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Operational implementation of prospective genotyping for personalized medicine: The design of the Vanderbilt PREDICT project

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Abstract

The promise of “personalized medicine” guided by an understanding of each individual’s genome has been fostered by increasingly powerful and economical methods to acquire clinically relevant features. We describe operational implementation of prospective genotyping linked to an advanced clinical decision support system to guide individualized healthcare in a large academic health center. This approach to personalized medicine includes patient and healthcare provider engagement, identifying relevant genetic variation for implementation, assay reliability, point-of-care decision support, and necessary institutional investments. In one year, approximately 3,000 patients, most scheduled for cardiac catheterization, were genotyped on a multiplexed platform including *CYP2C19* variants that modulate response to the widely-used antiplatelet drug clopidogrel. These data are deposited into the Electronic Medical Record and point-of-care decision support is deployed when clopidogrel is prescribed for those with variant genotypes. The establishment of programs such as this is a first step toward implementing and evaluating strategies for personalized medicine.

Keywords

Drug-Drug Interactions; Personalized Medicine; Pharmacogenetics; Translational Medicine;

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substantial contributions acquisition of data	X	X	X		X	X	X	X	X			X		X	X		X	X	X	X	X
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INTRODUCTION

An increasingly robust body of knowledge indicates that human genetic variation modulates disease susceptibility and drug responses. Compelling arguments have been put forward supporting the use of genetic variation information to choose among medications or dose [1,2]. The US Food and Drug Administration (FDA) now includes pharmacogenomic data in drug labels [3], some of which have acquired "Black Box" status. While incorporating information about individual genomic variability can improve health care [1], there are challenges to implementing this vision so that the fundamental idea remains largely untested.

The conventional approach to using genetic information to guide prescribing is reactive and often labor intensive: for instance, a practitioner must recognize the potential utility of knowing a patient's genetic variant status when considering a therapeutic, order the test, receive and interpret the result, and re-contact the patient to relay the treatment decision or alter a prescription if already dispensed. Unfortunately, as knowledge relating genomic data to healthcare expands, the systems to deliver information have not, and the current approach therefore is becoming increasingly impractical even for a limited number of drugs.

An alternate strategy is to deposit genomic information in patient records preemptively – that is, prior to its being needed in care [1,4]. In this scenario, when a drug is considered for a patient with known genetic variants modulating response, electronic decision support would alert the practitioner to potential decreased efficacy or adverse effect risks, and would recommend alternate therapies as appropriate. Implicit in this idea is that genetic information is stored and advice is provided in an advanced health information technology environment: no healthcare provider can reasonably be expected to have a personal fund of knowledge large enough to take appropriate action in an era of genomically-enabled personalized medicine without automated clinical decision support [5,6]. The preemptive approach presents substantial challenges, such as selecting the genetic variants for prospective testing and identifying which patients to test. Test results must be aligned with synthesized evidence, formatted to be acted upon by decision support algorithms and rules, and presented as clearly actionable guidance to prescribers.

Addressing these challenges is the key goal of a pharmacogenomics implementation project at Vanderbilt University Medical Center (VUMC) launched in September 2010. We describe the elements of this program, a 1-year report of initial implementation focused first on antiplatelet therapy following placement of cardiovascular stents, and its potential generalizability. The present implementation focuses on prospective assessment of genomic variants that have relevance for drug prescribing and is designated the Pharmacogenomic Resource for Enhanced Decisions in Care and Treatment (PREDICT). The long-term goal of the PREDICT initiative is to establish a framework and comprehensive infrastructure for preemptive incorporation of genomic and other high dimensional patient-specific data into the VUMC Electronic Medical Record (EMR). The PREDICT planning team was formed in September 2009 with the goal of developing and begin implementing the program within a year. The key elements of the planning process are shown in Figure 1 and the implementation steps and components are described here.

