



# Notable Pharmacogenomics Challenges in Clinical Informatics

Cyrine-Eliana Haidar, Pharm.D., BCPS, BCOP

Clinical Pharmacogenetics Coordinator

St. Jude Children's Research Hospital

[Cyrine.Haidar@stjude.org](mailto:Cyrine.Haidar@stjude.org)



# Outline

- CYP2D6 phenotype update
- “Possible” phenotypes
- CDS alerts for patients on chronic medications



# CYP2D6 Phenotype Assignment

- 1385 out of 4921 (28%) of *CYP2D6* genotypes needed to be corrected
- Resulted in a change in CYP2D6 phenotype frequencies in the population



# Consensus on *CYP2D6* Genotype to Phenotype Translation

Inferred <i>CYP2D6</i> phenotype	Previous CPIC definition (AS)	Previous DPWG definition (AS)	Consensus definition (AS)	Consensus contiguous definition (AS)
UM	> 2	> 2.5	> 2.25	> 2.25
NM	1-2	1.5-2.5	1.25	$1.25 \leq x \leq 2.25$
			1.5	
			2.0	
			2.25	
IM	0.5	0.5-1	0.25	$0 < x < 1.25$
			0.5	
			0.75	
			1	
PM	0	0	0	0



# Examples of results that needed changes in phenotypes

<i>CYP2D6</i> Diplotype	Previous Phenotype/AS	New Phenotype/AS	Summary
(*10/*10)2N	NM 1.0	<b>IM</b> <b>0.5</b>	Change in activity score and in phenotype
(*1/*4)2N	NM 1.0	<b>IM</b> <b>1.0</b>	No change in activity score but change in phenotype (AS=1)
(*1/*10)3N	NM or UM (possible UM) 2.0 or 2.5	<b>NM</b> <b>1.5 or 2.25</b>	Change from possible UM to NM due to change in AS
(*1/*40)3N	NM 1.0 or 2.0	<b>Possible IM</b> <b>1.0 or 2.0</b>	Change from NM to possible IM due to encompassing AS=1



# Summary of Changes

- Interpretive consult wording
  - Diplotype interpretation sentence
  - Activity score sentence
  - Phenotype assignment sentences (when applicable)
  - Dosing recommendations (when applicable)
- Problem list update (when applicable)
- Email notification to MDs about the CYP2D6 phenotype change for their patients (one email sent about all patients for each MD)
- Patient Result Letter in EHR and in portal
- Patient notification about updated results

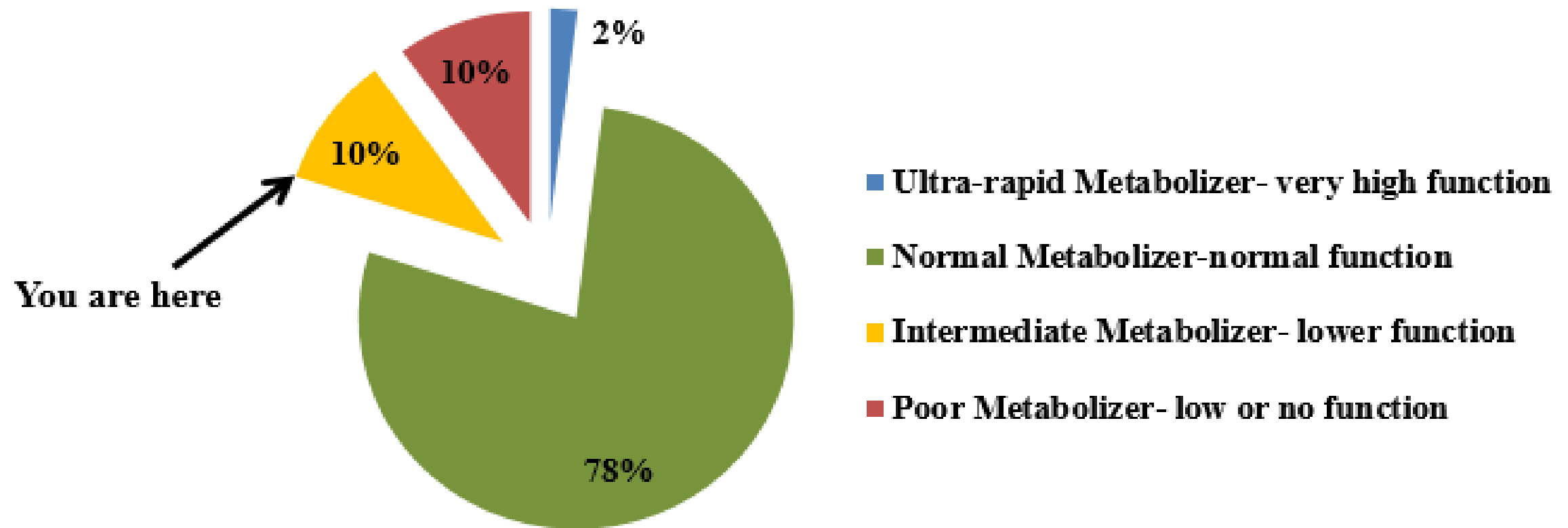


# Summary of Changes

- Consult databases updated to the new CYP2D6 phenotype assignments
- Update the phenotype frequencies in educational material:
  - CYP2D6 patient education sheet
  - CYP2D6 result notification letter to patients
  - PG4KDS website (CYP2D6 page)



