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SYSTEMATIC REVIEW

Approaches to assessing the provider experience with clinical pharmacogenomic information: a scoping review

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PURPOSE: Barriers to the implementation of pharmacogenomics in clinical practice have been thoroughly discussed over the past decade.

METHODS: The objective of this scoping review was to characterize the peer-reviewed literature surrounding the experiences and actions of prescribers, pharmacists, or genetic counselors when using pharmacogenomic information in real-world or hypothetical research settings.

RESULTS: A total of 33 studies were included in the scoping review. The majority of studies were conducted in the United States (70%), used quantitative or mixed methods (79%) with physician or pharmacist respondents (100%). The qualitative content analysis revealed five major methodological approaches: hypothetical clinical case scenarios, real-world studies evaluating prescriber response to recommendations or alerts, cross-sectional quantitative surveys, cross-sectional qualitative surveys/interviews, and a quasi-experimental real-world study.

CONCLUSION: The findings of this scoping review can guide further research on the factors needed to successfully integrate pharmacogenomics into clinical care.

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INTRODUCTION

Barriers to the expanded use of pharmacogenomics in clinical practice have been thoroughly discussed over the past decade.[1–4] While many of these barriers have been addressed, obstacles persist that preclude the successful application of pharmacogenomics into routine clinical practice. These obstacles include an underdeveloped clinical decision support (CDS) infrastructure, lack of third-party payer coverage policies and reimbursement, and limited clinician and patient understanding.[1,5–9] Several of these barriers were highlighted in recent work from the Implementing Genomics into Practice (IGNITE) consortium, which ranked 28 constructs for their importance to the future sustainability of genomic medicine.[10] Interestingly, three of the top five ranked constructs (1, 2, and 4) focused on provider needs and included: (1) expanded genomic education, (2) making CDS tools available, and (3) integrating genomic information into clinical workflow.

Numerous descriptive or cross-sectional studies assessing the attitudes of providers toward pharmacogenomics have been published. Descriptive papers often come from the implementation initiatives established at academic hospitals.[11–14] Cross-sectional studies focus on the attitudes, awareness, and concerns of physicians, community pharmacists, cardiologists, and psychiatrists. The findings of these studies demonstrate that the majority of physicians and community pharmacists, as well as specialists such as cardiologists and psychiatrists, have positive views of pharmacogenomics, yet feel unprepared to deliver it in their practices.[6,15–18] While these papers clarify the nuances and considerations necessary to establish pharmacogenomics in practice, they typically do not include a measurement or assessment of the interventions' impact on those delivering them to patients. Real-world assessments and intervention-based studies are crucial to provide actionable insights enabling clinical pharmacogenomics use for patient care.

With these considerations, the overall research goal of this scoping review is to assess how the prospective or retrospective experiences and actions of prescribers, pharmacists, or genetic counselors have been measured when using pharmacogenomic information in either real-world practice or a hypothetical research setting. This is an important gap in the literature to address as many studies to date have focused more on implementation strategies rather than collecting data on the decision making or experiences of the providers who will be responsible for acting on this information in clinical care.

MATERIALS AND METHODS

Study design

A scoping review is a synthesis of the existing literature on a topic in terms of the volume, nature, and characteristics of the primary research.[19] A scoping review was selected to assess the extent, range, and nature of evidence to summarize heterogeneous methods or disciplines, without pursuing a quality assessment of the literature.[20] The steps to conduct a scoping review are as follows: (1) clarify and link the review purpose and research question, (2) balance feasibility with breadth and comprehensiveness of the review process, (3) use an iterative team approach when selecting studies, (4) extract data, and (5) incorporate a quantitative summary and qualitative thematic analysis of results and state implications of study findings.[21] To increase the methodological transparency and uptake of these findings, the recent checklist extension by the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) published for scoping reviews (PRISMA-ScR) was used throughout this study.[22]

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Eligibility criteria

To be included in the scoping review, studies had to include an outcome that measured the experiences or actions of a physician or advanced-practice provider, pharmacist, or genetic counselor when engaged in actual or hypothetical pharmacogenomic testing scenarios. At least 50% of the data must have come from responses or decisions made by physicians (MD/DO), advanced-practice providers (nurse practitioners or physician assistants), pharmacists (RPh/PharmD), or genetic counselors (CGC). The scoping review excluded studies that were purely descriptive, anecdotal, or opinion in nature. To achieve our stated research goal, these exclusions focused our findings to studies that collected and reported provider decision making or experience data when acting on pharmacogenomic information. This exclusion approach eliminated cross-sectional provider studies focused only on attitudes and awareness, not actual use of pharmacogenomics, as well as studies that only describe the strategies and learnings of clinical pharmacogenomic implementation. Studies not primarily focused on pharmacogenomics, published before the year 2000, or published in a language other than English were also excluded.

Information sources and search

Potentially relevant papers were searched using the MEDLINE® and Embase® bibliographic databases. The search was executed in December 2020 and included studies published through the end of June 2020. Search strategies were developed by the lead author and refined through discussion with other authors. Two individual searches were performed in MEDLINE® and Embase® combining various alternative search terms for "pharmacogenetics" and "health personnel," "genetic counselors," "pharmacists," "physicians," "education," "surveys," or "questionnaire." "Nurse practitioner" and "physician assistant" were not included as explicit search terms, but appropriate studies that utilized these individuals as prescribers were included. The full search strategy is outlined in Supplement Table 1.

Selection of sources of evidence

Prior to beginning the selections, a screening form was developed and agreed upon by the authors. Two authors (N.J.K. and T.J.D.) independently and iteratively reviewed titles and abstracts, then full papers, making decisions to include or exclude at each stage. At the completion of each stage, the authors discussed their individual assessments and came to consensus on study inclusion.

Data charting and data elements

The data charting process used the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) checklist to determine which variables to extract from the included studies. Final variables were extracted by two authors (N.J.K. and T.J.D.) and included author and publication year, study location, research aims, study design and methods, population and setting, outcome (s) of interest, and major findings.

Synthesis of results

Finally, two authors (N.J.K. and M.R.) performed an inductive content analysis of the study designs and methods extracted during data charting to structure the results. This inductive analysis was first performed independently, with these authors

