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Research and Applications

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Barriers and facilitators of the use of clinical informatics resources to facilitate pharmacogenomic implementation in resource-limited settings

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Abstract

Objective: Understand perceived barriers to and facilitators of using clinical informatics applications for pharmacogenomic (PGx) implementation in resource-limited settings.

Materials and Methods: We conducted a qualitative research study using a semi-structured interview guide informed by the Consolidated Framework for Implementation Research (CFIR). Interview questions assessed CFIR contextual determinants related to: electronic health record (EHR) infrastructure; clinical informatics personnel and resources; EHR integration of PGx test results; PGx clinical decision support (CDS) tools; institutional resources; and partner receptivity. Transcripts were coded and analyzed to identify themes.

Results: We interviewed 24 clinical informaticists and executive leaders working in rural or underserved health care settings in Montana ($n = 15$) and Colorado ($n = 9$) and identified three major themes: (1) EHR infrastructure limitations, (2) insufficient supporting resources, and (3) unique contextual considerations for resource-limited settings. EHR infrastructure limitations included limited agency related to EHR build and interoperability concerns. Theme 1 highlighted challenges associated with integrating structured data into the EHR and inadequate vendor support. Theme 2 included limited familiarity with PGx across the care team, cost concerns, and allocation of non-financial resources. Theme 3 highlighted perceptions about the clinical utility of PGx within rural and underrepresented populations. Potential facilitators, such as being able to act nimbly, were found to coexist among the reported barriers.

Discussion and Conclusion: Our results provide insight into the clinical informatics infrastructure in resource-limited settings and identify unique considerations for clinical informatics-facilitated PGx implementation. Future efforts in these settings should consider innovative partnerships and strategies to leverage facilitators and minimize barriers associated with integrating PGx CDS applications.

Lay Summary

Drug-gene testing helps doctors pick the best medicine for each patient based on their genes. But this test can be hard to use in places with fewer resources, like small towns or areas with less money. Researchers talked to tech experts and hospital leaders in Montana and Colorado to find out what problems they face. They found three main issues: (1) Adding Results: It's hard to put test results into health records. (2) Not Enough Knowledge and Resources: Some health care workers don't know much about drug-gene testing. They also worry about its cost and availability. (3) Usefulness Questions: People wonder if this testing is helpful in small or less-served areas. These issues help us see the challenges of using this test where resources are limited. It may lead to better ways of using drug-gene tests in the future.

Key words: clinical informatics; implementation; rural; underserved populations; pharmacogenetics; pharmacogenomics.

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Introduction

Recent advancements in the use of pharmacogenomics (PGx) to inform drug selection and dosing have largely been facilitated by clinical informatics applications.[1,2] In the context of PGx, these applications primarily involve integration of PGx test results as discrete data in the electronic health record (EHR) and automated clinical decision support (CDS) tools that surface pre- and post-PGx test recommendations to clinicians at the point-of-prescribing.[1–5] However, clinical informatics-facilitated integration of PGx has primarily been limited to large academic medical centers, health systems, and resource-rich environments.[6–11] As such, PGx clinical implementation lags in resource-limited settings, including rural and underserved communities.

Implementation strategies that leverage meaningful, structured integration of PGx test results and automated CDS tools in the EHR have the potential to benefit resource-limited settings by supporting genetically-informed prescribing decisions, even when clinicians may have limited experience with PGx.[12] Unfortunately, few PGx implementation studies have been conducted in resource-limited settings, nor have studies systematically assessed clinical informatics resource needs in these communities.[12–15] Given the high population prevalence of actionable PGx variants, PGx has become a key component of many population health initiatives.[16,17] Importantly, level of urbanization contributes to differences in population health resources and subsequent medication therapy management, leading to potential inequities for patients living in rural areas or receiving care at underserved, low-resource health systems.[14,18] In line with these concerns, the National Academies of Sciences, Engineering, and Medicine hosted a roundtable focused on understanding disparities in access to genomic medicine.[19] A portion of the discussion centered on providing genomic medicine in resource-constrained environments, with recommendations to create and optimize tools within EHRs. Yet, there exists little guidance for pragmatic ways to advance clinical informatics in these settings, particularly for PGx integration. Clinical informaticists and executive leaders are uniquely positioned to provide expert opinions on the challenges of integrating new applications into their health care institutions; however, to our knowledge, no studies have evaluated their perspectives as they relate to using these tools for PGx implementation.

Objective

The objective of our study was to evaluate the perspectives of clinical informaticists and executive leaders about the barriers to and facilitators of using clinical informatics applications for PGx implementation in rural or underserved facilities across Montana and Colorado. We aim to use our findings to inform strategies for clinical informatics-facilitated PGx implementation in resource-limited settings. By gathering perspectives from key decision-makers within these facilities, we identified pragmatic considerations for implementing PGx in health systems serving often overlooked communities.

Methods

Study setting, sample, and recruitment

For this qualitative research study, we conducted 22 semi-structured interviews of 24 clinical informaticists and executive leaders from resource-limited settings, specifically rural and underserved facilities in Montana and Colorado (2 interviews included a pair of interviewees). Of the interviews, 14 were conducted at sites in Montana ($n = 15$ participants) and 8 were conducted at sites in Colorado ($n = 9$ participants). Convenience sampling was used to identify potential participants, with additional participants referred by colleagues who were already enrolled. Participants were excluded if they were less than 18 years of age or if they were unable to participate in the interview virtually or over the phone. Participant recruitment occurred via email outreach between January and June 2022. Participants were offered compensation in the form of a $30 electronic gift card. All interviews were conducted virtually via videoconferencing using Zoom (San José, CA, United States). The study was approved by the Colorado Multiple Institutional Review Board and the University of Montana Institutional Review Board with participant consent captured via a postcard consent form.

