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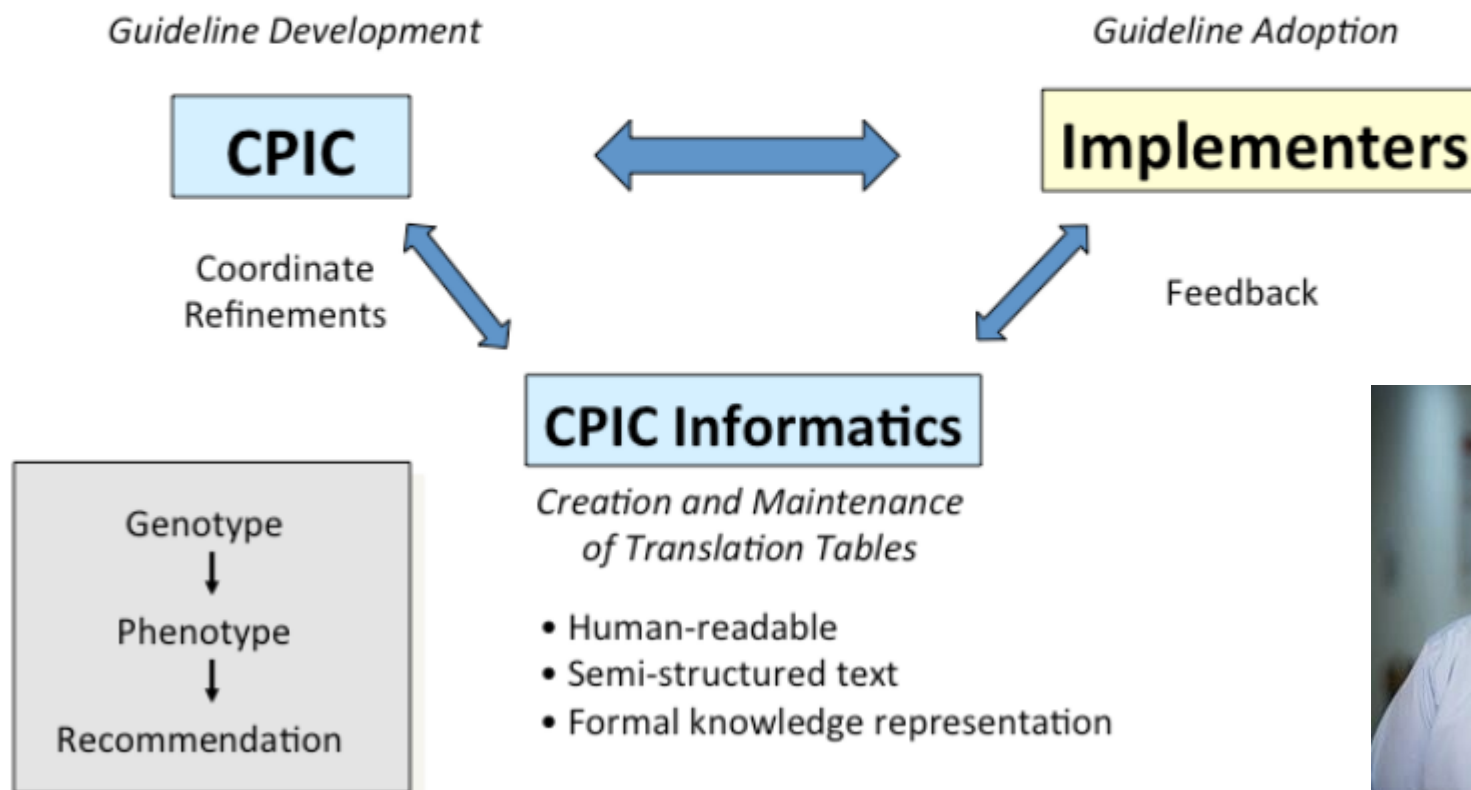


Ryan Whaley



Mark Woon

CPIC Informatics: Supporting Guideline Implementation

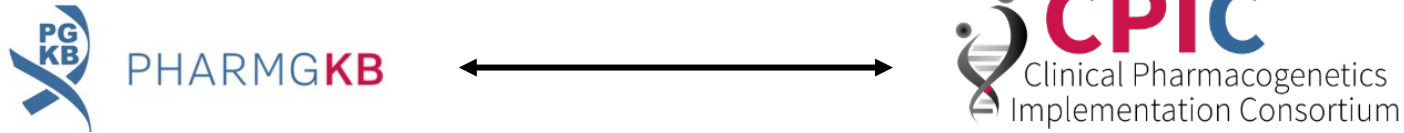


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CPIC was formed in 2009 to provide freely available, evidence-based, and updated PGx clinical practice guidelines



2000

2009

2023



730 members (clinicians and scientists)



32 guidelines (and counting!)