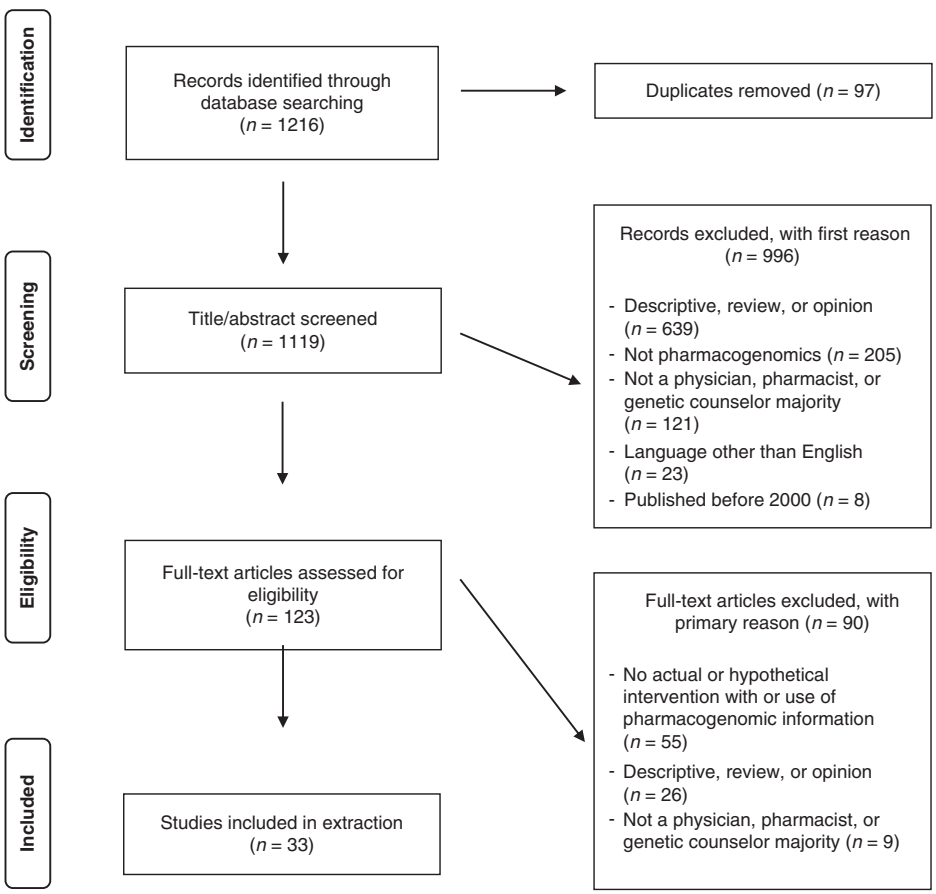

Fig. 1 After removing duplicates, 1,119 articles were screened against the eligibility criteria, the full text of 123 articles were reviewed, and ultimately 33 articles were included in the scoping review.

coming together to discuss initial findings and codes. These codes were then applied to each included study by the lead author. The authors met once more to ensure coding consistency before finalizing the results.

RESULTS

Fig. 1 provides an overview of the number of studies screened, determined eligible (with reasons for exclusion at each stage), and included in the review findings.

Characteristics of sources of evidence

A total of 592 unique studies were identified from MEDLINE®. The search of Embase® produced 527 unique studies that were not captured in the MEDLINE® search. A total of 33 studies underwent complete data extraction (Table 1). All studies, except for three, were conducted in the United States and Europe.[23–25] Among the 33 studies, 24 contained only physician participants, 7 involved both physicians and pharmacists, and 2 only included pharmacists.[26,27] None of the studies included respondents who identified as genetic counselors.

Table 1. General characteristics of included studies ($n = 33$).

Characteristics	*n*	%
Region of origin		
United States	21	64
Netherlands	3	9
Canada	2	6
United Kingdom	1	3
Italy	1	3
Norway	1	3
Northern Ireland	1	3
New Zealand	1	3
Multiple countries	2	6
Years published		
2019–2020	8	24
2015–2018	17	52
2010–2014	7	21
2005–2009	1	3
2000–2004	0	0
Study participants		
Physicians	24	73
Physicians and pharmacists	7	21
Pharmacists	2	6
Methods used		
Quantitative	20	61
Qualitative	7	21
Mixed methods	6	18
Study design		
Hypothetical clinical case scenarios	10	30
Real-world studies on prescribing/testing decisions	10	30
Cross-sectional qualitative interviews	6	18
Cross-sectional quantitative surveys	6	18
Quasi-experimental	1	4

Results of individual sources of evidence

Table 2 outlines the extracted data for each included study. The qualitative content analysis revealed five major methodological approaches: hypothetical clinical case scenarios, real-world studies evaluating prescriber response to recommendations or alerts, cross-sectional quantitative surveys, cross-sectional qualitative surveys/interviews, and a quasi-experimental real-world study. The following sections define each methodological approach, identify specific study aims, and briefly describe major study findings.

Hypothetical clinical case scenarios

Studies in this section engaged with a provider in an exercise that mimics some form of real-world clinical decision making. Of the ten studies included in this section, three themes were identified: information seeking, prescribing tasks, and other. The first of these themes, information seeking, includes three studies directly measuring the time to complete certain tasks involving pharmacogenomic information use.[28–30] The specific tasks were (1) modifying the appropriate dosage for a hypothetical patient based on pharmacogenomic alert messages triggered by the medication ordered and patient-specific laboratory, (2) searching online resources for pharmacogenomic information (UpToDate® and PharmGKB) to guide hypothetical clinical decisions, and (3) identifying correct dosages using algorithm-produced interpretations of genetic tests during organ transplantation immunosuppressive treatment. These studies cut across physician specialties, from internists to cardiologists to oncologists, and included multiple disease states and/or pharmacogenes. The sample size was small for these studies, ranging from 6 to 10 physicians. The variability between the findings of each of the included studies was high given the inherent differences among clinical decision support systems (CDSS) and study tasks. One study used two scenarios to gauge improvements task completion times.[30] Comparisons across studies were difficult to establish due to variability in information-seeking tasks.

The second theme, prescribing tasks, included three studies where the prescribers were presented with hypothetical scenarios and evaluated on the actions they might take with pharmacogenomic information.[31–33] All studies in this section used quantitative methods. The sample size was larger for this theme compared to information seeking, ranging from 15 to over 200 physicians. The measured variables included the percentages of physicians who would change a decision or initial orders based on new pharmacogenomic information, response to or dismissal of CDSS messages, as well as prescriber-reported evaluations of whether the alerts or information were helpful to decision making. Overall, these providers agreed that the alerts were helpful and there was high utilization of the CDS resources.

The third theme, other, included four studies among three unique approaches.[34–37] The first two focused on assessments of PGx-CDS usability, using both quantitative and qualitative assessments.[34,35] The third evaluated psychiatrists' use of irrelevant genomic information (average symptom change associated with a genetic biomarker when pre- and post-symptom scores were already given).[36] Finally, a survey examined the intercountry differences as drivers of oncologist test ordering. Similar to the previous section, providers involved in the studies cut across specialties and quantitative outcomes were reported. However, the sample in one study included both physicians and pharmacists.[34] Attitudes toward the CDSS (measured as the usability, trustworthiness, usefulness, and workflow integration subscale totals) were moderately positive (mean score: 42.3 of 64), younger psychiatrists were significantly more likely to use irrelevant

Table 2. Peer-reviewed summary of studies that met inclusion criteria for scoping review.