Interview guide and data collection

Study team members collaborated to iteratively design a semi-structured interview guide that was informed by the Consolidated Framework for Implementation Research (CFIR).[20] The interview guide was designed to evoke deductive themes, that is, findings that are directly comparable to data previously published in the literature, as well as inductive themes, aimed at identifying new theories not available as existing knowledge.[21,22] The final interview guide contained 23 open-ended questions (Supplementary Data), which included the following topics: EHR infrastructure and data integration (5 questions); clinical informatics personnel and resources (3 questions); existing CDS tools and build processes (4 questions); PGx tests and EHR integration (4 questions); institutional resource availability and allocation (2 questions); clinical EHR workflows (3 questions); and receptivity of key personnel (2 questions). Probing questions were asked, as needed, to clarify or prompt elaboration on responses. For the two interviews that included a pair of interviewees, the questions were posed, and responses were provided from one or both participants. Often, one of the participants would "take the lead" in answering the question and then give the other participant an opportunity to provide additional comments. Interviews lasted approximately 45 minutes and were conducted by 3 study team members (J.B.-R., J.L.M., K.E.B.).

Qualitative analysis

Interviews were audio-recorded and transcribed verbatim by MH Transcripts (Kingman, AZ, United States), with deidentified interview transcripts uploaded to Dedoose (Los Angeles, CA, United States) for data management and thematic analysis. Three of the study team members (J.B.-R., J.L.M., K.E.B.) analyzed the first 5 transcripts to iteratively develop an initial codebook based on participant responses. The initial codebook functioned as a list of codes (eg, words, phrases, or other segments of text associated with a given theme) that could be collaboratively reviewed and continually updated as more interviews took place. If study team members discovered that new codes were needed to enrich the codebook, they would discuss the new code with other members, and if deemed appropriate, add the code to the codebook. Each time a new code was added, the previously coded transcripts would be

rereviewed to ensure appropriate application of all available codes. The study team captured naturally emerging codes until reaching thematic saturation. The resulting codes were analyzed for discrepancies or potential bias in coding procedures, with open discussions among J.B.-R., J.L.M., and K.E.B. occurring until consensus was reached, leading to the finalized codebook. Inter-rater reliability was determined using Cohen's kappa via Dedoose software. Cohen's kappa coefficient was greater than 90% for each team member. Once the codebook was finalized, team members recoded all transcripts, updating previously applied codes as appropriate. For the 2 interviews containing a pair of interviewees, the coding was done for each interview as a whole.

J.B.-R., J.L.M., and K.E.B. analyzed the data, and grouped codes related to common concepts to formulate clusters of themes and sub-themes. Related concepts were decided upon based on iterative discussions among the study team members, focusing on relationships between participants' responses. Dedoose software was used to assess the frequency of assigned codes, and the strength of code relationships. Once preliminary themes were derived, the entire study team discussed the findings and further revised the themes until consensus was reached among all study team members. Data from participant demographic surveys were analyzed using descriptive statistics (SPSS software version 28.0, Armonk, NY, United States).

Results

Participant characteristics

A total of 56 clinical informaticists and executive leaders from selected resource-limited settings across Montana ($n = 18$) and Colorado ($n = 38$) were invited to participate in the study, with 24 individuals agreeing to participate. Nonresponse to study recruitment emails was the primary reason for lack of participation.

Table 1 shows participant and setting characteristics. Of the 24 participants, most were women (66.7%) and primarily White (83.3%). The average age at the time of the study interview was 45.5 ± 9.8 years (range: 31-68 years). Eleven participants (45.8%) had a professional degree, 8 (33.3%) had an undergraduate college degree, 4 (16.7%) had a graduate degree, and 1 (4.2%) had certifications in nursing and information technology. On average, participants completed their terminal degree 16.6 ± 10.2 years prior to the study interview. Most participants held multiple roles within their organization with 17 listing "administration/leadership," 16 listing "informatics," and 10 listing "clinical (patient-facing)" as a significant portion of their job responsibilities. No participants selected "expert" to describe their experience with PGx, with most (54.2%) selecting their experience as "novice," followed by "none" (37.5%), and "intermediate" (8.3%). Most participants (91.7%) reported receiving minimal or no education or training in PGx. Clinical PGx testing in settings represented by these interviewees was low, with only one participant reporting an institutional-level clinical PGx testing program within their organization. The specific EHRs used at participants' organizations included MEDITECH (20.8%), Epic (16.7%), Cerner (16.7%), Intergy (12.5%), eClinicalWorks (8.3%), CPSI (8.3%), and Health Share (4.2%), with three participants (12.5%) representing community networks in which the participants worked with multiple EHRs. The settings where participants worked included short term acute care hospitals (37.5%), Critical Access Hospitals (25%), Urban Indian Health Programs (12.5%), community managed care networks (8.3%), Federally Qualified Health Centers (8.3%), health information exchange (4.2%), and state rural health office (4.2%). Of the settings with information about the number of inpatient beds at the institution, the median was 54 beds (range 3-590).

