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SUMMARY WITH CRITICAL APPRAISAL

Pharmacogenomic Testing for Medication Selection: A Rapid Qualitative Review

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Authors: Andrea Smith, Hannah Loshak

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Abbreviations

PGx	pharmacogenomics

Context and Policy Issues

Pharmacogenomics is a rapidly expanding field that studies how a patient's genetic factors can influence how they respond to medications.[1] Estimates are that medications are effective in just 30%-60% of patients because of differences in how individuals respond to medications.[2]

Pharmacogenomic (PGx) testing can also predict which patients will suffer from adverse effects. Clinicians can use PGx testing in deciding which medications to give a patient, and at what dosage. Health care systems are exploring ways to implement PGx testing to support getting more patients onto the right treatment quickly."[1] By minimizing adverse effects and tailoring effective dosing, PGx testing may reduce unnecessary medications, hospital admissions, and health care use and expenditure.[1]

Currently, PGx tests have been developed for a wide range of conditions from depression to cancer. Within Canada, a number of direct-to-consumer pharmacogenomic tests like myDNA[3] and Genecept Assay[4] are currently available. With their increasing availability and use, it is important to understand how those engaging with PGx testing understand and experience them.[5]

The purpose of this review is to examine qualitative studies and methods to describe how patients and providers view, use and experience PGx testing for medication selection, and how PGx testing fits into existing health care pathways and systems.

Research Questions

How are pharmacogenomic tests for medication selection understood and experienced by users (i.e., patients and clinicians)? How do patients and clinicians interpret and use the results of pharmacogenomic tests, and how do these tests fit into existing pathways and structures of care?

Key Findings

- This rapid qualitative evidence synthesis included 13 primary studies on the views and understanding of patients and providers on PGx testing.
- Overall, PGx testing was seen by patients and providers as being beneficial. Although sometimes more information in and of itself was desired, most patients and providers described PGx testing as helping narrow down their choices to the "best" medication to avoid adverse reactions.
- However, patients and providers alike expressed worries around how PGx testing would limit patient centered care by limiting patients' choices of medications. For patients, particularly those with mental health conditions, they worried about not having their personal experiences with medications heard by providers. Having to select less effective or more expensive medications to avoid potential adverse reactions flagged by PGx test results was also raised as a substantial concern.

- Issues around the ordering of PGx testing revealed that providers' opinions varied about whether to order tests at medication initiation or after. Providers described comfort and familiarity with PGx tests as affecting their decisions to order testing.
- The potential for genetic discrimination by insurers and employers raised concerns about privacy and confidentiality. Limited access to PGx test results was considered a key strategy for mitigating this risk.
- PGx test results can shape patient care over their life course. The potential for secondary findings from PGx testing made patients worry about how these results would affect them in the present and the future. The potential for the results of PGx tests to impact current and future family members also troubled patients and providers.
- There was limited information on the use of and views on PGx by disease or by type of testing. Findings point to the need for faster results from PGx testing in life-limiting or rapidly progressing conditions. In areas such as mental health, PGx testing was used less routinely, and generally applied where patients experience adverse reactions or limited effectiveness. Providers and patients expected PGx test results to be one of several types of information in decision making.

Methods

Literature Search Methods

A limited literature search was conducted by an information specialist on key resources including Medline and PsycINFO via OVID, and Scopus. The search strategy was comprised of both controlled vocabulary, such as the National Library of Medicine's MeSH (Medical Subject Headings), and keywords. The main search concept was pharmacogenomic testing. Search filters were applied to limit retrieval to qualitative studies or studies relevant to the perspectives and experiences of patients and providers. Where possible, retrieval was limited to the human population. The search was also limited to English language documents published between January 1, 2015 and April 20, 2020.

Selection Criteria and Methods

One reviewer screened citations and selected studies. In the first level of screening, titles and abstracts were reviewed and potentially relevant articles were retrieved and assessed for inclusion. The final selection of full-text articles was based on the inclusion criteria presented in Table 1.

Table 1: Inclusion Criteria

Setting	Clinical care settings
Population	Patients and clinicians offering or receiving pharmacogenomic testing to guide medication selection
Intervention	Pharmacogenomic testing to guide medication selection
Comparison	Existing pathways of care, medication selection processes
Evaluation	Patients' and clinicians' understandings, perceptions, experiences of pharmacogenomic testing

Exclusion Criteria

Articles were excluded if they did not meet the inclusion criteria outlined in Table 1, they were duplicate publications, or were published prior to 2015.

