training, clinicians developed knowledge and understanding of pharmacogenomics concepts through various mechanisms. Specialty care providers discussed developing initial pharmacogenomics knowledge prior to the informatics intervention from research studies about the relationship between clopidogrel and the gene encoding the metabolizing enzyme,

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CYP2C19, presented in the literature and at academic conferences. Primary care providers in our sample had less prior exposure to pharmacogenomic concepts and expressed less confidence in their pharmacogenomics knowledge base. One clinician described the uncertainties inherent in clinical knowledge by stating, *"I feel like the things that I know, I know, but I'm fully aware that there's a much larger pool of what can … be applied to that I don't know. So, I know my ignorance."*

Interviewers asked each subject, "How do you define the term 'pharmacogenomics'?", eliciting a wide variety of reactions and responses. Several interview subjects laughed at the question, expressing uncertainty about the concept. For example, one respondent stated, *"I don't know. Trying to identify patient-specific ways that patients use or break down or get rid of medications."* Other clinicians responded confidently and concisely. The degree of precision and detail in definitions of pharmacogenomics varied widely. For example, some subjects responded with a fairly simple definition, *"I define it as understanding a patient's profile to help you make a better decision about the appropriate medication use."* Other subjects provided more detail in their responses, *"It's the use of genetic polymorphisms to determine even before first dose… potentially which drug, which dose of the drug, potential side effects, adverse effects from the drug. I guess in a nutshell… that would be my definition."*

PREDICT implementation initially targeted specialty care providers in cardiology. Cardiology clinicians cited outreach efforts by clinical and informatics leaders to promote the upcoming pharmacogenomics tool implementation as a key factor in their development of knowledge about and use of the testing. Methods used for knowledge dissemination included Grand Rounds and smaller practice group meetings. Clinicians typically discussed several key clinical and research leaders who provided an initial introduction and ongoing dialog related to pharmacogenomics,

> "Probably at the department level through larger group presentations. I recall [program faculty leader] being an influential voice to introduce this. I also worked closely with one of the key members of the pharmacogenomics team…. So, that has been a steady source of conversation over the last two years."

The types of initial exposure to pharmacogenomics discussed by primary care providers focused more on general communication channels, such as electronic medical center newsletters and journal articles.

Despite outreach efforts, questions remained about rapidly changing pharmacogenomics knowledge. One cardiologist described the balance between knowledge dissemination and the types of knowledge needed to apply information in practice,

> "Well, I think we could be more informed of some of the pharmacogenetic principles frankly in a more understandable way than the state-of-the-art grand rounds lecture on one hand and the patient communication piece on the other. There's something in between that is clear, concise, pitched at the general practitioner's level that is missing in this whole operation."

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Because of the rapid evolution and expansion of pharmacogenomics knowledge, clinicians discussed the need for continuing education. Clinicians discussed concerns about their knowledge becoming quickly obsolete. One cardiologist summarized this concern by saying,

> "I wish I knew more because sometimes I think we, I feel like we practice in a vacuum, especially on something so super specialized as this. So, you know it, and you learn it, and you know very well in six months what you know is not current. I mean, there's no way that it is."

In summary, we identified both positive aspects and gaps in the outreach efforts related to education and concerns by clinicians about continuous engagement to maintain their knowledge of research advancements.

Pharmacogenomics usage in practice

Test ordering and reporting—A clear theme across interviews was that clinicians understood the rationale for obtaining pharmacogenomics information, but integrating this knowledge into healthcare practices raised complex questions and concerns. One strong proponent of obtaining pharmacogenomics panel data summarized this view,

> "I think more information is always better about patients. So I believe that it's important to try to obtain this genetic information, pharmacogenomic information on my patients. That's step number one. Step number two is what do you do with the information? We're still learning."

Standard laboratory reporting of genomic test results was sometimes unclear to clinicians, leading them to seek answers from the interpretive information present in other sections in the EHR. For example,

> "There is so much information that comes back when [the laboratory test report] shows results that you say, "Okay, I don't know what this means. I'm going to go to [the EHR] where it's really simple and it tells me it's a poor metabolizer or intermediate metabolizer." Those are words I can understand as opposed to getting all the genetic information."

Some clinicians felt that even these distilled phenotype terms were difficult to interpret, in part because the nomenclature that was familiar to the clinical genetics research community was not transparent to end-users.

