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Lessons Learned When Introducing Pharmacogenomic Panel Testing into Clinical Practice

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ABSTRACT

Objectives: Implementing new programs to support precision medicine in clinical settings is a complex endeavor. We describe challenges and potential solutions based on the Indiana GENomics Implementation: an Opportunity for the Underserved (INGenious) program at Eskenazi Health—one of six sites supported by the Implementing GeNomics In pracTicE network grant of the National Institutes of Health/National Human Genome Research Institute. INGenious is an implementation of a panel of genomic tests. **Methods:** We conducted a descriptive case study of the implementation of this pharmacogenomics program, which has a wide scope (14 genes, 27 medications) and a diverse population (patients who often have multiple chronic illnesses, in a large urban safety-net hospital and its outpatient clinics). **Challenges:** We placed the clinical pharmacogenomics implementation challenges into six categories: patient education and engagement in care decision making; clinician education and changes in standards of care; integration of technology into electronic health record systems; translational and implementation sciences in real-world clinical environments; regulatory and reimbursement considerations, and challenges in measuring outcomes. A cross-cutting theme was the need for careful attention to workflow. Our clinical setting, a safety-net health care system, presented some distinctive challenges. Patients often had multiple chronic illnesses and sometimes were taking more than one pharmacogenomics-relevant medication. Reaching patients for recruitment or follow-up was another challenge. **Conclusions:** New, large-scale endeavors in health care are challenging. A description of the challenges that we encountered and the approaches that we adopted to address them may provide insights for those who implement and study innovations in other health care systems.

Keywords: clinical decision support, electronic health records, pharmacogenomics, precision medicine.

Introduction

Implementing new programs to support precision medicine in clinical settings is a complex endeavor. Strong evidence supports using genetic tests to inform prescribing in some scenarios, but there are many implementation challenges. The US Food and Drug Administration (FDA) has placed genetic testing recommendations and black box warnings on 135 labels [1]. Guidelines are being written regarding gene-drug pairs to inform decisions about switching medications or altering doses [2]. The Clinical Pharmacogenetics Implementation Consortium (CPIC) [3] has published guidelines for 33 medications and is planning for an additional 122 [4]. CPIC helps address one of the barriers to implementation: "lack of clear, curated, peer-reviewed guidelines that translate laboratory test results into actionable prescribing decisions" [3].

Even when clear guidelines exist, successful implementation requires educating clinicians, making pharmacogenomic information available to clinicians in a timely fashion, and reimbursing providers for pharmacogenomics-related activities [3,5–13]. In particular, the inconsistent quality and completeness of the data of an electronic health record (EHR) present various challenges including defining phenotype cohorts (with regard to exposures and outcomes) and accounting for patients' adherence to prescribed medications [14]. Nevertheless, many centers are actively working on piloting or implementing pharmacogenomics and are integrating it with EHRs and clinical decision support systems (CDSSs). The Electronic Medical Records and Genomics network is a leading example [15]. A survey of 10 sites of this network found that all had been able to incorporate pharmacogenomics into their existing CDSSs, and that delays resulted not from pharmacogenomics per se but rather from more general and typical health information technology (IT) implementation challenges related to staffing levels and communication [16].

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The Indiana GENomics Implementation: An Opportunity for the Underserved (INGenious) program at Eskenazi Health is one of six sites supported by the Implementing GeNomics In pracTicE network grant of the National Institutes of Health/National Human Genome Research Institute. INGenious is a testing program for a large panel of genes and medications and seeks to examine its value; it is being integrated, to the extent possible, into an EHR. To address the growing spectrum of guidelines, INGenious configured a custom multigene microarray (for 14 genes and 43 genetic variants) that may allow investigators to evaluate the impact of testing for 27 commonly prescribed pharmacogenetically active medications.

Unlike most previous pharmacogenomics programs, INGenious is being implemented in a safety-net population with diverse chronic illnesses, and across a broad spectrum of care. The setting is a county-owned urban hospital and its clinic system, with approximately 15,000 hospitalizations and almost 1 million outpatient visits per year. Most patients have publicly financed health care coverage (approximately 40% with Medicaid or Medicare, another 40% with county- or other state-financed care). It is important to study safety-net settings. Here, the introduction of innovative techniques and technologies is often delayed compared with places where employer-based or private coverage predominates. Challenges in patient education, recruitment, and informed consent processes may differ in safety-net settings as well. A recent study in academically affiliated safety-net clinics found that heavy use of EHR computers by clinicians was associated with worse patient satisfaction and less clinician-patient rapport [17].