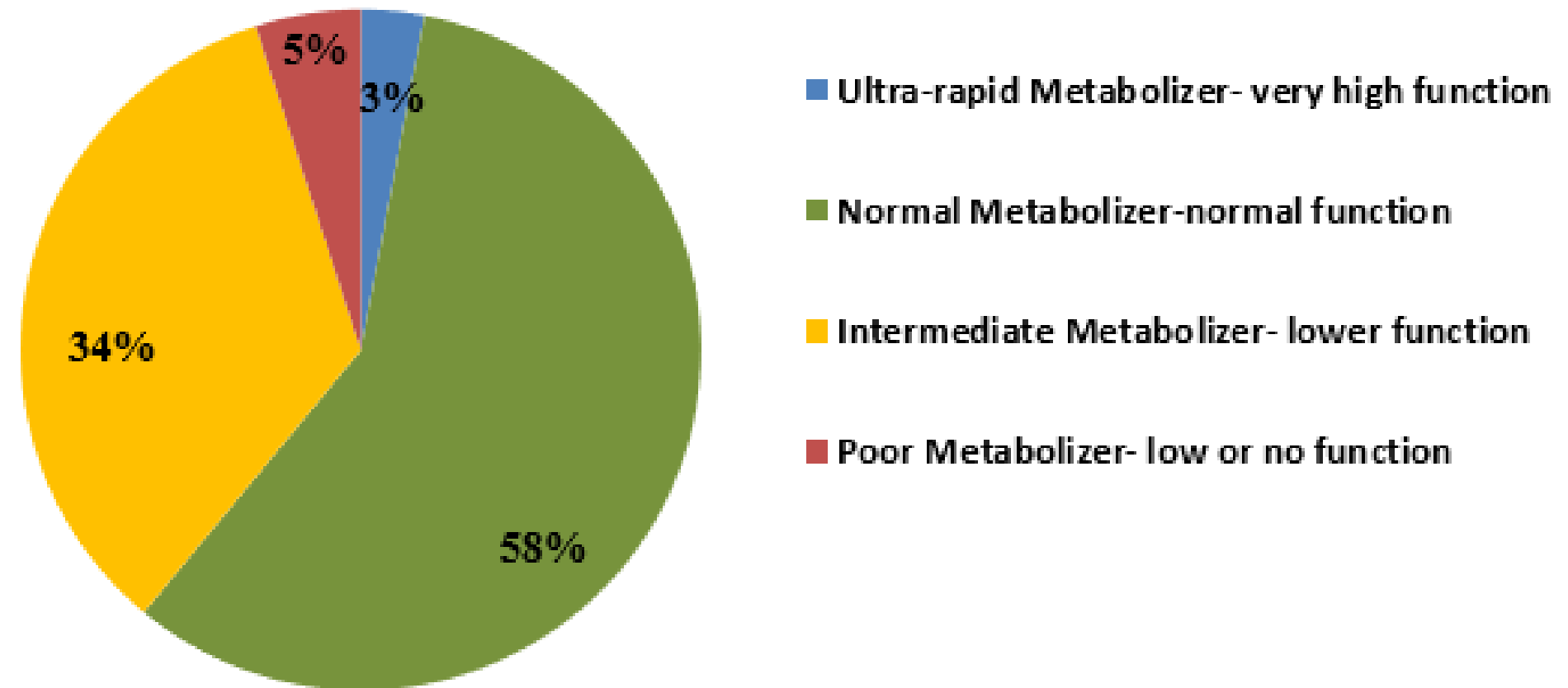
# CYP2D6 Phenotype Frequency Update (Old)



The exact percent of each group varies by ethnic group.



# CYP2D6 Phenotype Frequency Update (New)



The exact percent of each group varies by ethnic group.