RESULTS

Overview

The PREDICT team established the overall goal of the PREDICT program to prospectively genotype patients for "high-value" genetic variants that could improve drug selection and

dosing to decrease medication related adverse events. The evidence review process identified the relationship between variant *CYP2C19* genotypes and reduced clopidogrel efficacy [7–11], included in the FDA's March 2010 relabeling of the drug [12], as the first PREDICT implementation interaction. The evidence for a pharmacogenomic contribution to clopidogrel response is sufficiently strong that our initial implementation was executed as a quality improvement initiative. This report therefore describes the multiplexed genotyping we have undertaken and includes a major focus on the process for moving *CYP2C19* genotype information into routine healthcare processes at VUMC.

Patient attitude pilot survey

An initial step was to take advantage of the patient portal oMyHealthAtVanderbilt.com, currently used by >140,000 patients at our medical center, to survey patient attitudes. An optional patient survey link was placed on the portal and available over 4 days in May 2010, and a total of 644 patients responded. Patient demographic characteristics are shown in Table 1. While 84% percent of respondents found prospective genotyping for use in future care acceptable, they also felt that the practice is not yet routine relative to other common laboratory tests (Table 2): 87% identified cholesterol levels as routine, while only 20% felt similarly about genetic tests conducted to avoid adverse drug outcomes ($p<0.0001$ via Chi-square). "Routine" had no pre-specified definition provided to participants, and the goal was to elicit relative perspectives.

Patient focus groups

Focus group discussions generated a wide range of findings related to clinical pharmacogenomics [13]. Patients expressed preference for brief verbal notification of testing from their provider rather than a process requiring them to sign a formal patient consent document. Patients expressed a wide-range of preferences about whether they would want to be informed of their personal ancillary findings related to genetic susceptibility to disease, but came to a consensus that (1) patients should have a choice about how much and which types of ancillary findings they would receive, (2) providers should not be provided with test results that are not communicated to patients, and (3) work to implement PREDICT should not be delayed by issues related to ancillary findings.

Patient notification of test ordering

To raise awareness of the program, information related to PREDICT has been included in the standard Consent to Treatment forms all patients sign upon registration. Electronic prompts within the patient chart remind providers and other members of the care team to discuss the testing program verbally, document the conversation, record preferences, and provide the brochure. In this way, patients are notified of the PREDICT program and have the opportunity to have questions addressed. [A copy of the brochure is available in Supplementary Figure 1.]

Drug-gene interaction evidence synthesis and review

In 2009, clopidogrel was the third most commonly prescribed drug in the United States, and the primary indication for its use is in patients with coronary artery disease and in particular in the prevention of stent thrombosis in patients treated with drug-eluting stents. While clopidogrel was marketed in 1997, it was only in 2006 that bioactivation by *CYP2C19* was identified as a major factor in its anti-platelet efficacy [14]. In 2009, multiple reports from single centers reported that individuals homozygous for *CYP2C19*2*, a loss of function allele, displayed increased cardiovascular event rates during clopidogrel prescribed for coronary stenting [7–9,15]. More recently, meta-analyses have confirmed this risk and have extended it to include individuals who are heterozygous (termed *CYP2C19*1/*2*) for this

variant, and suggested variants in the intestinal transporter encoded by *ABCB1* may also contribute [10,11,16,17]. *CYP2C19*17* is a "gain-of-function" allele that has been associated with increased bleeding during clopidogrel treatment [18]. However, the evidence for this outcome is not as strong as for the *2 allele, and the FDA label does not recommend acting on this genotype. Accordingly, the initial implementation described here does not consider different management in subjects carrying this variant. The development of an implementation plan started with review of these data by a subcommittee of the standing Pharmacy and Therapeutics (P&T) committee described further in Methods, and that review agreed with the FDA label and consensus statements from professional societies [12] that there is substantial individual variability in response to clopidogrel, and that individuals with decreased *CYP2C19* activity display an increased incidence of stent thrombosis and other cardiovascular events. In addition, a retrospective case-control validation study using data from BioVU, a resource that links DNA extracted from discarded blood samples to deidentified medical records [19], found a statistically significant increase in coronary events in patients with variant *CYP2C19* genotypes treated with clopidogrel after coronary stenting (hazard ratio 1.54, 95% CI 1.16–2.06, p=0.003) [20]. At VUMC, approximately 4000 patients underwent coronary angiography in 2008, and clopidogrel was ultimately prescribed in 1735 (42.5%). Accordingly, the initial group of patients targeted for preemptive genotyping in PREDICT were those scheduled for coronary arteriography, prior to any decision to prescribe clopidogrel.

