Perspective

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Pharmacogenomics

Healthcare provider education to support integration of pharmacogenomics in practice: the eMERGE Network experience

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Ten organizations within the Electronic Medical Records and Genomics Network developed programs to implement pharmacogenomic sequencing and clinical decision support into clinical settings. Recognizing the importance of informed prescribers, a variety of strategies were used to incorporate provider education to support implementation. Education experiences with pharmacogenomics are described within the context of each organization's prior involvement, including the scope and scale of implementation specific to their Electronic Medical Records and Genomics projects. We describe common and distinct education strategies, provide exemplars and share challenges. Lessons learned inform future perspectives. Future pharmacogenomics clinical implementation initiatives need to include funding toward implementing provider education and evaluating outcomes.

First draft submitted: 28 February 2017; Accepted for publication: 7 May 2017; Published online: 22 June 2017

Keywords: clinical decision support • education • pharmacogenetics • pharmacogenomics • pre-emptive testing

Mapping the first human genome in 2003 has catalyzed sustained interest in understanding how genetic variation contributes to health and disease. To facilitate large-scale discovery and implementation science within genomic medicine, the National Human Genome Research Institute organized and funded the Electronic Medical Records and Genomics (eMERGE) Network [1] in 2007 and has maintained funding for the network, which is now in its third phase. The primary goal of eMERGE is to combine clinical information from electronic health records (EHRs) with genomic data obtained directly from participants or stored in US biorepositories [2]. eMERGE has discovered new genotype–phenotype associations, validated new variant panels and deployed these within routine practice to improve patient care [3,4].

Following the success of eMERGE Phase I (September 2007–July 2011), the aim of eMERGE Phase II (August 2011–July 2015) extended Phase I discoveries by incorporating genetic variant information into the EHR to enhance genetic risk assessment, prediction and diagnosis, and to individualize treatment. The multisite eMERGE-Pharmacogenomic (PGx) initiative was supplemental to Phase II and launched in collaboration with the Pharmacogenomics Research Network in 2012 to implement evidence-based genotype-guided therapy in clinical care, as well as further efforts in variant discovery and return of results from PGx sequencing [5]. Supplemental funding was awarded for sequencing 84 key pharmacogenes and building clinical decision support (CDS) tools at each site within a 1–3-year time frame. All sites were expected to develop a pre-emptive algorithm to identify patients who had the potential to require a medication informed by one or more sequenced pharmacogenes [5]. Network sites selected gene/drug pairs that

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typically had established Clinical Pharmacogenetics Implementation Consortium (CPIC) guidelines for genotype-guided prescribing.

Importantly, implementing and evaluating educational approaches were not part of the eMERGE-PGx initiative's aims. As a consequence, education efforts were unfunded. Aware that education was essential, investigators within the eMERGE Network were challenged to consider how to develop and implement healthcare provider education strategies to support integration of PGx into clinical practice.

Though many providers believe PGx testing can provide value, adoption has been slow [6]. Previous reports have revealed that physicians [7–9], nurses [10], genetic counselors [11] and pharmacists [12] report lack of preparedness to use PGx in practice due to limited or no PGx education, unfamiliarity with genetic testing for drug response, and lack of confidence in using PGx in practice. One path to increased adoption and effectiveness of genetic testing thus lies in providing education to healthcare providers, including targeted, relevant interventions for specific provider groups such as primary care providers [13]. To this end, our goal is to provide the historic, descriptive experience of ten institutions' approaches to provide PGx education, common and distinct education strategies, and exemplars. Furthermore, we offer insights and recommendations to inform other institutions considering the integration of PGx.

Institutional reporting

From October 2015 through January 2016, the coauthors from each eMERGE-PGx site conducted a minimum of monthly workgroup phone calls to discuss site-specific educational initiatives. Educational elements were identified from education program development and evaluation literature that characterize components of effective instruction and evaluation [14,15]. The coauthors were asked to provide information about target audiences for the education, personnel responsible for education, needs assessments, education content provided and delivery methods, implementation and evaluation methods, barriers and challenges, lessons learned and assessment of education impact. Information was systematically gathered for each site's education initiatives and stored in a REDCap® database [16]. Information was collected from 23 April–10 July 2015. Responses were analyzed to identify themes, independently reviewed for accuracy and summarized in table format. Member checking was used to ensure accuracy of each site's report. After recognizing that context of organizations' past experience with PGx was missing, the coauthors were asked to provide this information, including provider education that was done prior to the eMERGE-PGx initiative.