Author and publication year	Study location	Research aims	Study design and methods	Population and setting	Outcome(s) of interest	Major findings
Bain et al., 2018[38]	United States	To determine the feasibility of implementing a pharmacist led PGx service for the Program of All-Inclusive Care for the Elderly (PACE).	Prospective evaluation of PACE implementation processes including reviewing policies and procedures, observations documented pharmacists, genetic variants prevalence, and drug–gene interactions.	2 senior pharmacists and a pharmacy resident led PGx consultations in a centralized pharmacy serving 15–20% of PACE participants in 21 states.	Rates of prescribers' acceptances of the PGx consultation recommendations.	89% of recommendations were accepted by the prescriber. 100% of recommendations were accepted in the following: continue drug, drug dose adjustment, and consider drug regimen change. 38.5% of recommendations were accepted for implementing drug dose adjustment or drug regimen change.
Bank et al., 2019[45]	Netherlands	To investigate whether genotype-guided dosing in primary care using a PGx test panel in the Netherlands is feasible, and to investigate the frequency of a actionable genotypes in a panel of genes and corresponding gene–drug interactions, if applicable.	A prospective multicenter observational study of the routine clinical practice to test the feasibility of pharmacist-initiated pharmacogenomics testing in primary care. Retrospective analysis of defined daily dosages, pharmacy visits, and drug related interventions were collected.	Eligible patients to be genotyped was determined by previous medication use and pharmacist evaluation of suitability for inclusion. Physicians and pharmacists (jointly) were responsible for making medication decisions using the patient genotypes.	Adherence to DPWG guidelines based on patient genotypes.	62 of the 200 patients (31%) genotyped had a gene–drug interaction that required action by a physician–pharmacist team. For 52 (89%) of these patients, the health care providers adhered to DPWG guidelines. In 5 cases, the gene–drug pair *CYP2D6* and venlafaxine was present while treatment continued, 1 case the dose-maximum for escitalopram was surpassed, and 1 case in which the physician was motivated to continue based on previous toleration.
Blagec et al., 2016[34]	Austria and United States	To evaluate the perception and usability of a web- and mobile-enabled CDSS (Medication Safety Code) for pharmacogenetics-guided drug therapy among physicians and pharmacists.	Quantitative assessment of physician and pharmacist attitudes toward MSCs using two hypothetical use cases. 25 follow-up questions measured usability, trustworthiness, usefulness, and workflow integration.	39 physicians and pharmacists, with an overwhelming majority from Austria or Germany (~90%).	Scores on the usability, trustworthiness, usefulness, and workflow integration subscales and total scale score.	Average usability score was 10.6 of 16, 10.5 trustworthiness, 11.4 usefulness, and 9.9 workflow integration. Average score was 42.3 of 64. No difference between physicians and pharmacists, or respondents aware or unaware of genome guided prescribing and CDSS.
Borden et al., 2019[51]	United States	To study provider attitudes of and perceived barriers to the clinical use of pharmacogenomics before and during participation in an implementation program.	Between 2012 and 2017, providers were recruited. These providers completed a semistructured interview about PGx and received training on and access to a CDS with patient-specific PGx reports. Providers completed surveys before and during study participation.	Providers were recruited from the 1200 Patients Project at the University of Chicago. This includes 7 primary care, 3 oncology, 2 cardiology, 2 gastroenterology, 1 executive health, hepatology, nephrology, and pulmonology. Median years in practice was 17.5.	Provider adoption of PGx information. Provider-reported barriers to PGx results accession. Provider-reported utility of the Genomic Prescribing System.	Patient-specific results were accessed at 64% of visits, and medication changes were influenced by PGx information 42% of the time. Providers reported they had enough time to evaluate the information and the results were easily understood. If providers did not log into the GPS, nearly 40% reported this was due to a full schedule, and just over 25% said that they did not expect any new patient information.

Table 2 continued

Author and publication year	Study location	Research aims	Study design and methods	Population and setting	Outcome(s) of interest	Major findings
Devine et al., 2014[28]	United States	To evaluate an early prototype, commercial CPOE system with PGx-CDS alerts in a simulated environment, identify potential system user interface improvements, and understand usefulness of PGx knowledge embedded in an EHR.	Convergent, parallel, mixed methods design using five hypothetical clinical case scenarios featuring medication order triggered PGx alert messages. Audio–video recordings coded positive and negative evaluation heuristics.	7 cardiology fellows and 3 oncology fellows at the University of Washington.	Time to completion of prescribing task. Themes and improvements identified using the heuristic evaluation technique.	Physicians spent 3.6 to 4.9 minutes per prescribing task. 9 themes emerged from the heuristic evaluation. 5 included improvement suggestions for the CPOE user interface, 2 suggested including PGx information in alerts, and 3 emphasized relevant guidelines and dosing recommendations needs.
Dressler et al., 2019[53]	United States	To assess feasibility and perspectives of PGx in rural primary care physician (PCP) practices when they are trained to interpret/ apply results and testing cost are covered.	PCPs agreed to two, 1-hour continuing medical education sessions. PCPs were also given the option of having their own test done. Pre-education module and posteducation module surveys were conducted, in addition to an interim survey. Phone interviews were also conducted at the end.	94 PCP physicians were invited to participate in the study conducted between September 2016 and October 2017. Participants had to be located within one hour of the Mission Hospital in western North Carolina.	Physician responses to the poststudy survey and interviews, interim survey.	Postsurvey study results demonstrated improved awareness, more comfort with using PGx information, a better understanding of relevance and the pharmacist's ability to summarize the patient results. Added clinical value came through a better patient–doctor relationship and better medication management. PGx as a practices competitive edge was mixed, as well as the response to preemptive vs. reactive testing. Barriers included better guidance on who to test, use of the info over time, EHR support, and pricing.
Dunbar et al., 2012[23]	New Zealand	To assess clinician experiences ordering an AmpliChip® *CYP450* test kit, receiving results, utilization of the results, and perceived advantages and disadvantage.	Clinician was directed to prescribe "as usual," then complete an order form for the patient to get the testing done. Results were fed back to the clinicians directly. Ordering clinicians then completed qualitative interviews.	Across 3 District Health Boards within New Zealand, 42 clinicians ordered tests and 33 were interviewed.	PGx test results utilization and perceived advantages and disadvantages.	Test results confirm clinical decisions, provides reassurance, provides additional patient response information, influences dosing, and improves doctor–patient relationship. Nonuse reasons were result delays, inappropriate setting, and unnecessary information. Advantages were dose determination, adverse effect reduction, and external application. Drawbacks were clinical judgment interference, cost, and practicalities.
Ferreri et al., 2014[39]	United States	To determine the feasibility of implementing a PGx service in a community pharmacy.	Prospective evaluation of the program's feasibility following a retrospective data abstraction of prescription fills for clopidogrel.	A single pharmacy within a regional chain known for providing clinical services.	Rate of prescriber acceptance to a clinical pharmacist practitioner (CPP) recommendation across five different genotypes.	Majority of CPP recommendations were approved by prescriber. 100% approval across genotypes *1/*1 (EM), *17/*17 (UM), and *2/*17 (IM). 50% approval in genotype

