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Enhancing Clinical Decision Support through Integration of Pharmacogenetic Data in the Epic Genomic Module

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ABSTRACT

The University of Florida's Precision Medicine Program (PMP) centers its efforts on progressing pharmacogenomics (PGx) to enhance patient outcomes. The UF PMP, working together with the UF Health Pathology Laboratory (UFHPL), leveraged HL7 standards to embed PGx data within Epic's Genomic Module, thereby strengthening the clinical handling and application of pharmacogenomic information." A major advancement in the Genomic Module is its use of genomic indicators, which highlight clinically relevant genetic findings right inside the electronic health record (EHR). By showcasing key phenotype details and integrating with existing clinical decision support (CDS) alerts, these indicators help clinicians make faster and more informed treatment choices that are guided by a patient's genetic profile. This improvement signals a major evolution in how genetic insights are applied in clinical settings, shifting from stand-alone PDF documents to a more dynamic and meaningful display of pharmacogenomic information. By weaving these data into everyday care processes, clinicians gain actionable, genome-informed guidance that supports tailored treatment choices and strengthens the overall practice of individualized medicine.

Keywords: Precision medicine, Pharmacogenetics, Electronic health records (EHR), Clinical decision support systems, Genomics, Health informatics

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Introduction

Integrating genomic data into clinical systems has the potential to transform healthcare by offering treatment insights tailored to a patient's unique genetic profile [1]. Since 2011, the University of Florida has been an early leader in this area through its Pharmacogenomics and Precision Medicine Program (PMP), with a strong emphasis on pharmacogenomics (PGx) implementation [2, 3]. Most PGx testing is performed in-house by the UF Health Pathology Laboratories, which provide both individual gene assays—such as CYP2C19, CYP2D6, TPMT, and NUDT15—and a broader testing panel, GatorPGx. This panel evaluates eight key genes (CYP2C19, CYP2D6, CYP2C9, CYP3A5, CYP4F2, the CYP2C gene cluster, SLCO1B1, and VKORC1) that influence medication response and metabolism.

A central feature of UF's PMP has been the integration of health information technology into the electronic health record (EHR), including the creation of clinical decision support (CDS) tools that help clinicians make drug therapy choices informed by drug–gene interactions [4]. Initially, these PGx-focused CDS tools primarily generated pop-up alerts during medication prescribing. Although Epic has long supported such alerts, the introduction of genomic indicators through the Genomic Module represents a major enhancement to how genetic data can be managed and displayed. A new master file—known as the

VAR database—was created to store a wide range of variant types, including SNPs, indels, and structural changes, enabling more detailed and scalable genomic data handling. With this improved data infrastructure in place, Epic

added genomic indicators to make genetic findings easier to access and interpret. These PGx indicators provide several functions: they offer clinician- and patient-friendly interpretations, flag potential drug–gene issues with suggested actions, and connect directly to the relevant laboratory reports. They can also be linked with decision support mechanisms that assist clinicians in making complex therapeutic choices. For instance, when a patient carries a variant that alters how a drug is metabolized, a PGx indicator can be used to trigger an alert to help the prescriber avoid harmful reactions or choose a better-suited medication. Recognizing the importance of more advanced genomic integration, UF Health opted in 2021 to adopt Epic's Genomic Module.

Incorporating detailed genomic information into clinical systems brings a set of technical challenges, especially when it comes to accurately entering and interpreting the data. To overcome these issues, UF applied health informatics strategies to create a process that simplifies the interpretation of pharmacogenomic results and produces standardized outputs in HL7 format that can be seamlessly processed by the Genomic Module. HL7 serves as a globally recognized framework for exchanging clinical and administrative information between healthcare software platforms, promoting uniform, well-structured communication and reducing the likelihood of data errors or misinterpretation. A typical HL7 message begins with a header generated by the EHR and is composed of several distinct segments—MSH for the message metadata, PID for patient identifiers, ORC for order control, OBR for the test order information, OBX for reporting observations or results, and NTE for any supplemental comments. Each segment contributes specific pieces of information, allowing the message to convey complex clinical data in a clear, organized format. Using HL7 for genomic integration offers notable advantages: it allows laboratories to include detailed genetic descriptions, such as variant-level annotations and interpretive comments, while shortening the turnaround time for reporting and reducing manual processing errors [5, 6].

The broader aim of this initiative was to implement Epic's Genomic Module in a way that strengthens how PGx data supports post-analytic therapeutic decision-making. Because this integration is technically intricate, this work concentrates on the operational elements—specifically, the steps involved in transmitting results to the EHR through HL7 and establishing the downstream clinical decision support mechanisms.

Materials and Methods

UF Health Pathology Laboratories (UFHPL) operates on the Epic electronic health record (EHR) platform, which includes the Beaker laboratory information system (LIS). Epic offers multiple laboratory-oriented modules—such as Beaker Clinical Pathology (CP) and Beaker Anatomic Pathology (AP)—each tailored to different testing needs. At UFHPL, molecular test results are entered through Beaker CP, which supports storage of data in structured, searchable fields. The process described below outlines how pharmacogenomic (PGx) data was incorporated into Epic's November 2021 Genomics Module release, enabling complex genetic information to appear in the EHR in a structured form and supporting the use of discrete genomic indicators for clinical decision support.

To enable this functionality, a customized middleware system was created to connect PGx data to Beaker CP while leveraging an existing HIPAA-compliant technical framework. This framework centers on a Linux-based server that maintains secure links to Epic Bridges/NextGen Connect and to a shared network directory [7, 8]. Serving as a protected data conduit, the middleware ensures secure and accurate transfer of clinical information between the local network environment and Epic's integration tools. Epic Bridges then processes incoming HL7 messages, checking content against expected values through Epic's integration engine before the data is incorporated into the EHR.