523 institutions



29 genes

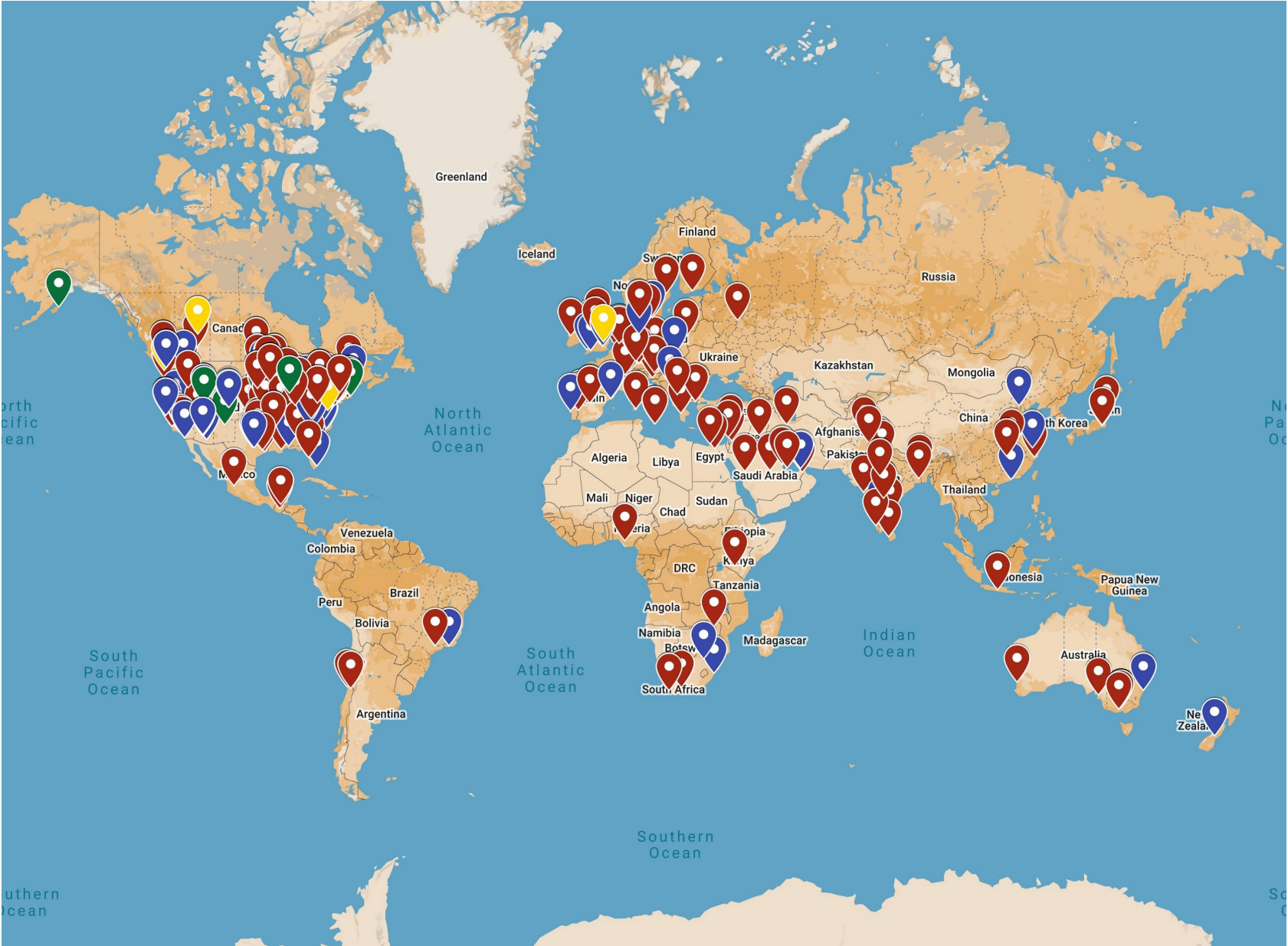


49 countries



>150 drugs

CPIC is a global organization



28 guidelines; 32 genes and >150drugs



- *TPMT, NUDT15*
 - MP, TG, azathioprine
- *CYP2D6*
 - Codeine, tramadol, hydrocodone, TCAs, tamoxifen, SSRIs, ondansetron, tropisetron, atomoxetine, metoprolol
- *CYP2C19*
 - TCAs, clopidogrel, voriconazole, SSRIs, PPIs
- *VKORC1*
 - Warfarin
- *CYP2C9*
 - Warfarin, phenytoin, NSAIDs, fluvastatin
- *CYP4F2*
 - Warfarin
- *CYP2C8*
 - NSAIDs
- *HLA-B*
 - Allopurinol, CBZ, Oxcarbazepine, abacavir, phenytoin
- *HLA-A*
 - CBZ
- *CFTR*
 - Ivacaftor
- *DPYD*
 - 5FU, capecitabine, tegafur
- *G6PD*
 - 48 drugs
- *UGT1A1*
 - Atazanavir
- *SLCO1B1*
 - Simvastatin
- *IFNL3 (IL28B)*
 - Interferon
- *CYP3A5*
 - Tacrolimus
- *CYP2B6*
 - Efavirenz, sertraline, methadone
- *RYR1, CACNA1S*
 - Inhaled anesthetics
- *mtRNR1*
 - Aminoglycosides
- *ABCG2*
 - Rosuvastatin
- *OPRM1, COMT*
 - Opioids (CPIC level C-no recommendation)
- *HMGCR*
 - Statins (CPIC level C-no recommendation)
- *SLC6A4, HTR2A*
 - SSRIs (CPIC level C-no recommendation)
- *ADRB1, ADRB2, ADRA2C, GRK4, GRK5*
 - Beta-blockers (CPIC level C-no recommendation)