Organizational context

The ten eMERGE sites consisted of three large healthcare systems (Geisinger Health System [Geisinger], Group Health Cooperative with the University of Washington ['Group Health'] and Mayo Clinic); three pediatric medical centers (Boston Children's Hospital, Cincinnati Children's Hospital Medical Center [CCHMC], Children's Hospital of Philadelphia [CHOP]) and four academic medical centers (Marshfield Clinic with Essentia Institute of Rural Health [Marshfield], Icahn School of Medicine at Mount Sinai [Mount Sinai], Northwestern University and Vanderbilt University Medical Center [Vanderbilt]). Vanderbilt has a long history in PGx discovery research and in 2010 expanded into clinical implementation as an institutional initiative and principle site within the Pharmacogenomics Research Network [17]. Vanderbilt's pre-emptive PGx testing served as the model for other sites within the eMERGE PGx initiative, and has been described elsewhere [18,19].

Prior to initiating eMERGE-PGx in August 2012, CCHMC, Mayo Clinic and Group Health had been providing PGx testing as a clinical service for 8 years (Table 1). In common among these sites, eMERGE PGx investigators were able to modify, expand or continue education efforts for providers. Mayo Clinic, CCHMC and Group Health had early institutional initiatives supported by significant internal funding and leadership support to implement PGx services, which included provider education. Mayo Clinic's early faculty development focused on preparing physicians to use PGx in practice by raising awareness and providing general education. Mayo Clinic's RIGHT protocol (Right Drug, Right Dose, Right Time - Using Genomic Data to Individualize Treatment) began in 2012 [20] during which education efforts were supported and coordinated as part of a large, institutional, strategic PGx initiative that included special emphasis on education for pharmacists [21].

CCHMC began its pharmacogenetics initiative with institutional seed money in 2003. It was an expectation that a Genetic Pharmacology Service would be implemented in 2004 and providers would have the knowledge necessary to use the service. Before launching the service, several broad education strategies, such as pediatric and nursing grand rounds and departmental inservices about pharmacogenetics, were used to make prescribers aware of the tests that would be available as well as the purpose, potential benefits and limitations of pharmacogenetic testing [22,23]. By January 2005, psychiatrists were the primary users of the service with up to 2000 new tests ordered per year [24]. Although there was no formal PGx initiative prior to eMERGE II, Group Health's Pharmacy

Table 1. Sites with pharmacogenomic implementation and education prior to 2012 Electronic Medical Records and Genomics-pharmacogenomic initiative.

Site	Gene/drug pairs	PGx service type (years)	CDS support	Education target audience(s)	Education strategies	Adopters/regular users
Children's Hospital of Philadelphia	Genotyping only *CYP2C9*, *CYP2C19*, *VKORC1-1639G>A*	GC model (1 year)	Results summary letter sent to PCP; PGx-specific letter given to patients to share with providers outside EHR	NA	NA	Genetics, Neurology – offered as part of WES
Cincinnati Children's Hospital	*CYP2D6*/codeine, *CYP2D6*/SSRIs, tricyclic antidepressants, *CYP2C19*/SSRIs, tricyclic antidepressants, *CYP2C9*/warfarin, *VKORC1*/warfarin, *TPMT*/thiopurines	Prescriber point-of-care (8 years)	Passive alerts in electronic ordering system; Result reports with therapeutic recommendations including dose adjustment or drug selection alternatives	All prescribers staff nurses, pharmacists	Specialty division faculty and staff inservices; profession-targeted grand rounds; inpatient unit-based posters and resource binders; patient information handouts for every unit and online	Psychiatry integrated into standing inpatient orders by 2005; infrequent use by other prescribers
Group Health	Genotype only, *HLA-B*15:02*	Prescriber point-of-care (8 years)	Best practice alert whenever carbamazepine prescribed regardless of HLA status	All prescribers in Group Health Cooperative	Specialty division faculty and staff in services	Neurology, psychiatry and sometimes primary care
Mayo Clinic	*CYP2D6*/select SSRIs	Prescriber point-of-care (8 years)	None	Clinic wide education: physicians, pharmacists, nurses	Specialty division faculty and staff in services; profession-targeted grand rounds (physicians, nurses, pharmacists), CME courses, newsletters, resource websites	Psychiatry physicians and nurses
Vanderbilt University	*CYP2C19*/clopidogrel, *SLCO1B1*/simvastatin, *CYP2C9*/warfarin, *VKORC1*/warfarin, *TPMT*/thiopurines, *CYP3A5*/ tacrolimus	pre-emptive and reactive genotyping ordered by provider (2 years)	Active and passive alerts in electronic ordering; pharmacy support for specific use cases	Prescribers	Grand rounds; in-service; educational website www.mydruggenome.org; brochure	Physicians and other providers who prescribe

CDS: Clinical decision support; CME: Continuing medical education; EHR: Electronic health record; GC: Genetic counselor; HLA: Human leukocyte antigen; NA: Not applicable; PCP: Primary care provider; PGx: Pharmacogenomic; WES: Whole exome sequencing.

and Therapeutics Committee and Medical Technology Assessment Committee monitored drug safety concerns and approved an alert for all carbamazepine prescriptions recommending *HLA B1502* testing prior to carbamazepine for patients with self-reported Asian ancestry. All committee decisions were published and made available to providers on Group Health's intranet, which was accessible to providers.