Assay Performance

The VeraCode ADME Core Panel that includes 184 variants relevant for drug responses was selected as the initial genotyping platform for the program. To maximize reporting efficiency, patient call rates were established at 97.30%. Average observed call rates for controls is 98.6%. After implementation of the assay for patient testing, repeat testing was performed on 150 patients to measure the concordance of results. The loci showing the highest discordance was GSTT1 CNV and DPYD*9B, SLC22A6 and CYP2D6*9. However, CYP2C19 genotype results demonstrated 100% concordance in all patients. Seven subsequent monthly QC plates have shown similar findings with GSTT1 CNV and DPYD*9B showing the highest discordant results and indicating that patient management utilizing these results will not be instituted. Likewise, on these QC plates, no discordant results have been observed for CYP2C19 on an additional 200 patient specimens tested in duplicate. Importantly, CYP2C19 allele frequencies for *2/*2 and *17/*17 homozygotes and *2 and *17 heterozygotes are as expected when compared to the NCBI dbSNP (Table 3). Ten loci are considered poor performing markers with locus call rates <95% and include CYP1A2*1C (94.47%); ABCC2 – I1324I (94.4%); SLC22A2-M165I (94.19%); DPYD*9B (92.97%); UGT2B17-CNV (91.68%); CYP1A2*3 (91.65%); UGT2B15*2 (91.43%); TPMT*4 (88.65%); GSTM1*B (50.42%) and GSTT1 (46.51%).

Clinical decision support systems/architecture

After genotype results are generated, they are stored in a database that is separate from the electronic medical record. Data is archived to a privately owned path on the secure PREDICT application server to protect patient confidentiality. Genetic data that has not been approved for use is stored in a sequestered Oracle database which resides at the VUMC data center behind their firewall. This data is not accessible by patients or providers but is linked to the patient. The data will be stored long term and will not be released until appropriate, i.e. a new genotype is deemed actionable. Patient genotyping data is also protected through The Genetic Information Nondiscrimination Act of 2008 (GINA), the Federal law that prohibits discrimination in health coverage and employment based on genetic information.

Genotypes that have been validated by the established quality control metrics, and reviewed and approved for clinical implementation by the P&T process above are deemed "actionable". After an actionable genotype is recorded, it is converted into a standard notation and interpretation (e.g., *CYP2C19*2, "Poor Metabolizer: Reduced anti-platelet effect"*), stored in the EMR as a molecular diagnostic lab result, and displayed within a "Drug-Genome Interaction" (DGI) section of the patient summary page of the EMR (Figure 2A). Decision support modules were developed in collaboration with informaticists, medical geneticists, clinical pharmacologists, clinicians practicing in relevant fields, and the P&T committee. Current decision support modules are integrated with inpatient computerized provider order entry (CPOE) and the outpatient electronic prescribing application.

