Kelly E. Caudle, Pharm.D., Ph.D., BCPS, FCCP

St. Jude Children's Research Hospital

CPIC staff

Roseann S. Gammal, PharmD, BCPS

Li Gong, PhD

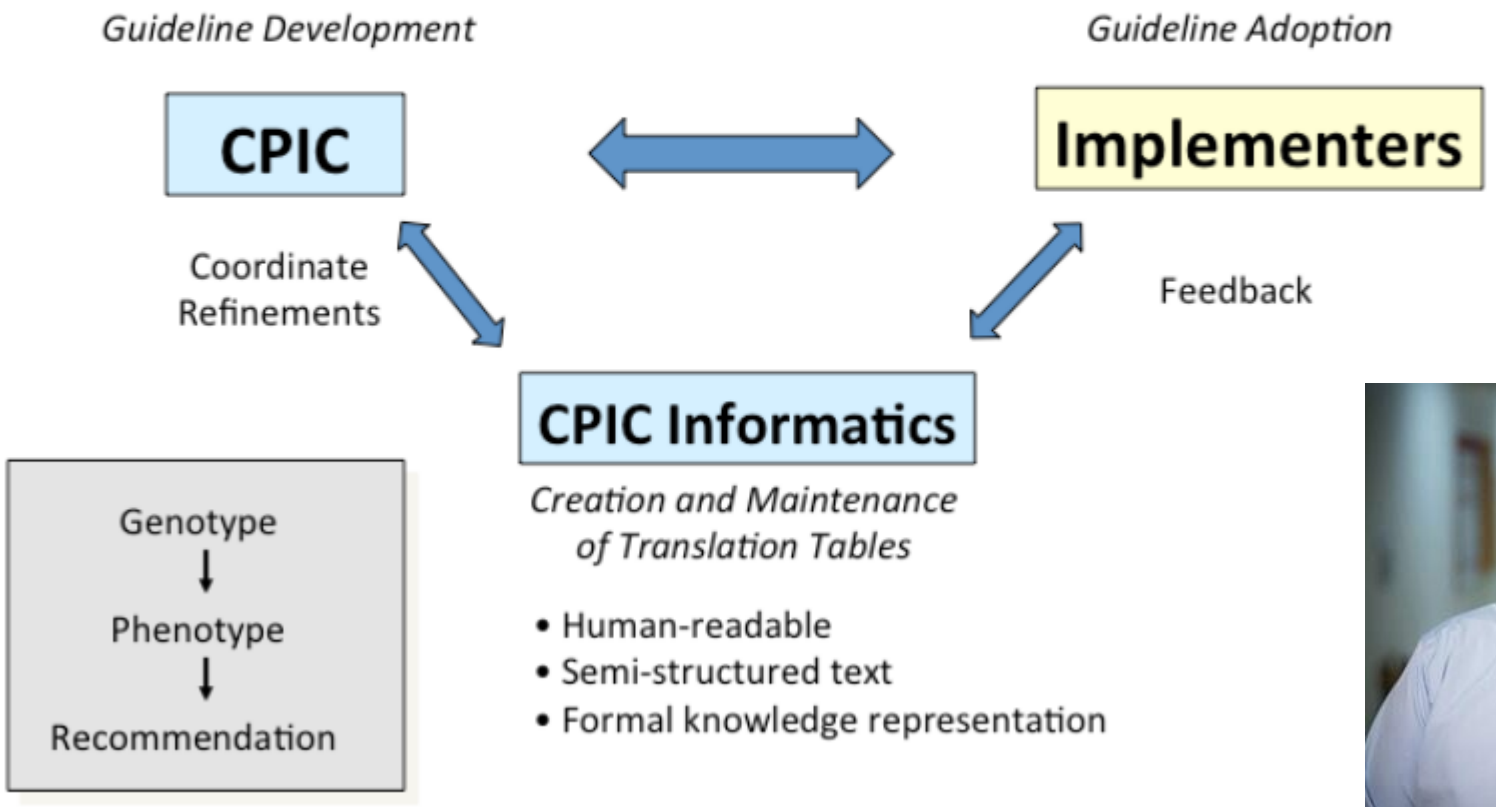
Katrin Sangkuhl, PhD

Ryan Whaley

Mark Woon

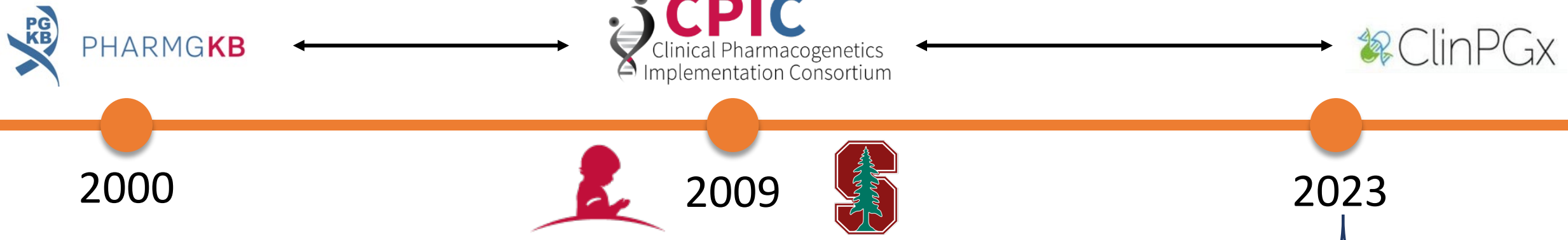
CPIC Informatics: Supporting Guideline Implementation