Critical Appraisal of Individual Studies

One reviewer assessed quality in terms of the credibility, trustworthiness (confirmability and dependability) and transferability of the included qualitative studies using the ten items from the Critical Appraisal Skills Programme (CASP) Qualitative Checklist.[6] Results of the critical appraisal were used to understand the methodological and conceptual limitations of the included publications in specific relation to this review. In particular, the critical appraisal contributed to the analysis by identifying the limits of transferability of the results of included publications to this review.

Data Analysis

Descriptive Analysis

One reviewer extracted descriptive data of study characteristics and of study participants. These are presented in tabular form in Appendices 2 and 3 and are summarize narratively.

Analytic Approach

One reviewer conducted the analysis, drawing on the principles of thematic synthesis[7] and grounded theory.[8] Data analysis was an iterative process involving a close reading of the included publications, making marginal notes, diagraming, and writing analytic memos to construct the synthetic findings. The constant comparison method was used to compare data, marginal notes and analytic memos within and across studies.

The reviewer began by reading and rereading included publications multiple times while making marginal notes on paper and memos (in Microsoft Word) to capture observations, analytic thoughts and methodological insights. During repeated close readings of the included publications, the reviewer underlined and commented on lines or sections were found to be salient. Similar to the inductive logics of line-by-line coding, this process allowed the reviewer to begin making connections throughout the empirical data presented within the body of included publications. Diagraming was used to make connections between concepts across the included publications and to the research questions. Analysis continued until themes were described and supported by data from the included publications. The reviewer reflected on the results of the critical appraisal to aid with interpretation and analysis. The objective of the analysis was to describe how PGx testing for medication selection is viewed, used, and experienced by patients and providers and how it fits into existing pathways and structures of care.

Summary of Included Literature

Quantity of Research Available

A total of 780 citations were identified in the literature search. Following the screening of titles and abstracts, 756 citations were excluded and 24 potentially relevant reports from the electronic search were retrieved for full-text review. Of these potentially relevant articles, 11 publications were excluded for various reasons, and 13 publications met the inclusion

criteria and were included in this report. Appendix 1 presents the PRISMA[9] flowchart of the study selection.

Summary of Study Characteristics

Additional details regarding the characteristics of included publications and their participants are provided in Appendices 2 and 3.

Study Methods

One included publication was described as a rapid assessment process design,[10] and one as a descriptive study.[11] The authors of the remaining 11 included publications did not report the study design.[5,12-21]

Five included publications reported using thematic analysis to analyze their data,[11-13,18,20] and two did not describe the methods they used to analyze their data.[15,17] Of the remaining six, one each was described as using grounded theory,[21] thematic development,[14] descriptive coding,[19] content analysis,[5] inductive analysis,[16] and one as using a grounded hermeneutic approach.[10]

Eight of the 13 included publications used interviews to collect data.[10-13,16,17,19,21] Four used focus groups,[5,15,18,20] and one used both interviews and focus groups.[14]

Country of Origin

Twelve of the included publications were conducted in the US[10-21] and one was conducted in Quebec, Canada.[5]

Study Population

Six of the included publications included only health care providers[10,12,13,15,19,21] and two included only patients.[18,20] Five publications included both patients and providers.[5,11,14,16,17]

Studies explored the use of PGx testing in a variety of health care settings. Three publications were conducted in primary care,[5,10,18] and three across health care services.[16,20,21] Two were conducted in pharmacies,[12,19] and two were conducted in oncology.[11,17] One each was conducted in solid organ transplant clinics,[14] cardiology,[13] in mental health clinics.[15]

Experience with PGx Testing

Of the 11 publications that included providers, three described their provider participants as being users of PGx testing[11,17,21] and four reported that the majority of their provider participants had either no or limited experience ordering or interpreting PGx tests.[10,13,14,19] It was unclear to what extent provider participants in the remaining four publications [5,12,15,16] had experience with PGx testing.