Table 2 continued

Author and publication year	Study location	Research aims	Study design and methods	Population and setting	Outcome(s) of interest	Major findings
						**1/*2* (IM), other 50% started aspirin EC 325 mg daily. 75% approval in genotype **1/*17* (UM). Clopidogrel was discontinued in the other patient.
Goodspeed et al., 2019[54]	United States	To evaluate input from mental health clinicians on EHR-integrated CDS, PGx, and the reaction of psychiatric clinicians to a CDS prototype.	3 focus groups: one to determine specific needs for clinicians in mental health and two to analyze interactions with a CDS prototype.	16 nurse practitioners and physicians employed in a mental health care setting.	Desired CDS features, focusing on pharmacogenomics and potential negative or unintended consequences of CDS integration.	3 themes emerged: desired clinical decision support features of mental health clinicians, pharmacogenomics use in practice, and unintended and negative consequences of clinical decision support integration at the point of care.
Haga et al., 2017[52]	United States	To investigate provider utilization of pharmacist support in the delivery of PGx testing in a primary care setting.	2 primary care practices, one with an in-clinic pharmacist and one with an on-call support pharmacist. A survey assessed PGx testing attitude, knowledge, and experience before and after a PGx seminar.	Twelve primary care providers from two internal medicine clinics within the Duke University Health System.	Perceptions and comfort using PGx. Patient charts provided number of PGx tests ordered in each trial arm. Variables of interest were number of times a pharmacist was consulted (pretest or post-test), and how the results were applied to treatment.	5 of 9 providers strongly or somewhat agreed that felt more informed about PGx testing. 6 felt more comfortable discussing PGx with patients after. 63 tests were ordered, 48 being ordered from the pharmacist in-house arm. Physicians consulted pharmacists in 13 of the 15 cases in the in-house pharmacist group compared to 7.5 of 15 in the on-call group.
Heale et al., 2017[29]	United States	To investigate physicians' information needs and information-seeking behavior when exposed to pharmacogenomics case vignettes.	Mixed methods approach with a prestudy questionnaire of PGx attitudes and knowledge, observation of information seeking in 3 case vignettes, and a poststudy questionnaire and interview.	A purposive sample of 6 physicians, 5 male and 1 female.	Time spent by physician on information seeking, time between navigational actions and number, number of searches entered. Categories of the information needs from poststudy assessment.	Average session time was 8:22 minutes (2:41 to 15:08), time between navigation was 0:53 (0:03 to 8.27), page navigations per subject was 8 (1 to 18), and number of searches was 2.3 (1 to 8). Follow-up identified 6 information needs: alternative therapies, testing guidance, testing frequency indication, testing importance evidence, genetic effects, and information searching aid.
Ielmini et al., 2018[46]	Italy	To identify if psychiatrist's treatment was consistent with the treatment suggested by PGx test and to assess if clinicians had changed treatment at 3-month follow-up visit according to the results of the PGx test.	Observational study with a follow-up at 3 months. At baseline, patients received genetic tests and were given 4 scales. At the follow-up, changes to treatment and adverse events were recorded.	Psychiatrist decision making for 30 bipolar type 1 and 2 patients who received PGx test at 2 psychiatric institutes.	Patients' overall assessment and clinical evolution, anxiety-depressive symptoms, manic symptoms, and side effects of ongoing pharmacological therapy.	At baseline, 13% of patients received optimal therapy. At follow-up, 40% of patients had therapy changes consistent with the PGx test results and 32% maintained a therapy disagreeing with results. A within-group reduction in adverse events observed in patients who received therapy modification.

Table 2 continued

Author and publication year	Study location	Research aims	Study design and methods	Population and setting	Outcome(s) of interest	Major findings
Lærum et al., 2013[30]	Norway	To develop a prototype for automated interpretation of genetic tests and evaluate hospital physicians' reactions to it in a specific use case.	Algorithm applied to interpretation of *CYP3A5* and impact on metabolism of immunosuppressive drug tacrolimus. Scenarios involved viewing and resolving 2 treatment scenarios. Physician asked to identify correct dosing while speech and actions on screen were recorded.	9 experienced and less-experienced physicians, five of whom completed specialties after qualifying as a medical doctor. One physician had a PhD in molecular genetics.	Median time to resolve the two scenarios presented and the speech and actions recorded while using the application. Reactions to the application after completing the scenario.	Average seconds to complete scenario 1 was 164 (110 to 339). Most physicians did not immediately grasp the concept of "interpreted report" versus original genetic data. Scenario 2 took less than half the time to resolve. Physician attitude to the application was generally positive. Some details were too extensive, unclear, or difficult to understand.
Lemke et al., 2017[55]	United States	To explore primary care physicians' views of the utility and delivery of direct access to PGx testing in a community health system.	Study participants received complimentary PGx testing kits for themselves and patients. 30-minute qualitative semistructured interviews conducted to identify viewpoints related to PGx clinical decision making.	15 primary care physicians in the NorthShore University Health System, a 4-hospital community health system.	Broad themes and associated subthemes from the qualitative analysis were the primary outcome.	3 themes were perceived value and utility of PGx testing, implementation challenges, and provider and patient needs. Subthemes were test findings guiding primary care decision making and how test information leads to specific positive outcomes.
Manzi et al., 2017[43]	United States	To describe the development and implementation of a comprehensive clinical pharmacogenomics service within a pediatric tertiary care urban teaching hospital,	Retrospective evaluation of first two years of *TPMT* single-gene sequencing operation and subsequent actions of the clinician based on CDSS alerts.	160 alerts across 31 patients with 69 unique practitioners at Boston Children's Hospital.	Rate of prescribers who canceled orders after alert, modified dose initiation, and percentage of tests order prior to initial prescription.	23% of prescribers canceled orders after *TPMT* alert. 71% of prescribers modified the dose after receiving the alert for the initial prescription. 90% of tests were ordered prior to the drug being ordered.
McMichael et al., 2017[36]	Northern Ireland	To demonstrate how attribute nonattendance analysis can be used in medical decision making to assess whether psychiatrists' treatment recommendations were influenced by on the genotype information, despite knowing patient's response to treatment.	Psychiatrists given patients' pre or post treatment symptom scores for two schizophrenia treatments, told whether patients had a genotype linked to a 30% increase in effectiveness in one treatment and asked for treatment choice. 26 vignettes assessed the effect of attributes on treatment recommendations.	67 practicing psychiatrists from Northern Ireland recruited during continuous professional development meetings in 3 hospitals.	Psychiatrists estimated probability that they will either ignore or attend to information about the patient genotype when already presented their pre and postsymptom scores.	84% probability that psychiatrists did not consider irrelevant genotype information. Psychiatrists with less than one year of clinical experience were more likely to incorporate irrelevant genetic information into patient treatment (46% probability). Psychiatrist with 15 years of experience had 7% probability of incorporating the same information.
Moaddeb et al., 2015[26]	United States	To characterize PGx test experiences and feasibility, including time to provide the testing, patient interest, perceptions of patients' post-test comprehension, pharmacist and prescribing physician interactions, and	Pharmacists completed surveys at two time points for each patient that was offered PGx testing. One for when the testing was offered, and another after testing was completed and test results were	Community pharmacists in North Carolina across 5 community pharmacies.	Length of the pretest counseling, the medium, and time to result communication with patient; pharmacists' beliefs of patients' understanding of results; and percentage	Over 80% of pretest counseling was under 5 minutes, 84% of results communicated by phone, pharmacists believed 95% of patients understood the results very well or somewhat well, and 90% of pharmacist interpretations were correct.