Sites new to PGx were challenged within the 3-year funding period to build infrastructure necessary for initiating PGx implementation for the eMERGE PGx initiative. Education at these sites tended to focus on making relevant providers aware of the specific results that would be seen in the EHR and modifying existing CDS structures to provide point-of-care education when results became available. For example, Geisinger first had in-person meetings with leaders of relevant departments and providers of impacted service lines. A general message about the new program was sent to all providers through the EPIC inbox. Due to the limitations of the EHR system at that time, Geisinger investigators needed to decide whether to present educational material or alternative medication choice in their EPIC Best Practice Alert (BPA). Sensitive to clinician concerns about workflow, they developed alternative medication choice language that was responsive to the feedback they received during in-person meetings.

Educational needs assessment

Conducting a needs assessment can help identify perceived or actual learner needs, allow alignment and cohesion with program goals, establish benchmarks and measure progress, and discover potential challenges [14]. All sites noted the requirement to educate clinicians regarding PGx for their eMERGE-PGx study or as part of deploying CDS in support of integrating PGx information in the EHR. While gathering information and evidence to understand learning needs is a key part of developing effective education, many of the sites had very limited resources and did not conduct formal needs assessment to identify target audiences or inform educational approaches. Half of the sites used informal needs assessment methods such as prior experience, referring to the literature and/or consulting with other eMERGE partners to determine educational needs and develop educational strategies, or engaging one or more clinician champions in the specialties where the eMERGE PGx testing was targeted (Table 2).

The other five sites conducted formal needs assessment to determine education and training gaps among clinicians. Needs assessment data were collected using a combination of questionnaires/surveys, focus groups and semistructured interviews. At Northwestern, survey results and physician advisors indicated that point-of-care education was preferred by primary care physicians. In response, carefully worded result templates, BPAs and patient and physician fact sheets accessible within the EHR were created. Similar to Northwestern's findings, Mayo Clinic pharmacists' and prescribers' needs assessment (Table 2) resulted in the prioritization to develop resources that support prescribing at the point-of-care, which included competency training for pharmacists and online resources linked to BPAs. Secondarily, providers noted a desire for basic PGx education. At Group Health, PGx scenarios were used in focus groups and provider interviews to identify provider knowledge gaps, preferences and concerns regarding PGx implementation, including educational needs, as previously described [25]. With the exception of Mount Sinai which reported targeting PGx education to residents and fellows, eMERGE institutions targeted practicing providers (Table 2).

Educational methodologies used

During the workgroup calls, commonalities emerged despite the fact that sites independently developed PGx education to support their specific eMERGE II PGx projects. All sites used two or more approaches to education (Table 3). Strategies used to educate providers can be divided into five categories: face-to-face (meetings and grand rounds presentations); direct-to-provider (email, print mail); point-of-care education (education embedded in CDS alerts, inbox messaging and result reports); resource development (online or print FAQ, online training); and links to online resources. Integrating genomic information into the EHR has been a goal of Vanderbilt University's Pharmacogenomic Resource of Enhanced Decision in Care and Treatment program since 2009 [26] and Mayo Clinic's RIGHT program since 2012 [20]. Implementing PGx as part of large-scale efforts requires understanding provider awareness and education gaps prior to the development of educational material and launch into the clinical practice [26].

Considering that provider education was intended to support incorporation of PGx and CDS into the EHR at all sites, most (9/10) sites prioritized the development of point-of-care resources embedded in result reports or linked to CDS alerts to provide education at the point-of-prescribing (Table 3). Many examples of the alerts used at eMERGE sites can be found within the CDS_KB library at the National Human Genome Research Institute funded site [27]. Implementing education as part of electronic CDS has been suggested as a promising approach for diffusion of innovation to provide 'just-in-time' information within the workflow [28]. While some have indicated that this

Table 2. Site education characteristics for Electronic Medical Records and Genomics-Pharmacogenomic 2012–2015.

