Clinical Pharmacogenetics Implementation Consortium (CPIC) Guideline for *CYP2D6*, *CYP2C19*, *CYP3A4*, *CYP3A5*, and *CYP1A2* Genotypes and Antipsychotics

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Overview

- Background and scope of work
- Evidence review
- Proposed recommendations (DRAFT)
- Next steps

Antipsychotic Medications

- Originally indicated for the treatment of schizophrenia
- Growing list of other indications*
  - Augmentation with antidepressants for mood and anxiety disorders, Bipolar disorder, aberrant behavior in ASD/ID, Tourette's, etc
  - Growing utilization, especially in mood disorders
    - E.g. Quetiapine, aripiprazole, risperidone, olanzapine all on 2023 top 300 prescribed drug list
    - ~23.8 million prescriptions and ~4.8 million patients in 2023 (just these four drugs)
- 30-75% discontinuation rate of therapy within a year of starting a new medication
  - Adverse Events
  - Lack of efficacy

Medical Expenditure Panel Survey (MEPS) 2014-2023. Agency for Healthcare Research and Quality (AHRQ), Rockville, MD. Database version 2025.8

*Specific indications may differ by drug

Antipsychotic Pharmacology

- Subcategorizations evolving
  - Pre 2024: 1st and 2nd generation antipsychotics (also called typical and atypical antipsychotics)
  - 2024 approval of first new muscarinic-focused agent (e.g., xanomeline/trospium - Cobenfy)
- Primary mechanism of action: dopamine-2 (D2) receptor antagonism
- Blockade of D2 receptors accounts for the reduction of delusions and hallucinations
- Serotonin-2A receptor (5HT2A) antagonism
  - Mostly 2nd generation agents
- Other receptors antagonized depending on agent
  - Alpha1/2, H1/2, muscarinic, 5HT2C, D1 (Clozapine: 19+ receptors affected)

Antipsychotic Metabolism

Commonly Used First Generation (Typical) Antipsychotics

Drug	Metabolism Pathways
Chlorpromazine	CYP1A2, **CYP2D6,** CYP3A4
Fluphenazine	**CYP2D6**
Haloperidol	CYP1A2, **CYP2D6, CYP3A4**
Loxapine	CYP1A2, CYP2C19, CYP2C8, CYP2D6, CYP3A4
Molindone	CYP2D6, CYP3A4
Perphenazine	CYP1A2, CYP2C19, **CYP2D6,** CYP3A4
Pimozide	CYP1A2, **CYP2D6, CYP3A4**
Thioridazine	**CYP1A2,** CYP2C19, **CYP2D6**
Thiothixene	**CYP1A2**
Trifluoperazine	CYP1A2, CYP2D6