Themes for using clinical informatics applications for PGx implementation

Analysis of the interviews identified three major themes: (1) EHR infrastructure limitations, (2) insufficient supporting resources, and (3) unique contextual considerations for resource-limited settings. Each theme contained between 2 and 4 subthemes. Each subtheme was related to its associated major theme but emerged separately as part of the thematic analysis.

EHR infrastructure limitations

Lack of EHR control was voiced as a major barrier to local PGx implementation and technical build efforts. Several participants reported that their organization's EHR was associated with, and dependent upon, an EHR leased from a larger health system (Table 2, Subtheme 1.1, quotes a and b). When asked whether their institution would be well-positioned to conduct EHR-based PGx results integration and CDS tool development, multiple participants discussed *limited agency over their EHR* and *restricted build customizability* (Table 2, Subtheme 1.1, quote c). These factors—along with dependence on external information technology resources—were also noted as hindrances to institutional preparedness for new EHR initiatives (Table 2, Subtheme 1.1, quote d). However, the concept of limited EHR agency was not universal in this cohort, with one participant reporting their EHR was very customizable, noting it as a strength of their institution (Table 2, Subtheme 1.1, quote e).

Several participants discussed *difficulty connecting technologies*—internally between different departments within their health system (eg, inpatient vs ambulatory) and externally to outside institutions—as a potential challenge to system-wide PGx implementation efforts. One participant expressed frustration at the disjointed state of their EHR, explaining that nursing staff and other clinicians operate on different systems and are unable to access each other's platforms (Table 2, Subtheme 1.2, quote a). Some participants discussed how communication between different areas of their health system (eg, between a hospital and a satellite clinic) would be problematic for new implementation programs. This was largely due to some locations using multiple EHRs with variable technical capabilities, adding to participants' concerns regarding their approach to implementing system wide, cohesive EHR initiatives (Table 2, Subtheme 1.2, quote b). It was also noted how disparate systems within one organization required more information technology maintenance (Table 2, Subtheme 1.2, quote c). Additionally, some participants mentioned challenges associated with sharing information between their EHR and the EHRs of other institutions (Table 2, Subtheme 1.2, quote d), ultimately hindering the ability to efficiently transfer patient data. One participant concluded that, in rural and underserved settings, variability existed in organizational readiness to establish interoperability pipelines between institutions and health systems (Table 2, Subtheme 1.2, quote e).

Table 1. Participant characteristics.

Characteristic	Participants ($N = 24$)
Recruitment site	
Montana	15 (62.5)
Colorado	9 (37.5)
Setting	
Short term acute care hospital	9 (37.5)
Critical Access Hospital	6 (25.0)
Urban Indian Health Program	3 (12.5)
Community managed care network	2 (8.3)
Federally Qualified Health Center	2 (8.3)
Health information exchange	1 (4.2)
State rural health office	1 (4.2)
Age at time of interview (years)	45.5 ± 9.8
Female	16 (66.7)
Time since completion of terminal degree (years)	16.6 ± 10.2
Race	
White	20 (83.3)
American Indian or Alaska Native	2 (8.3)
Native Hawaiian or Pacific Islander	1 (4.2)
Asian	1 (4.2)
Non-Hispanic Ethnicity	22 (91.7)
Education status, most advanced degree	
Professional degree	11 (45.8)
PharmD	6
MD/DO	2
MPH	1
MBA	1
Other	1
Undergraduate college degree	8 (33.3)
Graduate degree	4 (16.7)
MS	3
PhD	1
Other	1 (4.2)
Current job position/title[a]	
Administration/leadership	12 (50.0)
Informaticist	9 (37.5)
Pharmacist	7 (29.2)
Information technologies	6 (25.0)
Nurse	3 (12.5)
Physician	2 (8.3)
Other	2 (8.3)
Physician assistant/nurse practitioner	1 (4.2)
Participant job effort[a]	
Administration/leadership	17 (70.8)
Informatics	16 (66.7)
Clinical (patient-facing)	10 (41.7)
Primary EHR associated with participant's organization	
MEDITECH	5 (20.8)
Epic	4 (16.7)
Cerner	4 (16.7)
Multiple[b]	3 (12.5)
Intergy	3 (12.5)
eClinicalWorks (ECW)	2 (8.3)
CPSI	2 (8.3)
Health Share	1 (4.2)
Experience with PGx	
Novice	13 (54.2)
None	9 (37.5)
Intermediate	2 (8.3)
Expert	0 (0.0)
Received formal training in PGx	
No	22 (91.7)
Presence of institutional-level clinical PGx testing at participant's organization	
No	16 (66.7)
Unsure/don't know	7 (29.2)
Yes, as part of clinical practice	1 (4.2)
Yes, under the auspices of research	0 (0.0)
Yes, both clinical practice and under the auspices of research	0 (0.0)

Data are presented as mean ± standard deviation (range) or *N* (%) and were recorded at the time of study visit, unless otherwise specified. Some percentages may be greater than 100% due to rounding.

[a] Participants could choose more than one response; therefore, total percentage is greater than 100%.

[b] Participants were associated with Community Care Networks which interacted with EHRs across multiple organizations.

Abbreviations: PharmD: Doctor of Pharmacy; MD: Doctor of Medicine; DO: Doctor of Osteopathic Medicine; MPH: Master of Public Health; MBA: Master of Business Administration; PGx: pharmacogenomics.