Site	Gene/drug pairs implemented for eMERGE PGX	Target audience(s)	Needs assessment	Educational personnel
Boston Children's Hospital	*CYP2C9*/warfarin *VKORC1*/warfarin	Physicians	Not conducted	Clinical pharmacogenomics team
Children's Hospital of Philadelphia	*CYP2D6*/codeine *CYP2C19*/clopidogrel *TPMT*/thiopurines	Prescribers[†] Genetic counselors	Not conducted	Clinical geneticist
Cincinnati Children's Hospital	*CYP2D6*/opioids	Surgical and pain management prescribers[†] Nurses	Informal	Clinical nurse specialist in genetics and anesthesiologist with expertise in opioid PGx
Geisinger Health System	*CYP2C19*/clopidogrel *SLCO1B1*/simvastatin *IL28B*/interferon	Physicians Prescribers[†]	Informal	Clinical geneticist
Group Health	*HLA-B*1502*/carbamazepine *HLA-B*5701*/abacavir	Physicians Pharmacists	Formal[‡]	Clinical geneticist
Marshfield Clinic	*CYP2C19*/clopidogrel *SLCO1B1*/simvastatin *CYP2C9*/warfarin *VKORC1*/warfarin	Physicians Prescriber[†] Pharmacists	Formal[‡]	Clinical pharmacogenomics team
Mayo Clinic	*CYP2D6*/opioids *CYP2D6*/tamoxifen *CYP2C19*/clopidogrel *SLCO1B1*/simvastatin *CYP2C9*/warfarin *VKORC1*/warfarin *HLA-B*5701*/abacavir *HLA-B*1502*/carbamazepine *TPMT*/thiopurines	Physicians Prescribers[†] Pharmacists Genetic counselors	Formal[‡,§,#]	Multidisciplinary education team: Pharmacists Clinical pharmacologist Genetic counselor Trained medical educator
Icahn School of Medicine at Mount Sinai	*CYP2C19*/clopidogrel *SLCO1B1*/simvastatin *CYP2C9*/warfarin *VKORC1*/warfarin	Physicians Residents Fellows	Not conducted	Clinical geneticist Pharmacogenomicist
Northwestern University	*CYP2C19*/clopidogrel *SLCO1B1*/simvastatin *CYP2C9*/warfarin *VKORC1*/warfarin	Physicians	Formal[§,#]	Genetic counselors
Vanderbilt University	*CYP2C19*/clopidogrel *CYP2C9*/warfarin *VKORC1*/warfarin *TPMT*/thiopurines *CYP3A5*/tacrolimus	Prescribers[†] Recruiting nurses	Formal[‡,§,#]	Program staff, faculty and clinical pharmacists

Needs assessment types:
[†]Prescribers include physicians, advanced practice registered nurses and physician assistants.
[‡]Interview.
[§]Survey.
[#]Focus group.
eMERGE: Electronic Medical Records and Genomics; PGX: Pharmacogenomic.

is a preferred choice for learning new information to support prescribing [29,30], caution is advised against overuse to prevent alert fatigue [31].

Because education was supportive of PGx test and related CDS implementation, education was targeted primarily at those providers who prescribed the PGx

Table 3. Educational approaches and resource links for Electronic Medical Records and Genomics-pharmacogenomic 2012–2015.

Site	Direct-to-provider	Face-to-face	Point-of-care	Resources	Links to online resources
Boston Children's Hospital	Consent for participation	Meetings		Online video	www.pharmgkb.org/
Children's Hospital of Philadelphia		Department and staff meetings Grand rounds	Education linked in CDS alert	Online	http://myresults.org/
Cincinnati Children's Hospital	Print ROR to physicians	Department and staff meetings; real-time education by Champion	CDS alert Result report	Online FAQ	www.cincinnatichildrens.org/service/g/genetic-pharmacology/faq
Geisinger Health System		Department leadership meetings	Inbox messaging, Education embedded in CDS alerts	Online FAQ	http://clinicalgenome.org/ www.pharmgkb.org/view/dosing-guidelines.do?source=CPIC
Group Health/ University of Washington	Print ROR to providers		education embedded in CDS alerts	Online FAQ	www.fda.gov/Drugs/DrugSafety/Postmarket-DrugSafetyInformationforPatientsandProviders/ucm123927.htm www.fda.gov/Safety/MedWatch/SafetyInformation/SafetyAlertsforHumanMedicalProducts/ucm075124.htm
Marshfield Clinic	Email at program onset, print ROR	Required training for physicians, Grand rounds	Education embedded in CDS alerts	Print FAQ	http://myresults.org/
Mayo Clinic	Educational email, print ROR to physicians	Department leadership meetings Grand rounds	Education embedded in CDS alerts	Required online training for pharmacists Online FAQ	PGx online resource (intranet only) http://myresults.org/
Icahn School of Medicine at Mount Sinai		Department and staff meetings	Education embedded in CDS alerts	Prerecorded training video for providers	www.pharmgkb.org/ www.pharmgkb.org/view/dosing-guidelines.do?source=CPIC
Northwestern University	Educational email		Education embedded in CDS alerts	Online FAQ	www.pharmgkb.org/view/dosing-guidelines.do?source=CPIC
Vanderbilt University	Email at program onset, brochures	Department and staff meetings, Grand rounds	Education embedded in CDS alerts	Website Online FAQ	www.mydruggenome.org/dgi.php