Of the seven publications that included patients, two reported that their patient participants had been offered PGx testing.[16,18] It was unclear to what extent patient participants in four studies had experience with PGx testing.[5,11,14,17,20]

Summary of Critical Appraisal

Overall, the quality of the included studies was assessed to be low to moderate. Although reporting constraints may have played a role in the amount and detail of information on methods provided, the included studies offered scant description of how they recruited their

participants, and often had low numbers of participants that were not justified, for example by a form of saturation. This led the reviewer to conclude that the recruitment strategy of was a key issue in many of the included studies. Further, the methods used to analyze study data were judged to be low in many of the included studies, as they did not reflect general principles or strategies underlying qualitative methods. Transferability of some of the included studies was limited due to a research focus on the development of clinical decision supports or PGx reports. Taken together, these issues affected the trustworthiness of the individual included studies. Additional details on the critical appraisal of the included studies are provided in Appendix 4.

Results

Perceptions and expectations of the benefits of PGx testing

Where publications explored patients' and providers' ideas on the benefits of PGx testing, most reported that their views were generally positive.[5,10,14,15,18,20,21] Some providers and patients described that they saw test results as useful in that they provided more information.[18,20,21] As one patient participant put it, "I think it's a great idea. Who wouldn't want more information about the proper medication to take."[20] (p. 23) In other words, patients and providers valued PGx tests because they provided information per se, independently from how they used or applied the information. One provider participant, described by the study authors as a "strong proponent" of ordering PGx testing, explained:

> 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.[21] (p. 6)

In this light, more information was valued in and of itself, and if PGx testing provided more information, then it was perceived as a positive endeavor.

Others articulated expectations of how they expected PGx test results to be directly useful.[5,10,15,16,18,20] For many patients and providers, the key benefit to PGx test results was the ability to select medications that avoided or reduced adverse reactions.[5,16,18,20] Various metaphors were invoked by patients and providers to describe how they saw PGx testing as getting them closer to a desired outcome of effective and safe medication use. [10,15,20] For example, one patient participant described how: "You could jump off anywhere downtown and get to a store, but you want to get off closer to the store you're going to."[20] (p. 23) Similarly, one mental health provider stated: "the analogy I use with patients is it's like moving me closer to the dart board. I'm trying to hit the bullseye and I keep missing but let's figure out something that might get you closer."[15] (p. 7)

The ability to quickly identifying the "optimal drug" was seen by patients and many providers as being able to avoid lost time, pain and suffering.[11,16,20] One patient participant described what they felt could have happened if they had undergone PGx testing: "[t]hat's right, if I would have had this [PGx testing for simvastatin], we could have saved a lot of grief and money, and you know, gone right to the top."[16] (p. 293) Similarly, one mental health patient participant said: "the idea of a genetic test – I know there's some controversy there – but that it could help limit, or define, [the best] medication, that's very appealing. I mean, I have had *bad years* on the wrong thing."[20] (p. 23) Patients very clearly expressed that they welcomed the use of PGx testing based on their personal experiences of adverse reactions.[11,16,20]

Worries about the impact of PGx testing on patient centered care

Some patients described being troubled by how the results of PGx testing might be used deterministically by providers and that it would be exclusively relied on without accounting for patient specific factors.[18,20]

> I can see this testing as a protection for doctors, kind of a cop-out. They won't have to work quite as hard to dig and find out, 'What shall I prescribe this person and how much?' Because they will have this [test result] – 'Oh, okay, we'll use that.' So it's kind of a protection for doctors.[20] (p. 24)

Patients hoped that their other health conditions and medical history would continue to be considered during medication selection: "It's not the only piece of information. If you have had [gastrointestinal] surgery, for example, and you can't absorb a medication, that's not something that's going to show up on your genetic profile."[20] (p. 24) Providers too echoed these concerns, and articulated that it was another piece of information that must be considered alongside a patient's medication and health history.[15,19]

While some of the findings pointed to the ways in which providers saw PGx as not determining but as narrowing the choices of medications, these concerns mapped onto patients' medication worries or experiences of not being taken seriously. In one study, several patient participants who had been prescribed medications for their chronic psychiatric conditions recounted incidents where they described their accounts of problems with medications were listened to.[20] In light of not being heard or of being ignored, patient participants were concerned that PGx test results would be used to further dismiss their own personal experience.