Many participants stated that their institution did not have an on-site clinical laboratory capable of performing PGx testing. As such, participants discussed *challenges of integrating structured genetic results* into their organization's EHR (Table 2, Subtheme 1.3, quote a). In the absence of structured (discrete) results integration, there were concerns about how the data would be formatted and where it would be entered, for example, as PDFs within miscellaneous sections of the EHR (Table 2, Subtheme 1.3, quotes b and c). Some participants stated that additional technical interfaces would be needed to facilitate transfer of orders with laboratories and to incorporate results as structured data within the EHR (Table 2, Subtheme 1.3, quote d). Other participants anticipated the need for manual results entry, which prompted uneasiness about the potential for human error (Table 2, Subtheme 1.3, quotes e and f). In contrast, some thought that results integration would be straightforward if the process was facilitated by a third-party vendor (Table 2, Subtheme 1.3, quote g).

When asked to describe areas in which their organization's EHR could be improved, several participants talked about challenges associated with *inadequate EHR vendor support*, primarily related to upgrades and new functionalities (Table 2, Subtheme 1.4, quote a). For example, one participant explained how lack of vendor support for EHR upgrades led to confusion about loss of existing functionalities and unforeseen changes to CDS applications after the upgrade (Table 2, Subtheme 1.4, quote b). Another participant talked about situations in which vendors do not routinely provide training about new EHR functionalities, limiting the ability of clinicians to assess the utility and value of these applications in their settings (Table 2, Subtheme 1.4, quote c). In contrast, some thought EHR vendor support was a strength, allowing their organization to keep pace with changing technical regulations in the field (Table 2, Subtheme 1.4, quote d).

Insufficient supporting resources

Many participants expressed *limited familiarity with PGx*, as evidenced by a large majority (91.7%) selecting "none" or "novice" when asked about their experience with PGx. This suggests that widespread educational efforts would be needed to overcome knowledge gaps across disciplines and enable successful PGx integration efforts at their institution. It was suggested that educational efforts should focus on the availability, purpose, and potential benefits of PGx testing (Table 3, Subtheme 2.1, quote a). Participants voiced that

Table 2. Subthemes and representative quotes for Theme 1, "EHR infrastructure limitations."

Subtheme 1.1. Institutions with limited agency of their EHR face significant barriers related to build customizability

a) *"And then I'll say in some of our rural facilities that are owned by larger hospital systems, the hospital system actually controls what you can get out of the EMR."*—Participant 6, Colorado
b) *"We can't do our own build. That's the whole thing about being in that co-op, we're basically in a co-op. So everybody has to succumb to their co-op builds."*—Participant 11, Montana
c) *"And then, I would also say some of the rural health centers are utilizing EHRs that their bigger health systems use. And then, they're also at somewhat of the mercy of the larger health centers or the larger health system that they're a part of to make those decisions for them so they may not have necessarily the decision-making power to do certain things within their EHR."*—Participant 2, Colorado
d) *"I don't have control of [system] access, but yet, those that have the control are not on site. And that's probably what set us up the worst to start with because we could not get into this system at all until like a week before go live. And it's because that IT [information technologies] level is off-site and really hands off. And that makes for a really shaky go live."*—Participant 18, Montana
e) *"I'd say our EHR is actually very customizable. That probably is one of the strengths that [institution's EHR] has that other EHRs don't have is the ability to customize."*—Participant 20, Montana

Subtheme 1.2. Interoperability challenges exist within many resource-limited health systems

a) *"It's really difficult because it's disjointed at the moment. I think it's going to get there. But the nursing is on a different platform than the providers, and it's very, very confusing for everybody at the moment. Because one's on a web-based platform, and one is not. One's on an application-based platform. And it's a struggle at the moment."*—Participant 18, Montana
b) *"We also have some problems [. . .] connecting between the hospital and the clinic because [. . .] they usually have to use different electronic medical records because ambulatory medical records don't have the capabilities of what a hospital record has and the hospital one doesn't necessarily have what ambulatory needs. So sometimes those can talk together and a lot of times they can't. So that becomes a problem."*—Participant 6, Colorado
c) *"We are currently operating on two different sides of code you know pharmacy and lab are on one set of codes and the physicians with CPOE and the nursing as far as their documentation are a second set of codes that causes some communication difficulties between the different modules. It requires quite a bit more maintenance from an IT side of things because things don't talk to each other properly all the time. So that that's one of the limitations."*—Participant 14, Montana
d) *"But interoperability, I think, is the hardest part. A lot of our patients end up going up to Missoula. And [health system] is the dominant player up there, and they're on Epic. So getting information back and forth becomes a little tedious and is a little bit cumbersome sometimes. But that's what you get when you're going in between different EHRs."*—Participant 10, Montana
e) *"So I do see a huge variance between who's ready to establish these interoperability pipeline components for getting inbound/outbound data feeds and just building a more longitudinal record within their EHR system."*—Participant 2, Colorado