One of the main hurdles in the integration process involved automating the conversion of pharmacogenomic results into the proper standardized terminology required for entry into the EHR as discrete data. Manually performing this conversion is labor-intensive and prone to inconsistencies. For each gene, laboratories must report a genotype using star-allele notation, a corresponding predicted phenotype, and in some cases an activity score [9]. The phenotype—defined according to CPIC's star-allele system—classifies a patient's drug-metabolizing ability as Ultrarapid, Normal, Intermediate, or Poor [9]. Generating these designations often requires an extra interpretive step. Many laboratories rely on commercial tools like Allele Typer™ to translate raw variant data into star alleles, especially for genes with complicated architectures such as CYP2D6 [10].

To remove the need for third-party interpretation tools, a new workflow was designed using a Python-based pipeline capable of converting instrument-generated outputs directly into genotype and phenotype assignments. The system reads CSV files produced by the assay, offering enough flexibility to update or expand assay content when needed. The QS_Translator.csv file provides the information used by the Python script to classify each

probe as Normal, Heterozygous, or Mutant, simplifying the handling of nucleotide-level calls and allowing new assays to be incorporated with minimal effort. After this step, the PGX_Translator.csv file—containing probe definitions, assay identifiers, and all possible genotype outcomes—is used to determine the star-allele genotype. The script then generates phenotype assignments using the GT_PT_Translator.csv file, which includes phenotype categories, activity scores, interpretive comments, and instructions on whether results should trigger an abnormal flag in the EHR. The UF Health PMP team reviewed the terminology to ensure full alignment with CPIC's current recommendations [9].

All associated files are publicly available at https://github.com/UF-Health-Molecular-Pathology/PGX_HL7 and may be adapted to meet the needs of individual laboratories. Institutions should update the QS_Translator.csv with probe details specific to their assays, adjust PGX_Translator.csv to reflect their genotype definitions, and revise GT_PT_Translator.csv for institution-specific reporting requirements. Within the Python script, the gene_symbol_replacements function must be tailored to the genes included in each assay, and the append_OBX_segments function should be modified to match local Epic configuration for Long Read Report (LRR) and Variant (VAR) mapping.

Figure 1 summarizes the system architecture and outlines the pharmacogenomics (PGx) workflow. Elements shown in bold represent the newly automated steps enabled by the custom middleware, while components marked with dotted outlines and shaded hatching depict the former manual process. Steps that appear unchanged occur in both workflows. The process starts when a provider places and signs a PGx order in Epic, after which the patient sample is collected and tested. In the updated automated pathway, once the laboratory receives the specimen, an outgoing ancillary order (AIK8) is sent to Epic Bridges. This transmission carries the necessary patient and order details so that resulting can later be filed correctly. DNA extraction and TaqMan PCR are then performed, and the resulting data are reviewed before being exported for interpretation. Under the older manual approach (indicated by the grey dotted line), the exported data were uploaded into Allele Typer™ (Life Technologies) for genotype annotation. The interpreted results were printed and then entered into Beaker by hand for review. With the automated workflow, these steps are replaced by an internally developed Python script that analyzes the assay output and assigns genotype and phenotype results. The script formats the findings into HL7-compliant messages, aligns them with the original AIK8 order, generates an AIK7 results message, and automatically transmits it to Beaker through NextGen Connect and Epic Bridges. Both workflows ultimately meet at the same endpoint: a final review to confirm accuracy before the results are verified and uploaded to the patient's electronic chart.

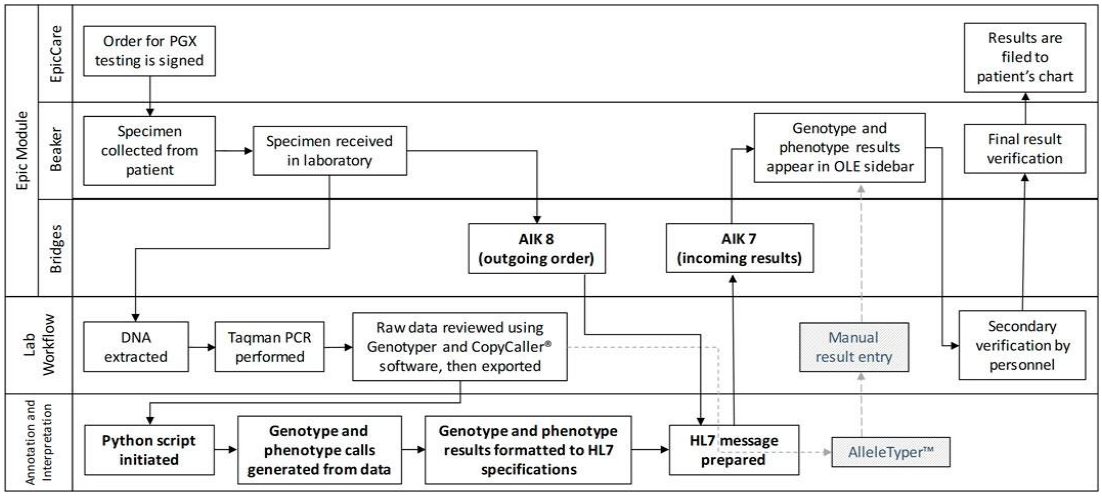


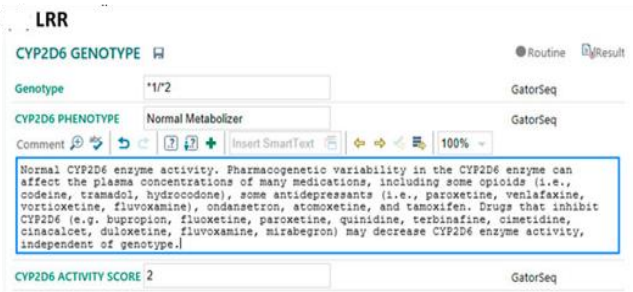
Figure 1. presents a Rummler–Brache diagram outlining the pharmacogenomics (PGx) workflow. Steps shown in bold denote the newly automated process supported by the custom middleware, whereas items outlined with dotted lines and shaded in grey reflect the former manual approach. All remaining components occur in both versions of the workflow.