> "I think poor metabolizer is a good word, a good phrase… Indeterminate would suggest that we have no idea what the mutation does. Whereas, intermediate… a more suitable word might be partial metabolizer."

Due to the highly specialized content of pharmacogenomics tests, some clinicians expressed concern about the clinical relevance and information overload of reporting genomic information to the EHR. As one clinician expressed, *"One gets diluted, tired, and then ignorant of things that are posted on every single patient, especially if we're not using it very often."*

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Translating results into clinical decisions—Once tests results were reported, clinicians integrated pharmacogenomics test data into their clinical decision-making processes to varying degrees. Clinicians expressed strong desires for, as one clinician described it, *"decision support that's informational that doesn't disrupt the flow of the work."* The need for CDS in general to be well integrated into clinical workflow has been a repeated theme of informatics research on CDS[26] so the extension of this perspective to pharmacogenomics CDS was unsurprising.

Interview subjects provided suggestions for several different approaches to CDS, focused on the idea that CDS needs to be clear and concise but also provide the ability to seek out more information quickly and easily if desired. One clinician laid out a rationale as follows,

> "I'm a very quantitative person… intermediate doesn't mean anything to me. So… can you tell me poor metabolizer? Could you quantify that in some way? 10, less than 10%? Some number that tells me or even something that's just color coded and it says, "Prescribe something else. Don't do these drugs,"

Another physician suggested,

> "Most importantly, the information has to be pushed to the ordering physicians so that the ordering physician gets the information. With that push has to be very easy links to… written advisor statements invented by the experts that tell us what is recommended. And then, there should be another link to the original data for people that want to know exactly what the evidence is one way or the other."

Clinicians in our interview sample viewed pharmacogenomics data as just another element to integrate into clinical decisions, much like routine laboratory tests. At the same time, they pointed out that multiplexed pharmacogenomic testing as assessed by PREDICT encompassed potential pharmacogenomics interactions beyond ones that currently have clear treatment guidelines in their field. Other subjects expanded on this concept, to discuss how the current state of pharmacogenomics knowledge may not give a full picture of the potential variation in drug response.

> "That's part of the frustration at this particular point with pharmacogenomics, in terms of having a patient walk into the door and really not knowing that information that you think may be vital to their care in terms of trying to individualize their care at that particular point, but as we go forward, as information starts to compile and build, connects and make modifications in terms of therapy."

Clinicians reported that making medical decisions related to pharmacogenomics data involved a complex effort to balance cost, risk, and benefit. Alternative medications suggested by the literature and adopted by the program for use within CDS could create higher out of pocket costs and new safety concerns in addition to the promise of improved efficacy. Clinicians discussed the challenges inherent in integrating program guidance with the social situation of the patient and uncertainties with how much genome tailored therapy would improve outcomes. *"I mean it's a huge financial burden on patients to make the change. So we have to prove that it actually changes outcome."*

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Explaining test ordering and results to patients—Initially, clinicians discussed pharmacogenomics testing in detail with patients before ordering tests, but reduced the amount of explanation over time.

> "So, at the beginning, we started all this, I went through this detailed explanation of what we were ordering, and what I found from patients is that the response all along is, 'Oh, please order it. It's stupid not to order this particular test. I definitely want to know the information.' At this point, it's become a shorter conversation in terms of, 'I want to do this. I think it's smart. This is why,' and everybody says, 'Fantastic. Please do and can my daughter get it? Can my uncle get it? Can my grandmother get it?'"

Other clinicians felt that in-depth explanations of specific pharmacogenomic testing details were unnecessary in initial decisions to test.

> "I'm usually somebody that likes to simplify things an awful lot for understanding for both my patients and for me. So, you know, how can I make this as simple as possible so that they get the big picture of why I'm doing the test, but not overwhelm them with its purpose."

Clinicians discussed some of the language they used in explaining pharmacogenomics testing to patients,

> "I try to explain that this is a piece of the puzzle. That we can get lots and lots of people's data and then we can be able to sort of make more, I don't say responsible, but medically sound decisions based on evidence and not guess work."