CDS: Clinical decision support; FAQ: Frequently asked question; ROR: Return of result.

test medication. For example, sites that created and implemented *CYP2C19*/clopidogrel PGx tests (Table 2) focused initial education efforts toward cardiologists and cardiology interventionists. Mayo Clinic instituted the most expansive number of gene/drug tests requiring a much broader education approach that is later described in Exemplars. Consistent with previous reports of provider preferences for PGx resources [9], materials were created to provide PGx information for commonly asked questions, such as currently available PGx lab tests and the corresponding interpretations, specific gene/drug pairs implemented and indications for using PGx in practice. Sites used a combination of locally developed printed and Web-based resources with links to other resources (Table 3). Only three sites developed formal training curricula; these were mandatory for a subset of providers at Marshfield, all pharmacists at Mayo Clinic and optional for providers at Mount Sinai. CCHMC, Geisinger, Marshfield Clinic and Vanderbilt University offered continuing medical education credits in conjunction with select education.

All sites reported that they provide ongoing education to support PGx integration into practice using a combination of targeted, direct-to-provider communications and broader institutional strategies, such as grand rounds, and/or meetings to educate about PGx and to create awareness of PGx CDS implementation efforts (Table 3). It may be tempting to draw an association between the breadth of PGx services offered and the extent of the comprehensiveness of the educational efforts, however, without further examination, this is speculation. Though didactics are an efficient method for delivering education and raising awareness broadly, critics argue that it does not promote active learning or application into practice [32]. No sites reported using incentives as a motivator for participation or learning.

Educational evaluation

Educational experts agree that evaluating the effectiveness and outcomes of education is critical to creating and conducting better education, and ultimately, improving learning [14]. Formative assessment strategies (e.g., interviews, surveys, focus groups, observation) may be used to determine method or delivery suitability, while summative assessment (e.g., pre-/post-test, observation, event analysis) strategies may be used to measure the degree to which outcomes have been met. Few institutions conducted evaluations of the educational interventions due to limited resources (time, personnel and finances). Mayo Clinic sent an informational packet to 159 providers of patients who had received pre-emptive PGx in conjunction with the eMERGE collaboration. Of respondents who recalled seeing the packet, 70% (19/27) reported that it was helpful [33]. Additional studies have shown that despite early education efforts, physician confidence when integrating PGx into daily practice spans a spectrum [34]. As part of the their large-scale PGx implementation program evaluation, Vanderbilt interviewed 15 physicians and nurse practitioners [35] and reported that clinicians were challenged to stay abreast of rapid changes in PGx evidence without ongoing educational support. Clinician interviews to obtain feedback on physician preparedness to manage PGx results are in process at Northwestern University.

Exemplars

Exemplar incorporating PGx as a strategic initiative

At Mayo Clinic, education efforts were supported and coordinated as part of a large, institutional, strategic PGx initiative that was initiated in 2001 by a 5-year, limited educational grant from the Eisenberg Foundation. Regular quarterly updates at departmental meetings, presentations at grand rounds, newsletters and a Website provided information and resources for physicians to learn more about how genomic medicine would impact practice. In addition, a 3-day PGx continuing education session was offered [36]. While physicians, pharmacists and nurses had all indicated that they were interested in PGx, there was common agreement that it was 'not yet ready for prime time.' To advance the translation of genomic medicine into the practice, Mayo Clinic established the Center for Individualized Medicine in 2012. From this Center, a multidisciplinary team comprised of a clinical pharmacologist, pharmacists, genetic counselor, project manager and medical educator was created to develop and coordinate PGx education across the practice, as previously described [21]. Collectively, the PGx Education Team comprised approximately two full-time-equivalents staff and became a formalized entity with a reporting relationship to the institutional PGx Task Force. As a result of this initiative, a new cooperative relationship was established with the Pharmacy Department that has ultimately assumed responsibility for ongoing pharmacist training efforts and continues to serve as a resource for PGx education [37].