Creating the genomic indicators required close collaboration among the PMP team, UFHPL, and UF Information Technology. The PMP group reviewed CPIC guidance to ensure alignment with current recommendations and drafted the explanatory text that clinicians and patients see for each gene. UFHPL produced the VAR records, which supply the structured variant data on which the indicators rely. UF IT then connected these indicators to

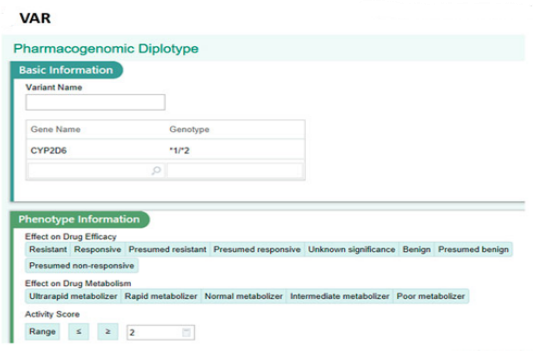
the VAR database using Epic's PGx Turbocharger package—a collection of clinical decision support (CDS) tools, translation logic, indicator definitions, provider-facing descriptions, and medication-interaction content. Although the package includes support for all CPIC Level A gene–drug pairs, the implementation focused on only a portion of them and required significant refinement of Epic's default translation logic. Epic's translation logic includes two main elements: (1) mapping tables that link specific genotypes to their associated phenotypes—customized here to reflect only the SNPs tested by UFHPL—and (2) rules that use these tables to determine when an indicator should be added to a patient's chart. For instance, if a patient's CYP2C19 genotype corresponds to an intermediate metabolizer phenotype, the appropriate indicator is assigned automatically. The logic was extended so that it would also apply to older results that were entered before the Genomics Module was deployed, using LRR components. A specialized utility processed these historical results to populate indicators retrospectively. Working with PMP experts, further refinements were made for select variants where the available evidence diverged somewhat from CPIC's recommendations. The CDS framework was also updated so that rules evaluate genomic indicators rather than older-style discrete result components, and existing CDS messages were revised to pull content from the standardized text built for the indicators. With these enhancements, genomic indicators now activate PGx-specific CDS and simplify the maintenance and oversight of precision-medicine workflows within the EHR.

Results and Discussion

When integrating the Genomics Module into clinical workflows, it is essential to recognize the differences in how data are stored within Epic for Clinical Pathology (CP) versus the Genomics Module. CP results are maintained in the LRR (Long Read Report) database, where each individual result component must have its own discrete record. This approach provides highly granular data but generates a large number of records for each test. For example, as illustrated in **Figure 2a**, CYP2D6 results in LRR are recorded separately for each attribute, such as genotype, phenotype, and activity score. By contrast, the Genomics Module stores results in the VAR (variant) database, which consolidates each type of result into a single set of records. This approach streamlines both data storage and retrieval. **Figure 2b** demonstrates that in the Genomics Module, result components are not tied to individual genes, so it is unnecessary to create a separate record for each gene–result combination. **Figure 2c** provides a comparison of the result components required for the same gene panel in LRR versus VAR, highlighting the simplified structure of VAR.



a)



b)

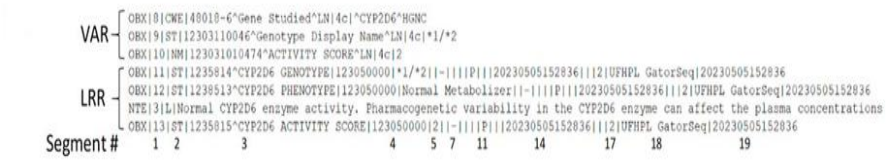
LRR and VAR Component Mapping

Result Type	Component	Mapping
LRR	CYP2C Cluster Genotype	1235884
	CYP2C19 Genotype	1235856
	CYP2C19 Phenotype	123859
	CYP2C9 Genotype	1235870
	CYP2C9 Phenotype	1235872
	CYP2C9 Activity Score	12358722
	CYP2D6 Genotype	1235814
	CYP2D6 Phenotype	1238513
	CYP2D6 Activity Score	1235815
	CYP3A5 Genotype	1235875
	CYP3A5 Phenotype	1235876
	CYP4F2 Genotype	9865
	SLCO1B1 Genotype	1235882
	SLCO1B1 Phenotype	1235883
	VKORC1 Genotype	1235886
VAR	Gene Studied	48018-6
	Genotype Display Name	12303110046
	Activity Score	123031010474