Although the purpose of this study was to discuss challenges in the clinical implementation of a pharmacogenomics program, an additional aspect of this program's design was a controlled trial (ClinicalTrials.gov Identifier NCT02297126). We will briefly describe the trial here because it was inextricably intertwined, logistically, with the introduction of the clinical pharmacogenomics program. When a potentially eligible subject is prescribed 1 of the 27 medications, the EHR prompts the clinician (with a pop-up alert) to enroll the patient in the trial. If the clinician agrees, the CDSS randomizes the patient to the control arm or the intervention (genotyping) arm. To help ensure that usual care is provided to subjects in the control arm, those patients are not approached for informed consent. If randomized to the genotyping arm, the patient's name, location, and incident medication are electronically relayed to a research assistant, who attempts to approach the patient for consent (for genotyping and the trial).

In this descriptive case study, we describe challenges and the approaches taken to address them during the implementation of the Eskenazi Health pharmacogenomics initiative.

Methods

We conducted a descriptive case study of the implementation of a pharmacogenomics program with wide scope (14 genes, 43 variants, and 27 medications) and a diverse population (patients who often have multiple chronic illnesses, in a large urban safety-net hospital and its outpatient clinics). We authors each have a distinct specialty or discipline and reflect varied perspectives including scientific, clinical, economic, medical and molecular genetics, laboratorian, and project management.

We listed and categorized the program's challenges (and their potential solutions), in the context of the literature of the implementation of pharmacogenomics (or other types of programs and technologies). The themes that we identified were developed informally at first, on the basis of the regular weekly meetings in which challenges and approaches to addressing them were discussed. We then refined the categorization through iterative discussion. Our charge, a priori, had been to write about challenges in the adoption of new technology. If we consider clinical pharmacogenomics as the new technology, then all the categories of challenges that we identified apply. In contrast, if we consider technology more narrowly (e.g., as EHRs, automated CDSSs, and new hardware and software for laboratory-developed tests [LDTs]), then some of the categories that we identified (e.g., with respect to the education and engagement of patients and clinicians) are not specific to technology but rather are broader challenges, ever-present in the evolution of medical care.

Challenges

On the basis of consensus, we placed the clinical pharmacogenomics implementation challenges into six categories: patient education and engagement in care decision making, clinician education and changes in standards of care, integration of technology into EHR systems, translational and implementation sciences in real-world clinical environments, regulatory and reimbursement considerations, and challenges in measuring outcomes.

Patient Education and Engagement in Care Decision Making

Educating patients about clinical pharmacogenomics is imperative for both clinical implementation and recruitment into a study. Key steps are to appreciate and to overcome the preconceived ideas that patients have about genetic testing. In this regard, our patient education efforts emphasize how pharmacogenomics data can inform a clinician to make better medication choices. We position the patient's pharmacogenomics data as a critical tool to ensure that the medication a clinician prescribes is effective and safe. During subject recruitment, we also stress the absolute privacy of a patient's genetic testing data. We believe that educating patients within this framework of clinical utility and data privacy will be effective. In addition, the research assistants who recruit the patients are available to answer questions that patients may have, and the clinicians who see the patients have received education about our clinical pharmacogenomics program and may serve as an additional source of information.

On a more operational level, we also recognized that our patients are in our internal medicine and other outpatient clinics for a relatively short period of time, and so any educational efforts must be efficient. We developed bright, colorful, and easy-to-comprehend brochures; we emphasized pictures rather than being narrative in explaining clinical pharmacogenomics and the trial. The brochures are available at check-in (see Supplemental Materials found at http://dx.doi.org/10.1016/j.jval.2016.08.727).

Clinician Education and Changes in Standards of Care

It was also imperative to identify and to align key clinicians in support of the pharmacogenomics endeavor. Because clinical pharmacogenomics encompasses knowledge from a broad spectrum of medical subspecialties, identifying clinicians with interest and expertise in this field was a challenge. We identified key clinicians on the basis of our awareness of previous research on clinical pharmacology that they had conducted within their subspecialties or within our division of clinical pharmacology. Once identified, these individuals played a critical role in the education of their colleagues and in advocacy for our project. We also successfully engaged the support of higher level leaders (of medical departments and patient care areas) on the hospital campus. Fortunately, hospital and clinic leaders were receptive to