CPIC guideline progress; prioritization based on member feedback

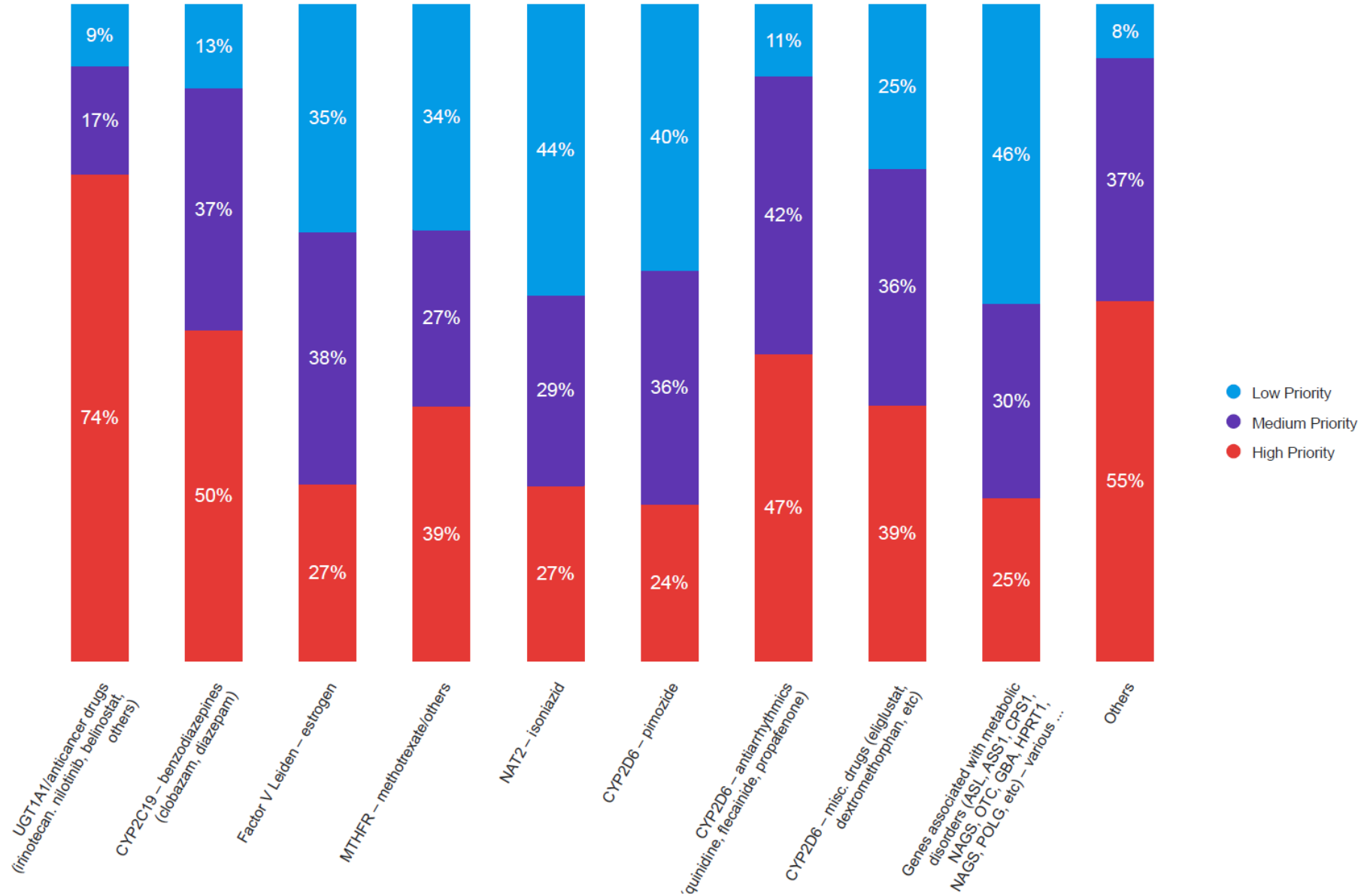
New guidelines

- *CYP2D6, CYP2C19, SLC6A4, HTR2A/SRRIs, SNRIs, others*
- *CYP2B6/methadone- In press*
- *CYP2D6, ADRB1, ADRB2, ADRA2C, GRK4, GRK5/Beta-Blocker-In press*

Guidelines in Progress

- *CYP3A5/Tacrolimus – In evidence review.*
- *CYP2D6/Antipsychotics – In evidence review; the authors are discussing adding more genes*
- *NAT2/Hydralazine – In evidence review*
- *UGT1A1/irinotecan- On hold because of re-prioritization*
- *DPYD/fluoropyrimidines- Evidence review underway*
- *TPMT-NUDT15/thiopurines update-authorship plan underway*
- *CYP2D6/ondansetron-recruiting authors now*