Subtheme 1.3. Incorporation of external information as structured data in the EHR is challenging, particularly for external PGx laboratory tests

a) *"And another biggest barrier is we don't have [a lab] on-site. We don't have the capability for a lab. And depending on the send out, I don't know if the send out is interoperable with ours."*—Participant 8, Colorado
b) *"But anything that doesn't have an integration or discrete data fields flowing through would probably end up in another tab or like a media tab. Which nobody really likes"*—Participant 10, Montana
c) *"Generally [genetic testing is] done at an outside hospital. And so the results will be a PDF format that might be in reports or other notes or something along those lines."*—Participant 15, Montana
d) *"[. . .] It would depend on who we were sending those sorts of laboratory and genomic testing to. It would potentially mean setting up more interfaces for that data, those orders to flow through and the results to fall back into our structured data."*—Participant 16, Montana
e) *"And so if you're doing it at an outside lab, then somebody at our institution is going to have to input it manually into our EHR"*—Participant 1, Colorado
f) *"So I think if we were to enter [PGx results] manually, one primary concern that would come up and has been discussed is how do we make sure that's accurate, or entered correctly."*—Participant 24, Montana
g) *"So, but for this, like integrating, if like our lab vendor offered this, [. . .] I think it would probably be pretty straightforward to integrate."*—Participant 12, Montana

Subtheme 1.4. Inadequate EHR vendor support is a barrier to implementation efforts

a) *"Yeah, I mean the technical support with our EHR is really bad."*—Participant 12, Montana
b) *"You're like, 'Oh my gosh, these upgrades sound great.' And then once they did the upgrade, it was like, 'Oh, these upgrades are really nice, but that functionality that we had last week is gone. And that was actually really nice.' Like, some of our clinical decision support stuff started breaking. And couldn't reliably count on it."*—Participant 4, Colorado
c) *"[EHR vendor is] not proactively training us on their new stuff. They are informing us [. . .] but where's that vendor support to train the clinical people in that area, because without that training, without that product knowledge, I don't know if the clinical people can make an educated decision on whether that's a good move or not, because we just don't have that knowledge with these new programs that are available."*—Participant 14, Montana
d) *"From a technical standpoint, another strength of EHR is that it's pretty well supported by the vendor. It's Epic. So pretty much, if there's a new federal regulation or some of the more recent demands of interoperability and information sharing, we're well supported to keep up with all of the latest mandates and functions."*—Participant 7, Colorado

many resource-limited organizations do not have in-house PGx expertise or a PGx specialist, which evoked concerns about whether clinicians would know what to do with the information and how PGx testing would be optimally integrated into clinical workflows (Table 3, Subtheme 2.1, quotes b and c). Overall, PGx knowledge was viewed as a key facilitator of integrating PGx into a system (Table 3, Subtheme 2.1, quote d), highlighting the need for education across multiple disciplines and stages of the PGx integration process.

Participants often described *cost as a major barrier* to integrating PGx at their institution. Cost concerns centered around PGx testing, along with the technical and personnel costs needed to support clinical integration. As a result, many participants perceived PGx implementation to be cost prohibitive in their setting. Although this concern is not limited to rural and underserved settings, cost may be a decisive barrier in settings that lack ample resources for projects perceived as non-critical. For example, one participant remarked that

Table 3. Subthemes and representative quotes for Theme 2, "Insufficient supporting resources."

Subtheme 2.1. Limited familiarity with PGx hinders integration efforts

a) *"I think just education on the availability of [PGx] tests and the purpose for using them. [. . .] So I think that's the biggest barrier, really, is just education around the topic and the benefit of providing pharmacogenetic testing to drive better medication prescribing."*—Participant 4, Colorado

b) *"And how do we pick the patients? Why are we checking this patient and not another? What's our population? I guess that's not infrastructure, but then you need the expertise."*—Participant 7, Colorado

c) *"We don't have anyone that specializes in [PGx] to even read it. Unless we had an outside consult. But I'm sure if the physician saw it, they'd be like, "Well, what am I supposed to do with this?" And then, do we want it to show, again, to which drugs [do] you want it to show?"*—Participant 8, Colorado

d) *"It seems like they would need extensive knowledge on [PGx] as well to be able to build this into the system."*—Participant 23, Montana

Subtheme 2.2. Cost is a major barrier to implementing PGx in resource-constrained settings

a) *"I think for us, it would just be cost. I think [. . .] these [pharmacogenomic lab results] would be expensive and that we have [. . .] kind of a low threshold financially for ordering anything outside of a basic lab panel. That would be, I think, our biggest barrier."*—Participant 22, Montana

b) *"I think just some of the barriers are cost [. . .] currently we've got 20 of our 41 rural hospitals operating in the red and so cost is a huge driver."*—Participant 6, Colorado

c) *"I think one of the barriers would definitely be cost and buy-in of whether they're really necessary."*—Participant 15, Montana

d) *"I think that you'd be hard-pressed to, at this point in time, be able to warrant it based on the cost of putting something like that in place and understanding [what] the return on that investment either from a patient safety or an efficacy perspective is. I just don't know how measurable that would be."*—Participant 16, Montana

e) *"[. . .] as you talked about some of those major players like clopidogrel. I think when if we can just show that by having this clinical support built, we're going to improve patient outcomes, and then therefore decrease further down the line costs if they had another cardiac event or side effects related to the ability to metabolize the drug or whatever it might be. I think they would definitely be in full support of that."*—Participant 4, Colorado