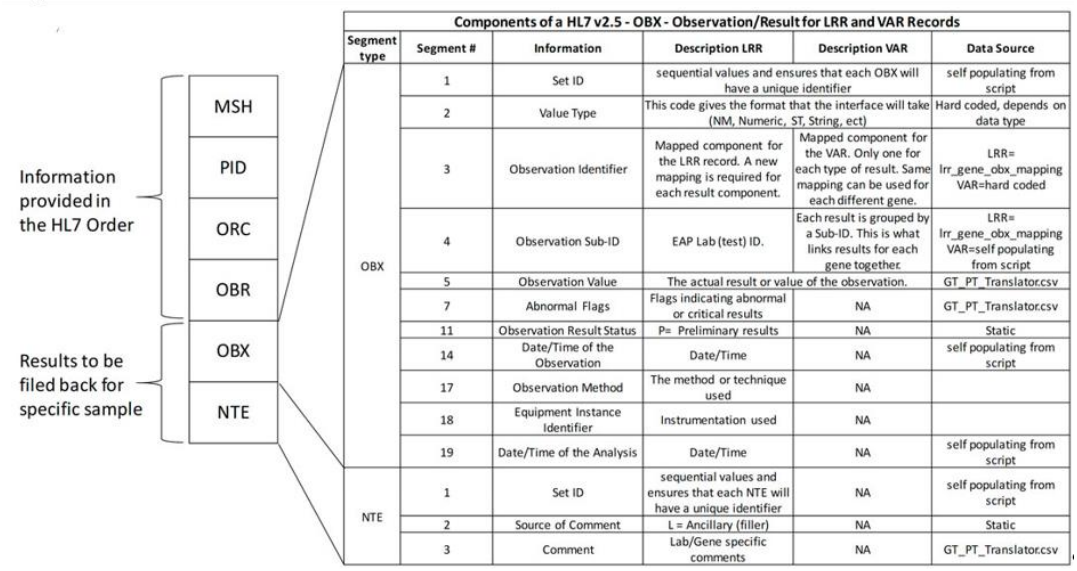
c)

Figure 2. illustrates the result entry interfaces and component mapping: (a) shows the Beaker Clinical Pathology (CP) screen for Long Read Report (LRR) results, (b) displays the Beaker Genomics Module interface for Variant (VAR) results, and (c) compares the required components for LRR versus VAR result types.

During the initial rollout of the Genomics Module, both LRR and VAR data were included in the results to address usability considerations. While the VAR view provides a comprehensive genomic perspective, it is not fully integrated into the results review tab, where clinicians are accustomed to accessing LRR results. Including both data types ensured continuity, offering a more complete and user-friendly presentation of genomic findings. HL7 messaging was used to transmit these results efficiently. **Figure 3a** shows a sample HL7 message for CYP2D6 that contains both VAR and LRR components within OBX and NTE segments. Each segment is broken into fields, separated by the pipe (|) symbol. **Figure 3b** details the specific OBX and NTE components for both result types. A Python script generates the HL7 message, populating each segment to ensure accurate representation. For example, OBX-1 (Set ID) provides a unique identifier for each OBX segment, automatically generated by the script. OBX-2 (Value Type) is hard-coded to indicate the data format. OBX-3 (Observation Identifier) maps each LRR result individually, while VAR requires only a single mapping per result type that can apply across multiple genes. OBX-4 (Observation Sub-ID) stores the EAP Lab test ID for organizing gene-specific results, and OBX-5 (Observation Value) contains the actual results, pulled from GT_PT_Translator.csv. OBX-7 (Abnormal Flags) identifies abnormal or critical results, also sourced from GT_PT_Translator.csv, and additional fields such as OBX-11 (Observation Result Status) and timestamps are handled by the script. The NTE segment provides a structured way to include lab-specific comments, ensuring that all relevant information is captured and clearly presented.



a)



Components of a HL7 v2.5 - OBX - Observation/Result for LRR and VAR Records

Segment type	Segment #	Information	Description LRR	Description VAR	Data Source
OBX	1	Set ID	sequential values and ensures that each OBX will have a unique identifier		self populating from script
	2	Value Type	This code gives the format that the interface will take (NM, Numeric, ST, String, ect)		Hard coded, depends on data type
	3	Observation Identifier	Mapped component for the LRR record. A new mapping is required for each result component.	Mapped component for the VAR. Only one for each type of result. Same mapping can be used for each different gene.	LRR= lrr_gene_obx_mapping VAR=hard coded
	4	Observation Sub-ID	EAP Lab (test) ID.	Each result is grouped by a Sub-ID. This is what links results for each gene together.	LRR= lrr_gene_obx_mapping VAR=self populating from script
	5	Observation Value	The actual result or value of the observation.		GT_PT_Translator.csv
	7	Abnormal Flags	Flags indicating abnormal or critical results	NA	GT_PT_Translator.csv
	11	Observation Result Status	P= Preliminary results	NA	Static
	14	Date/Time of the Observation	Date/Time	NA	self populating from script
	17	Observation Method	The method or technique used	NA	
	18	Equipment Instance Identifier	Instrumentation used	NA	
	19	Date/Time of the Analysis	Date/Time	NA	self populating from script
NTE	1	Set ID	sequential values and ensures that each NTE will have a unique identifier	NA	self populating from script
	2	Source of Comment	L = Ancillary (filler)	NA	Static
	3	Comment	Lab/Gene specific comments	NA	GT_PT_Translator.csv

b)

Figure 3. depicts HL7 messaging for transmitting genomic data. Panel (a) shows a portion of an HL7 message for CYP2D6, containing both Variant (VAR) and Long Read Report (LRR) results represented in Observation (OBX) and Notes (NTE) segments. The segments are divided into specific fields, separated by the pipe (|) character, with numbered segments corresponding to the detailed layout shown in panel (b). Panel (B) provides an in-depth view of the OBX and NTE segments, highlighting the components for LRR and VAR records and showing how the Python script populates each field in the HL7 message.

