Primary Intended Outcomes
1. Improve the safety of medication use through personalized medicine
2. Integrate the use of genomic data into the pharmacy practice model

Relevant PPMI Recommendations

B23. The following characteristics or activities should be considered essential to pharmacist-provided drug-therapy management in optimal pharmacy practice models:
   B23f. Adjustment of medication regimens based on genetic characteristics of the patient.

B24. Every pharmacy department should:
   B24e. Ensure institutional safe medication use.

E3. My institution has worked to advance drug therapy management services by pharmacists in the past three years.

Situation Analysis
Boston Children’s Hospital is a 380-bed stand-alone quaternary care pediatric hospital. As one of the premier pediatric research hospitals in the world, Boston Children’s has been recognized for the outstanding discoveries made in the field of genomics. As a result, personalized medicine has been on our wish list for many years as a method for improving medication safety. Recent advances in technology coupled with a decrease in cost of testing enabled the creation of a pharmacogenomic service.

The Clinical Pharmacogenomics Service (CPS) was created to facilitate the incorporation of pharmacogenomic information into the medication management cycle to promote safer medication use. The service is directed by a pharmacist and provides consultations for the clinicians at Boston Children’s Hospital who request assistance with the interpretation and application of relevant pharmacogenomic (PGx) data for patient care.

The service is managed by an Oversight Committee that is composed of clinical experts who ensure the safe and rational movement of drug/gene pairs and return of results to the electronic medical record (EMR). The CPS is also responsible for the creation, maintenance and monitoring of related decision support rules in the EMR. The service has established collaborations with Lab Medicine and the Information Service Department to build the necessary infrastructure for return of PGx results to the medical record.
**Service Description**

The CPS officially went live with all EMR functionality on August 1, 2012, including a pharmacogenomic specialty lab view and a consult note structure. To date, we have completed several consults assisting various surgical and medical services with the application of PGx results that were either relayed by the family or provided in hard copy from outside labs.

The first drug/gene pair moved into the EMR was thiopurines/TPMT. In conjunction with the DNA lab, we created and implemented an interpretation report generator that converts the raw data output from the DNA lab into a clinical report. Together with ISD, we constructed a specialty view for pharmacogenomic results, allowing the clinician to view all the applicable PGx results in one place.

Additionally, we created the decision support rules that fire for the prescribers and the pharmacists on order entry/order verification for any of the three thiopurine derivatives (6-mercaptopurine, azathioprine or 6-thioguanine) when the patient has a variant status of heterozygous or homozygous deficient.

Additional drug/gene pairs will be evaluated by the CPS Oversight Committee and moved into the EMR in the near future. All pharmacists received introductory training on the service and the utilization of PGx data in dosing of thiopurines. Several pharmacists completed an expanded competency to serve as PGx service consultants.

This service has been so successful that we were presented with a Pediatric Pharmacy Advocacy Group Best Practice Award at their annual meeting in Indianapolis on May 3, 2013.

In addition to the clinical service, the pharmacogenomics service also has a research mission. We have successfully deployed and analyzed a prescriber survey addressing knowledge and attitudes about PGx. A second study underway is retrospectively studying the relationship between genotype and reported adverse drug reactions. A third study has just received IRB approval and will enroll patients from participating clinics and genotype them on a broad PGx platform, assessing the patient’s response to medication and outcome in the context of their genotype and phenotype.

**Key Elements for Success**

1. A good working relationship with all invested parties is key, as it is in almost any large-scale implementation. Performing pharmacogenomics measurements with decision support from front to back has been successful for us because all of the key stakeholders were involved and committed. At minimum, hospital leadership, the genetic diagnostic lab, the informatics department, the pharmacy department, and the key medical service(s) that will be affected by the first gene/drug pair implementation must be part of the process.

2. Establishing a multidisciplinary oversight committee with a reporting hierarchy within the institution is essential. The committee is responsible for which drug/gene pairs are the most suited for return in the institution based on published guidelines, clinical utility, volume,
and numerous other factors. They are also responsible for weighing the implications of returning genetic data to the medical record, in what context, and with what level of guidance to the frontline clinicians.

3. Start with something small and manageable and build it all the way from beginning to end. Trying to develop decision support rules, incidental finding policies, storage capability, and revisable reporting around whole genome sequence data is NOT a manageable first step for most institutions.

**Resource Utilization**

**Personnel:** One pharmacist dedicated at 80 percent effort, with dedicated bioinformatics (15 percent), and intermittent ISD support.

**IT and other infrastructure:** Up front build upon existing EMR infrastructure. Estimated a combined 40 hours from various ISD personnel.

**Supply Expense:** None

**Return on Investment:** To date we have run 84 TPMT samples pre-emptively at a cost of $55,200 (we saved $19,000 by bringing the assay in house). Nine samples (10.7 percent) have returned with a variant requiring dosage adjustment. Without dose adjustment, the patients could have experienced severe myelosuppression requiring hospitalization. The average length of stay for an ADR requiring hospitalization (no ICU) is four days, or about $14,000. Thus, the total cost from the ADRs could have been as high as $126,000. The net savings of avoiding the ADRs is estimated at $70,800 from this single drug/gene pair.

**Recognized Intangible Benefits**

Our staff have a greater appreciation of the role that a person’s genetics can play in medication tolerance. We have identified an area of great possibility for pharmacist involvement as we move into the future of personalized medicine, particularly as it relates to pediatrics.

**Outcome Measures**

1. Number to treat variables
2. Number of alerts fired
3. Adverse effects observed when following the PGx dosing guidelines

**Lessons Learned**

1. The future steps are bigger and more complex, so build a solid foundation from beginning to end for something smaller and achievable.

2. Engage staff and present plenty of background. Most of the prescribers and pharmacists have not thought about the inner workings of DNA replication since pharmacy school, and the vast majority did not have any prior instruction on pharmacogenomics.

**Other Considerations**

Nothing will ever finish within the expected time frame. Build a timeline and try to stick to it, understanding there will be unforeseen roadblocks along the way. Time from inception to implementation was six months with a highly motivated team. Also, don’t be surprised if the first patient population you target does not work out.
Suggestions for Other Hospitals/Health Systems

We could not have been successful without the gracious input from the staff at St. Jude Research Hospital. Attend programs on setting up scalable pharmacogenomics programs, and reach out to those who have gone before you. This will be particularly helpful if they use the same EMR platform that your institution uses.

Helpful References