Subtheme 2.3. Resource allocation for CDS tool development is challenging, particularly for complex builds and given competing demands

a) *"[. . .] it's back to that more hours, more people. It's just a resource constraint. That's generally all that it ever comes down to. [. . .] So you don't have time to build decision support yet because you just need to get a drug database built, drug interactions, basic interactions, basic allergies like there's a lot of work that goes into that—[. . .] and if you have resources that say well, we need to get the basic architecture the system done versus these add-ons [. . .] you're going to divert all your resources to the critical basic structure to make sure it works before you start having the ability to design these."*—Participant 19, Montana

b) *"[. . .] we have to draw a line somewhere saying here's the things above the line that we're going to tackle that are new this year and here's what we just don't have the time, or the money, or the resources to do and I think that's one challenge where probably pharmacogenetics would fall; [. . .] how does it compete with the other things we're trying to manage day in and day out being short-staffed."*—Participant 16, Montana

c) *"And so then, it would require somebody on their end, at least somebody that would be able to translate this data or this information to our system and make it usable. So yeah, I would say complexity is a big one in there, a lot of moving parts. . ."*—Participant 23, Montana

d) *"If it's significantly complex or labor intensive when compared to our perceived value, then we could say, 'Wow, it'd be nice, but it's really too much work for what we're going to get out of it.' So we might pass over it."*—Participant 7, Colorado

their institution had a low financial threshold for ordering any testing outside of basic lab panels (Table 3, Subtheme 2.2, quote a). Another participant, representing a community managed care network, referred to nearly half of their rural hospital partners as "operating in the red," again highlighting cost as a major factor influencing decision-making (Table 3, Subtheme 2.2, quote b). Cost conversations were also intertwined with questions about the necessity and value of PGx testing in the face of limited resources and competing demands (Table 3, Subtheme 2.2, quotes c and d). One participant, however, stated their institution would likely be supportive if armed with the knowledge that PGx testing and CDS tools led to improved patient outcomes and decreased costs down the line (Table 3, Subtheme 2.2, quote e).

The interviewees voiced that *allocating resources to PGx would be challenging*, particularly for complex CDS builds and given competing institutional demands. When discussing clinical informatics PGx integration, many participants evoked sentiments reminiscent of the idiom—"we have bigger fish to fry." One participant talked about the need to allocate resources towards building "basic critical structures," perceiving PGx CDS tools as nice-to-have, but not essential (Table 3, Subtheme 2.3, quote a). Regarding institutional resource constraints, another participant described a threshold beyond which certain endeavors, for example, PGx implementation, would likely be deprioritized in favor of projects focused on improving daily workflows (Table 3, Subtheme 2.3, quote b). There was also a perception that building PGx CDS tools would be complex and difficult, potentially requiring disproportionate resource allocation and work effort when compared to perceived value (Table 3, Subtheme 2.3, quotes c and d).

Unique contextual considerations for resource-limited settings

Many of the study participants *recognized the overall value of PGx testing* but were *uncertain of its utility* in the populations served by their organizations. Several of these conversations centered around the perception that the small size of these communities would potentially limit the impact of PGx testing (Table 4, Subtheme 3.1, quotes a and b). Patient beliefs about genetic testing—and concerns for utility in underserved populations—were also voiced. For example, one participant spoke about how PGx testing would be useful in American Indian and Alaskan Native (AIAN) patients, but that research needs more racial diversity, so that findings could be more readily translated to underrepresented populations (Table 4, Subtheme 3.1, quote c). Another participant expressed how genetic testing is a sensitive topic among AIAN communities, owing to historical mistrust between patients and the health care system (Table 4, Subtheme 3.1, quote d). As a result, consideration would need to be given to

Table 4. Subthemes and representative quotes for Theme 3, "Unique contextual considerations for resource-limited settings."

Subtheme 3.1. Participants recognize the value of PGx testing but are uncertain of its utility in their specific populations
a) *"So for this genetic testing, if you're in a rural area, you're really just trying to take care of people by and large. I'm not saying that we wouldn't do genetic testing or that we don't, because they're definitely medically relevant. But the focus is certainly more on primary care and making sure your patients are taken care of. [. . .] One of the drawbacks is if we were to go ahead and do a lot of genetic testing here in [the community], we don't have a huge sample size."*—Participant 10, Montana
b) *"So it's that ratio of, do those prioritization[s]—is it really impacting patient safety? How many patients is it impacting? If it's impacting a very low percentage of our patient population, then it could be de-prioritized."*—Participant 7, Colorado
c) *"[. . .] I think that from a clinician standpoint that [PGx is] needed, that it's something that should be implemented just because we have a very delicate population that we take care of. Our mission statement is for American-Indian Alaskan Native patients and I witnessed, not just here but in all of my 17 years of healthcare, that this population does not metabolize medication the same. . . But I wish that we had pharmacogenetic[s] specifically in regards to American-Indian people."*—Participant 22, Montana
d) *"There is a lot of distrust between native communities and really, health facilities in general and so, there would have to be clear understanding of what this type of information is being used for and what [it] is not being used for and the securities around that information, too. So yeah, I think it is a relatively sensitive topic."*—Participant 23, Montana
e) *"And if our population [patients at Vail Resort, Colorado] were a sicker population, it would definitely be beneficial. But I would feel bad if it were to pop up on a patient from California. You get this result, and if it truly affects them, do you really give it to them? Do you give [it] to their primary care? Because they'll be leaving. Usually they leave in a couple days. You fix them, and then they leave."*—Participant 8, Colorado
Subtheme 3.2. Smaller institutions can nimbly implement changes within their system
a) *"I think personally, one of the other strengths, I think of our Epic instance is that we are only one institution. And so we do not have to get buy-in from multiple institutions for instance, on processes [. . .] because it's just us."*—Participant 1, Colorado
b) *"So the strengths are that because we're a small system, we have pretty good communication as far as what needs to be changed and usually those changes are done fairly quickly because we only have one guy that we have to talk to."*—Participant 22, Montana
c) *"But because we're so small, and sometimes honestly, [making decisions involves] like two people. [. . .] I don't have to wait. Compared to the large hospital that I worked in before that is a part of a multisystem [. . .] it could be done in two days versus six weeks. So since we have that local control, I would say changes happen very fast"*—Participant 5, Colorado
d) *"I'm able to work with every single department and every single practitioner on both behavioral health and medical side and then leadership as well. The fact that we're all kind of a smaller, very cohesive group that can all work together I think is a major strength for us. So there's not a lot of disconnect out there."*—Participant 23, Montana
e) *"Strengths would be the fact that we do have a protected time once a week where we can get a lens from every single part of the organization. So we can try and mitigate against any domino effect of a decision. So it's really nice to have somebody from each department to be there and speak up for the department."*—Participant 20, Montana