Patients raised worries that PGx test results might be used to deny people a medication that might be effective over their life course:[20] "…because of certain percentages, you might not be good on a certain drug, maybe, and they make this whole list of all these good drugs you can't have. So they would refuse certain medicines to you, your whole life."[20] (p. 24) This worry was particularly relevant for those with lifelong chronic conditions, highlighting the way PGx test results may shape patient care over their life course. Similarly, patients articulated that they might want the most effective drug, even if it means enduring side effects:[18] "if I know it could be really effective… even if there might be some side effects then I might be more willing to push through, knowing the benefits."[18] (p. 8)

Some providers reported that using PGx test results in decision making required them to balance the benefits of potentially more efficacious drugs with concerns about higher out-of-pocket medication costs.[21] As one mental health provider revealed: "half the time I think of something and they are like that's not going to be covered so I can't use that.[15](p. 6) While these concerns exist more broadly in medication selection, PGx test results contributed to patients and providers facing these scenarios.

Ordering PGx testing

Primary care providers in one Canadian study (Quebec) emphasized that in order to be useful in decision making, PGx testing had to be rapid.[5] The importance of rapidity was especially true of cancer, where timely testing in the face of rapidly advancing disease was desired by providers.[11] One oncology provider shared their experience: "We've had two patients whose disease was at a galloping pace and unfortunately they died from their disease before we could get the results of the genetic testing… where it did reveal that they had a mutation."[11] (p. 4)

Some felt PGx testing should be routine, while others thought that it would be best used with patients who were experiencing difficulties (i.e., adverse reactions, lack of efficacy) with their medications. Some providers describe "saving it" for poor responders (mental health providers,[15] solid organ transplant clinicians[14]). One mental health provider described: "I save it for people who are either getting really bizarre side effects from multiple classes or multiple treatment failures in multiple classes [of medications]."[15] (p. 7) "I think PGx testing can be useful in patients [who had solid organ transplant] in whom it's difficult to establish adequate trough level."[14](p. 1297)

The ease of access (e.g., cost, availability, interpretability) to PGx testing appeared to have influenced providers' views on when and on who they would use testing. For providers, interpretability of PGx test results affected when they would order medications: "I try very hard to avoid ordering test that I don't know how to interpret for the patient, or that I can't refer them to something regarding interpretations."[21](p 9) Other providers described how they would only use those tests that specifically related to their patient and the treatment plan.[22]

Providers felt that those who ordered the medication should be responsible for communicating the PGx test results and modifying treatment. This related to how comfortable clinicians were with interpreting and using PGx testing. A primary care provider described how:

> Simvastatin is bread and butter of primary care. I feel like we deal with it more than any other specialty, so for this drug I think primary care should take charge… but it's some drug that we don't prescribe that often, then definitely the [clinician] that prescribes it the most.'[16](p. 293)

Similarly, a primary care provider articulated "I would not do this [PGx testing] for sure, I would not have the time, I wouldn't be able… I would talk to the pharmacist about it. If you [pharmacists] know there is something wrong with one cytochrome, you could warn me if I prescribe something related to that."[5](p. 592)

Clinical use of PGx testing mapped onto worries about cost, which was often stated by providers as their greatest implementation concern.[5,10,11,14] I In the US this played out in terms of who was left paying for PGx testing (e.g., laboratory, health insurer, or patient),[17] similar concerns echoed in the Canadian context. As one pharmacist stated: "Who will pay for this? The government? Will it be covered? Will taxpayers agree with that?"[5](p. 592) In Canada additional worries were raised about the affordability of PGx for the public health care system.[5]

Secondary findings and implications of PGx testing for family members

The potential for secondary findings from PGx testing, for example, learning of an increased risk of disease, was raised by patients and providers.[13,14,16,18] This lurking possibility was expressed by one patient participant: "[t]here must be other information attached to whatever they found that made me genetically different from other people."[18] (p. 6) Patients worried about how these secondary findings would affect them in the present and the future. Providers did not agree on whether secondary findings should always be communicated to their patients, and tended to be more hesitant to return results where there was no action that patients could take to reduce their disease risk.[14,16] Providers cited the potential need to consider referring patients to genetic counselling to support the interpretation and communication of secondary findings from PGx test results.[13]

The impact of results of PGx tests on family members also troubled patients and providers.[5,14,20] One provider articulated their view that the patient's family was also implicated with PGx testing: "[b]ecause if he [the patient] receives a genetic test positive for slow metabolizer, then maybe some family members are slow metabolizers as well."[5] (p. 592) This issue of secondary findings and the potential impact of PGx testing on patients' family ties into ethical and social dimensions of using genetic information for medication selection, including informed consent, and privacy and confidentiality.