The data implicating *CYP2C19*2* as a modulator of response to clopidogrel did not translate unambiguously into standardized clinical recommendations [21,22]. However, the approach that our program ultimately adopted was to recommend use of prasugrel for patients with genotypes associated with decreased clopidogrel effectiveness. (The option of recommending a higher dose of clopidogrel was not supported by any data at the time, or since [23].) Use of prasugrel in patients with acute coronary syndrome has been associated with a 20% reduction in adverse cardiovascular events at 12 months compared to clopidogrel but at the expense of an increased risk of major bleeding [24]. In patient subgroups with elevated rates of bleeding events (e.g., those aged >75 years), prasugrel is contraindicated and so in PREDICT, the drug is not recommended in these patients. Figure 2B shows the point of care decision support guidance that is triggered when a prescription order is initiated for a patient with a variant *CYP2C19* genotype. The guidance implemented in September 2010 focused on *CYP2C19*2/*2* homozygotes only; with the availability of data from subsequent meta-analyses [10,11], the guidance was later extended to *CYP2C19*1/*2* heterozygotes in 2011. Provider behavior in response to genotypes and outcomes of individuals are being followed for Quality Improvement program evaluation at a later date.

Initial uptake and CYP2C19 variant assay results

The program was launched on September 15, 2010. As of August 1, 2011, 3449 patients had undergone left heart catheterization, and genotyping was ordered in 2165 (63%). The results of *CYP2C19* genotyping are shown in Table 3; as expected of a largely Caucasian patient population, 19% were heterozygous for the *2 allele, and 3% were homozygous. Genotypes are classified as "Normal Metabolizer" (two copies of the CYP2C19*1 allele), "Intermediate Metabolizer" (one copy of either the *2,*3, or *4 allele), "Poor Metabolizer" (two copies of either the *2, *3, or *4 allele), or "Rapid Metabolizer" (two copies of the *17 allele). "Indeterminate" is used to note variants that have insufficient evidence to be clinically actionable or variants that could not be called due to low genotyping performance or low signal.

DISCUSSION

We have gleaned lessons that might be beneficial for other sites considering such a program, listed below:

- Commitments across multiple disciplines as well as by institutional leadership are necessary: the requisite disciplines include clinicians, geneticists, informaticists, user interface experts, pharmacists, pharmacologists, clinical pathologists, and program managers. Major institutional commitments are critical for salary support for faculty and staff effort; purchase of new equipment for clinical genotyping; and funding for genotyping for the initial set of patients. The estimated total is ~$5 million in the first two years. Seeking payer reimbursement for genetic screening to guide drug therapy as specified in approved FDA labels is a next phase of the

program. With this in place, we expect the program to ultimately generate cost savings to payers and patients through reduced adverse outcomes associated with lack of efficacy and toxicity.

- Collaboration with interventional cardiology was essential. This involved specific domain expertise as well as buy-in to the program by users. We anticipate that each new drug-genotype rollout will require expertise in terms of pharmacogenomic content as well as domain expertise from physicians who work within the specific targeted practice settings. The initial testing rate was approximately 75%, and it is possible that the mechanics of ordering a new test or uncertainties over how to interpret the result may have resulted in some clinicians' omitting the test order from the pre-catheterization protocol.
- A key initial step for implementation was to establish attitudes in our patient population. To accomplish this goal we leveraged the MyHealthAtVanderbilt.com portal and conducted patient focus groups. We recognize that this group of patients may differ in some ways than the general VUMC population; for example, survey participants are likely to be more familiar with diagnostic testing since receipt of lab results is a common reason to access the portal. However, this population represents 27% of the current VUMC population and is growing[25]. These methods provided strong support for using genetic information to guide choice of drugs or dosage, and provided invaluable input for implementation of PREDICT.
- The procedure for developing and refining decision support rules is time consuming; it required careful review of the literature and input from multiple constituencies, including clinicians, pharmacy, informatics, and genomics, and repetitive iterations of the formats in which it would be provided (Figure 1). There were advantages to starting the program with clopidogrel: the drug is widely-used; there was good evidence that failure of drug efficacy confers risk of substantial morbidity; there is a single common risk allele in subjects of European descent; and the assay is reliable. The drug prescribing information also has a "Black Box" warning from the FDA. However, even this "simple" example highlighted the nuances and complexities of an implementation program. For example, there is an evolving set of data relating genotypes to outcomes: since initiating PREDICT in September 2010, there have been over 60 manuscripts published that might influence the approach to clopidogrel and CYP2C19. These include clinical outcomes in poor metabolizers[11,26], interaction with proton pump inhibitors[27,28], evaluations of other antiplatelet therapies[29], dose adjustments based on genotype[23,30,31], comparison to ticagrelor[32], further characterization of rare 2C19 alleles[33], use of platelet aggregometry testing [34] and platelet inhibition response[11,26–33,35]. Indeed, our initial implementation focused on patients with the *2/*2 genotype, and was extended to those with the *1/*2 genotype in March 2011, after publication of a large meta-analysis describing poorer outcome in both homozygotes and heterozygotes[11]. Maintaining ongoing awareness of evolving pharmacogenetic evidence for purposes of translation to practice is a daunting task, and with the ever-increasing number of genetic tests and medications approved for pre-treatment genetic tests, additional program staff may be necessary to keep up with the field. An increase in institutional funding may be necessary to do so.
- While the evidence for a genetic predictor to clopidogrel response is strong, there is controversy over the utility of genotyping [22]. The best approach to managing patients carrying allele(s) indicating increased risk for drug failure and yet who are not eligible for alternate therapy (such as prasugrel) is unclear. The role of genomic variants in other settings in which clopidogrel is used, such as neurovascular disease, is unknown.