how PGx was integrated in health systems serving these populations, namely Urban Indian Health Centers and Tribal/Indian Health Services. Study participants who worked in small tourist towns (eg, ski towns in Colorado) also brought up another potential factor influencing PGx utility—the transient nature of patients treated in tourist areas. For example, there were questions about the long-term utility of PGx results for patients who were tested and treated in the acute setting but who then returned home to other parts of the country (Table 4, Subtheme 3.1, quote e).

Another unique contextual finding in this study was that *smaller institutions are nimble*, potentially allowing changes to be made quickly within their systems. One participant commented that being a single institution was a strength of their EHR, as they did not need approvals from multiple institutions to change processes (Table 4, Subtheme 3.2, quote a). Participants from smaller institutions also discussed factors such as good communication, smaller teams, and interdepartmental cohesiveness as being facilitators of streamlined processes and the ability to adapt and iterate quickly (Table 4, Subtheme 3.2, quotes b-e).

Discussion

To the best of our knowledge, this study is the first to evaluate the barriers to and facilitators of integrating PGx clinical informatics applications in resource-limited settings—with a focus on Montana and Colorado. By interviewing informaticists and healthcare leaders, we identified 2 major perceived barriers to the development and use of PGx clinical informatics tools: EHR infrastructure limitations and insufficient supporting resources. We also identified unique contextual considerations that highlight the strengths of resource-limited settings in favoring PGx integration in rural and underserved settings, including nimbleness, fewer decision-makers, and excellent internal communication. Many of our findings may be generalizable to other informatics initiatives in resource-limited settings, but we also highlight issues that are unique to PGx informatics implementation.

EHR infrastructure limitations related to customizability and interoperability were key considerations for participants. Our data revealed that, unlike large academic medical centers and resource-rich environments, smaller institutions in resource-limited settings often lease their EHR instance from a larger hospital system or share an EHR license with a network of health systems. Most participants viewed lack of EHR control as a major barrier to PGx implementation, which restricts local change, integration of new applications, and EHR customization. One potential solution is to ensure EHR leasing contracts have been reviewed for undue restriction of system customization and are continually reviewed upon contract renewal, fostering a cooperative partnership between lessors and lessees.[23] Further compounding these issues were concerns about technical interoperability, both within an organization and between health systems. Some participants viewed the technical components of their EHR as disjointed, which was associated with skepticism about the ability to implement PGx testing in a cohesive and systematic way in their settings. Unfortunately, local customization and maintenance of non-standardized CDS builds can be resource intensive due to the technical infrastructure and staff expertise required,[24] leading to the need for balancing

standardization and customizability for these institutions.[25] As such, the further development of shareable CDS systems adhering to national standards, such as the Substitutable Medical Applications and Reusable Technologies Health IT specifications, may help these organizations find an appropriate balance.[26–28] With respect to interoperability, HL7 Fast Healthcare Interoperability Resources (FHIR) specifications are available to support standardized data exchange between computer systems.[29,30] These specifications may help address challenges related to incorporating external PGx results as structured data in the EHR. In addition, some organizations have moved to state- or region-wide health information exchange systems to promote more seamless data transfer between institutions.[31] There is also the potential to leverage additional applications—such as ancillary genomic systems and commercially available "out-of-the-box" PGx CDS tools—to offset existing EHR technical limitations and technical burden; however, the cost of these tools is likely prohibitive for resource-limited settings.[32,33]