Table 2 continued

Author and publication year	Study location	Research aims	Study design and methods	Population and setting	Outcome(s) of interest	Major findings
		prescribing changes based on results.	communicated. Testing was offered for *CYP2C19* and/or *SLCO1B1*.		of result interpretations done correctly.	Pharmacists reached out to a physician 4 times across 56 patients.
Nguyen et al., 2019[37]	United States	To apply user-centered design methods to develop and evaluate a prototype of a PGx-CDS user interface for thiopurine medications to assist providers with their prescribing decisions.	Qualitative interviews to assess providers' information needs and evaluate the usability of a PGx-CDS user interface.	14 physicians within a large, Midwestern Veterans Affairs (VA) Medical Center and a colocated, major academic health-care system.	Quantitative usability data collected on four measures of usability: learnability, usability errors, efficiency, and satisfaction.	11 themes emerged: need for PGx-CDS for TPMT, impact of PGx-CDS on clinical workflow, lab testing preferences, perceived barriers to PGx implementation, PGx-CDS content, PGx-CDS display, references within PGx-CDS, genetic result content, display of patients' genetic results, PGx care coordination, and examples of related software and CDS systems.
Nishimura et al., 2016[31]	United States	To determine if physicians find clinical decision support alerts for pharmacogenomic drug–gene interactions useful and assess their perceptions of usability aspects that impact usefulness.	Case scenario approach, physician prescribed dual antiplatelet therapy. Regardless of choice, a PGx alert for clopidogrel and *CYP2C19* variant was shown, followed by 15-item questionnaire and open-ended questions on their response to the alert.	55 physicians (58% attending physicians) at the University of Washington who worked in major medical centers, outpatient and specialty clinics, and emergency departments.	Physician response to the alert in an actual clinical interaction. Usefulness of the alert in general, quality of the alert's visual design, appropriateness of the alert in a clinical workflow, and usefulness of the pharmacogenomic content.	40% of physicians would cancel and 49% would modify initial aspirin or clopidogrel order after alert. 4% would override the alert. 7% reported they would contact a pharmacist. 90% agreed or strongly agreed alert was helpful, text was helpful for decision making, and appropriate alert time. 30% were unsure of data usefulness.
Nutescu et al., 2013[40]	United States	To determine the procedural feasibility of a pharmacist-led interdisciplinary service for providing genotype-guided warfarin dosing for hospitalized patients newly starting warfarin.	Prospective, observational study of genotype-guided warfarin therapy patients. Outcomes were initial genotype and consult order time, time to results appearing in EHR, time to initial consult and genotype-guided dose recommendation, and warfarin doses.	The EHR system for the University of Illinois. Clinical dose recommendations were made by the pharmacogenetics consult team.	Adherence of the medical staff to doses recommended by the pharmacogenetics service. Acceptance of the dose recommended defined as within 0.5 mg.	353 dose recommendations were provided for 80 patients. 73% of warfarin doses were within 0.5 mg of recommended dose. Recommendation adherence increased over time: 66% in months 1 and 2, 76% in months 3 and 4, and 80% in months 5 and 6.
Overby et al., 2015[32]	United States	To assess via a pilot study the physician, technology, and task characteristics of effective communication and clinical impact of using a prototype CDSS embedded in the EHR to deliver PGx information.	Clinical experts developed hypothetical clinical scenarios prompting prescribing tasks, and revisions of scenarios that included presentation of PGx information. Each participant was presented with five scenarios.	15 oncology and 7 cardiology fellows practicing at the University of Washington.	Assessments of clinical impact measured by prescribing uptake, prescribing intent, and change in personalized drug dosing (PDD).	Across both high and low actionable alerts, fellows used gene specific resources in 88% of tasks and alert message evidence in 74% of tasks. 65% of physicians changed dose after using PGx-CDS. A decrease was only observed for capecitabine and mercaptopurine/ thioguanine.

Table 2 continued

Author and publication year	Study location	Research aims	Study design and methods	Population and setting	Outcome(s) of interest	Major findings
Payne et al., 2011[50]	United Kingdom	To compare the preferences of patients and health care providers for the key attributes of a PGx testing service.	A discrete choice experiment through an online survey that consisted of five, four-level attributes resulting in 1,024 possible scenarios, done alongside a prospective randomized controlled trial (TARGET study).	138 health-care providers (83% physician) with experience of prescribing and advising on azathioprine.	5 attributes were level of information given, predictive ability of the test, how the sample is collected, turnaround time for a result, who explains the test result.	Health-care providers were willing to wait 2.2 days for 1% improvement in predictive accuracy, 8.9 days for high levels of information provision. They were willing to wait 9.5 days and give up 4.4% in predictive ability for physicians to deliver results over pharmacists, and 6.1% for hospital doctors delivery. No differences in sample collection preferences.
Peppercorn et al., 2013[33]	United States	To assess the use of the *CYP2D6* test for tamoxifen metabolism outside of clinical trials and the attitudes of community-based oncologists and breast cancer specialists about testing among breast cancer patients eligible for tamoxifen therapy.	Cross-sectional survey evaluated *CYP2D6* test knowledge, use outside of trials, patient and third-party requests, and hypothetical test result responses. Associations between practice setting and *CYP2D6* knowledge, tamoxifen test use, and practice patterns were evaluated.	Random sample mail survey of breast cancer oncologists from National Comprehensive Cancer Network and community-based oncologists from American Society of Clinical Oncology.	Response to hypothetical test results presented through three scenarios regarding managing management of patients on tamoxifen who obtained commercially available *CYP2D6* results from an external source.	For premenopausal women with a poor metabolizer (PM) genotype, 33% would make no therapy changes and 56% would. In those with an intermediate genotype 66% made no change, whereas 20% would change. Only 14% of respondents would not change therapy.
Peterson et al., 2016[47]	United States	To solicit clinicians' perceptions of clinical utility, preparedness to effectively use PGx test results, and questions of responsibility for disclosure and clinical use of multiplexed results.	Online survey design with questions based on a previous publication by Stanek et al. and contributions by two authors. Two clinical scenarios were presented to determine which providers should be responsible for clinical action.	Cardiology, primary care, and endocrinology clinicians at Vanderbilt University who ordered a PGx test or cared for a patient with a PGx result. 88% of respondents were physicians.	Responses to the question of which providers were responsible for clinical action with a PGx result.	Cardiology and noncardiology providers agreed multiple providers should receive results, but 50% agreed patients should be notified. 90% of cardiology providers selected the treating specialist and 80% selected the drug therapy prescriber. 95% of noncardiology providers selected the prescriber. 80% of cardiology and 74% of noncardiology chose the treating specialist to act on results. 50% of both groups chose the provider who ordered the PGx test.
Peterson et al., 2016[41]	United States	To investigate how physicians respond to an enterprise-wide PGx implementation utilizing either a clinical decision support and a pharmacist-led surveillance system.	In a new implementation program, coronary stent patients receiving clopidogrel were genotyped *CYP2C19* variants. Poor and intermediate drug metabolizers were flagged and reported to attending cardiologists to see if alternative antiplatelet agents were prescribed.	Prescribing decisions were tracked for 514 patients with poor or intermediate drug metabolizer status of 2,676 that received a coronary stent and were discharged on clopidogrel therapy.	Time to a genotype-tailored antiplatelet prescription within 12 months of the stent procedure. Interception rates from the pharmacist surveillance system.	At 12 months, 57.6% of poor metabolizers and 33.2% of intermediate metabolizers received alternative treatment. *CYP2C19* was most predictive factor of prescribing changes. Pharmacist-led surveillance intercepted 481 of 514 patients for alternative therapy. 304 patients were recommended for therapy change and 130 changes were made.