Michelle Whirl-Carrillo, Ph.D.
Stanford University



James M. Hoffman, Pharm.D., M.S.
St. Jude Children's Research Hospital

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



730 members (clinicians and scientists)

523 institutions

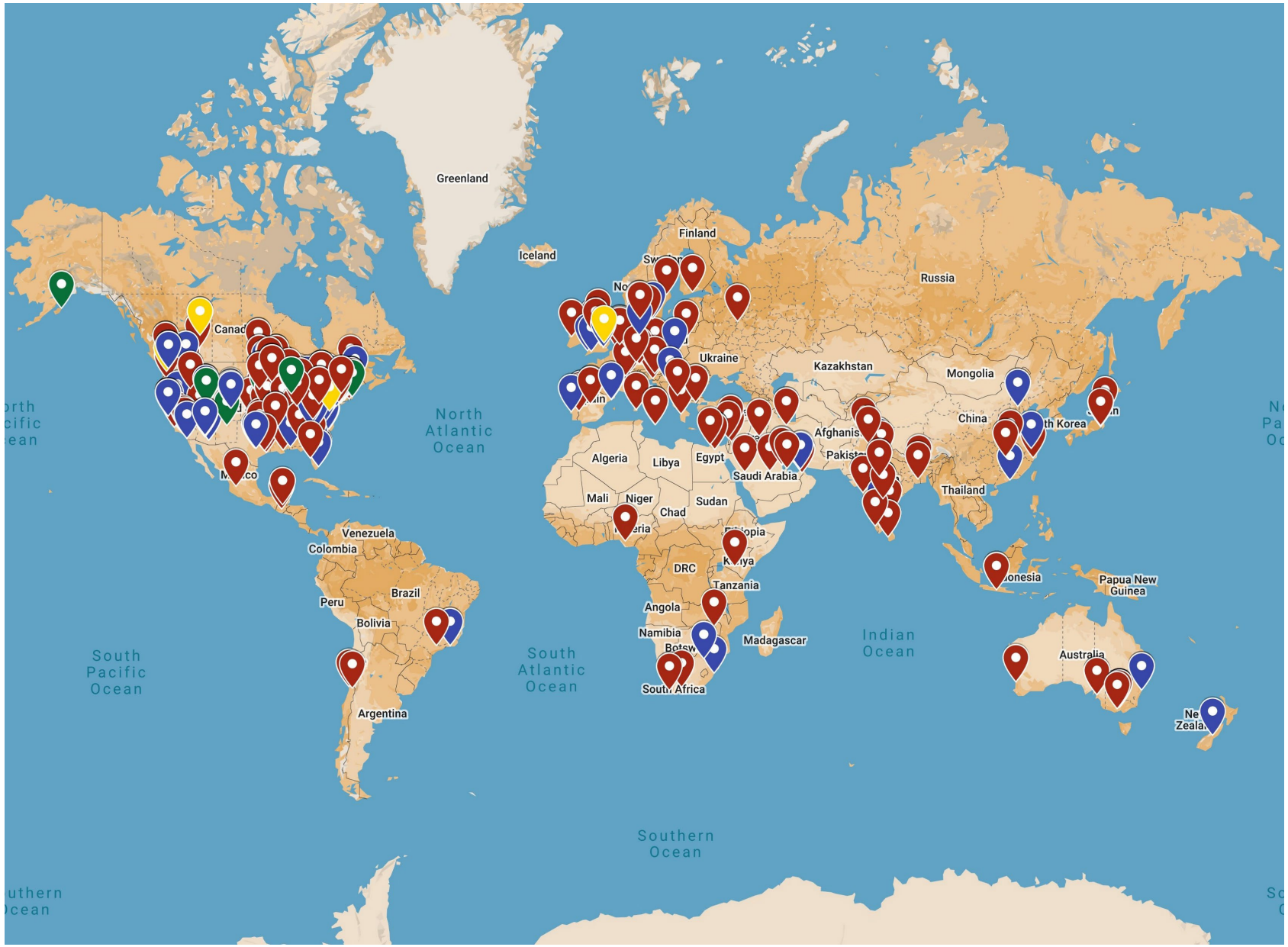
49 countries

32 guidelines (and counting!)