After the HL7 message is generated, the data are exported into two output formats: HL7 and PDF. The PDF serves as a tool for internal laboratory review and documentation control. As shown in **Figure 4**, the PDF contains complete genotype and phenotype information, along with individual sample calls, allowing laboratory technologists to easily review and verify results. Each PDF also includes the generation date and the original file names used to produce the data, ensuring traceability and transparency. This dual-output approach helps maintain data integrity while supporting streamlined and efficient clinical workflows.

PGX TaqMan Genotype and Phenotype Result Review

07_25_2023_15_53_11

['CN GPGX-QS-23-52 Results.csv', 'GPGX-QS-23-52_20230613_120247_Export.csv']

	Sample_ID	Gene_Symbol	Genotype	Phenotype	Activity_Score
366	100072135	CYP2C Cluster	G/G	Report Genotype Only	NA
3	100072135	CYP2C19	*1/*1	Normal Metabolizer	NA
297	100072135	CYP2C9	*2/*3	Poor Metabolizer	0.5
90	100072135	CYP2D6	*1/*4	Intermediate Metabolizer	1
248	100072135	CYP3A5	*1/*3	Intermediate Metabolizer	NA
378	100072135	CYP4F2	*1/*3	Report Genotype Only	NA
280	100072135	SLCO1B1	*1/*5	Decreased Function	NA
385	100072135	VKORC1	G/A	Report Genotype Only	NA

	Sample_ID	Assay_ID	Probe_Information	Gene Symbol	if_Call	Then_convert	Genotype	Phenotype	Activity_Score
366	100072135	C__31983399_10	CYP2C rs12777823 (WT=G MUT=A)	CYP2C Cluster	G/G	WT	G/G	Report Genotype Only	NA
3	100072135	C__25986767_70	CYP2C19*2_c.681G>A (WT=G MUT=A)	CYP2C19	G/G	WT	*1/*1	Normal Metabolizer	NA
46	100072135	C__27531918_10	CYP2C19*6_c.395G>A (WT=G MUT=A)	CYP2C19	G/G	WT	*1/*1	Normal Metabolizer	NA
15	100072135	C__27861809_10	CYP2C19*3_c.636G>A (WT=G MUT=A)	CYP2C19	G/G	WT	*1/*1	Normal Metabolizer	NA
77	100072135	C__30634128_10	CYP2C19*10_g.C>T (WT=C MUT=T)	CYP2C19	C/C	WT	*1/*1	Normal Metabolizer	NA
53	100072135	C__30634130_30	CYP2C19*8_c.358T>C (WT=T MUT=C)	CYP2C19	T/T	WT	*1/*1	Normal Metabolizer	NA
31	100072135	C__30634136_10	CYP2C19*4_c.1A>G (WT=A MUT=G)	CYP2C19	A/A	WT	*1/*1	Normal Metabolizer	NA
66	100072135	C___469857_10	CYP2C19*17_g.-806C>T (WT=C MUT=T)	CYP2C19	C/C	WT	*1/*1	Normal Metabolizer	NA
345	100072135	C__25625804_10	CYP2C9*8 (WT=G MUT=A)	CYP2C9	G/G	WT	*2/*3	Poor Metabolizer	0.5
297	100072135	C__25625805_10	CYP2C9*2 (WT=C MUT=T)	CYP2C9	C/T	HET	*2/*3	Poor Metabolizer	0.5
306	100072135	C__27104892_10	CYP2C9*3 (WT=A MUT=C)	CYP2C9	C/A	HET	*2/*3	Poor Metabolizer	0.5
316	100072135	C__27859817_40	CYP2C9*5 (WT=C MUT=G)	CYP2C9	C/C	WT	*2/*3	Poor Metabolizer	0.5
353	100072135	C__30634132_70	CYP2C9*11 (WT=C MUT=T)	CYP2C9	C/C	WT	*2/*3	Poor Metabolizer	0.5
331	100072135	C__32287221_20	CYP2C9*6 (WT=A MUT=-)[]	CYP2C9	A/A	WT	*2/*3	Poor Metabolizer	0.5
234	100072135	C_30634117C_K0	CYP2D6*8; 1758G>T; (WT=C MUT=A)	CYP2D6	C/C	WT	*1/*4	Intermediate Metabolizer	1
113	100072135	C__11484460_40	CYP2D6 (*4 and *10) 100C>T (WT=G MUT=A)	CYP2D6	A/G	HET	*1/*4	Intermediate Metabolizer	1
121	100072135	C__27102414_10	CYP2D6 4180G>C (WT=C MUT=G)	CYP2D6	C/G	HET	*1/*4	Intermediate Metabolizer	1
132	100072135	C__27102425_10	CYP2D6 2850C>T (WT=G MUT=A)[]	CYP2D6	G/G	WT	*1/*4	Intermediate Metabolizer	1
155	100072135	C__27102431_D0	CYP2D6*4; 1846G>A; (WT=C MUT=T)[]	CYP2D6	C/T	HET	*1/*4	Intermediate Metabolizer	1
161	100072135	C__32388575_A0	CYP2D6*7; 2935A>C; (WT=T MUT=G)[]	CYP2D6	T/T	WT	*1/*4	Intermediate Metabolizer	1
178	100072135	C__32407229_60	CYP2D6*9; 2615_2617delAAG; (WT=TCT MUT=-)	CYP2D6	TCT/TCT	WT	*1/*4	Intermediate Metabolizer	1
190	100072135	C__32407232_50	CYP2D6*3; 2549delA; (WT=T MUT=-)	CYP2D6	T/T	WT	*1/*4	Intermediate Metabolizer	1
197	100072135	C__32407243_20	CYP2D6*6; 1707delT; (WT=A MUT=-)	CYP2D6	A/A	WT	*1/*4	Intermediate Metabolizer	1
206	100072135	C__34816113_20	CYP2D6*29; 3183G>A; (WT=C MUT=T)	CYP2D6	C/C	WT	*1/*4	Intermediate Metabolizer	1
216	100072135	C__34816116_20	CYP2D6*41; 2988G>A; (WT=C MUT=T)	CYP2D6	C/C	WT	*1/*4	Intermediate Metabolizer	1
103	100072135	C___2222771_A0	CYP2D6*17; 1023C>T; (WT=G MUT=A)	CYP2D6	G/G	WT	*1/*4	Intermediate Metabolizer	1
90	100072135	Hs00010001_cn	CYP2D6_ex9 (Copy Number)	CYP2D6		2.0	*1/*4	Intermediate Metabolizer	1
248	100072135	C__26201809_30	CYP3A5*3 (WT=T MUT=C)	CYP3A5	T/C	HET	*1/*3	Intermediate Metabolizer	NA
257	100072135	C__30203950_10	CYP3A5*6 (WT=C MUT=T)	CYP3A5	C/C	WT	*1/*3	Intermediate Metabolizer	NA
272	100072135	C__32287188_10	CYP3A5*7 (WT=- MUT=A)	CYP3A5	-/-	WT	*1/*3	Intermediate Metabolizer	NA
378	100072135	C__16179493_40	CYP4F2 c.1297C>T; (WT=C MUT=T)	CYP4F2	C/T	HET	*1/*3	Report Genotype Only	NA
280	100072135	C__30633906_10	SLCO1B1*5 c.521T>C; (WT=T MUT=C)	SLCO1B1	C/T	HET	*1/*5	Decreased Function	NA
385	100072135	C__30403261_20	VKORC1-1639G>A; (WT=C MUT=T)	VKORC1	C/T	HET	G/A	Report Genotype Only	NA