Table 2 continued

Author and publication year	Study location	Research aims	Study design and methods	Population and setting	Outcome(s) of interest	Major findings
St. Sauver et al., 2016[49]	United States	To assess the perspectives of clinicians and the impact of PGx alerts on prescribing practices who received informational materials through a clinical decision support in the electronic drug prescribing system.	Email survey to understand perspectives on implementation and use of PGx testing in clinical practice. Once the survey was returned, the number of PGx-CDSS alerts were extracted from the EHR.	159 primary care physicians at the Mayo Clinic in Rochester, Minnesota.	Clinician perspectives and response to an alert if they remember receiving one. CDSS alerts were grouped into two categories: alert recommended caution with the prescription or the alert recommended an alternate prescription.	36 clinicians reported PGx alert responses. 12 had positive response, 19 had negative, and 5 reported both. EHR and CDSS data from 27 clinicians and 50 alerts were included. 26 alerts recommended caution with prescription. 3 resulted in prescription change, 23 did not. 24 alerts suggest a prescription change. 7 resulted in a prescription change, 17 did not.
Ubanyionwu et al., 2018[44]	United States	To report the results of prescribers' responses to a PGx-based CDSS alert designed to prompt TPMT status testing.	Retrospective, chart review to evaluate prescriber compliance with a pretest CDS alert that warned of potential thiopurine drug toxicity resulting from deficient TPMT activity.	The Mayo Clinic's Rochester campus electronic health record system between 20 November 2014 and 31 August 2015.	The proportion of patients for whom a test to ascertain TPMT status was ordered and number of guideline-supported doses ordered after CDSS alert.	Of 500 CDSS alerts generated, 101 *TPMT* phenotyping or *TPMT* genotyping were ordered. Alert fatigue may contribute to this. 24 patients were provided with thiopurine dosing recommendations, only 12.5% received concordant doses.
Unertl et al., 2015[48]	United States	To describe the knowledge and attitudes of clinicians participating in a large pharmacogenomics implementation program.	Semistructured interviews of subjects recruited through email or in person and compensated for their time.	13 physicians and 2 nurse practitioners from either a primary care or cardiology practice at Vanderbilt University.	Key themes categories and the multiple themes representing these categories.	3 themes: preparation and knowledge, PGx use in practice, and future implementation challenges. Clinicians acknowledged complexity and unfamiliarity with representations and nomenclature. Strong support for ongoing engagement with implementation team. Concerns included long-term responsibility of results and handoffs.
van der Wouden et al., 2019[42]	Netherlands	To quantify the potential real-world impact of implementation of PGx panel in a clinical decision support system.	Cross-sectional prospective multicenter observational cohort study.	Community pharmacists and general practitioners within the Dutch health-care system.	Number of newly initiated drugs for which potential drug–gene interactions are encountered, since enrolment, and whether these interactions are actionable.	PGx panel results were recorded in 96% and 68% of pharmacist and general practitioner EHRs, respectively. Most were reported as contraindications in the EHR, others as a separate PDF. Reasons for not reporting included lost paper reports or no aberrant variants among genes tested. 84% of health-care providers adhered to DPWG guidelines when the patient had an actionable drug–gene interaction. Much higher health care utilization was found in those patients with a provider adhering to the guidelines.

Table 2 continued

Author and publication year	Study location	Research aims	Study design and methods	Population and setting	Outcome(s) of interest	Major findings
van der Wouden et al., 2020[27]	Netherlands	To study pharmacist perceived remaining barriers, preventing and enablers facilitating implementation of pharmacist-initiated PGx panel-testing in primary care.	Semistructured interviews.	15 pharmacists in primary care.	PGx implementation enablers and barriers.	Five barrier themes and two enabler themes emerged. Barrier themes included unclear procedures, undetermined reimbursement for PGx test and consult, insufficient evidence of clinical utility for PGx panel-testing, infrastructure inefficiencies, and health-care provider PGx knowledge and awareness. Enabler themes included pharmacist perceived role in delivering PGx and believed clinical utility of PGx.
Walden et al., 2015[25]	Canada	To assess physicians' perception of PGx testing and their experience using the test results to help prescribe antidepressant and antipsychotic medication.	Survey sent to physicians 6–8 weeks after receiving a PGx report, coinciding with the first patient follow-up visit at 6 weeks to allow time for the physician to decide if therapy changes should be made.	168 Canadian physicians who ordered PGx test for psychiatric medications, consisting of psychiatrists (33.9%) and general practitioners (40.5%).	Assessed physician attitudes towards PGx testing using Pharmacogenetics in Psychiatry Follow-up Questionnaire.	Respondents agreed PGx testing will become common standard in psychiatric treatment and were satisfied with genetic information provided. Clinician scientist reported a higher mean in their reported ease of understand PGx information.
Walden et al., 2019[24]	Canada	To assess the implementation of pharmacogenetic testing in clinical practice, determine the clinical utility of pharmacogenetic testing by following patients before and after their physician received the genetic report, and evaluate physicians' and patients' opinions of pharmacogenetic testing.	Questionnaires using the Pharmacogenetics in Psychiatry Follow-Up Questionnaire (PIP-FQ).	61 physicians at the Centre for Addiction and Mental Health, Toronto, Canada.	Physicians' opinions regarding their patients' clinical status after given genetic information for *CYP2D6* and *CYP2C19*.	Of the physicians who completed the survey and assessed their patients prior to receiving the questionnaire, 23% ($n = 14$) of physicians reported that their patient had an improved outcome following pharmacogenetic testing. 41% ($n = 25$) of physicians reported no change in patient outcome. There was not a single physician who indicated that their patient had a worse outcome following pharmacogenetic testing.
Wegwarth et al., 2009[35]	Germany and United States	To investigate oncologists' decision making on using PGx tests for cancer treatment and to examine cross-cultural differences between the USA and Germany.	Pilot study revealed cues influencing PGx test ordering decisions and were used to create 9 hypothetical scenarios. To determine information importance, three models were applied: weighted additive model, equal-weighted model, and simple sequential model.	The pilot study consisted of 7 US and 12 German oncologists. The main study was comprised of 109 US and 111 German oncologists.	Whether respondents would use the test for making a treatment decision or not, and the type of information most influential in this decision.	US oncologists opted for test in 6.5 of 9 scenarios, and German oncologists in 5.4 scenarios. The most influential information to US oncologists was test cost, and test guideline recommendation for German. When therapy side effects were more severe, nonguideline recommended test orders increased 20%.