29 genes

>150 drugs

CPIC is a global organization



28 guidelines; 32 genes and >150drugs

CPIC™ Clinical Pharmacogenetics Implementation Consortium

- *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

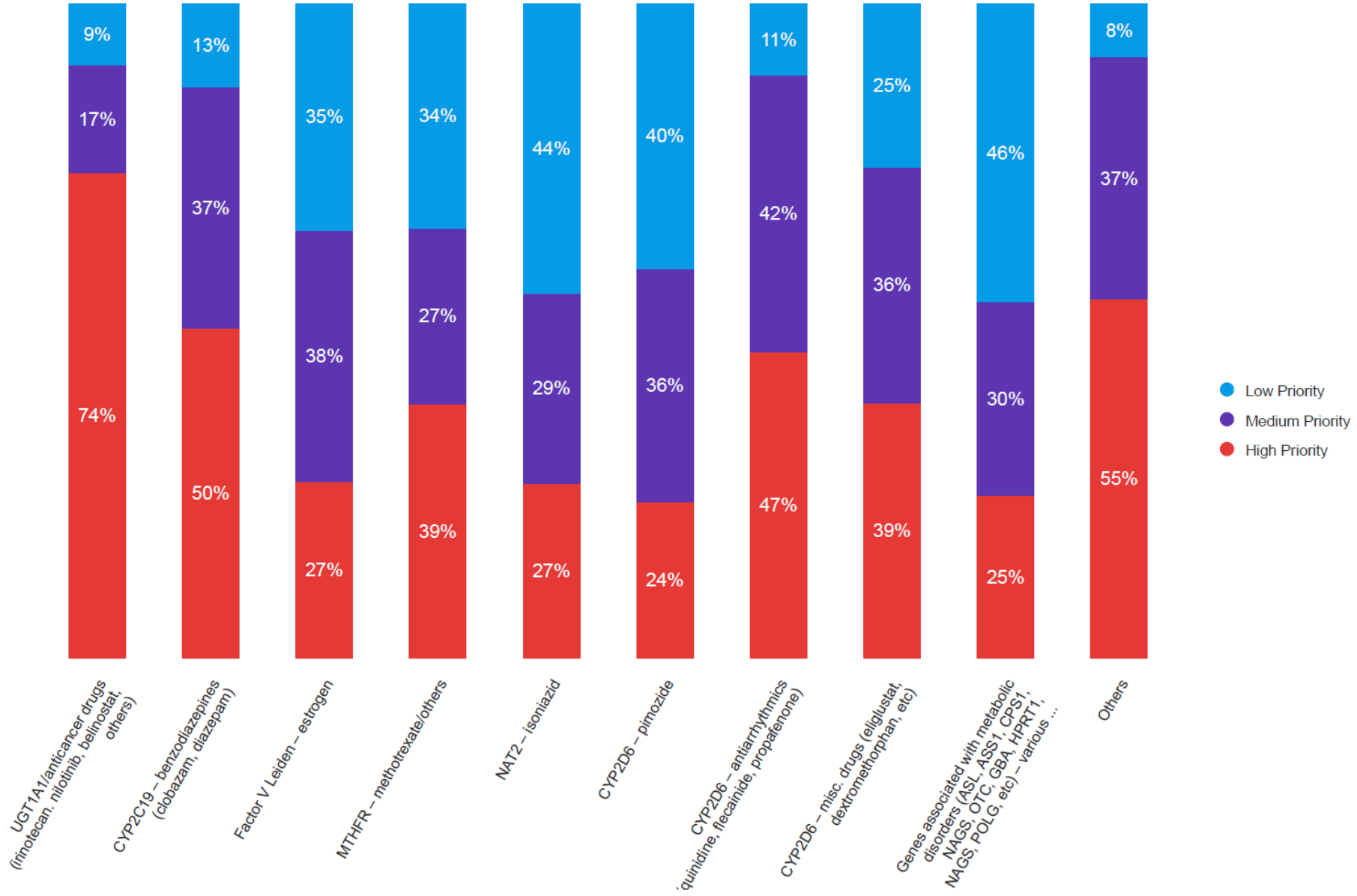
New guidelines

- *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

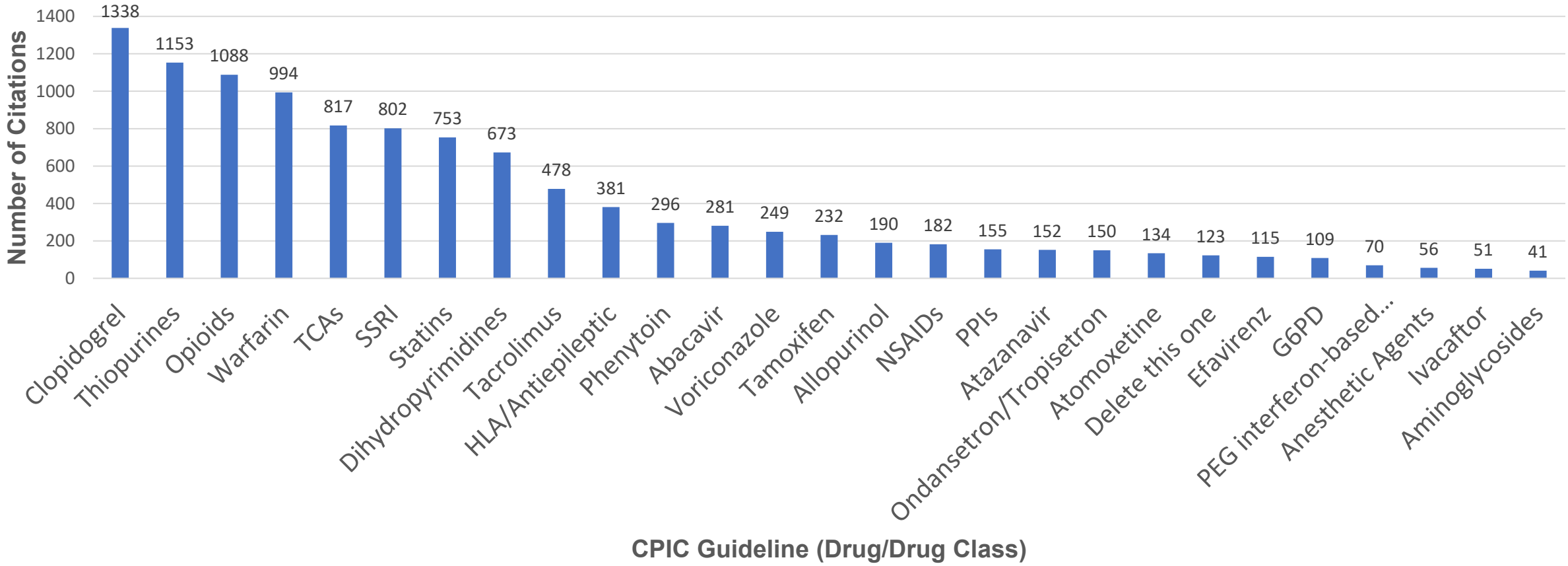