- There is a need to perform and continuously monitor assay performance in a CLIA setting. The initial platform that we chose performed well in determining *CYP2C19**2 phenotype, but as described above, there were a number of assays that did not meet clinical performance expectations. Additionally, with rapidly emerging genotyping technologies, the future use of DNA samples for additional testing is a possibility, as leftover DNA is currently stored, but this has not been explored in detail by PREDICT implementation teams and warrants further examination.

We are in the process of adding additional drug-gene pairs, including warfarin/*CYP2C9-VKORC1* and simvastatin/*SLCO1B1* to PREDICT. Each new drug-gene pair presents issues analogous to those we encountered with clopidogrel: an evolving set of evidence and SNPs, variability across ancestries, newer drugs in the same therapeutic class, and changing regulatory advice. Nevertheless, the principles we describe above represent important starting points for any program that proposes to implement genotype data into clinical workflow. The fundamental design principle that we embrace is that genotype data are best used in such an effort when they are available in the EMR prior to drug prescription, "pre-prescription genotyping".

MATERIALS AND METHODS

Drug-gene variant evidence synthesis and review

The selection of drug-gene variants pairs to be implemented started with consideration of available published evidence, followed by formulation of an initial implementation plan. The criteria for including a drug-genome interaction (DGI) in the program included: an established body of evidence in the biomedical literature linking DGI to patient outcomes, therapeutic guidance from the FDA [36,37], risk allele frequency, and the severity and costs of adverse events that could be averted by genome tailored prescribing. The decision for initial implementation was also guided by practical considerations, such as whether the genotyping platform selected for initial implementation contained the genotypes of interest; the potential complexity of decision support rules; the number of providers involved; and availability of faculty with content expertise. Our initial implementation plan also included local validation of drug-genome associations in BioVU [19], the resource that links DNA samples to de-identified clinical data from the VUMC EMR, so that we had confidence that the conditions of interest did exist in the patient population that would be affected by the intervention.

The original implementation plan was developed by a multidisciplinary team that included individuals with expertise in pharmacy operations, clinical laboratory operations, pharmacogenomics, biomedical informatics, and ethics, as well as clinicians with content expertise. In the case of clopidogrel, interventional cardiologists were involved with the design and implementation of the program. The review process was facilitated by a CTSA studio [38] and final approval was given by the Pharmacy and Therapeutics (P&T) Committee. A Therapeutics Subcommittee of P&T composed of a cross-section of VUMC clinicians, pharmacogeneticists, and pharmacists was organized to perform a preliminary review for any proposed drug-genotype variant. For each actionable genotype, the entire process of genotype validation, review and approval for clinical implementation took approximately one year.