Clinicians described a clear pattern that, as they became more familiar with this type of testing, they began to view the test in a similar light as other clinical tests in terms of explanation required before testing. One substantial caveat to this explanation pattern is that during the time interviews were conducted, the PREDICT test was institutionally supported and offered free of charge to patients. Some clinicians expressed reservations regarding whether patients would be receptive to genetic testing once it was charged to their insurance plan and they were responsible for co-pays and deductions. For example, one specialty care provider stated, *"Patients do not want to pay for testing particularly if it's not… if they don't see upfront the benefit of it. I think it's going to be harder to convince people that that is added value."*

When receiving test results, clinicians faced the challenge of interpreting and communicating the information to patients and families. Their level of familiarity with pharmacogenomics impacted this interaction.

> "I think that you had a lot of clinicians who were blindsided because all of a sudden, patients start finding out they were intermediate metabolizers and this is before anyone knew what to do with that. And so, I think, you know, you had patients asking their doctors, 'Well, I got this, you know, this is what they said I am. You know, what do I do?' And the doctors would go, 'Uh, I don't know.'"

In some cases, a sense of lack of preparedness led to conversations with patients being conducted in less detail than clinicians would normally pursue. One clinician explained,

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"The conversations with patients are more on a high level and not so detailed because of that sense of unpreparedness." Clinicians expressed unease about explaining implications of results that were of indeterminate or intermediate significance, *"You had patients asking their doctors for advice based on their pharmacogenomics result before the doctors knew how to respond."*

Secondly, specialty care providers felt underprepared to explain drug-gene interactions that involved drugs they did not prescribe, *"I try very hard to avoid ordering tests that I don't know how to interpret for the patient, or that I can't… refer them to something regarding interpretation."*

Providers expressed interest in a formal set of patient education materials that anticipated questions and concerns. *"We might benefit from bullet-point thoughts of what patients are hearing because we're having to unravel some of their exceeding expectations when they get here."*

Future of pharmacogenomics in practice

Ownership and responsibility for results—Providers discussed how the persistent nature of pharmacogenomics data presents new challenges related to long-term data ownership, responsibility, and liability. For example,

> "Does that information [the full range of PREDICT results] remain undiscovered if I don't actively push it to the primary care physician or can it automatically get to them so that they can use that information for the 48 other drugs that I'm not going to be prescribing?"

Clinicians explained a gap between current policies and the range of data in the informatics intervention, with several clinicians exploring the need for formal clear policies to explain responsibility and ownership for pharmacogenomics data.

> "I think it'd be nice if there were some clarity about the responsibility for the ordering physician in terms of notifying the other physicians involved in the patient's care just so people know exactly what's expected of them when they order the test."

While clinicians felt clear lines of responsibility and ownership were necessary, they expressed concerns about the level of pharmacogenomics knowledge among referring clinicians outside the academic medical center environment. The need to educate busy community clinicians about the results and recommended action was an area that some clinicians felt needed to be explored in detail,

> "I think it's going to be important to come up with good processes to educate referring physicians as well as ordering physicians and specialists on how to handle this information. Who do you need to notify? Who's responsible for acting on the information? Who's responsible for educating the patients on it as well?"

Although many clinicians came to view pharmacogenomics testing as another routine laboratory test in their practices, there were clear concerns about challenges related to the persistence of pharmacogenomics data over time.

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Future of pharmacogenomics evidence development

Regardless of how well the pharmacogenomics test ordering and results were integrated into clinical practice, subjects discussed the need to continue scientific exploration of outcomes related to treatment changes. One clinician discussed the future of pharmacogenomics by saying,

> "So, [pharmacogenomics testing] has changed my practice even though the outcomes data are not there yet. And I feel comfortable about that because my change has been validated in a cohort of patients outside of known genetic information. In randomized trials. I also think it's important to get into the mindset where we are, as, as clinicians, routinely thinking about optimizing drug therapy for patients based on their genetics."

Closing the loop on the current approach to pharmacogenomics was critical to multiple clinicians interviewed for this study. As one clinician stated,

> "I'm not sure where it's headed as far as using it for science in terms of having a strong database where we're linking PREDICT data with clinical outcomes."

Continuing along the path to personalizing treatment decisions for patients based on genetic data requires demonstrating the value of this approach, particularly on improving patient outcomes.