CDS clinical decision support, *CDSS* clinical decision support system, *CPOE* computerized physician order entry, *DPWG* Dutch Pharmacogenetics Working Group, *EHR* electronic health record, *EM* extensive metabolizer, *IM* intermediate metabolizer, *PGx* pharmacogenomics, *UM* ultra-rapid metabolizer.

genomic information than their colleagues with more than 15 years' experience, and US oncologists opted for testing more than their German counterparts.

Prospective or retrospective real-world studies of prescribing/testing decisions

This section includes ten studies, seven of which were prospectively designed, two that used a retrospective chart review method, and one that used a quantitative follow-up survey. These studies were further divided into three themes: evaluation of prescriber actions based on pharmacist or pharmacist-led surveillance service recommendation,[38–41] prospective or retrospective evaluation of prescriber decision making based on a CDSS alert[42–45] or communication of pharmacogenetic test results, the means of which was not explicitly stated,[46] and finally, physician opinion of their patients' clinical status following pharmacogenomic testing.[24]

Among the four studies in the first theme evaluating pharmacist-led services, the primary aim was to ascertain the frequency with which prescribers accepted these recommendations and for what types of patients (i.e., phenotype) did this occur. Study sample size ranged widely from actions taken on 18 to 514 patients. Prescriber response to the pharmacist recommendation was separated by the metabolizer status of the patient in two of the studies.[39,41] Acceptance of pharmacist recommendations overall was high in three of the studies (73%, 89%, and 100%).[38–40] However, lower acceptance rates were observed in the fourth study when the pharmacist recommended therapeutic modification, reporting a therapy change in 57.6% of poor metabolizers and only 33.2% of intermediate metabolizers.[41] The authors point to previous studies that conclude that cardiologists remain uncertain about the clinical significance of a *CYP2C19* intermediate metabolizer, as well as the increased out-of-pocket patient cost when switching patients to ticagrelor or prasugrel.[47,48]

In the second theme, evaluating prescriber decision making, the outcome of interest was adherence to an internal CDSS or interpreted results and guidance from the testing lab/company. Two of the five studies in this theme produced outcomes from a retrospective chart review to evaluate adherence to testing.[43,44] Interestingly, both studies used a "pretest CDSS alert," meaning that rather than guiding the provider on prescribing, it informed them that testing is indicated prior to any initial dosing. Pretest alerts resulted in about 20% of recommended tests being ordered in one study[44] and 90% of tests being ordered in the other study.[43]

The final study in this section stood on its own in terms of methodological approach. Focused solely on mental health, this study captured psychiatrist *opinions* regarding their patient's status following pharmacogenomic testing. No physicians reported a worse outcome for their patients and 23% indicated an improvement.[24]

Cross-sectional quantitative surveys

The cross-sectional quantitative survey section included six studies that employ unique methods to measure response from providers involved in pharmacogenomics.[25,26,47,49–51] Given the uniqueness of each study, no themes were developed here. Five studies had between 18 and 159 physician respondents.[25,47,49–51] In the other study, the reader is informed of the number of participating pharmacies ($n = 5$) and the number of patients engaged by these pharmacists ($n = 69$).[26]

One study was based on an actual implementation project across a series of community pharmacies.[26] This study captured pharmacists' perspectives and experiences with delivering pharmacogenomics and their perceptions of the patients' experiences. The survey was offered after the communication of *CYP2C19* and *SLCO1B1* test results. In a second study, a discrete choice experiment was conducted along with a randomized controlled trial involving azathioprine use.[50] This study examined the tradeoffs health-care providers were willing to make across numerous variables including predictive ability of the test, wait time for results, and information provision. A third study evaluated both psychiatrists' and general practitioners' attitudes toward pharmacogenomic testing for antidepressant and antipsychotic medications at the time of a patient follow-up visit, 6–8 weeks after test results were received.[25] The smallest of the studies surveyed several physician specialties and evaluated the percent of time results were accessed, the number of medication changes, and the reasons for not accessing results or changing medications.[51] The last three studies were conducted in academic pharmacogenomic implementation programs. The fifth study aimed to uncover cardiology and noncardiology providers' perceptions of who should be notified of pharmacogenomic results and who should be primarily responsible for managing the patient.[47] The sixth study assessed the positive or negative aspects of a pharmacogenomic alert.[49]

The results of the discrete choice experiment study revealed several interesting tradeoffs patients and health care providers were willing to make for higher levels of information and predictive ability. Both patients and physicians were willing to wait 2 days for a 1% improvement in test accuracy. Yet, patients were more willing to wait 19 days to obtain more information compared to 8 days for health-care providers.[50] In the study of cardiology and noncardiology providers, there was a strong agreement that results should be returned to both the specialist treating (90% vs. 90% agreement) and the original prescriber (80% vs. 96%), as well as agreement that the specialist should be responsible for acting on the result (80% vs. 74%).[47]

Cross-sectional qualitative research methods

Five of the six studies included in this section utilized interviews.[22,27,48,52,53] The remaining study utilized three focus groups with clinicians.[54] The number of interviews ranged from 15 to 94 individuals. One focused on mental health providers and elicited specific reasons for and against using test results.[23] A second study targeted primary care physicians to understand the value and utility of pharmacogenomics, as well as its use to guide clinical decision making.[55] The third study included both primary care and cardiology providers and utilized a thematic approach to measure the knowledge and attitudes of clinicians participating in a large pharmacogenomics implementation program.[48] The fourth study was one of only two included studies in this review to focus solely on pharmacists as the respondent.[27] The last study was part of a prospective, observational, feasibility study that included pre- and post-study evaluations with primary care providers.[53]

Each interview-based study identified between three and five themes, with several similarities. The first study's themes were test ordering and result receiving experiences, result utilization, and perceived advantages and disadvantages. Mental health–care service clinicians acknowledged the advantages of utilizing the test results but described difficulties when ordering and receiving tests.[23] The second study's themes were perceived value and utility of pharmacogenomic testing, challenges to implementation in practice, and provider and patient needs. Providers recognized the benefits of pharmacogenomic testing but also discussed challenges such as privacy concerns, costs, insurance coverage, and test interpretation.[55] The third study identified three theme categories: preparation and knowledge, pharmacogenomics usage in practice, and future management of genomic variants. Providers expressed an inability to stay updated on new evidence and conveyed support for clinical decision support.[48] Results of particular interest include the noted advantages of test results for decision confirmation and reassurance. However, perceived

disadvantages included using genomic results at the expense of clinical judgment and worries of handoffs to providers outside established implementation programs.[23,48] The prospective feasibility study found that once primary care physicians (PCPs) used pharmacogenomic information, they realized better relationships with patients and medication management skills. Reactions to pharmacogenomics producing a competitive edge were mixed, and respondents desired more testing guidance and electronic health record (EHR) support.[53] The focus group study used a thematic approach to the analysis, but was singularly focused on capturing mental health clinician reaction to a CDS prototype, features left to be desired, and potential concerns or unintended consequences.[54]

Quasi-experimental

Only one study used a quasi-experimental approach, a methodology involving the manipulation of one or more variables, but without random participants assignment.[52] Framing the study as a pilot, the authors used a two-armed intervention trial to assess provider utilization of pharmacist support in pharmacogenetic testing. The study arms consisted of six physicians within a pharmacist-in-house clinic and seven physicians within a pharmacist on-call clinic. This study found that physicians in the pharmacist in-house arm ordered significantly more tests (48 of 63 total tests ordered) and consulted pharmacists at nearly twice the rate compared to the pharmacist on-call arm.