CPIC allele function expert panels

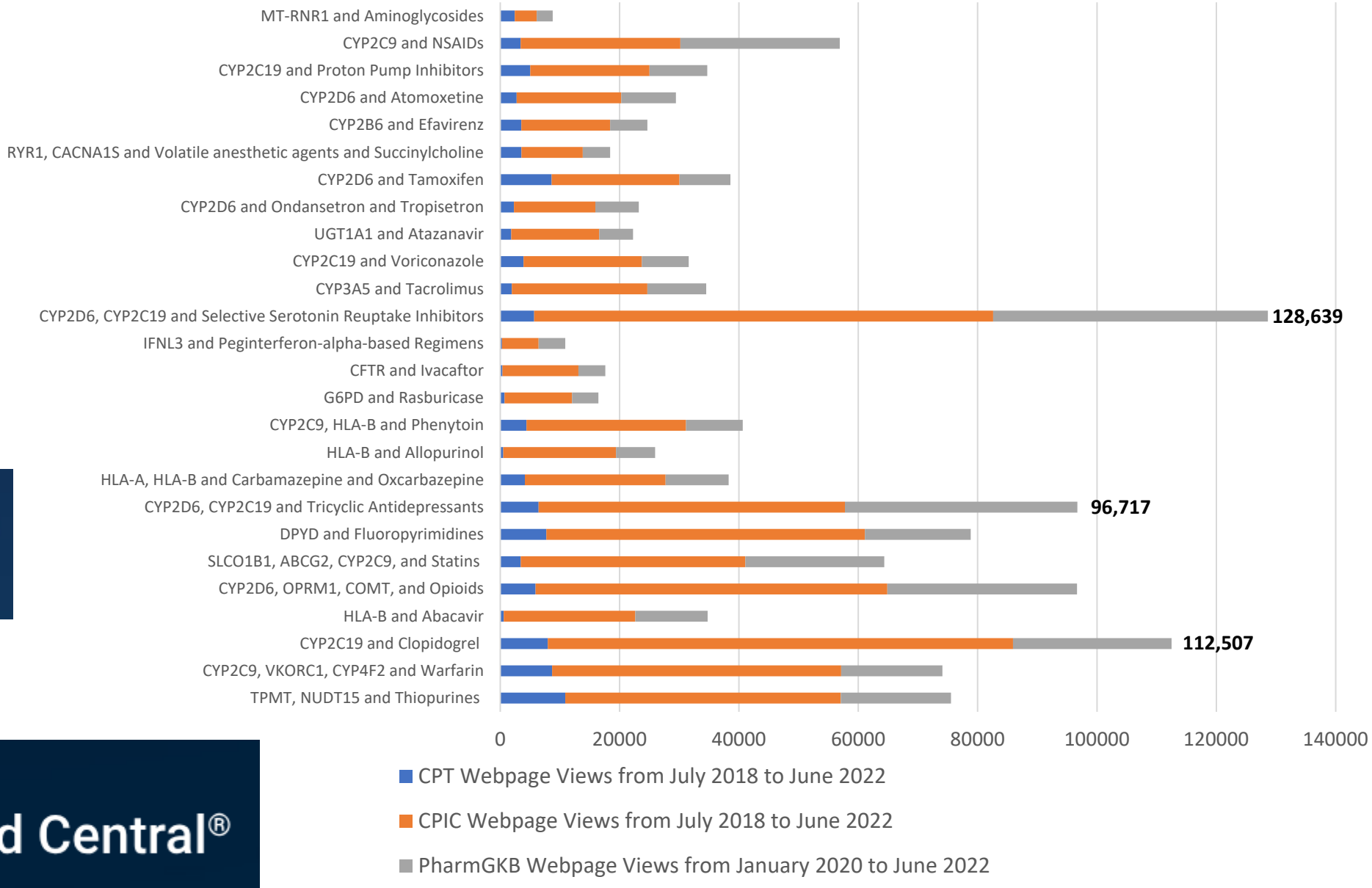
GENE: CYP2C19				
Allele/cDNA/rsID	Allele Clinical Functional Status	References	Strength of Evidence	Summary of Findings
*1	Normal function	7487078, 32602114, 22027650, 2932	Definitve	CYP2C19*1 is assigned normal function ba
*2	No function	8195181, 22027650	Definitve	CYP2C19*2 is assigned no function based