Troubled by the potential for genetic discrimination

Patients and providers expressed worries around who would have access to patients' genetic information and the potential for it to be accessed and misused by unauthorized persons.[5,14,18,20] These concerns around confidentiality and privacy were often raised in reference to fears of discrimination by insurers (in terms of eligibility and coverage).[5,14,18,20] In relation to these worries, patients articulated a range of views of whether this information should be included in the medical record and be available to be accessed by others within the health care system.[5,16,20] Limiting access within medical records, particularly electronic ones, appeared to be the primary mechanism by which patients and providers thought privacy and confidentially could be mitigated.

Differences in type of PGx tests

Patient participants in one study were probed on their views on single-indication testing, PGx panels, and whole genome sequencing.[20] Overall, patients saw whole genome sequence as being the most risky as it would give them information about their having a potentially increased risk for conditions for which there was nothing they could do.[20] Additionally, panel tests were seen as particularly challenging as providers who viewed that they did not have the expertise to order them.[17]

Limitations

This review has several notable limitations that stem from the available set of literature. Within the studies, there was limited information on the use of PGx testing by disease area (e.g., cancer, mental health). This is significant for two reasons. First, the review findings point to the length of time of treatment and for decision making as affecting how PGx testing is experienced. Second, different disease areas have different societal dimensions, with mental health often viewed as having the potential for stigma, which may affect the implications of using genetic information such as PGx testing.

Additionally, there was limited information available on differences between types of testing (e.g., indication-specific testing, PGx panels, whole genome sequencing). The findings of this review suggest that this is likely an important consideration due to differences in the type and amount of information tests can provide and the extent to which issues around interpretability of results and secondary findings may arise.

Twelve of the 13 included studies were conducted in the US. The role of private for-profit health care and the absence of a single payer system in the US means that how PGx testing is experienced and used in Canada is likely to differ from the US in important ways that this review was not able to identify.

Conclusions and Implications for Decision or Policy Making

This rapid qualitative evidence synthesis used thematic analysis to analyze the findings of 13 included publications. The findings of this review echo a recent meta-data analysis by Veilleux et al. that explored patient and provider preferences in understanding PGx testing.[23] Like the current review, the authors found that patients saw the benefits of PGx testing as being able to get the right dose of the right drug to reduce adverse reactions and ineffective medications.[23] Worries around how PGx test results might result in patients having to trade off fewer adverse reactions for less effective medications, the high cost of testing and who bears it, and the potential for discrimination based on PGx test results by insurers were prominent.

Moreover, the current review builds on patients' worries about the potential for discrimination based on PGx test results and draws out concerns relating to privacy and confidentiality within health care systems. The findings describe how the potential for secondary findings from PGx test results (e.g., information on an increased genetic risk of a particular disease) can affect patients and their families in unanticipated ways. Because of the genetic nature of PGx testing, results carry with the patient over time and extend to their current and future family, and ethical issues figure prominently in the implementation and use of PGx testing. Of note, none of the studies raised issues around informed consent. A recent systematic review concluded that informed consent practices for PGx testing vary widely, and as a result, there is a need for a standardized set of principles of information that should be part of the consent process.[24]

Pharmacogenomics is a rapidly changing area and how it is used for medication selection is likely to change in the future. Changes including types of tests (e.g., whole genome sequencing, gene expression) and the types of medications for which they are developed mean that PGx testing is an evolving area. Potentially significant changes may occur in terms of the placement of PGx testing (i.e., at diagnosis and medication initiation versus when treatment is not effective or resulting in adverse effects) and the integration of PGx testing into clinical decision aids and electronic health records. The findings of this review suggest that attending to the specific clinical area is likely to impact how patients and providers interact with PGx testing, pointing to the need to attend to those differences. Lastly, PGx testing is likely to continue to require policies and resources to support clinicians in ordering, interpreting and using PGx testing. Clarity around who can order the test and responsibility for medication adjustment, and who can access PGx test information in the future will help with the implementation of PGx testing in health care systems.