Exemplar incorporating PGx as part of a pharmacology service

At CCHMC, the Genetic Pharmacology Service was initiated in 2004 and PGx testing became routine for psychiatrists to inform psychotropic prescriptions and for providers who prescribed thiopurines. Although *CYP2D6* testing to inform codeine use had been available for over 8 years, surgeons had limited awareness of PGx testing and its potential. When made aware

of the test, clinicians reported that waiting 2–4 days for results to inform analgesic selection or changes was of little value for pain management. As part of the eMERGE PGx project, patients being evaluated for possible scoliosis or pectus excavatum surgery were targeted for pre-emptive *CYP2D6* testing. The existing codeine *CYP2D6* result templates were modified to include therapeutic recommendations based on CPIC guidelines [38] and the existing CDS was modified to trigger alerts when tramadol, oxycodone, hydrocodone as well as codeine were prescribed within the EHR system. A pediatric anesthesiologist, with an expanding clinical research program in opioid PGx, was the site's clinician champion. The anesthesiologist and a clinical nurse specialist in genetics conducted small group instruction to surgical faculty and staff. Because the champion had direct daily contact with targeted providers, he was easily accessible when provider, surgical staff and acute pain management team questions arose. CCHMC's existing Genetic Pharmacology Service responded to education needs as questions arose from other providers who ordered *CYP2D6* opioids elsewhere throughout the organization. After the eMERGE PGx project ended, surgeons from the pectus excavatum clinics created a standing order for the *CYP2D6* test for all children prior to surgery to inform postsurgical pain management. Select surgeons in the scoliosis clinic are also ordering the test to inform pain management prior to surgery. Providers in the chronic pain management team recently requested the test as a standing order for all patients admitted for stem cell transplant or solid organ transplant.

Exemplar incorporating PGx as part of a centralized, institutional effort

CHOP and Geisinger developed oversight committees or advisory groups as part of their infrastructure to implement PGx. CHOP initiated a PGx service a year prior to the eMERGE PGx initiative, using a genetic counseling model for testing and returning results for *CYP2D6*, *CYP2C19* and *TPMT* (Table 1). To facilitate PGx implementation outside the genetic counseling model at CHOP, a subcommittee was established with representation from several divisions – the Center for Applied Genomics, Clinical Genetics, Pharmacology, Information Systems and General Pediatrics. Provider education was focused on providing links to education within the CDS alert and presenting upcoming changes to targeted providers during their regularly scheduled department and staff meetings. Similarly at Geisinger, a multidisciplinary PGx Advisory Group with representatives from genetics, pharmacy, pathology and laboratory medicine, health plans and the informatics/EHR team was formed. Tasks included developing a more comprehensive educational strategy to support the implementation of PGx after the eMERGE PGx project ended.

Exemplar incorporating mandatory PGx education

Mount Sinai School began a PGx implementation program called CLIPMERGE PGx during the eMERGE PGx initiative [39]. As part of its recruitment strategy, the research team conducted hour-long training sessions for outpatient providers in Internal Medicine, including resident trainees and attending physicians. Training content included a general overview of PGx and a brief review of the literature surrounding simvastatin, warfarin and clopidogrel PGx. Providers were also introduced to sample BPAs and drug-gene specific education materials that could be accessed whenever they encountered a BPA. Providers were surveyed prior to and following the training sessions to measure their attitudes toward adopting genome-guided prescribing through CDS prior to enrolling in the study. Providers who thought genotype data were useful for making prescribing decisions were more likely to have positive attitudes toward adopting genome-guided CDS [40]. The surveys also suggested that providers lacked overall familiarity and comfort in interpreting and utilizing genomic information. The education session was videotaped and made available to any provider willing to participate in the study and/or learn about the program.

Challenges

Regardless of the approaches used to educate providers, all sites described one or more challenges in five general categories (Table 4): operations (e.g., scheduling and coordination), technical (e.g., limitations of EHR environment), resources and personnel (e.g., subject matter experts), learner attributes (e.g., attitudes and turnover) and communication (e.g., low attendance for oral presentations). The majority reported challenges with learner attributes including restricted time, turnover and attitudes. Time restraints were characterized by poor attendance at presentations, competing demands and physicians' self-reported lack of time for education. Institutions were challenged to provide education for large numbers of physicians and medical trainees exacerbated by the inherent turnover of these populations at academic medical centers. Finally, challenging provider attitudes included skepticism about the clinical utility of PGx. In their study of provider education following the return of results to RIGHT participants, Mayo Clinic physicians reported a lack of confidence when applying PGx results for prescribing [33]. These findings are consistent with other studies describing

education barriers that reported limited time for education [41], concern with the limited evidence of clinical utility [7] and lack of PGx education [42].