*3	No function	7969038, 9103550, 22027650	Definitve	CYP2C19*3 is assigned no function based
*4	No function	9435198, 21358751	Limited	CYP2C19*4 is assigned no function based
*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

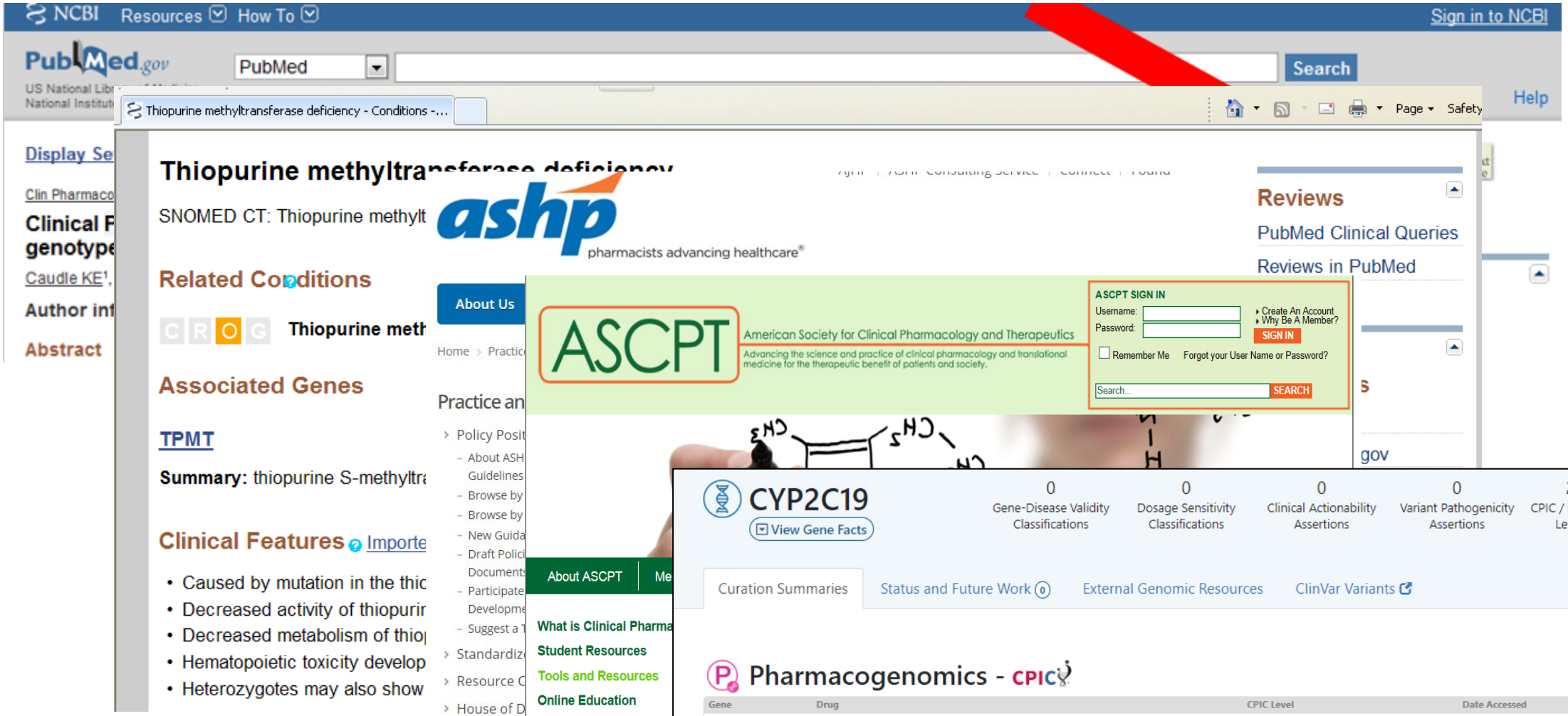
CPIC guidelines are highly cited (over 11,000 times in all)