Figure 4. displays the PDF output generated during data processing. This PDF provides a preliminary review of the data prior to its integration into the Electronic Health Record (EHR), offering a complete overview of genotype and phenotype information along with individual sample calls.

Figure 5 illustrates how the data are visualized within the EHR. Panel (a) shows results stored in the standard Clinical Pathology (CP) LRR database, presented in the Results Review tab. This traditional view is static, lacks interactivity, and does not display genomic indicators or associated drug information. By contrast, the Genomics Module presents a more interactive and user-friendly interface for interpreting complex genomic data. Panel (b) demonstrates VAR results within the Genomics Module, highlighting its enhanced usability. Panel (c) shows how these results link directly to genomic indicators, giving clinicians quick access to relevant genomic insights. The PGx genomic indicators provide several key functions, including interpretation text tailored for both providers and patients, alerts for potential drug–gene interactions with actionable recommendations, and links to the corresponding laboratory results. By integrating these indicators into the Genomics Module, clinicians can more efficiently review and utilize genomic information, supporting informed clinical decision-making and improving the workflow for precision medicine.

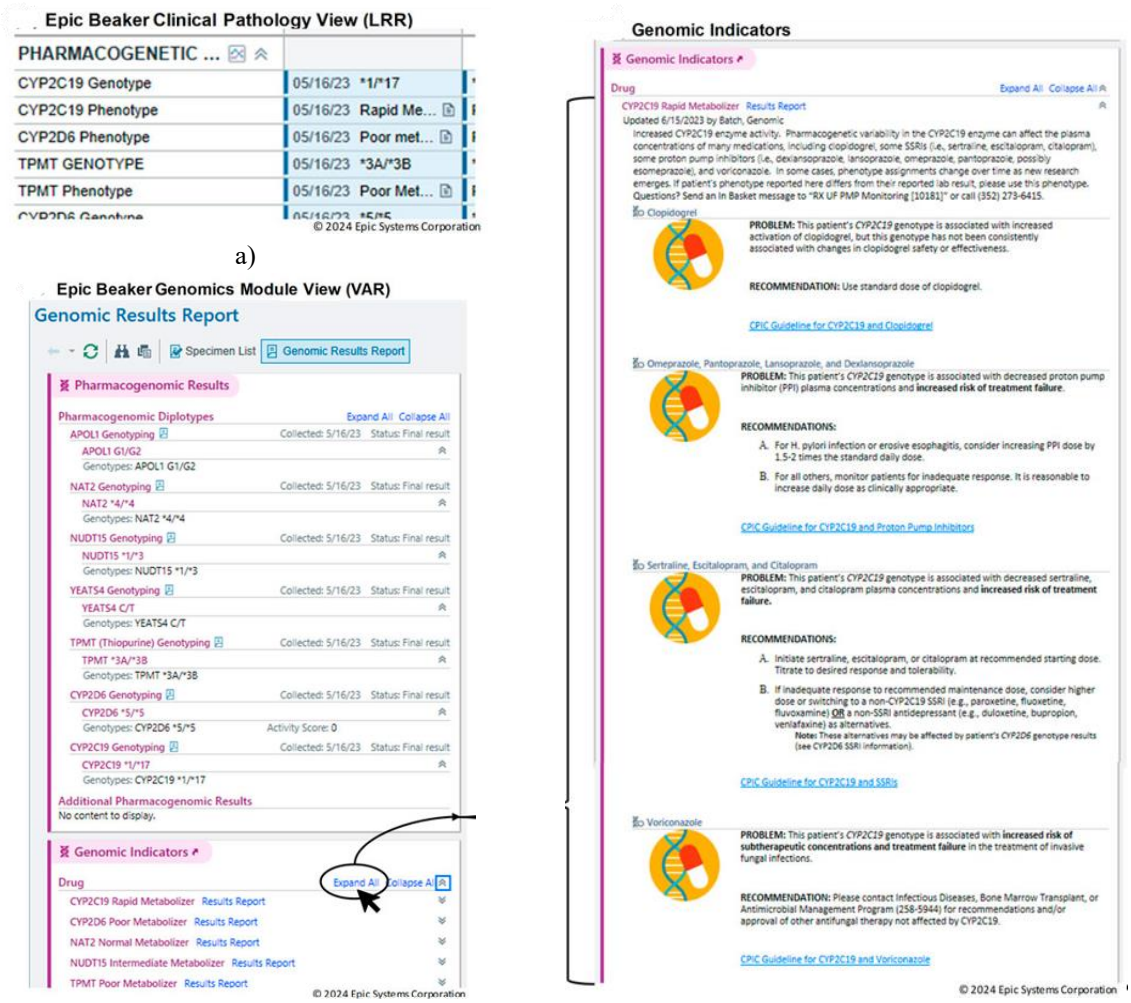


Figure 5. illustrates how genomic data are visualized in the Electronic Health Record (EHR). Panel (a) shows results from the standard Clinical Pathology (CP) Long Read Report (LRR) database in the Results Review tab, while panel (b) presents Variant (VAR) results from the Genomics Module. Panel (c) highlights the connection from the Genomics Module results to genomic indicators, enabling clinicians to access key genomic information directly.