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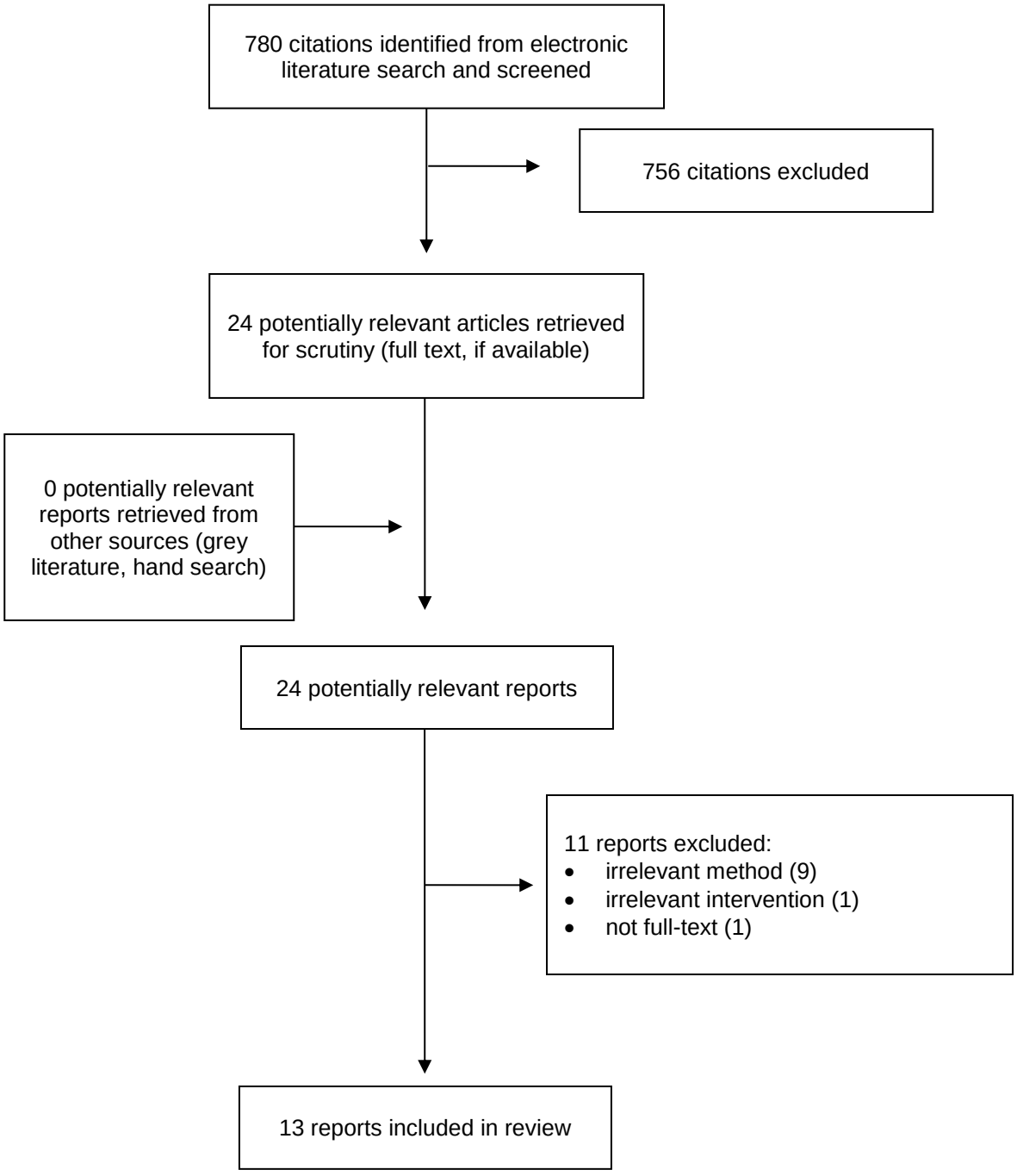
Appendix 1: Selection of Included Studies



Appendix 2: Characteristics of Included Publications

Table 2: Characteristics of Included Publications

Study citation, country	Study objectives	Study design and method of data analysis	Setting	Inclusion criteria	Data collection strategy
Berenbrok 2019, US[12]	To describe the educational needs of community pharmacists to support the implementation of clinical PGx services at community pharmacies	NS; thematic analysis	Community pharmacies	Pharmacists working at community pharmacies	Semi-structured interviews
Deininger 2019, US[14]	To assess stakeholder perspectives on the clinical utility of PGx for solid organ transplant	NS; described as theme development	University hospital heart, kidney and liver transplant clinics	Patients who had undergone a kidney, liver or heart transplant within the past 10 years Physicians, pharmacists and nurse practitioners practicing at a university transplant clinic	Focus groups and interviews with transplant patients Interviews with providers
Deininger 2019, US[13]	To evaluate factors influencing cardiologist' perspectives about PGx testing in clinical practice	NS; thematic analysis	University hospital	Cardiologists working at a university hospital	Semi-structured interviews
Frigon 2019, Canada[5]	To understand the perceptions of primary care providers, pharmacists, and patients on implementing PGx in clinical practice	NS; content analysis, including discourse analysis on concrete examples	Primary health care including community pharmacies	Primary health providers and community pharmacists and patients receiving primary care	Focus groups
Goodspeed 2019, US[15]	To explore the views of mental health clinicians on what features they hope to see in a clinical decision support incorporating PGx for mental health, how they use PGx information, and potential negative and unintended consequences from using a mental health specific clinical	NS; NS	Mental health providers	Providers who volunteered after monthly staff meetings (location NS)	Focus groups