CPIC guidelines are highly viewed from CPT, CPIC and PharmGKB



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



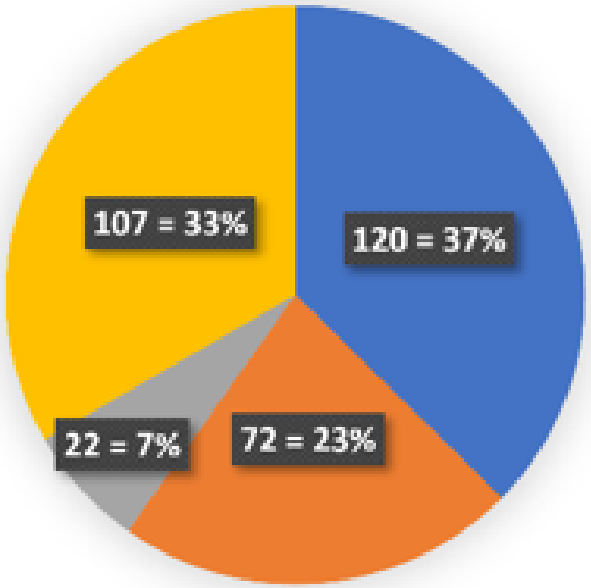
CPIC is a highly used resource for pharmacogenomic implementation

415 publications

2017-2022
"clinical implementation" AND
"pharmacogenetics OR
pharmacogenomics"

Excluded:
N=41 reviews (27 incl. CPIC)
N=36 surveys (5 incl. CPIC)
N=6 editorials
N=11 not available for review

321 publications



- using CPIC for Pgx data analysis prior to implementation
- using CPIC for clinical implementation of Pgx projects
- using CPIC to develop tools for implementation
- no mention of CPIC for implementation