Clinician communication

Since the primary initial PREDICT clinical site was the catheterization lab, the primary providers were the 13 interventional cardiologists performing the procedures and responsible for post procedure anti-platelet therapy. Four prelaunch sessions were held among this group. These involved review of the published and local data supporting the

intervention, discussion of the proposed format of the guidance as provided by VUMC's clinical decision support systems, and the mechanisms for providing a testing prompt within Vanderbilt's EMR to guide clinicians to order the genotyping test.

Patient attitudes – pilot survey

With Institutional Review Board approval, a pilot patient survey was conducted to gauge attitudes toward aspects of genetic testing. The survey was conducted by soliciting users of the MyHealthAtVanderbilt.com (MHAV) patient portal, a resource that provides general health information, messages healthcare providers, and displays to patients their laboratory results [25]. The optional survey link was made available on the MHAV patient portal home page after a user had logged into their account. If the individual elected to take the survey and opened the link, they were directed to the structured survey developed using REDCap Survey (http://redcap.vanderbilt.edu/consortium/index.php). The domains captured in this pilot survey were patient perspectives on medical testing, whether different types of diagnostic and genetic tests were considered routine, the ways health care institutions use and store their health information, and the importance of use of their genetic information in healthcare decisions.

Patient attitudes – focus groups

Previous studies to evaluate patient perceptions of pharmacogenetics have focused on general concerns related to privacy and management of ancillary findings, but have not attended closely to the practical issues of implementing clinical pharmacogenomics [39–45]. We conducted ten focus group sessions, including two conducted in Spanish, with Vanderbilt patients to elicit input the design and implementation of PREDICT [13]. Discussions addressed a number of issues, including preferences on how patients would like to be informed of PREDICT, how they would like to provide their consent for pharmacogenomic testing, what they would need to learn from their healthcare provider, and how they would like ancillary findings to be managed.

Ethics review and patient notification of test ordering

The initial deployment of the PREDICT program was undertaken as a healthcare quality improvement (QI) initiative based on the program objective to implement FDA regulatory guidance for prescribing [36,37]; thus, there is no research informed consent process as there would be for a study involving human subjects. However, given the seminal nature of the program, the Medical Center Ethics Committee reviewed the overall program plan prior to implementation to provide guidance. Pilot survey, focus group findings, and committee recommendations were used to develop consent procedures, brochure and other patient notification approaches, and ancillary finding policies. Brochures were subsequently developed with a 7th grade reading level based on the Fry Readability measurement.

Genotyping Assay

The VeraCode ADME Core Panel (Illumina, Inc. San Diego, CA) was chosen for genotyping studies. The assay targets 184 variants in 34 genes involved in drug absorption, distribution, metabolism and excretion (ADME) [46]. Due to the highly polymorphic nature of many of the regions assayed, a patient sample is analyzed in 3 separate reactions to optimize the assays and prevent competition from adjacent polymorphic regions within the same gene. Thus, a 96 well plate enables analysis of 32 specimens; the VUMC implementation includes 30 patient specimens as well as a control DNA specimen (with a known genotype at the 184 variants) and a negative control reaction tube with all reagents but no template DNA. Polymorphisms in *CYP2C19* analyzed in this panel include both common (*2, *17) and rarer (*3, *4, *5, *6, *7, *8, *12) variants.

Implementation within the institution's CLIA high complexity molecular diagnostics laboratory required additional institutional investments, including space for designated pre- and post-PCR work stations; personnel; laboratory informatics system work stations; specific instrumentation required for the assay, and an automated DNA extractor. To accommodate the anticipated workflow, 4 medical technologists were trained to perform the assay, with other laboratory staff providing daily assistance as needed for DNA extraction. General workflow was designed to process samples and return results within 3 business days from the sample draw.