Guideline Prioritization

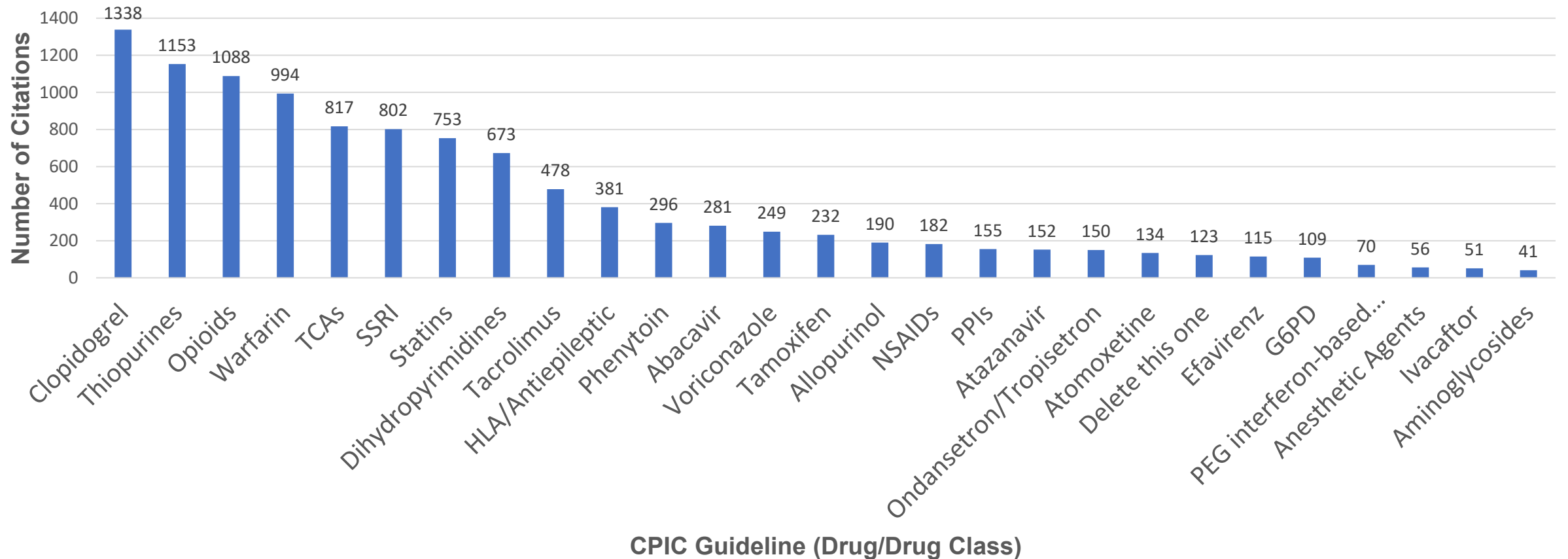


CYP2C19 allele function expert panels

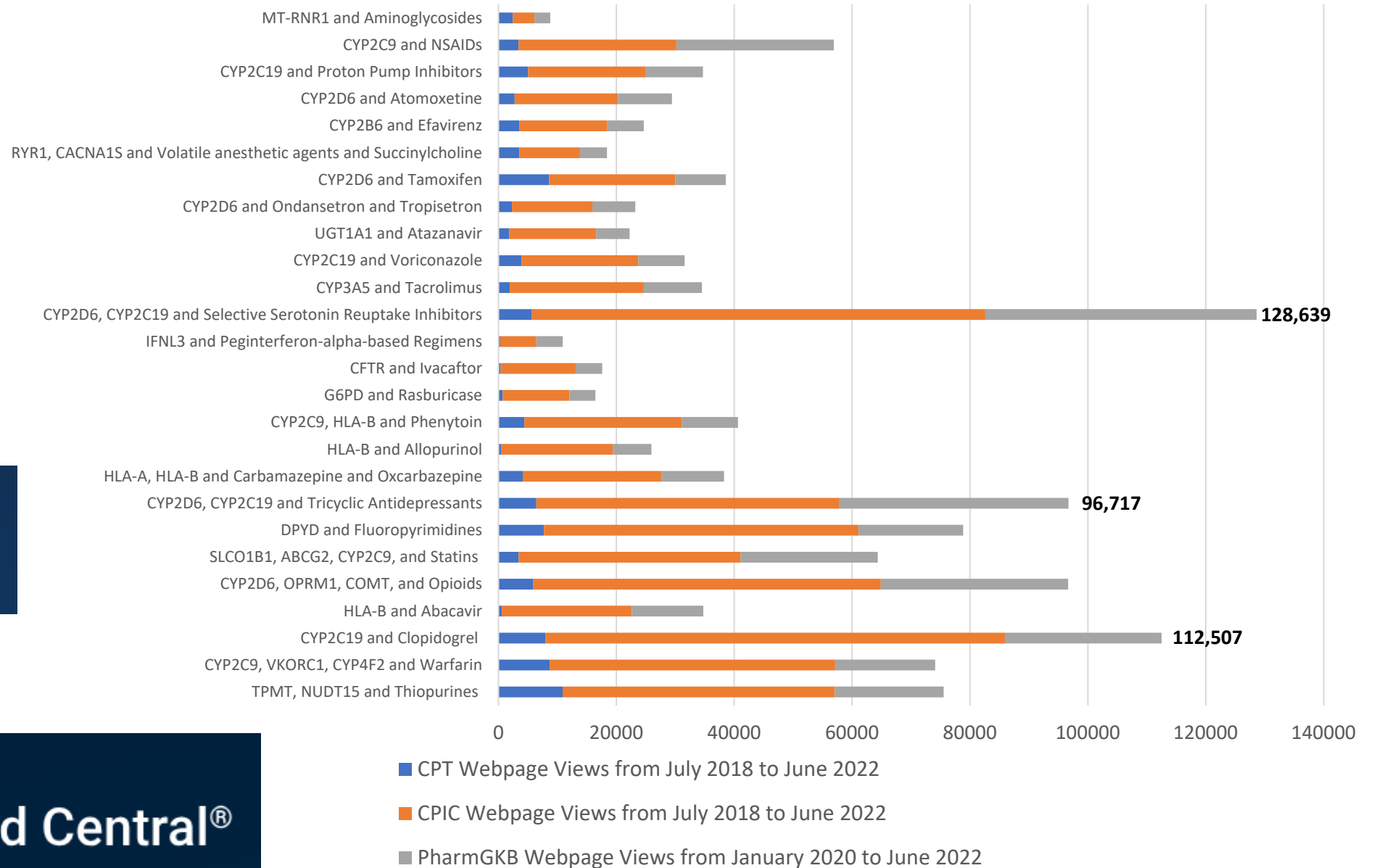
GENE: CYP2C19				
Allele/cDNA/rsID	Allele Clinical Functional Status	References	Strength of Evidence	Summary of Findings
*1	Normal function	7487078, 32602114, 22027650, 2932	Definitve	CYP2C19*1 is assigned normal function based on
*2	No function	8195181, 22027650	Definitve	CYP2C19*2 is assigned no function based on
*3	No function	7969038, 9103550, 22027650	Definitve	CYP2C19*3 is assigned no function based on
*4	No function	9435198, 21358751	Limited	CYP2C19*4 is assigned no function based on
*5	No function			
*6	No function			
*7	No function			
*8	No function			
*9	Decreased function			
*10	Decreased function			
*11	Normal function			
*12	Uncertain function			
*13	Normal function			
*14	Uncertain function			