- 67% (214/321) used CPIC
- 21% (46/214) were outside of US

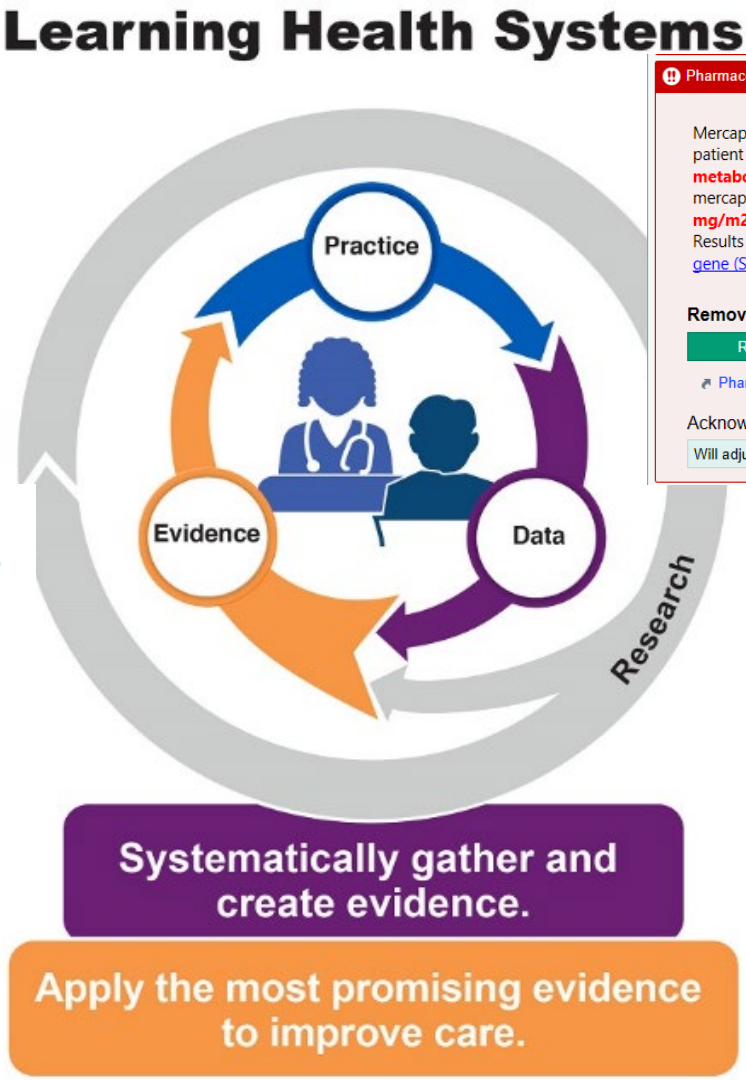
CPIC guidelines have been implemented at St. Jude

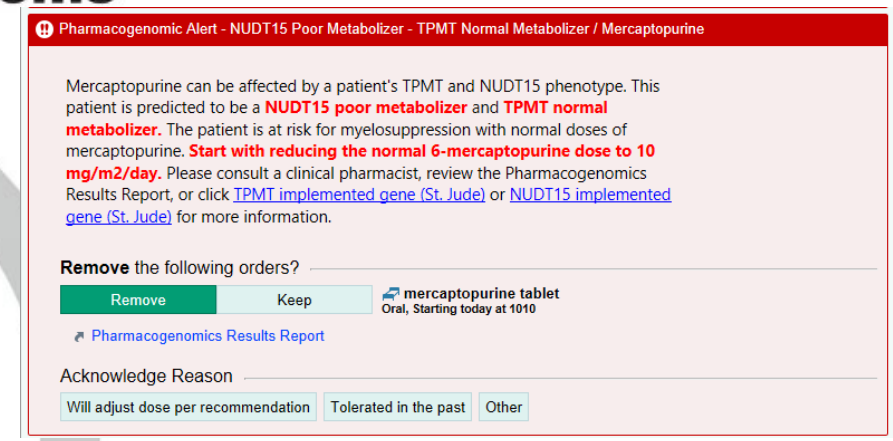
CPIC™
Clinical Pharmacogenetics Implementation Consortium

Clinical Pharmacogenetics Implementation Consortium Guideline for Thiopurine Dosing Based on *TPMT* and *NUDT*15 Genotypes: 2018 Update

Mary V. Relling[1], Matthias Schwab[2,3,4], Michelle Whirl-Carrillo[5], Guilherme Suarez-Kurtz[6], Ching-Hon Pui[7], Charles M. Stein[8], Ann M. Moyer[9], William E. Evans[1], Teri E. Klein[4], Federico Guillermo Antillon-Klussmann[10,11], Kelly E. Caudle[1], Motohiro Kato[12], Allen E.J. Yeoh[13,14], Kjeld Schmiegelow[15,16] and Jun J. Yang[1]