Assay validation

Prior to implementation for patient testing, the assay was validated by the laboratory by comparing the observed genotypes for all 184 variants with the previously reported genotypes for these variants in 54 control DNA cell line samples repeatedly tested on training plates and by several technologists. The average concordance was 99.58% (SD=0.4844%) from 23 cell lines (ParagonDx, Jacksonville, WY) and 98.36% (SD=1.91 %) from 31 additional cell line samples (Coriell, Camden, NJ).

Assay quality control

In addition to control parameters included by the manufacturer to monitor the performance of each run, a previously validated control specimen is included on each plate to measure the performance and reproducibility of each variant on each plate. Other quality control indicators established and monitored include the: locus call rate; patient and control call rates; variant allele frequencies; and monthly QC plates containing specimens previously tested and reported in the prior month. The locus call rate represents the percentage of patients for which a result is obtained at a given marker and indicates the overall performance of an individual variant. A "no call" result can either indicate complete failure of the assay at that site or potentially reduced stringency within a particular run and the inability of the assay to discriminate among possible variants. The patient and control call rates indicate the percentage of variants for which a result was obtained for a given patient. The variant allele frequencies generated are compared to those listed in NCBI dbSNP and the monthly QC plates assess the reproducibility of the assay. Due to the amount of data collected, reports were generated using bioinformatic tools and submitted to laboratory personnel for review.

Quality assurance of implementation

To monitor the initial clinician response to PREDICT and ensure the timely transmission of information, we deployed a multi-user web-based application to allow a team of nurses and pharmacists to view which eligible patients had an actionable genotype result. Prescribing providers who had not yet received clinical decision support or reacted to a variant genotype (for example, if the patient's genetic result was returned after they were discharged) were notified with an electronic clinical message via the EMR, which is a standard means of clinical communication within the institution. The QA mechanism enabled the follow-up of genetic results that returned following discharge and prior to a follow-up visit with a Vanderbilt provider.

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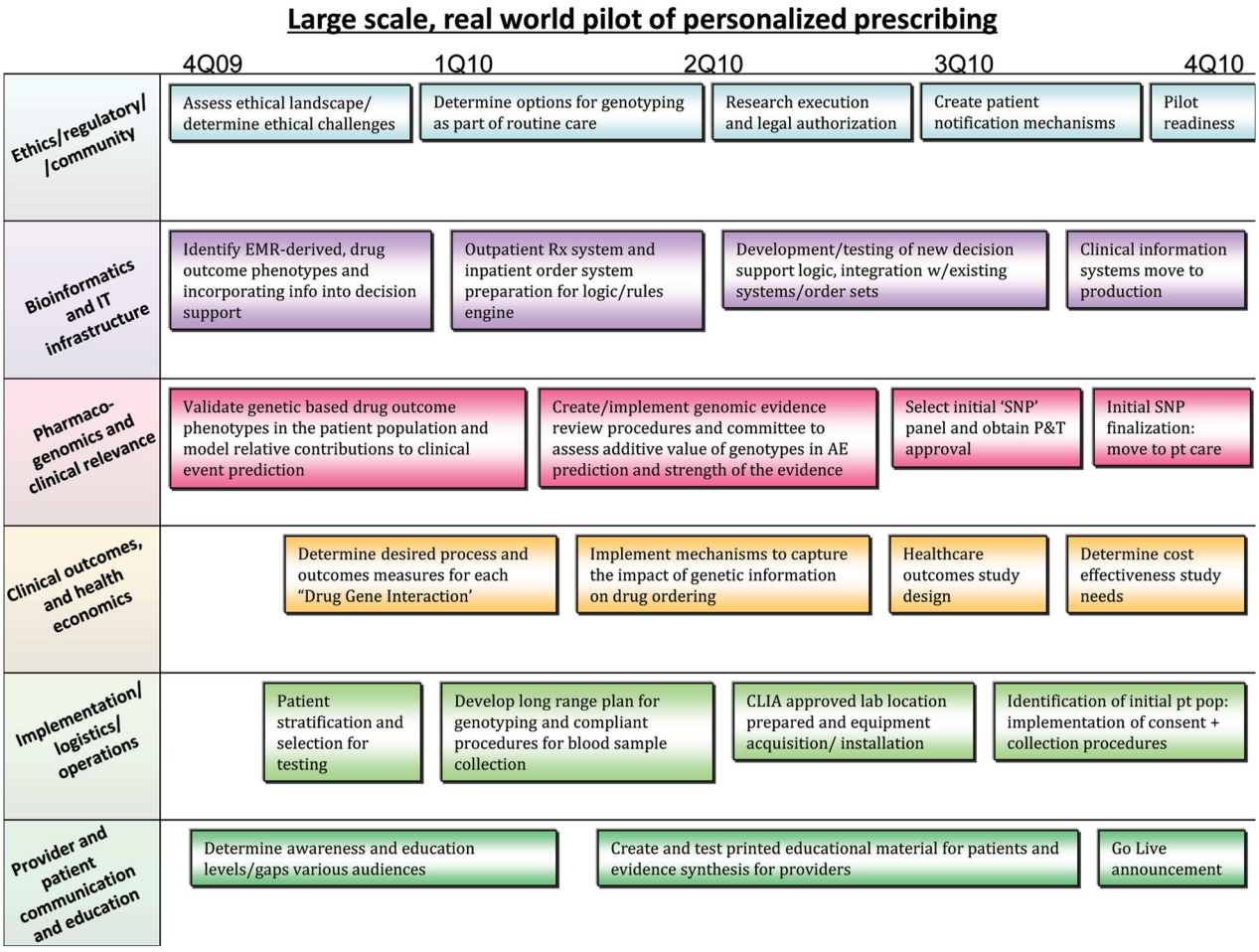