Discussion

This study provides insights into the barriers facing the dissemination of personalized medicine. First, clinicians acknowledged the complexity of genomic data; the unfamiliar representations and nomenclature used to describe results led to difficulties with interpreting, communicating, and applying the data to clinical care. Strong support was expressed for ongoing engagement with the implementation team to keep clinicians updated on the latest research results. Providers also strongly supported the use of thoughtfully designed and well-integrated CDS tools to facilitate genome-informed decisions. However, they identified gaps in the program related to long-term responsibility for genomic risks when patients leave the institution, and hand-offs to community providers.

Several prior qualitative and survey studies have identified providers' concerns about incorporating genomic information into their practice. Interviews of hospital pharmacists working in Australia indicated their knowledge, education, and time constraints were barriers to use of pharmacogenomics.[27] Similarly, surveys of providers about pharmacogenomics identified enthusiasm for the concept but infrequent ordering and lack of preparation to receive the results [17, 18, 28]. One study with a similar qualitative design assessed primary care physician attitudes within the context of the MedSeq randomized clinical trial. Interviewed primary care physicians receiving whole genome sequencing results and rated the results as less valuable than family history expressing uncertainty about how to act on them.[29] Our study, which was conducted within the context of a supportive implementation program, reiterated some of the concerns raised by practitioners in the other studies regarding new types of data and the impact of personalized medicine on care.

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However, the target clinician group, clinical context, and content of the genotyping panel were unique and these factors likely significantly impact provider attitudes.

Pharmacogenomics testing was viewed by practitioners in our study as similar to other laboratory tests, particularly when explaining the need for such testing to patients. Practitioners identified, however, that pharmacogenomics results also had different attributes from routine laboratory results. Testing was to address specific treatment questions, but the PREDICT pharmacogenomics panel test covered a wide range of genetic variants. Pharmacogenomics testing creates persistent data whose meaning and interpretation will evolve over time. This persistent value requires assignment of long-term responsibility for interpretation and management. Ordering clinicians expressed concerns regarding hand-off of responsibility for managing drug-gene interactions for drugs not prescribed by the ordering clinician. Primary care physicians in the community had limited preparation to interpret and manage drug-gene interaction data, raising questions about how long-term responsibility for managing drug-gene data can best be transitioned from ordering practitioners to referring and general practitioners. Pharmacogenomics testing represents an important and emerging frontier in health data, requiring communication, coordination, and longitudinal follow up that is rarely handled effectively in the current fragmented structure of healthcare.

The study has several limitations. The themes were derived from a small sample of clinicians that may not be fully representative of all opinions within our institution or among other types of subspecialists who encounter genomic results. We have not compared attitudes between primary care physicians and specialists which would require additional data from a broader spectrum of clinicians. Indeed, we expect oncologists who have greater clinical experience applying molecular diagnostics in practice would be more comfortable with genomic results. Although much of the data gathered in this study has broad relevance, pharmacogenomics implementations vary widely and some details may be implementation specific. Interviews were conducted when the institution supported the cost of pharmacogenomics testing; however, clinicians in the study were already anticipating the evolution to testing reimbursed by insurance. Costs of testing and treatment alternatives may change rapidly with updates to program and insurance policies, and we anticipate further evolution of provider perspectives. Finally, all clinicians interviewed were affiliated with an academic medical center, leaving a significant area for future research: studying the perspectives of healthcare practitioners in the community.

Conclusions and Future Perspective

A qualitative study of clinician views of pharmacogenomics defined gaps in the current implementation and suggestions for future improvement. In particular, pharmacogenomics implementations need to focus on education of both practitioners and patients. Continuous educational outreach may be required to assist with rapid pace of knowledge development. Clinical decision support and long-term responsibility for pharmacogenomics panel data are important areas to be addressed by new policies and new program features. With the emerging implementation of next generation sequencing of both somatic and germline variants, we anticipate attitudes will change as additional evidence is generated. Future

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investigations of clinicians' views of genomic medicine should include a broad spectrum of specialists, including those who have already embraced targeted therapy and those who are poised to incorporate targeted therapy into their clinical practice.

Executive Summary

A qualitative study of clinician views of pharmacogenomics highlighted ongoing interest in incorporating genomic information into routine clinical care and defined gaps in the current pharmacogenomics implementation and suggestions for future improvement. Study subjects reported the following themes:

- **Preparation and knowledge**
  - Clinicians expressed support for the idea that pharmacogenomics is rapidly becoming part of standard practice
  - Clinicians found it challenging to keep pace with the rapid generation of new drug-gene interaction evidence without ongoing educational support
- **Pharmacogenomics usage in practice**
  - Clinicians expressed concerns about communicating to patients the rationale for applying pharmacogenomic results to prescriptions and the need to balance genomic information with other clinical, social, and financial factors
- **Future of pharmacogenomics in practice**
  - Clinicians expressed unease with taking long-term responsibility for genomic variation that was either not directly related to their care plan or outside their specialty.