Challenges related to availability of supporting resources included concerns about limited familiarity with PGx across disciplines, costs of PGx testing and associated CDS tools, and balancing resource allocation when faced with competing demands. More widespread, multidisciplinary educational efforts will be needed to disseminate PGx evidence and facilitate its integration into clinical practice, particularly in resource-limited settings that lack PGx domain expertise. One potential solution would be increased collaboration between resource-rich and resource-limited institutions, with PGx training being offered remotely and conveniently to rural and/or underserved areas.[34] Cost concerns emerged as a significant barrier to clinical informatics-facilitated PGx implementation, consistent with other studies across various settings.[35–37] Several participants perceived PGx CDS tool development as too resource-intensive to meet the priority threshold of the institution, similar to findings from previous research.[35,38] We also noted an important difference between the way we framed traditional informatics teams and responsibilities, and the way participants described their informatics departments. In resource-limited communities, there are a limited number of highly trained informatics personnel, with informatics responsibilities often falling on a single individual or shared among clinicians who also have patient care and administrative responsibilities. As a result, informatics resource allocation is often directed toward building and maintaining "basic critical structures" rather than considering innovative system-wide informatics projects. To address the concern of inadequate resources limiting the ability of some organizations to utilize PGx, a state-wide project in Minnesota that creates sharable databases to disseminate CDS tools and build structures for accessing PGx results provides an example solution.[39] For PGx to become a reality in resource-limited settings, a multipronged strategy will likely be necessary, potentially including shared informatics personnel among institutions, shared PGx resources and, ideally, centralized and interoperable CDS tools.[37,40,41]

Unique contextual considerations of PGx implementation in resource-limited settings included questions about the clinical utility of PGx in small populations. With greater than 99% of patients likely to carry at least one actionable PGx variant among 5 commonly tested genes[17,42] and hundreds of medications with actionable clinical PGx recommendations, PGx testing is likely to impact clinical care, even in small populations. Addressing technical and non-technical barriers will be key to realizing the potential benefits of PGx-guided care in rural and underserved populations. Participants in Montana also discussed the lack of PGx data in AIAN populations and the historical mistrust these communities have towards medical and research establishments. These concerns are in line with calls for more diverse patient representation in PGx research studies, to extend the equitable application of clinical PGx testing by identifying population-specific genetic variants and associated drug therapy recommendations.[43,44] In addition, structural inequities, social determinants of health, and data stewardship will need to be addressed to fully integrate PGx testing in rural and underserved communities.[45,46] Despite these uncertainties and concerns, participants recognized the value of PGx testing and identified characteristics including nimbleness, good internal communication, and interdepartmental cohesiveness as strengths that may favor smaller institutions for PGx implementation. For example, it was noted that rural and underserved institutions often have smaller decision-making teams, affording them the ability to quickly implement changes, demonstrating that barriers such as limited EHR agency and facilitators such as nimbleness often coexist in these settings. Paradoxically, this suggests that although PGx implementation has historically been limited to larger health systems, smaller institutions in rural and/or underserved areas could be leveraged to facilitate more streamlined PGx integration processes.

There are several limitations of our study that merit discussion. First, our participants represent a relatively narrow geographical region and some participants worked in settings serving specific groups (eg, AIAN populations). As a result, our findings may not be generalizable to other resource-limited settings. Second, selection bias because of convenience sampling is possible, as participants who had more opinions about or familiarity with PGx may have been more likely to take part in the study. In addition, participants were largely from similar clinical informatics and executive leadership networks in these small rural and underserved communities. This may influence study generalizability, as the participants may have similar views and experiences. However, while experience in clinical informatics and/or executive leadership were requirements for study participation, many participants were also clinical practitioners who held patient facing roles, thus insights from a variety of areas were obtained and thematic saturation was reached, ensuring depth in the exploration of identified themes among study participants. We also acknowledge that inclusion of 2 interviews containing a pair of interviewees may have influenced study findings, with stronger voices overshadowing other voices in pair-based interviews versus single interviews. Third, we only obtained a general description of participants' EHR instances; thus, participants' statements may be based on their particular EHR settings which may not be directly comparable to others'. We also acknowledge that factors contributing to resource limitations are often complex, and health systems that serve communities with the most need do not necessarily face the same challenges.

Conclusions

Current literature suggests patients living in geographically remote and underserved areas—often with limited access to

care—see additional benefits to optimization of medication therapy with PGx, which highlights the importance of understanding the unique barriers and facilitators in these locations.[13,47] Clinical informatics tools have the potential to benefit resource-limited settings by systematizing PGx-informed prescribing decisions, even when clinicians have limited experience with PGx.[5] We found that EHR infrastructure limitations, insufficient supporting resources, and uncertainty about the clinical utility of PGx testing in underserved populations were identified as potential barriers to PGx integration, while smaller institutional size and nimbleness were identified as potential facilitators of integration efforts. Our study findings will inform future studies to test different PGx implementation strategies that mitigate barriers and leverage institutional strengths, with the goal of promoting more widespread integration of PGx clinical informatics tools. One of the more tractable ways to accomplish this goal is to explore partnerships between resource-limited institutions interested in implementing PGx and resource-rich institutions with strong PGx domain expertise, leveraging remote education, training, and collaboration tools. Through additional implementation research and cross-institutional collaborations, strategies can be developed to advance clinical informatics-facilitated PGx implementation in resource-limited communities.

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Author contributions

Study conception and design: Christina L. Aquilante, Erica L. Woodahl; data collection: Jade Bosic-Reiniger, James L. Martin, Karen E. Brown; analysis and interpretation of results: all authors; draft manuscript preparation: Jade Bosic-Reiniger, James L. Martin, Karen E. Brown, Christina L. Aquilante, Erica L. Woodahl; critical review and revision of the manuscript: all authors.

Supplementary material

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Conflicts of interest

The authors have no competing interests to declare.

Data availability

The data underlying this article cannot be shared publicly due to participant privacy concerns. Researchers interested in data access and collaboration are encouraged to contact the corresponding authors.

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