Planning for CPIC Database content, functionality, API

Listening Sessions

CPIC Informatics Call 11/27/18

CPIC Call 12/6/18

Developing new tools to expand and customize use of CPIC guidelines

- Make guidelines more computable
  - Implementation resources available on www.cpicpgx.org
  - Database for implementation resources
  - Application Programming Interface (API)
- Will enable use of CPIC knowledge in new ways across a broad potential user community

The established CPIC implementation resources provide a foundation for these new tools

- CPIC Informatics work group lead the development of resources that accompany each guideline
  - First set of resources published in 2014 (abacavir/HLA guideline update)
- Comprehensive translation tables from genotype to phenotype to clinical recommendation is one unique resource

CPIC™
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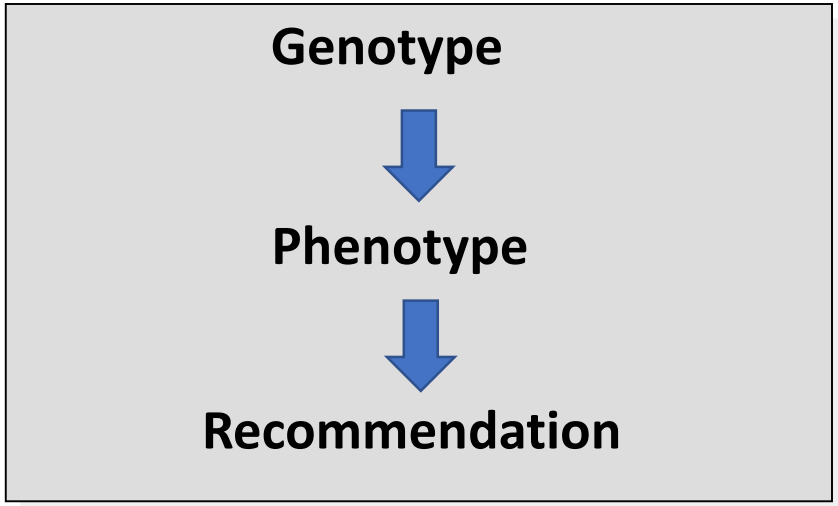

Developing knowledge resources to support precision medicine: principles from the Clinical Pharmacogenetics Implementation Consortium (CPIC)

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ABSTRACT

To move beyond a select few genes/drugs, the successful adoption of pharmacogenomics into routine clinical care requires a curated and machine-readable database of pharmacogenomic knowledge suitable for use in an electronic health record (EHR) with clinical decision support (CDS). Recognizing that EHR vendors do not yet provide a standard set of CDS functions for pharmacogenetics, the Clinical Pharmacogenetics Implementation Consortium (CPIC) Informatics Working Group is developing and systematically incorporating a set of EHR-agnostic implementation resources into all CPIC guidelines. These resources illustrate how to integrate pharmacogenomic test results in clinical information systems with CDS to facilitate the use of patient genomic data at the point of care. Based on our collective experience creating existing CPIC resources and implementing pharmacogenomics at our practice sites, we outline principles to define the key features of future knowledge bases and discuss the importance of these knowledge resources for pharmacogenomics and ultimately precision medicine.

Keywords: pharmacogenetics, knowledge bases, electronic health records, clinical decision support systems, precision medicine

Guideline for Tricyclic Antidepressants and CYP2D6 and CYP2C19

CPIC has updated the 2013 guideline for tricyclic antidepressants and *CYP2D6* and *CYP2C19* . See Tables 2, 3, and 4 of the guideline for updated recommendations.

Update (December 2016)

- Clinical Pharmacogenetics Implementation Consortium Guideline (CPIC®) for *CYP2D6* and *CYP2C19* Genotypes and Dosing of Tricyclic Antidepressants: 2016 Update

Supplemental tables:

Table provided with publication

- 2016 Supplement
- Drug Resource Mapping
  - Amitriptyline
  - Clomipramine
  - Desipramine
  - Doxepin
  - Imipramine
  - Nortriptyline
  - Trimipramine
- Amitriptyline Pre- and Post-test Alerts and Flow Chart
- Nortriptyline Pre- and Post-test Alerts and Flow Chart

CPIC Gene-specific Information Tables

These resources support CPIC guidelines by providing information regarding star (*) allele definitions, allele function, allele frequency by major ethnic groups, translations of diplotype to phenotype, example EHR consultation (genetic test interpretation) and gene resource mappings.