DISCUSSION

This scoping review examined the characteristics of 33 peer-reviewed studies, illuminating the prevailing methods utilized to examine pharmacogenomic use in practice. The decision to identify methods used in implementing pharmacogenomics was a reaction to the saturation of the literature with cross-sectional health-care provider awareness and attitude studies. A common thread in these awareness and attitude studies is that health-care providers find pharmacogenomics useful to patient care, but lack the knowledge to deliver it effectively.[8,15,16,56,57]

The studies identified in this scoping review demonstrate a continued focus on decision making within the EHR. Most of these studies employed hypothetical case-based scenarios designed to mimic real-world practice. These types of studies fit well at the intersection of the three genomic sustainability constructs outlined at the beginning of this review: clinician education, CDS tools, and workflow integration.[10] The importance of well-designed CDSS has been a central focus among leading pharmacogenomic implementation programs. The Clinical Pharmacogenetics Implementation Consortium's (CPIC) Informatics Working Group provides best practice suggestions for integrating CDSS with pharmacogenomics for clinical delivery.[58] Other leaders in the field point to the importance and challenge of developing standardized results and identifying who should receive a CDSS alert.[59,60] The feasibility of the studies in this section is driven by the translation of pharmacogenomic information into a discrete data field that can be called upon when applicable. EHRs without this functionality make it challenging for prescribers to use pharmacogenomic information efficiently.[61] Given the variability between studies, future research on prescriber interactions with a pharmacogenomic CDSS should pursue comparative and longitudinal study designs to elucidate the most effective way to deliver this information. Additional use of hypothetical clinical case scenarios methodologies would be useful for furthering our understanding of optimal CDS for pharmacogenomics. Digital pilot engagement meant to mimic the EHR may enhance provider competency ahead of the complex system integrations and improve adoption.

These review findings also indicate a concerted effort from several ongoing implementation programs to understand who should be acting on pharmacogenomic information and how well these providers perform. This was typically achieved in one of three ways: measuring adherence or compliance to a pharmacist or CDSS-based dosing and therapy recommendation, measuring engagement with the CDSS and subsequent medication changes, or measuring test ordering rates based on a pretest alert prior to dosing determination. Future studies should consider following providers over time to assess adherence behavior changes. Clinicians' limited exposure to pharmacogenomics has been previously noted in the literature.[7,15,56] This unfamiliarity may contribute to a hesitancy to adopt these suggestions immediately. Supplementing these studies with qualitative assessments of recommendation adherence would strengthen these studies, help identify areas in need of interventions, and better understand which providers are optimally positioned to deliver pharmacogenomic information across specialty.

There is a continued need to communicate the value and validity of pharmacist or CDSS-based recommendations more broadly. Pharmacist leadership and involvement with crafting the delivery of pharmacogenomics in clinical care has been strong and this leadership role should continue in new practice settings.[5,12,13,62] The individual institution's infrastructure will most likely guide whether a CDS- or pharmacist-guided recommendation is most appropriate for delivering clinical pharmacogenomics. Future studies focused on a patient-facing role for pharmacists in pharmacogenomics should implement prospective, observational studies and experimental designs. Findings from these study designs may be more impactful to the clinical community and will enable more rapid implementation in real-world settings.

The feasibility of delivering pharmacogenomics through community pharmacists is an ongoing area of research.[17,45,63] Two studies identified in this scoping review identified some of the key considerations to operationalize this approach, such as the time needed for a pharmacogenomic consult, perceived patient understanding, and the pharmacist's ability to interpret information correctly.[26,52] Both studies were conducted by the same group of researchers and in the same state, thus the findings' generalizability may be limited. However, these studies provide a model for future researchers to replicate and establish broader validity. Pharmacist engagement in pharmacogenomics at both the patient level and implementation level has clear support from leading professional organizations, including the American Society for Health-System Pharmacists and the American Pharmacists Association.[64,65] The growth of physician–pharmacist collaborative models, such as formal collaborative practice agreements, is a sustainable path to implementing pharmacogenomics services.[66] Furthermore, additional research surrounding the integration of genetic counselors into the physician–pharmacist collaboration would enhance patient experience and should be experimentally explored.

Our scoping review identified numerous study designs that reported both drug–gene agnostic and drug–gene specific findings across a variety of provider types and specialties. Clinical implementation of pharmacogenomics is progressing such that critical appraisals of the best implementation approach can be compared. Future research focusing on the implementation strategy for the same drugs, genes, clinical service, or testing approach across different institutions would be of particular value. Prospectively designing these studies to capture provider experience or decision making would further our understanding of the best implementation strategies. While most studies from this review included only physicians, future research should assess pharmacists' real-world experiences using pharmacogenomic information, making clinical decisions or suggestions based on this information, and their role in developing best practice. This will help achieve one of the research directions of Volpi et al.: to

study the pharmacist as the "clinical champion" for pharmacogenomics.[5]

This review contains some limitations. First, many of the studies included were published from mature pharmacogenomic implementation programs, likely due to the nature of our research question and inclusion requirements. As a result of this, the majority of included studies were conducted in academic medical centers. While this reflects a gap in previous literature and is not a limitation of our study, more insights would be gained from additional research exploring these same ideas in community pharmacies and hospitals. Second, the nature of a scoping review does not allow for the synthesis of results across studies and thus this was not our aim. However, this review identified key features of the pharmacogenomics implementation literature that can help guide future research priorities.

In summary, this scoping review compiles recent studies assessing the experiences or actions of health-care professionals engaged in pharmacogenomic information use. Our findings illustrate a range of study designs from the actual use of pharmacogenomic information to hypothetical scenarios designed to mimic the real world. Prospective and retrospective real-world data collection and quasi-experimental designs were common, and these studies likely best demonstrate how pharmacogenomic data can be efficiently and effectively implemented into routine clinical decision making. Given the diversity of settings implementing pharmacogenomics, less resource-intensive study designs, such as longitudinal surveys or interviews, still provide value and may be more feasible in resource-constrained environments. Depending on the health-care setting, resources available, and research question, any of these methods, when appropriately designed, may be useful to further understand the use of pharmacogenomic information.

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COMPETING INTERESTS

The authors declare no competing interests.

ADDITIONAL INFORMATION

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