CYP2C19 Diplotype	Coded Diplotype/Phenotype Summary	EHR Priority Notation
*1/*1	CYP2C19 Normal Metabolizer	Normal/Routine/Low Risk
*1/*2	CYP2C19 Intermediate Metabolizer	Abnormal/Priority/High Risk
*1/*3	CYP2C19 Intermediate Metabolizer	Abnormal/Priority/High Risk
*1/*4	CYP2C19 Intermediate Metabolizer	Abnormal/Priority/High Risk
*1/*5	CYP2C19 Intermediate Metabolizer	Abnormal/Priority/High Risk
*1/*6	CYP2C19 Intermediate Metabolizer	Abnormal/Priority/High Risk
*1/*7	CYP2C19 Intermediate Metabolizer	Abnormal/Priority/High Risk
*1/*8	CYP2C19 Intermediate Metabolizer	Abnormal/Priority/High Risk
*1/*9	CYP2C19 Likely Intermediate Metabolizer	Abnormal/Priority/High Risk
*1/*10	CYP2C19 Likely Intermediate Metabolizer	Abnormal/Priority/High Risk
*1/*11	CYP2C19 Normal Metabolizer	Normal/Routine/Low Risk
*1/*12	CYP2C19 Indeterminate	none
*1/*13	CYP2C19 Normal Metabolizer	Normal/Routine/Low Risk
*1/*14	CYP2C19 Indeterminate	none
*1/*15	CYP2C19 Normal Metabolizer	Normal/Routine/Low Risk

CPIC guidelines are highly cited (over 11,000 times in all)



CPIC guidelines are highly viewed from CPT, CPIC and PharmGKB



CPIC guidelines are endorsed by professional societies and cited in genomic resources

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Thiopurine methyltransferase deficiency - Conditions - ...

Display Settings
Clinical Pharmacology
Clinical Features
genotype
Caudle KE
Author information
Abstract

Thiopurine methyltransferase deficiency

SNOMED CT: Thiopurine methyltransferase deficiency

Related Conditions

CROG Thiopurine methyltransferase deficiency

Associated Genes

[TPMT](#)

Summary: thiopurine S-methyltransferase deficiency

Clinical Features

- Caused by mutation in the thiopurine methyltransferase gene
- Decreased activity of thiopurine methyltransferase
- Decreased metabolism of thiopurine drugs
- Hematopoietic toxicity develops
- Heterozygotes may also show clinical features

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ASCPT
American Society for Clinical Pharmacology and Therapeutics
Advancing the science and practice of clinical pharmacology and translational medicine for the therapeutic benefit of patients and society.

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CYP2C19
View Gene Facts

Gene-Disease Validity Classifications: 0
Dosage Sensitivity Classifications: 0
Clinical Actionability Assertions: 0
Variant Pathogenicity Assertions: 0
CPIC / PharmGKB High Level Records: 27 / 15
Follow Gene