Table 1: Description and intended use of the implementation resources in the CPIC Guideline and Supplement[a]

Name of Table in CPIC Guideline	Description	Intended Use
Translation of genotype test result into interpreted phenotype	Provides a crosswalk from genotype to interpreted phenotype. Includes diplotype in star allele nomenclature (if applicable).	Translates a laboratory result into a more clinically meaningful result. Phenotypes are helpful as discrete results in the EHR because they provide clinical context and can reduce the complexity needed in CDS rules.
Resources that demonstrate the genotypes that constitute the * alleles for gene X and their effect on X protein	Provides a crosswalk between pharmacogene star allele nomenclature, dbSNP identifier (rsID), variant nucleotide change, allele effect on protein.	Useful when evaluating limited published evidence to determine a potential phenotype and clinical recommendation.
Drugs that pertain to this guideline	Contains a list of the drugs covered in the guideline, referencing codes from standard terminologies (eg, RxNorm, DrugBank, ATC) and related databases (eg, PharmGKB).	Provides an unambiguous list of drugs that can be leveraged when creating CDS rules, using codes that are common in prescribing and pharmacy systems.
Genes that pertain to this guideline	Contains a list of genes covered in the guideline, referencing codes from standard nomenclatures and knowledge bases (eg, HGNC, NCBI, Ensembl, PharmGKB).	Useful when creating CDS rules; uses codes that can be cross-referenced to lab test results and used to look up data in knowledge databases.
Clinical implementation workflow for EHR	Contains the steps and decision flows needed to position a pharmacogenetic result in the EHR when a systematic CDS program is implemented.	Combine this workflow with the pharmacogenetic genotype/phenotype summary entries for appropriate results reporting. This workflow highlights where clinical care needs to be implemented for actionable results.[b]
Pharmacogenetic genotype/phenotype summary entries	Identifies required data to couple genetic result with an interpretation, including genotype, phenotype, EHR priority result notation, and example interpretation text.	Useful when reporting a genomic result to help clinicians understand the clinical relevance of genotype or phenotype information. It is important to have clinician input on the wording for these interpretations.
Point-of-care clinical decision support (table)	Describes the trigger conditions and example text for interruptive CDS alerts.	Useful when building the rules for interruptive CDS alerts. It is important to have clinician input on the final wording of these alerts.
Point-of-care clinical decision support (workflow)	Describes the evaluation criteria and decision flow needed to build rules for interruptive CDS alerts.	This workflow is combined with the point-of-care clinical decision support table to build interruptive CDS alerts. It should be customized to fit into local clinical workflows

[a]CPIC Guideline and Supplement are available at https://cpicpgx.org/guidelines/. An example of tables can be found here: https://www.pharmgkb.org/guideline/PA166105005.
[b]An actionable result is any result where a patient with that result and being prescribed a corresponding drug prompts a recommendation for a change in therapy. Also known as "priority" results in some settings.

Hoffman JM et al. *J Am Med Inform Assoc.* 2016 https://cpicpgx.org/guidelines/

Examples of potential use cases

Retrieve a summary of the drugs and genes that are associated with a CPIC guideline

- Uses the standard nomenclatures already in CPIC guidelines (e.g. RxNorm for medications and HGNC for genes)

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Filter available drug/gene information to specific local needs

- CPIC guideline may include information on 7 tricyclic antidepressants, but users may only want to download applicable information (e.g. CDS language) for the drugs on the hospital's formulary
- Further, show recommendations based on one gene (e.g. *CYP2D6)* for an antidepressant – not the second gene (e.g. *CYP2C19)* for which testing is not yet available at the site

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Retrieve all drugs with CPIC guidelines and return a summary of all actionable diplotype/phenotype data with the corresponding CDS alert language

- These data would be used on an ongoing basis
- This data may be sent to different applications and/or users