Challenges with resources and personnel were reported by the authors from four of the five sites which had implemented clinical PGx prior to eMERGE-II, but were not reported by any of the sites for which PGx clinical implementation was initiated concurrently with eMERGE-II. Most often, education development was led by one or more persons from the study team such as a clinical geneticist or nurse, or a small group such as genetic counselors or clinical genetics department (Table 2). The responsible individuals or groups had minimal or no protected work time, and often used discretionary time to develop education. Having access to and commitment from subject matter experts were noted barriers (Table 4). Others have also described the resource burdens required to implement education broadly across an institution [43], and the need for resources that are easily accessible, clinically oriented and peer-reviewed [9].

A variety of operational challenges were noted as well. Both Group Health and Northwestern University reported operational challenges related to delayed receipt of PGx results from the laboratory. At Northwestern University, the delay created confusion among physicians who had either forgotten about the study or who had started patients on medications prior to receiving the results. Due to the multiplicity of human resource systems across multiple academic centers and health systems, Mayo Clinic reported challenges identifying, contacting and enrolling appropriate learner populations. Vanderbilt noted similar barriers when educating providers outside the health system.

Though not reported by a majority of participating sites, communication and technical issues were also reported. Vanderbilt noted that educating attending physicians did not necessarily mean the information trickled down to physician residents and fellows. Mayo Clinic reported limited success targeting providers with educational email [44]. Low attendance at meetings and grand rounds and high turnover of staff were considered barriers associated with communication efforts. Technical barriers were identified with EHR and browser platforms. For example, some EHR CDS capabilities were limited to either presenting an alternative medication choice or educational material, but not both. Web browser incompatibility issues caused delays and hampered user access to required training.

Lessons learned and future perspective

Expectations for implementing genomics, including PGx, into practice will increase over the next 5 years as reflected in additional large federally funded programs such as the Clinical Sequencing Exploratory Research program [45], the Implementing Genomics in Practice consortium [46] and the Precision Medicine Initiative [47]. Technology for genome sequencing and analysis of genes important in drug response will continue to improve and become more cost effective. Technology to manage and distribute pharmacogenomic information in the EHR will also improve. But, technology enhancements do not preclude the need for provider education. The authors use the many challenges faced by the eMERGE-PGx sites to make recommendations based on a number of lessons learned.

Table 4. Challenges of provider education implementation.

Site	Operations	Technical	Resources and personnel	Learner attributes	Communication
Boston Children's Hospital			X	X	
Children's Hospital of Philadelphia	X	X	X		
Cincinnati Children's Hospital Medical Center			X		
Geisinger Health System		X			X
Group Health/ University of Washington	X		X		
Marshfield Clinic	X			X	
Mayo Clinic	X	X		X	X
Icahn School of Medicine at Mount Sinai				X	
Northwestern University	X			X	X
Vanderbilt University			X	X	

Lesson 1: develop a comprehensive tool-box, but be strategic

Using a singular approach or delivering education once is unlikely to have long-lasting or significant impact [48]. Traditional didactics, such as conferences and ground rounds, show limited impact in changing provider performance [32]. The coauthors used these strategies to raise awareness of PGx and the changes that were being instituted for site-specific eMERGE PGx projects. Increasing full time equivalents (FTEs) to implement education was not an option with supplemental funding targeted for CDS implementation. Therefore, strategies such as just-in-time learning linked to CDS at the point-of-care, which oftentimes included ready access to Web-based resources, were used by the majority of sites with the expectation that these tools would endure beyond the project. At sites where PGx had been implemented prior to eMERGE (CCHMC, Mayo, Vanderbilt) or that had additional funding (Mayo, Mount Saini, Vanderbilt) teams were in place that were available to develop additional educational resources if needed and engage in multiple sessions of targeted face-to-face learning, and direct real-time communication with providers who routinely ordered medication informed by implemented PGx tests. The coauthors recommend that multiple instructional methods at multiple and reoccurring time points be implemented to create enduring change that lasts beyond the implementation project.

Lesson 2: enlist champions as part of a change management strategy

Applying a change management model includes building a coalition to achieve action [49]. Understanding types and sources of resistance [50] to change, and then identifying champions whose voices are heard and respected in the organization can facilitate meaningful change [51]. Education initiatives were considered more successful and required less effort when physician or pharmacy practice champions were recruited early as change agents. Enlisting respected champions can enhance buy-in and mitigate resistance, trust and communication issues when leading education efforts [49,52–54]. The importance of engaging leaders who can endorse transformational change should not be underestimated [55,56].

