Peter H. O'Donnell, MD
Department of Medicine

The 1200 Patients Project: Evaluating How Results Delivery in the Genomic Era Might Promote Communication in the Doctor-Patient Relationship

Introduction/Background
Patients and providers both view the paradigm of "personalized medicine" as a goal for medicine in the 21st century. In reality, personalized care has been practiced for centuries, if one defines personalization as the consideration of all clinical, biologic, and environmental factors that make each patient unique. Such knowledge about—and understanding of—each individual patient is made manifest, in large part, through the quality of the doctor-patient relationship.

What changed through the sequencing of the first human genome in 2000 was the expectation that 'personalized medicine' would now also mean inclusion of genetic information. As one component of that, pharmacogenomics is the study of genetic factors governing drug response and toxicity. The field has led to discovery of genetic polymorphisms for hundreds of drugs, but thus far, information has infrequently been utilized in prescribing decisions. Implementation has been hampered by skepticism regarding the clinical utility of associations, poor physician knowledge about drug-gene relationships, limited avenues for testing, and time delays to receive results.

This research project is aimed at overcoming these barriers to realize the promise of pharmacogenomics in the clinic. We are prospectively enrolling 1200 adults receiving routine outpatient care from one of 12 early-adopter physicians at The University of Chicago. Consenting patients are preemptively genotyped across a panel of polymorphisms selected based upon clinically relevant, published evidence of their pharmacogenomic role. Patient-specific results are made available to early-adopters through a created research portal, or "genomic prescribing system" (GPS), which provides instantaneous pharmacogenomic consultations.

Through this individualized health care model, we are studying whether and how pharmacogenomic results are utilized by physicians if timely, interpretable results are provided, and whether inappropriate or high risk medications are less likely to be prescribed in patients for whom pharmacogenomic results are known. Importantly, we are studying how the availability of pharmacogenomic information—as one potential component of "personalizing" medical care— impacts the nature of the doctor-patient relationship.

Methods
This proposal is being carried out through an ongoing IRB-approved research study led by the applicant (clinicaltrials.gov study #NCT01280825). Enrolled patients' research results are being made available (exclusively) to their study provider through the GPS. At each patient visit, providers are being prospectively monitored for whether they access the GPS to query pharmacogenomic information about their patient during treatment decision-making. We are measuring the first Aim by determining the frequency of review of pharmacogenomic results by

study physicians at all encounters where medication changes occur. For Aim #2, surveys of study physicians and patients are being utilized to assess the impact of the GPS's results availability. Surveys assess factors that may have led to use or non-use of pharmacogenomic information. Providers are being asked whether the pharmacogenomic information influenced their medication choice; about other factors influencing their prescribing behavior; whether the pharmacogenomic information fit their patient's clinical situation; and whether the patient was involved in the ultimate treatment decision. Patient questionnaires administered concurrently are assessing patient-viewpoint perspectives: Did the physician share pharmacogenomic results with the patient? Was the patient the driver of a conversation about genetic results and "personalizing" care? Do patients feel included in the prescribing decision process?

Statistical Justification & Data Analysis: Data will be analyzed using a linear model for repeated binary data. Random effects will include provider and patient nested within provider. Patterns and influences will be captured through longitudinal following of each provider and patient. Over 1 yr of median patient follow-up, we estimate that 1080 patient-provider encounters will be measurable for prescribing behavior variance, equaling ~90 possible assessments/physician, and averaging at least 1/patient. We will quantitate presence of the Hawthorne effect by correlating responses with frequency of physician use of the GPS over time.

Results
We have 646 patients enrolled in the study. For 396 of these patients, genotyping has been performed and results are available to study physicians. Among these 396 patients, 92 have had a clinic visit with their enrolling physician since the time pharmacogenomic results were available. In 90% of these clinic encounters, patients have been taking at least 1 medication with relevant pharmacogenomic information available about the drug. This means that the potential relevance of the GPS information has been high in our currently-studied population.

In approximately 15% of the 92 clinic encounters since the GPS went "live", medications have been changed by the enrolling physician. We are currently studying the impact of the GPS on these medication changes through surveys that have been administered to physicians at the time of these prescription changes. We are also administering questionnaires to patients at every visit (regardless of whether a drug change occurred) to assess the above-mentioned measures regarding the doctor-patient relationship. Evaluations of additional clinic encounters are occurring continuously, as the number of study patient visits increases on a daily and weekly basis. Interim analysis of these data is planned by June 2013 and will be reportable then. We anticipate that by June 2013 approximately 200 such physician-patient clinic encounters with pharmacogenomic results available will be evaluable.

Discussion
We are early in the process of results delivery, and examining of the primary Aims is pending. By June 15, 2013 (when the dedicated research assistant who was hired for this project has her term end), an interim analysis will be conducted and summary results for project Aims 1 and 2 will be possible.