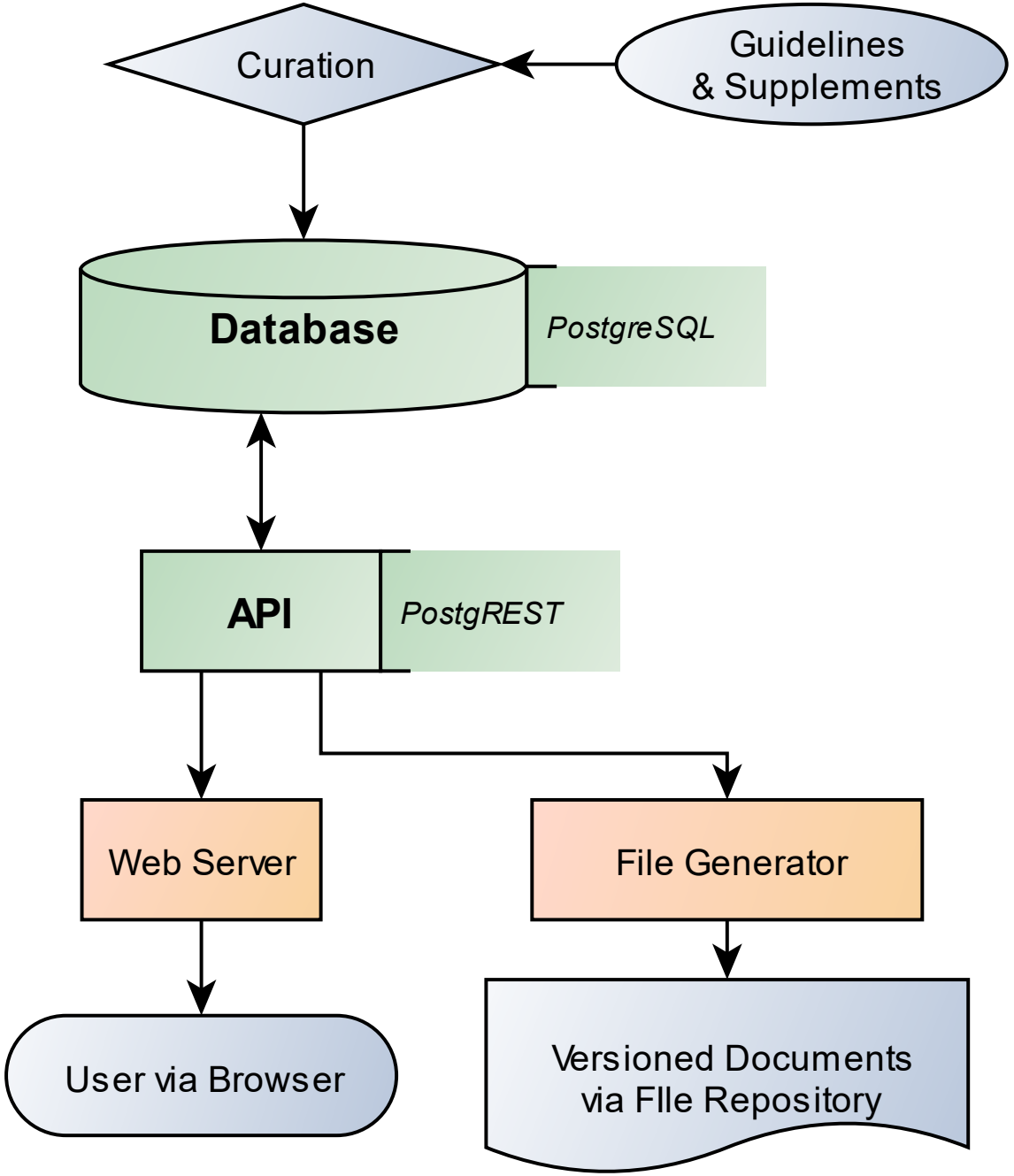
Query Examples

/diplotype_view?genesymbol=eq.UGT1A1&diplotype=eq.*27/*80


```
[
  {
    "genesymbol": "UGT1A1",
    "diplotype": "*27/*80",
    "phenotype": "Poor metabolizer",
    "ehrpriority": "Abnormal/Priority/High Risk",
    "consultationtext": "This result signifies that the patient has two copies of decreased function alleles (*_ and *_). Based on the genotype result this patient is predicted to be a poor metabolizer of UGT1A1 substrates. This patient may be at risk for an adverse or poor response to medications that inhibit or are inactivated by UGT1A1. Based on the genotype result, this patient is predicted to have low UGT1A1 function, which is generally indicative of Gilbert syndrome. This patient may be at high risk for toxicity from select medications that inhibit or are inactivated by UGT1A1. Please consult a clinical pharmacist for more information about how UGT1A1 metabolic status influences drug selection and dosing.",
    "activityscore": null
  }
]
```

/recommendation?genotypes=cs.”UGT1A1:Poor metabolizer”


```
[
  {
    "id": 104158,
    "guidelineid": 100034,
    "drugid": "RxNorm:343047",
    "implications": "Markedly decreased UGT1A1 activity; high likelihood of bilirubin-related discontinuation of atazanavir.",
    "drug_recommendation": "Consider an alternative agent particularly where jaundice would be of concern to the patient.\r\nIf atazanavir is to be prescribed, there is a high likelihood of developing jaundice that will result in atazanavir discontinuation (at least 20% and as high as 60%).",
    "classification": "Strong",
    "genotypes": [
      "UGT1A1:Poor metabolizer"
    ],
    "drug": {
      "name": "atazanavir"
    },
    "guideline": {
      "name": "CPIC Guideline for atazanavir and UGT1A1"
    }
  }
]
```


Curation
Guidelines
& Supplements
Database
PostgreSQL
API
PostgREST
Web Server
File Generator
User via Browser
Versioned Documents
via FIle Repository

Feedback: Questions to guide discussion

- How do you anticipate you would use the CPIC database/API?
- Of the existing CPIC implementation resources, what is the top priority to build in the database?
- What support or guidance would you need to use the CPIC database/API?
- How should the CPIC guideline development process change to support these new resources?

Next steps

- Evaluate feedback from both listening sessions and determine where additional information may be needed
- Additional review with CPIC leadership and steering committee
- Ongoing progress reports on CPIC Informatics calls with routine updates to all of CPIC