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Appendix: Ethnographic Interview Guide

Role and computer use

Goal: understanding the interview subject’s role in healthcare delivery and interaction with health information technology.

1. Can you describe your current role? What types of patients do you primarily see? What clinical department(s) do you normally work in?
2. How do you record clinical provider notes? *(Examples: StarPanel Notes, Dictation, Paper, Quill*)*
3. What tools do you use for ordering tests and procedures? *(Examples: OPOC, VOOM, HEO/WizOrder*))*
4. Are there any other health information technology systems that you use?
5. How would you describe your use of computers in healthcare?

Meaning and use of pharmacogenomics

Goal: understanding how interview subjects conceptualize pharmacogenomics and the role of pharmacogenomics in healthcare.

1. How do you define the term “pharmacogenomics”?
2. How were you first introduced to pharmacogenomics?
3. Where have you learned the most about pharmacogenomic testing? *(Examples: literature, professional meetings, Vanderbilt communications, media)*

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4. What types of evidence or guidance do you feel is most persuasive in adjusting your clinical practice?
5. How has your understanding or interpretation of pharmacogenomics changed over time (in general or for a specific drug-gene interaction)?
6. Have you received any informal or formal training in pharmacogenomics? Can you tell us more about any training you've received?
7. What role does pharmacogenomic testing have in your healthcare practice currently? What role do you think it will have in the future? How prepared do you feel to order pharmacogenomic tests and apply the results?

Experiences with PREDICT

Goal: gathering self-reported current usage of PREDICT, an example of how the subject currently uses PREDICT, and their anticipated future use.

1. How often do you think you order PREDICT tests right now? How often do you think you use the results of PREDICT tests?
   - **a.** Could you walk us through an example of a time that you used PREDICT to order a pharmacogenomic test? Why did you order the test?
   - **b.** What was the timeline for ordering the test?
   - **c.** Did you use the results of the test yourself, or did you pass the results onto another provider?
   - **d.** How did the patient respond to ordering the test?
2. Could you walk us through an example of a time you used the results from PREDICT tests in care?
   - **a.** Did the results change your care plan?
   - **b.** What would you have done without the results?
   - **c.** Was the patient aware that pharmacogenomic data was used in care planning?
3. Can you describe some of the reasons why you order PREDICT testing during clinical encounters?
4. The PREDICT testing is currently free for patients. What difference, if any, will it make to you when PREDICT testing is no longer free?
5. What circumstances would make you hesitate to order a PREDICT test or lead you to not act on recommended treatment changes?

Language/wording choices

Goal: understanding how phrasing of PREDICT prompts impacts provider understanding of those prompts.

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1. What are your thoughts on the PREDICT guideline recommendation language that is currently displayed? For example, some terms that are used include “poor metabolizer” and “intermediate metabolizer.” What do you think of these terms? Are there other terms you would suggest for guidelines?
2. Do you think including other types of information such as quantitative estimates of risk (e.g., absolute risk, relative risk) would influence your response to PREDICT communications?
3. Based on your own experience with pharmacogenomic guideline recommendations, could you rank these words from highest to lowest degree of obligation? *(Note: see list below)*
    a. Follow up question: could you discuss why you put these terms in this particular order?

General

Goal: wrapping up the interview, gathering any other open-ended comments subjects would like to share.

1. Do you have any suggestions on how to best integrate pharmacogenomic data into clinical workflow?
2. Is there any other feedback you’d like to give about your interaction with PREDICT?
3. Are there any questions about pharmacogenomic testing or about PREDICT that you think we should be asking that we haven’t asked?

Word list

May

Should Consider

Is Suggested

Should Be

Is Indicated

Is Recommended

Must

May Consider

Should

Should Be Considered

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May Be

* **Note:** Starpanel notes and Quill are two alternative electronic documentation tools used within the institution where all of the study subjects worked. Likewise, OPOC, VOOM, and HEO/WizOrder are names of provider electronic order entry tools within the institution.