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





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

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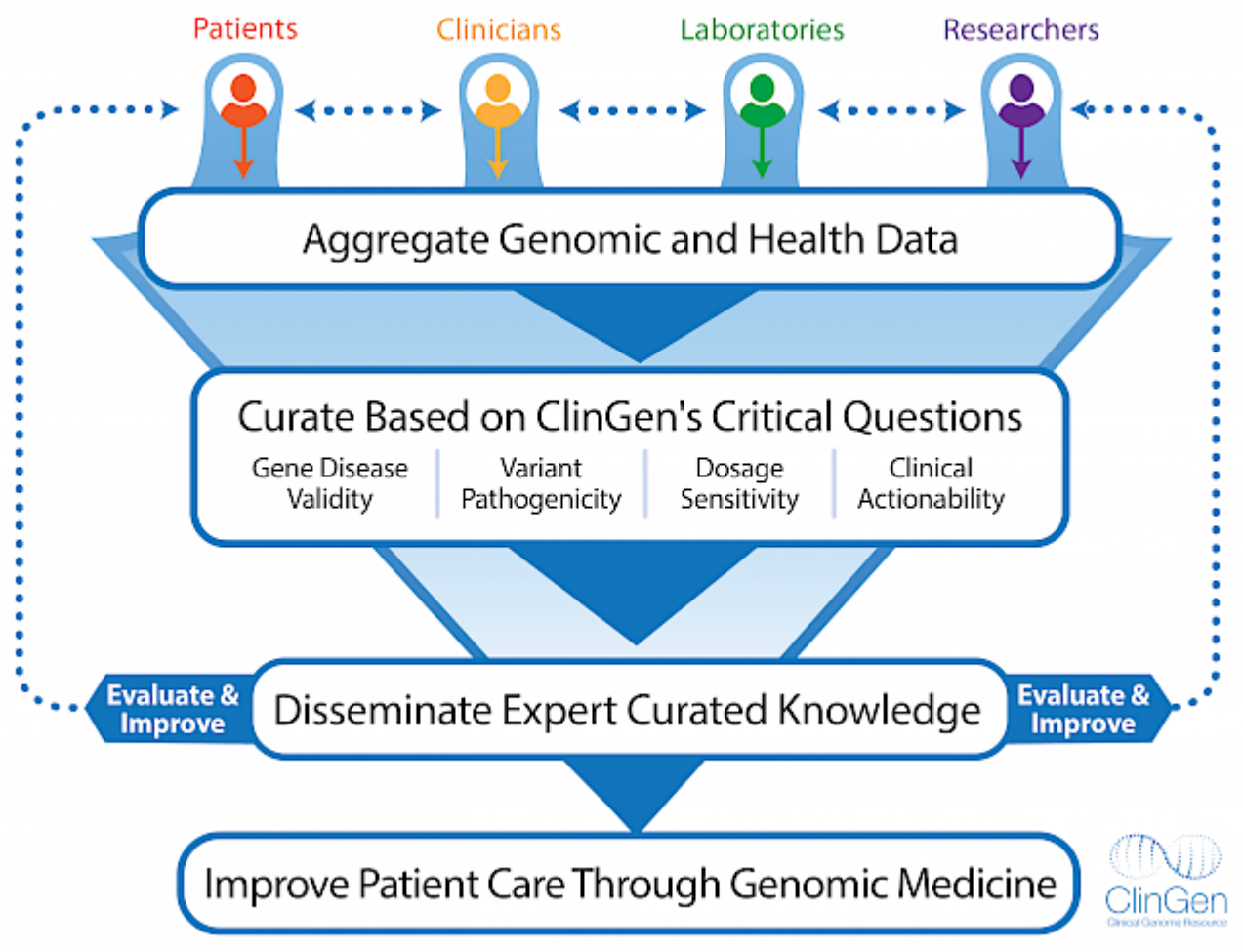
Clinical Pharmacogenetics Implementation Consortium

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*"

Kelly E Caudle [1,*], James M Hoffman [1,2] & Roseann S Gammal [3]

[1]Department of Pharmacy & Pharmaceutical Sciences, St. Jude Children's Research Hospital, Memphis, TN 38105, USA

[2]Office of Quality & Patient Safety, St. Jude Children's Research Hospital, Memphis, TN 38105, USA

[3]Department of Pharmacy Practice, Massachusetts College of Pharmacy & Health Sciences, Boston, MA 02115, USA

[*]Author for correspondence: Tel.: +1 901 595 3994; kelly.caudle@stjude.org

CPIC Co-Principal Investigators

Kelly E. Caudle, Pharm.D., Ph.D.
St. Jude Children's Research Hospital

Teri E. Klein, Ph.D.
Stanford University

Co-Investigator
Mary V. Relling, Pharm.D.
St. Jude Children's Research Hospital

CPIC Informatics Co-Directors
Michelle Whirl-Carrillo, Ph.D.
Stanford University

James M. Hoffman, Pharm.D.
St. Jude Children's Research Hospital

Stanford CPIC Coordinator
Michelle Whirl-Carrillo, Ph.D.
Stanford University

CPIC staff

Rose Gammal, Pharm.D.
St. Jude Children's Research Hospital

Li Gong, Ph.D.
Stanford University

Katrin Sangkuhl, Ph.D.
Stanford University

Ryan Whaley
Stanford University

Steering Committee

Teri E. Klein, Ph.D.
Stanford University

Kelly E. Caudle, Pharm.D., Ph.D.
St. Jude Children's Research Hospital

Michelle Whirl-Carrillo, Ph.D.
Stanford University

Mary V. Relling, Pharm.D.
St. Jude Children's Research Hospital

Dan M. Roden, M.D.
Vanderbilt University

Rachel F. Tyndale, Ph.D.
University of Toronto and CAMH

Larisa Cavallari, Pharm.D.
University of Florida

Stuart A. Scott, Ph.D.
Stanford University and Stanford Healthcare

Sara Van Driest, M.D., Ph.D.
Vanderbilt University

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