Figure 1.
Program components overview and timeline, with key milestones reflected

Figure 2.
Lab result presentation of genetic results in EMR and clinical decision support guidance within order entry system.

Table 1

Demographics of patient pilot survey respondents

DEMOGRAPHIC - AGE	**# OF RESPONDENTS**
Age 20–39	202
Age 40–59	292
Age 60–79	143
Age 80+	8
DEMOGRAPHIC - RACE	**# OF RESPONDENTS**
Caucasian	521
African-American	44
Asian	8
American Indian	1
Unknown	71
DEMOGRAPHIC - GENDER	**# OF RESPONDENTS**
Male	224
Female	421

Table 2

Responses as to whether a specific test was viewed as routine

Test	Routine	Not Routine	Not Sure	No Response
Cholesterol levels	87%	12%	1%	1%
Blood counts used to detect anemia or infection	73%	24%	3%	1%
Hemoglobin A1c (for diabetes management)	59%	32%	10%	<1%
Urine test for drug abuse	18%	78%	5%	1%
Testing for HIV/AIDS	24%	71%	5%	2%
Information in genes to avoid bad side effects from medicines	20%	69%	12%	1%
Information in genes to test risk for specific diseases	24%	70%	7%	1%

Table 3

Genotype data and dosing recommendation

Category	Genotypes	Recommendation	Total
Poor metabolizer	CYP2C19*2/*2	Alternative therapy	82 (2.6%)
Rapid metabolizer	CYP2C19*17/*17	Usual care	154 (4.9%)
Intermediate metabolizer	CYP2C19*2 Heterozygote, CYP2C19*3 Heterozygote	Alternative therapy	601 (19.1%)
Normal metabolizer	CYP2C19*1/*1, CYP2C19*17 Heterozygote, CYP2C19*4 Heterozygote	Usual care (e.g. clopidogrel 75mg)	2,059 (65.5%)
Indeterminant	CYP2C19*5 Heterozygote, CYP2C19*6 Heterozygote, CYP2C19*8 Homozygote, CYP2C19*8 Heterozygote, CYP2C19*12 Heterozygote	Usual care	249 (7.9%)