**HOW TO HANDLE  
“POSSIBLE”  
PHENOTYPES**





# CPIC Guidelines Possible/Likely Phenotype Terminologies

CYP2C19 Diplotype	Coded Diplotype/Phenotype Summary <sup>a</sup>
*1/*1	CYP2C19 Normal Metabolizer
*1/*2	CYP2C19 Intermediate Metabolizer
*1/*3	CYP2C19 Intermediate Metabolizer
*1/*4	CYP2C19 Intermediate Metabolizer
*1/*5	CYP2C19 Intermediate Metabolizer
*1/*6	CYP2C19 Intermediate Metabolizer
*1/*7	CYP2C19 Intermediate Metabolizer
*1/*8	CYP2C19 Intermediate Metabolizer
*1/*9	CYP2C19 Likely Intermediate Metabolizer
*1/*10	CYP2C19 Likely Intermediate Metabolizer
*1/*11	CYP2C19 Normal Metabolizer
*1/*12	Indeterminate
*1/*13	CYP2C19 Normal Metabolizer
*1/*14	Indeterminate
*1/*15	CYP2C19 Normal Metabolizer
*1/*16	CYP2C19 Likely Intermediate Metabolizer
*1/*17	CYP2C19 Rapid Metabolizer
*1/*18	CYP2C19 Normal Metabolizer
*1/*19	CYP2C19 Likely Intermediate Metabolizer

SLCO1B1 Diplotype	Coded Genotype/Phenotype Summary <sup>a</sup>
*1a/*1a	SLCO1B1 Normal Function <sup>c</sup>
*1a/*1b	SLCO1B1 Normal Function <sup>c</sup>
*1a/*2	SLCO1B1 Possible Decreased Function <sup>c</sup>
*1a/*3	SLCO1B1 Possible Decreased Function <sup>c</sup>
*1a/*4	Indeterminate
*1a/*5	SLCO1B1 Decreased Function <sup>c</sup>
*1a/*6	SLCO1B1 Possible Decreased Function <sup>c</sup>
*1a/*7	Indeterminate

# Utilizing SNOMED-CT Terms for “Possible” Phenotypes

Add New Problem

**Problems** Secondary Description

**\*Problem:** CYP2D6 ultra-rapid metabolizer  Freetext

Annotated display: Possible CYP2D6 ultra-rapid metabolizer

Qualifier:

**\*Confirmation:** Possible

**\*Classification:** Medical



# Annotated Display Will Display Possible Phenotype Nomenclature

< > Problem List

Classification View      Active Problems      Change View

Qualifier	Name of Problem	Onset Date	Classification	Annotated Display	Contributor ...
	COUGH	11/10/2002	Clinical		PowerChart
	CYP2C19 POOR METABOLIZER	4/13/2016	Medical	CYP2C19 POOR METABOLIZER	PowerChart
	CYP2D6 POOR METABOLIZER	11/18/2019	Medical	POSSIBLE CYP2D6 POOR METABOLIZER	PowerChart

Discussion about submitting for LOINC codes to automate this process



CDS ALERTS FOR  
PATIENTS ON **CHRONIC**  
MEDICATIONS

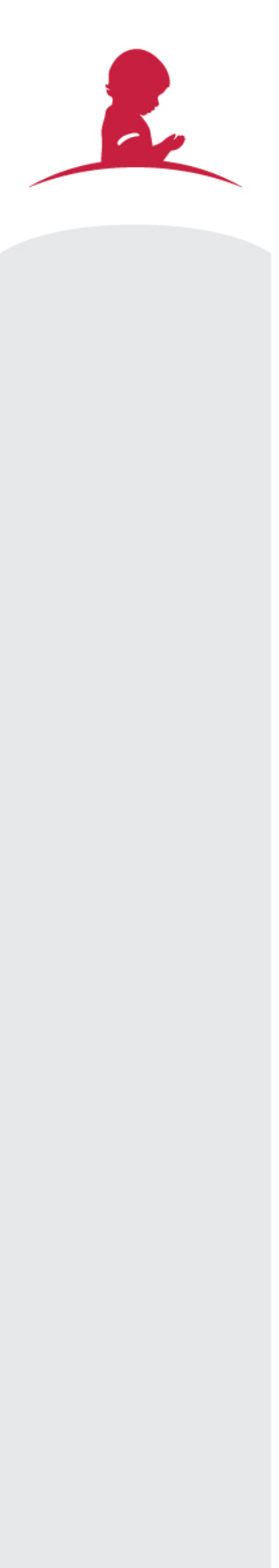


# CYP2D6 PM/Atomoxetine CDS Alert Recommendation

This patient is predicted to be a CYP2D6 PM and may be at an increased risk of a atomoxetine-related adverse events. Initiate with a dose of 0.5 mg/kg/day and **if no clinical response and in the absence of adverse events after 2 weeks, consider obtaining a plasma concentration 4 h after dosing. If response is inadequate and concentration is <200 ng/ml, consider a proportional dose increase to achieve a concentration to approach 400 ng/ml. If unacceptable side effects are present at any time, consider a reduction in dose.**



How do we create CDS alerts to take into account future recommendations?



Questions?