Clinical decision support (CDS) is a central component of personalized medicine, providing clinicians with timely, patient-specific alerts to guide therapeutic decisions [4]. **Figure 6** provides an example, showing a CDS alert for a CYP2C19 Poor metabolizer. By default, the alert suggests removing a clopidogrel order, but providers have the option to override it or dismiss the alert entirely. With the integration of the Genomics Module into clinical workflows, legacy CDS rules were redesigned to use genomic indicators as the primary triggers. Previously, alerts relied on LRR genotype or phenotype results, which met basic PGx-CDS needs but had key limitations. This

earlier approach could not easily handle complex scenarios, such as variable activity scores (e.g., CYP2D6 or CYP2C9) or updated guideline recommendations. Additionally, maintaining these rules was cumbersome because every possible genotype had to be accounted for. The adoption of genomic indicators as CDS triggers addressed these challenges. By the end of 2023, over 11,000 patient results had been converted to VAR format, involving the creation of 50 unique genomic indicators and the transformation of 50 CDS rules to the new format. Comparing the year before and the year after implementation, there was a 112% increase in provider interaction with alerts, rising from 1,518 to 3,218 alerts acted upon. This demonstrates the enhanced effectiveness and clinical utility of the updated system.

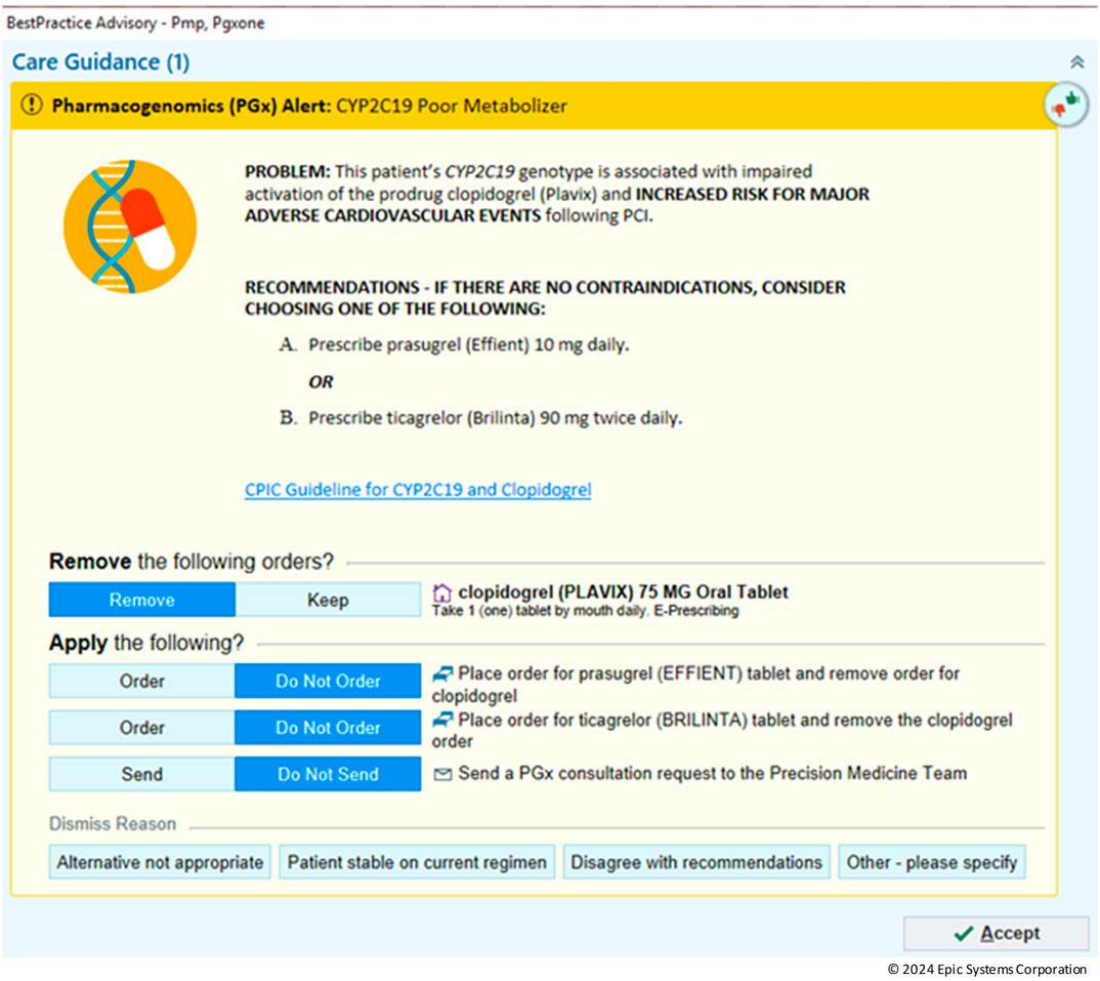


Figure 6. Example clinical decision support (CDS) alert.