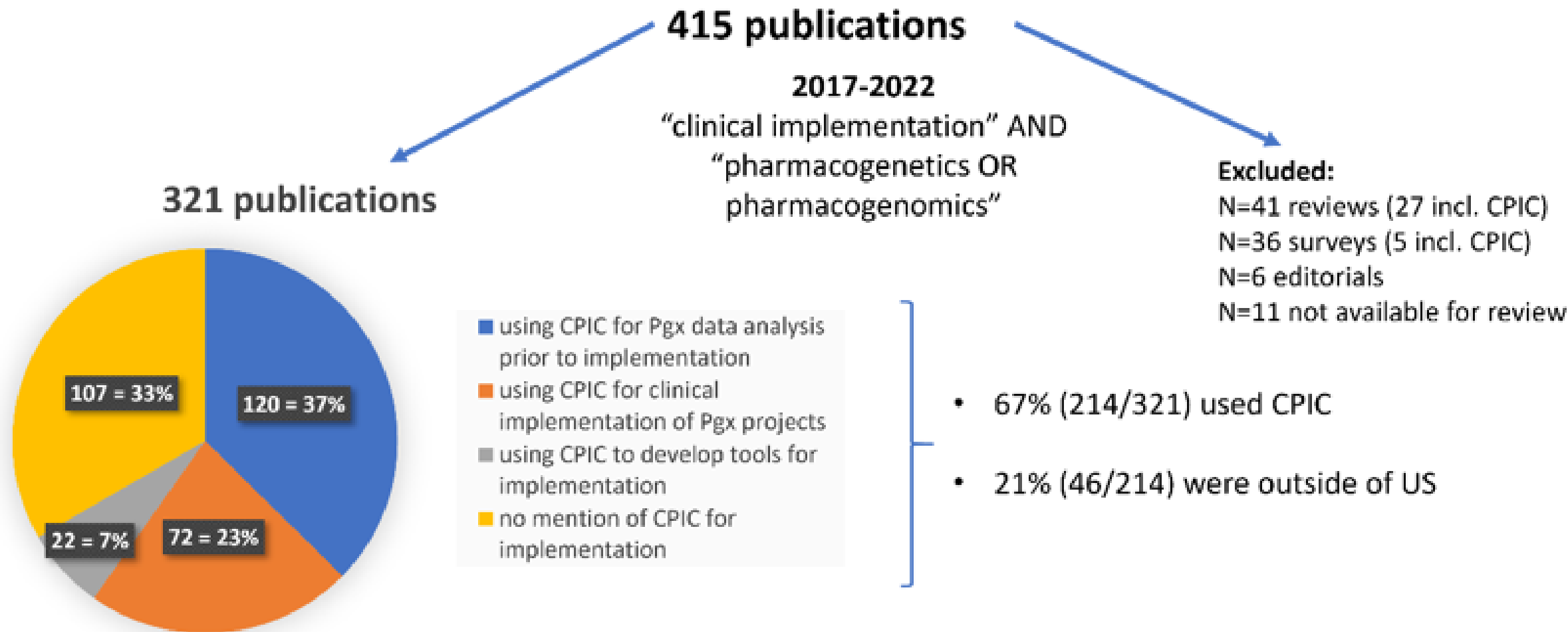
Curation Summaries Status and Future Work External Genomic Resources ClinVar Variants

Group By Activity

Pharmacogenomics - CPIC

Gene	Drug	CPIC Level	Date Accessed	CPIC Clinical Guidelines
CYP2C19	lansoprazole	Level A	08/29/2023	Guideline
	omeprazole	Level A		
	pantoprazole	Level A		
	dexlansoprazole	Level B		
	esomeprazole	Level C		
	rabeprazole	Level C		

CPIC is a highly used resource for pharmacogenomic implementation



CPIC guidelines have been implemented at St. Jude



Clinical Pharmacogenetics Implementation Consortium Guideline for Thiopurine Dosing Based on *TPMT* and *NUDT15* Genotypes: 2018 Update

Mary V. Relling¹, Matthias Schwab^{2,3,4}, Michelle Whirl-Carrillo⁵, Guilherme Suarez-Kurtz⁶, Ching-Hon Pui⁷, Charles M. Stein⁸, Ann M. Moyer⁹, William E. Evans¹, Teri E. Klein⁴, Federico Guillermo Antillon-Klussmann^{10,11}, Kelly E. Caudle¹, Motohiro Kato¹², Allen E.J. Yeoh^{13,14}, Kjeld Schmiegelow^{15,16} and Jun J. Yang¹

Clin Pharmacol Ther. 2019 May;105(5):1095-1105.

Learning Health Systems



Pharmacogenomic Alert - NUDT15 Poor Metabolizer - TPMT Normal Metabolizer / Mercaptopurine

Mercaptopurine can be affected by a patient's TPMT and NUDT15 phenotype. This patient is predicted to be a **NUDT15 poor metabolizer** and **TPMT normal metabolizer**. The patient is at risk for myelosuppression with normal doses of mercaptopurine. **Start with reducing the normal 6-mercaptopurine dose to 10 mg/m²/day**. Please consult a clinical pharmacist, review the Pharmacogenomics Results Report, or click [TPMT implemented gene \(St. Jude\)](#) or [NUDT15 implemented gene \(St. Jude\)](#) for more information.