Lesson 3: education is no magic pill

When trying to change provider behavior – education provides a partial answer. Creating infrastructures and enhancing workflows to support providers can result in more efficient, effective and long-lasting change [57,58]. This will include developing more effective CDS alerts [59] along with subsequent supportive education [60]. As with any new innovation or practice change [61], successful PGx implementation involves culture change. Expect uptake to be slow before adoption.

Lesson 4: building the plane while flying is not easy or free

The evidence to support PGx knowledge is constantly advancing and changing, as evidenced by regular updates of CPIC guidelines [62]. Keeping education content current, accurate and relevant demands continual funding and designated subject matter experts with protected time. Developing viable strategies to maintain and update education is paramount to supporting PGx implementation [63]. Additionally, developing resources and educational interventions that could be shared among healthcare institutions would result in economies of scale and reduced financial burden to institutions. Members of the eMERGE education workgroup created an online website [64] with drug/gene information to be used as a shared resource (Table 4). Additionally, the National Human Genome Research Institute funded a competency-based genomic education portal [65] that lists reviewed educational resources, many at no cost and some of which focus on PGx content.

Lesson 5: develop a long-term strategy

There was general consensus among all sites that regardless of the type and number of educational strategies implemented, the initial training was inadequate. An aging workforce and high-turnover rates among trainees and practitioners at large academic institutions will require ongoing education strategies [66]. Developing PGx education that is scalable and sustainable across multiple stakeholder groups impacted by PGx is imperative. Integrating PGx education as part of health professional preparatory schools, postgraduate education and continuing education should be part of long-term efforts for lasting change. In addition, adopting a more collaborative approach to resource development could reduce workload and enhance quality of education developed.

Conclusion

Future multisite pharmacogenomic initiatives will benefit from recognition that education is essential to achieving implementation aims. Technology to identify important drug response genomic variants and distributing results linked to CDS in the EHR are important tools but education is still needed for providers to use PGx testing to guide prescribing and to communicate results and their implications to patients. Education solutions for the ten eMERGE sites tended to be

local, reflecting the level of institutional priority, institutional culture, availability of resources, and scope and scale of implementation prior to and for eMERGE PGx projects. Though aims to assess the effectiveness and impact of education efforts were restricted at some sites due to limited resources and competing priorities, there was unanimous agreement that education efforts were insufficient to evoke meaningful, long-lasting change. All sites agreed that ongoing education is necessary to ensure provider acceptance and adoption. To this end, several institutions continue to develop and assess education efforts in support of integrating PGx into the practice.

Financial & competing interests disclosure

The Electronic Medical Records and Genomics Network was initiated and funded by the National Human Genome Research Institute through the following grants: U01HG006828 (Cincinnati Children's Hospital Medical Center/Boston Children's Hospital); U01HG006830 (Children's Hospital of Philadelphia); U01HG006389 (Essentia Institute of Rural Health, Marshfield Clinic Research Foundation and Pennsylvania State University); U01HG006382 (Geisinger Clinic); U01HG006375 (Group Health Cooperative/University of Washington); U01HG006379 (Mayo Clinic); U01HG006380 (Icahn School of Medicine at Mount Sinai); U01HG006388 (Northwestern University); U01HG006378 (Vanderbilt University Medical Center); and U01HG006385 (Vanderbilt University Medical Center serving as the Coordinating Center). This work was also supported in part by Mayo Clinic Center for Individualized Medicine. The authors have no other relevant affiliations or financial involvement with any organization or entity with a financial interest in or financial conflict with the subject matter or materials discussed in the manuscript apart from those disclosed.

No writing assistance was utilized in the production of this manuscript.

Executive summary

- The Electronic Medical Records and Genomics-Pharmacogenomic (PGx) initiative aimed to implement targeted sequencing for 84 key pharmacogenes and build clinical decision support tools at each site within a 3-year time frame.
- Vanderbilt's institutional initiative, which featured pre-emptive pharmacogenomic testing, served as the model for other sites within the Electronic Medical Records and Genomics PGx initiative.
- All sites reported a need to educate clinicians regarding PGx and the clinical decision support that was deployed to support PGx information integration in the electronic health record.
- Formal and informal needs assessments were used to understand learning needs.
- Most sites used point-of-prescribing education strategies as opposed to formal training curricula.
- Learner attributes and limited personnel and financial resources were the most frequently reported challenges.
- All sites agreed that ongoing education is necessary to ensure provider adoption.

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