Study citation, country	Study objectives	Study design and method of data analysis	Setting	Inclusion criteria	Data collection strategy
	decision support with PGx information				
Jones 2018, US[16]	To understand the information patients and clinicians would want from a PGx report	NS; described as an inductive analysis	A research initiative called MyCode combining genetic information with EHR in an integrated rural health delivery system	Adults who were patients in the integrated health system and participating in the MyCode research initiative Primary care providers, specialists and pharmacists working in the integrated rural health delivery system and who were engaged with the MyCode research initiative	Semi-structured interviews
Wu 2018, US[17]*	To describe the process of ordering and paying PGx tests in the context of cancer care	NS; NS	Oncology care using PGx testing and laboratories providing PGx testing	Patients who were prescribed medications whose ordering could have been affected by PGx testing Providers who prescribed medications whose ordering could have been affected by PGx testing Laboratory employees who had experience with PGx testing	Semi-structured interviews
Chase 2017, US[10]	To examine the barriers to using clinical decision supports in primary care	Described as a Rapid Assessment Process; described as a grounded hermeneutic approach	Five primary care sites using electronic health care records	Physicians, osteopaths, nurse practitioners, and physicians' assistants working at five primary care sites across the US	Semi-structured interviews
Lee 2017, US[18]	To understand the patients' views on PGx testing in a setting with an institutional implementation project	NS; thematic analysis	Primary care and specialist outpatient care with an PGx implementation study	Patients involved in a PGx implementation study who had either received PGx testing or who had received non-PGx standard of care	Focus groups

Study citation, country	Study objectives	Study design and method of data analysis	Setting	Inclusion criteria	Data collection strategy
Wu 2017, US[11]*	To explore providers' and patients' experiences and views on access to PGx testing and strategies used for gaining access	Descriptive study; thematic analysis	Oncology care in community and academic settings	Patients who were prescribed medications whose ordering could have been affected by PGx testing Providers who prescribed medications whose ordering could have been affected by PGx testing	Semi-structured interviews
Romagnoli 2016, US[19]	To understand pharmacists' information needs and resource requirements for PGx-based decision making	NS; described as descriptive coding	Pharmacies in a range of settings (i.e., tertiary care, community practice, private nursing homes)	Pharmacists identified through professional connections of the authors	Interviews
Trinidad 2015, US[20]	To explore patients' beliefs and attitudes about PGx to inform implementation and policy	NS; thematic analysis using constant comparison	Patients enrolled in a large HMO in the Pacific Northwest	Enrolled patients who had been prescribed antidepressant or carbamazepine and a cohort of enrolled patients who did not have any chronic conditions	Focus groups
Unertl 2015, US[21]	To describe the knowledge and attitudes of clinicians in a large PGx implementation program	NS: described as a grounded theory approach	PGx implementation program at a university medical centre	Physicians and nurse practitioners working in primary care and cardiology at a university medical centre at the time of a PGx implementation program	Semi-structured interviews

PGx = pharmacogenomics; NS = not stated; HMO = health maintenance organization; EHR = electronic health record

*Wu, 2017 and Wu 2018 use the same sample of patients and providers but report on different data and findings

