Pilot Implementation of Clinical Genomic Data into the Native Electronic Health Record (EHR): Challenges of Scalability

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Abstract
Integration of genomic data into the EHR is a critical step to achieving the goals of precision medicine. In this pilot study, we integrate the genetic variants from 1,317 patients for four actionable genetic conditions and seven pharmacogenes. We assessed this implementation for scalability to additional genes and a much larger patient population. Several challenges to scalability were identified, including: data standards for genomics, the laboratory to EHR interface, and maintenance of decision support.

Introduction
Genomic data has potential to improve health through targeted clinical management based on genetic sequence. The integration of genetic information into healthcare is considered a major priority with several national and international initiatives that have been launched to pursue this goal[1]. Despite this, only recently have EHR vendors allowed for the storage and access of discrete genomic data. Even with this new capability there remain many challenges related to adoption and implementation of such technologies. As part of the Electronic Medical Records and Genomics (eMERGE) network[2, 3] and through our MyCode® Community Health Initiative[4] Geisinger has exome sequencing data available for more than 145,000 patients. With the goal of integrating genetic data into the EHR for our entire sequenced population, we first performed a pilot study on 1,317 patients from the eMERGE patient cohort to assess the plausibility of scaling the deployment to more genes and a larger sequenced population.

Methods
We imported discrete pathogenic and likely pathogenic genomic variants for the Center for Disease Control Tier one conditions (Hereditary Breast and Ovarian Cancer Syndrome, Lynch Syndrome, and Familial Hypercholesterolemia), and variants from seven pharmacogenes (CYP2C19, SLCO1B1, DYPD, TPMT, IFNL3, CYP2C9, and VKORC1). Variants for hereditary hemochromatosis were also included to assess for challenges related to implementation of autosomal recessive conditions. We constructed context sensitive maintenance guidelines in the EHR for each of the disease conditions and built best practice alerts for medications impacted by the pharmacogenomic variants. Patient and provider facing information was developed for all disease variants as these were accessible through both the physician chart and the patient portal. Through the implementation process weekly calls were held with pertinent stakeholders to address challenges and barriers to implementation as they arose. A list of these challenges was maintained throughout the process. After implementation, we analyzed the noted challenges and identified barriers to scaling our implementation to more genes and our entire sequenced population.

Results
We were able to successfully implement all conditions for 1,317 patients with minimal compromises. Several challenges were encountered that affect our ability to scale the process. We encountered some vendor specific informatics challenges including the inability to store discrete variants for pharmacogenomics, instead resorting to star allele diplotypes, and having inadequate infrastructure for autosomal recessive conditions where the patient is a compound heterozygote. Although these were vendor specific issues, the vendors data implementation was based on the Health Level Seven International (HL7) V2.5 Clinical Genomics Report standard, which had deficiencies that contributed to these problems. Other global challenges include: 1) Need for standardization of genetic phenotypes. 2) Difficulty in sending discrete data from the genetic testing laboratory directly to the EHR. 3) Addressing the role of the Laboratory Information System (LIS) in the genomics process. 4) Inadequate and discordant standards for genomics in the HL7 genomic report format and the Fast Healthcare Interoperability Resource (FHIR) molecular sequence resource. 5) Challenges related to maintenance of patient/provider information and decision support in a rapidly changing field. 6) Lack of publicly available standard resources for patient/provider information. 7) Disparate implementation needs for clinical geneticists compared to primary care providers. 8) Differing perceptions of discrete genomic data versus a scanned PDF of the genetic report. 9) Classification and reclassification of variants.
Discussion

While we were able to achieve a successful integration of genomic data into the EHR, there are many challenges that need to be addressed prior to scaling our implementation. One of the greatest challenges is the long-term maintenance of gene/variant specific information and decision support. Genomic medicine is a rapidly changing field and many EHR systems including our own require support from vendor specific technical personnel to implement changes to patient/provider facing information and decision support. Engaging this technical team can be challenging given their responsibility to maintain all aspects of the EHR for the entire healthcare system. In addition, these personnel are not skilled in genomics requiring an alignment of teams to make any changes to the system. EHR vendors adhering to more open standards for genomics and decision support, including SMART on FHIR, and CDS hooks would allow for integration of external applications where maintenance can be performed by staff with genetics training and less technical skill. This is particularly important while we are in the “Wild West” phase of genomics where many of applications and developments are still in their infancy. Another important component to this, is the need for maintained resources such as PharmGKB that are Infobutton compliant and can allow for rapid access to the most current recommendations and information on a specific gene or variant. To our knowledge no vendor has implemented Infobutton support for genomics, and outside of pharmacogenomics no such Infobutton compliant resources exist.

Difficulty in passing data from the laboratory to the EHR is a considerable challenge and one of the greatest components of this challenge is the standardization of the genetic phenotype (i.e. disease, metabolizer status, gene specific phenotype, modifier variant phenotype). We were able to capture discrete genomic data from our primary genetic testing laboratory, however; neither the current FHIR molecular sequence resource or the HL7 V2.5 Genomic report standard were adequate for their reporting so the laboratory used their own proprietary JSON structured format. Even with the ability to pass discrete genetic data our efforts in this area were hampered by lack of standardized genetic phenotypes. We developed the ability to pass the phenotypes included in the pilot study but would have to specifically define and build out any additional phenotypes that might be discovered on exome sequencing to enable the lab to report all exome results this way. The initial role of our LIS in this process was unclear, since laboratory data currently enters the EHR from the LIS and our LIS did not have the ability to store or report discrete genomic variants. In our design, we opted to keep the existing pathway for ordering and reporting genomic testing through the LIS intact and build an additional messaging pathway that bypassed the LIS and delivered data directly to the EHR.

We opted to bypass automated processes to classify variants and accepted the laboratory classification as the value that first enters the EHR. Reclassification of variants based on clinician reinterpretation presented several challenges. Vendor specific challenges included the inability to reclassify at the variant level, requiring the updating of each patient with the same variant separately. Although variant reclassification was allowed and tracked appropriately in the EHR, this presented the possibility of having structured genomic data that was discordant with the scanned PDF. This demonstrates the need for bidirectional communication between the clinician and the lab when variants are reclassified, particularly if both parties submit their classification to ClinVar. While the need was expressed to automatically reclassify all patients with a given variant once reclassification was warranted, there was no clear process to manage this at scale.

Geisinger has developed extensive processes for the management and return of clinically actionable genetic results that may be able to be optimized through EHR integration. To most efficiently utilize Geisinger’s existing resource would require interfaces that allow non-technical clinical experts to manage the information and decision support around genetic variants. Moving genetic data from the lab to the EHR and managing it in a scalable way requires adequate standards for storing and transmitting genomic data and standard API’s that allow ancillary systems, including those in laboratories, to interface with the EHR. Classification and reclassification of variants remains a challenge. We have identified key areas to address to scale our clinical implementation.

References