The implementation of the Genomics Module, driven by Health Informatics strategies and collaborative efforts across multiple teams, has markedly improved the clinical delivery of pharmacogenomic (PGx) data. The impact of this initiative can be observed across three major areas. First, integration efficiency was greatly enhanced, enabling PGx data and automated workflows to be incorporated into the existing EHR system. This reduced the need for manual data entry and, as a result, improved overall data accuracy. Second, clinical decision support (CDS) was strengthened through the complete migration of both legacy and new PGx-CDS alerts to a framework based on genomic indicators, making the alerts more reliable and actionable. Third, there was increased adoption among users, reflected by the more effective delivery of comprehensive PGx information to providers and a measurable rise in both awareness and utilization of PGx results in clinical practice. Together, these outcomes highlight the successful deployment of the Genomics Module and its positive effect on PGx data management and clinical application.

Although other efforts have explored the integration of Genomics Modules into healthcare systems, this project addresses a central challenge in genomic implementation: automation coupled with adherence to HL7 standards [11]. Similar to Caraballo *et al*., this approach involved creating discrete genetic results, designing CDS rules, and embedding genomic data into EHR workflows. However, the current project extends beyond previous work by

offering a detailed technical roadmap for healthcare organizations seeking to implement or optimize genomic data management. It provides a comprehensive overview of the critical technical components required for successful integration, including the underlying data structures and system architectures that support genomic workflows. The emphasis on HL7-based automation is particularly significant, addressing the increasing need for accurate and efficient management of large-scale genomic data in modern clinical settings.

The adoption of HL7 standards greatly enhances the scalability and reproducibility of genomic data workflows [12, 13]. By applying health informatics principles, a streamlined solution was developed to simplify the interpretation of pharmacogenomic (PGx) data and produce standardized outputs in HL7 format compatible with Epic's Genomics Module. Detailed documentation and source code for implementing the Genomics Module and improving PGx management are available as an open-source resource on GitHub (https://github.com/UF-Health-Molecular-Pathology/PGX_HL7.git). This repository includes comprehensive guidance on the integration process, from analyzing PGx TaqMan Genotyping data from QuantStudio instruments to HL7-based communication between laboratory devices and the EHR.

Overall, the Genomics Module addresses many of the limitations associated with traditional PDF-based genetic reporting [11]. It consolidates scattered genomic information, giving healthcare providers a unified view of all genetic results, including PGx, germline, and somatic variants. Specifically for PGx, the module automatically interprets results and applies genomic indicators directly to the patient's record, providing clinicians with actionable, guideline-informed recommendations. This functionality not only streamlines the interpretation of complex genetic data but also enhances the precision and personalization of patient care. By offering a comprehensive overview of a patient's genomic profile, the Genomics Module supports informed clinical decision-making and contributes to the broader goals of personalized medicine. In this way, it equips providers with a powerful tool to integrate genomic insights into routine care, advancing the role of genetics in clinical practice [14].

Limitations

The implementation of precision medicine using the Genomics Module has faced several notable challenges: Integration with third-party instruments: While HL7 standards facilitate the incorporation of genomic results, connecting devices that do not have a direct interface with Epic—often requiring middleware such as Data Innovations—remains complex. In cases where this integration cannot be completed, results and genomic indicators may need to be manually entered to fully leverage the module's capabilities. Activity score interpretation: Currently, the ability to generate rules for translating genotype-derived activity scores is limited to UFHPL. Although genomic indicators can report and interpret these scores, they cannot directly derive them from alleles or duplications. Upcoming Epic updates are expected to allow healthcare providers and IT teams to create their own activity score rules, extending customization beyond the laboratory setting. Presentation of complex gene-drug interactions: The current layout of genomic indicators does not easily support medications influenced by multiple genetic variants. For example, sertraline is affected by both CYP2C19 and CYP2B6 variants, yet relevant information is distributed across separate indicators, requiring users to navigate multiple sections. Similarly, thiopurine drugs such as thioguanine, azathioprine, and mercaptopurine are impacted by both TPMT and NUDT15 genes, but their data are not consolidated. A more effective approach could involve organizing indicators by medication rather than by gene or implementing dynamic alerts that assess multiple gene-drug interactions simultaneously to improve usability. Phenoconversion considerations: The module does not fully account for phenoconversion, which occurs when drug-drug interactions inhibit or induce CYP enzyme activity, potentially altering a patient's metabolizer status. This limitation is largely due to the accuracy and completeness of active medication data in patient profiles rather than the module itself. Currently, clinicians rely on patient-specific consultation notes to address potential phenoconversion. These challenges highlight areas for future enhancements to increase the Genomics Module's utility in precision medicine. Potential improvements include better integration of third-party results, more effective categorization of results, expanded activity score reporting, optimized presentation of complex gene-drug interactions, and more comprehensive management of phenoconversion scenarios.

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