Appendix 3: Characteristics of Study Participants

Table 3: Characteristics of Study Participants

Study citation, country	Types and number of study participants	Sex (% female)	Age (range or mean)	Experience with pharmacogenomics	Type of disease or clinical area
Berenbrok 2019, US12	11 pharmacists	NS	NS	Unclear – some participants described learning through clinical practice	Community pharmacy
Deininger 2019, US14	36 patients 24 providers	27.8 58.3	Mean of 55 year Mean of 44 year	Patients did not report having experience with PGx 83% of providers reported having either no experience or as being novices	Solid organ transplant
Frigon 2019, Canada5	23 physicians 11 pharmacists 30 patients	74% 82% 70%	NS NS 19-78 years	NS NS NS	Primary care and community pharmacy
Goodspeed 2019, US[15]	16 mental health providers (mix of nurse practitioners and physicians, n=NS)	NS	50% were between 46-66 years old	NS	Mental health care
Jones 2018, US[16]	10 clinicians 10 patients	50% 62%	NS 71% were between 55-64 years old	Patients reported not having had PGx 2 clinicians had previously ordered PGx testing	General health care
Wu 2018, US[17]*	10 oncology providers 16 oncology patients 8 laboratory employees	NS NS NS	NS NS NS	Providers were users of PGx testing in their clinical practice Unclear if patients received PGx testing Laboratory employees were experienced with the ordering and payment of PGx testing	Oncology

Study citation, country	Types and number of study participants	Sex (% female)	Age (range or mean)	Experience with pharmacogenomics	Type of disease or clinical area
Chase 2017, US[10]	NS providers	NS	NS	Most providers were non-users of PGx testing	Primary health care
Lee 2017, US[18]	9 patients had participated in a PGx testing study and had PGx testing 13 patients who had received standard non-PGx care	50%	Mean of 59.5 years	3 patients recalled having PGx testing for medication selection	Primary care and subspecialist outpatient care
Wu 2017, US[11]*	10 oncologists and oncology nurse practitioners 16 oncology patients	70% 56%	30-59 years 30-60+ years	Providers were users of PGx testing in their clinical practice Unclear if patients received PGx testing	Oncology
Romagnoli 2016, US[19]	14 pharmacists	71%	NS	None of the providers reported using PGx testing or having patients who had received PGx testing in the past year	Pharmacy
Trinidad 2015, US20	27 patients prescribed antidepressants 17 patients prescribed carbamazepine 17 patients without chronic conditions	64	21-78 years	NS	Treatment of chronic psychiatric conditions
Unertl 2015, US21	15 physicians and nurse practitioners	NS	NS	Clinicians practicing at a medical centre with a PGx implementation program	Primary care and cardiology

PGx = pharmacogenomics; NS = not stated

*Wu, 2017 and Wu 2018 use the same sample of patients and providers but report on different data and findings

Appendix 4: Critical Appraisal of Included Studies

Table 5: Critical Appraisal of Included Publications Using CASP Qualitative Checklist[6]

First Author, Year	Clear statement of the aims of the research?	Qualitative methodology appropriate?	Research design appropriate to address the aims of the research?	Recruitment strategy appropriate to the aims of the research?	Data collected in a way that addressed the research issue?	Relationship between researcher and participants been adequately considered?	Ethical issues been taken into consider-ation?	Data analysis sufficiently rigorous?	Clear statement of findings?	Relevant to the current review?
Berenbrok 2019[12]	+	+	+	-	+	+/-	+	+	+	-
Deininger 2019[13]	+	+	+	-	-	+/-	+	+	+	+
Deininger 2019[14]	+	+	+	-	+	+/-	+	-	+	+
Frigon 2019[5]	+	+	+	+	-	+	+	+	+	+
Goodspeed 2019[15]	+	+	+	-	-	+/-	+	-	+	-
Jones 2018[16]	+	+	-	-	-	+/-	+	-	-	+
Wu 2018[17]	+	+	-	+	+	+/-	+	-	+	-
Chase 2017[10]	+	-	-	-	-	+/-	+/-	-	-	-
Lee 2017[18]	+	+	+	-	+	+/-	+/-	-	+	+
Wu 2017[11]	+	+	-	+	+	+/-	+/-	-	+	+
Romagnoli 2016[19]	+	+	-	-	+	-	-	-	-	-

First Author, Year	Clear statement of the aims of the research?	Qualitative methodology appropriate?	Research design appropriate to address the aims of the research?	Recruitment strategy appropriate to the aims of the research?	Data collected in a way that addressed the research issue?	Relationship between researcher and participants been adequately considered?	Ethical issues been taken into consider-ation?	Data analysis sufficiently rigorous?	Clear statement of findings?	Relevant to the current review?
Trinidad 2015[20]	+	+	+	+	+	+	+	+	+	+
Unertl 2015[21]	+	+	+	+	+	+/-	+	-	+	+

+ = yes; - = no; +/- = unclear based on information reported