Remove the following orders?

mercaptopurine tablet Oral, Starting today at 1010

[Pharmacogenomics Results Report](#)

Acknowledge Reason

Inherited *NUDT15* Variant Is a Genetic Determinant of Mercaptopurine Intolerance in Children With Acute Lymphoblastic Leukemia

Jun J. Yang, Wendy Landier, Wenjian Yang, Chengcheng Liu, Lindsey Hageman, Cheng Cheng, Deqing Pei, Yanjun Chen, Kristine R. Crews, Nancy Kornegay, F. Lennie Wong, William E. Evans, Ching-Hon Pui, Smita Bhatia, and Mary V. Relling

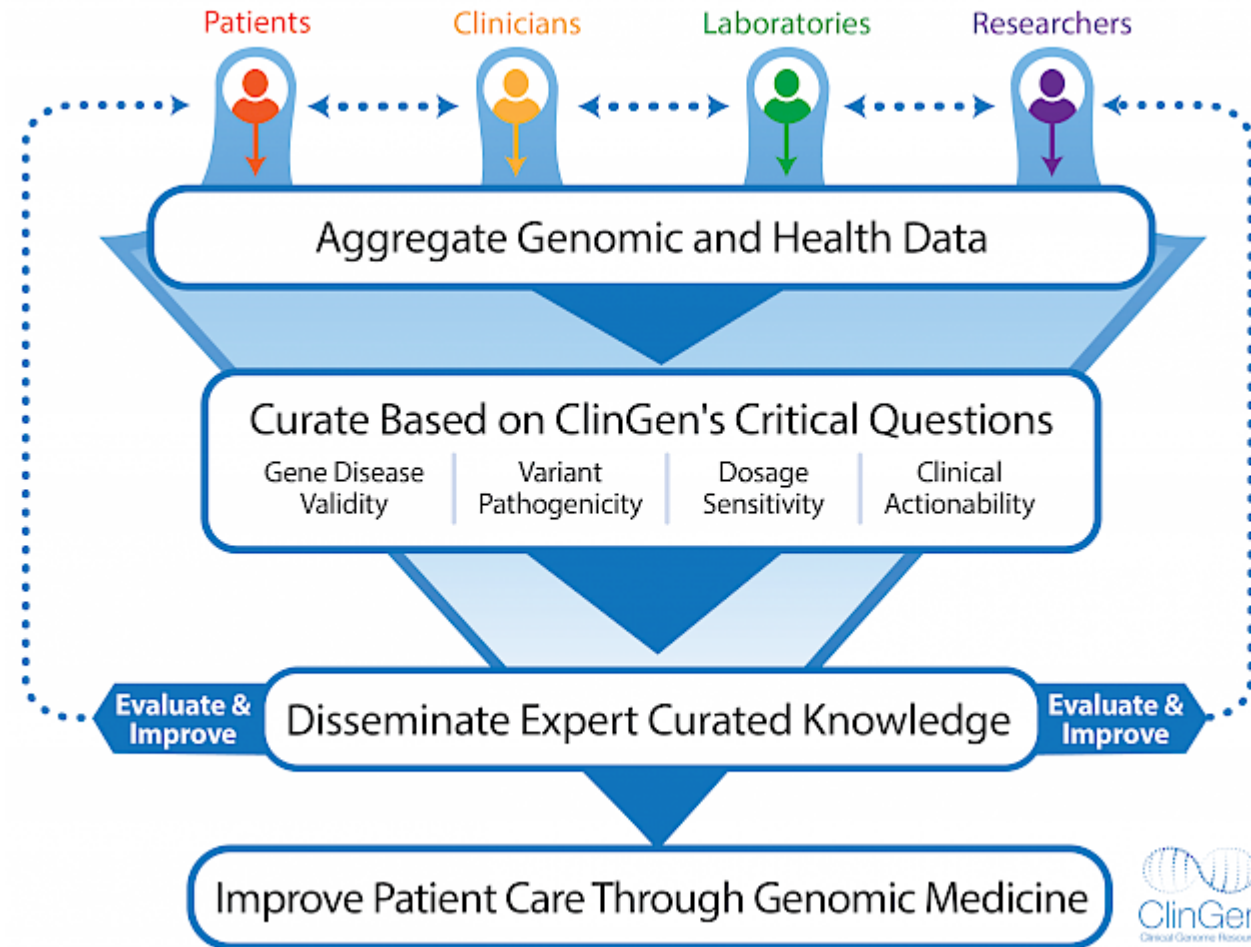
J Clin Oncol. 2015 Apr 10;33(11):1235-42.

The future....

**CPIC will continue to facilitate the adoption
of pharmacogenomics**



ClinGen is an authoritative central resource that defines clinical relevance of genes and variants for genetic diseases






More work for standardization

Future Medicine Ltd
Pharmacogenomics
Volume 24, Issue 4, March 2023, Pages 183-186
<https://doi.org/10.2217/pgs-2023-0020>

Editorial

Pharmacogenomics implementation:
*“a little less conversation, a little
more action, please”*

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Pharmacogenomics



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