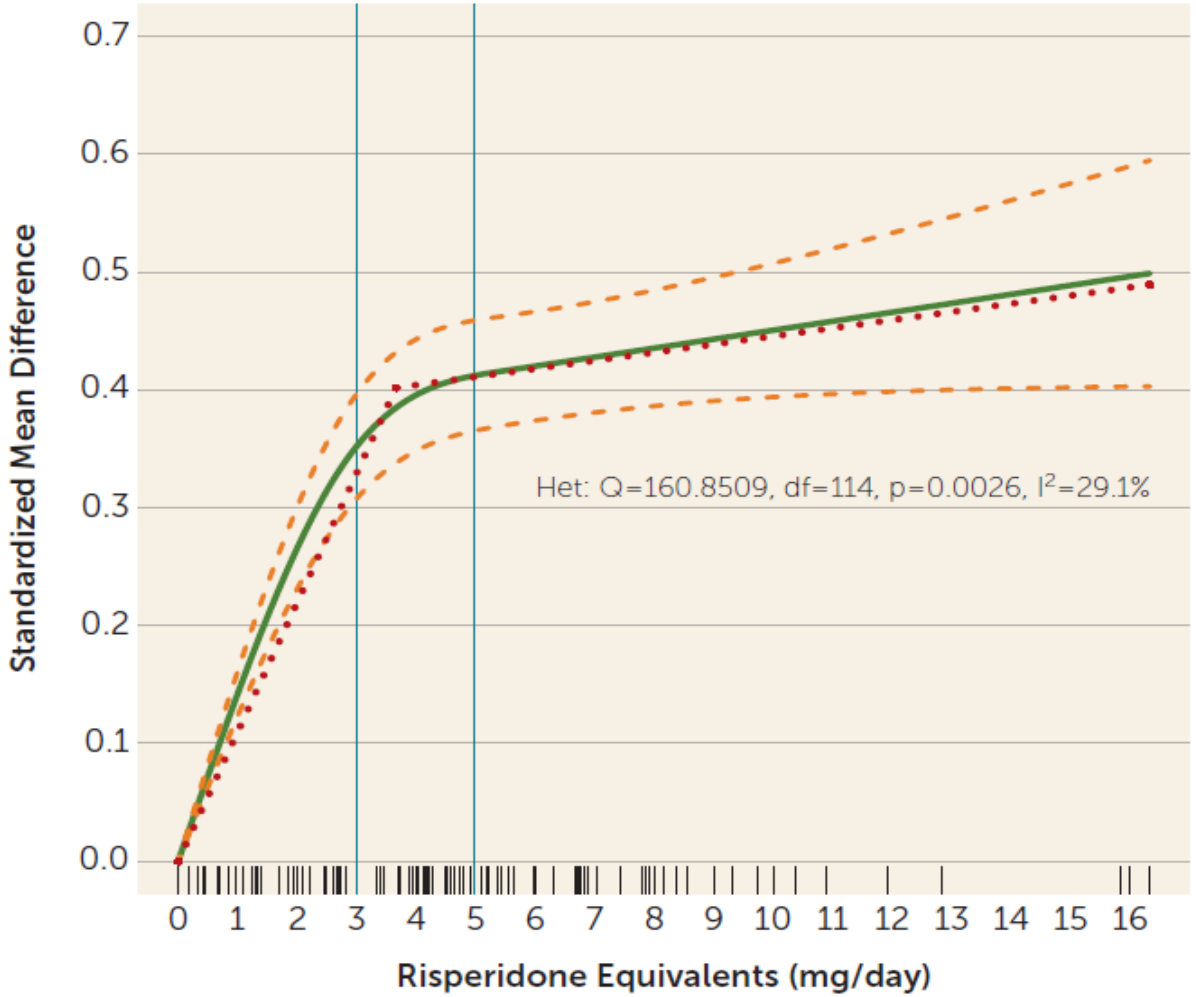
Commonly Used Second Generation (Atypical) Antipsychotics

Drug	Metabolism Pathways
Aripiprazole	**CYP2D6, CYP3A4**, CYP3A5
Asenapine	**CYP1A2, UGT1A4,** CYP2D6, CYP3A4, CYP2C19
Brexpiprazole	**CYP2D6, CYP3A4**
Cariprazine	CYP2D6, **CYP3A4**
Clozapine	**CYP1A2,** CYP2C19, CYP2D6, CYP3A4
Iloperidone	**CYP2D6,** CYP3A4
Lurasidone	**CYP3A4**
Olanzapine	Glucuronidation, **CYP1A2,** CYP2D6
Paliperidone	Limited CYP metabolism/renal
Quetiapine	**CYP3A4,** CYP2D6
Risperidone	**CYP2D6,** CYP3A4
Ziprasidone	CYP1A2, CYP3A4

Antipsychotic Medications: dosing & drug exposure are important

- Assessment of PBO-controlled dose finding studies of n=20 antipsychotics
- N=68 acute schizophrenia studies
  - Dose-response up to 95% effective doses then plateau
- Known dose-dependent side effects
  - Movement d/o, somnolence/sedation, anticholinergic
- Serum concentrations predict D2 receptor occupancy (optimal range: 60-80%)
- TDM guidelines for antipsychotics published (updates in progress)
  - Variability in use in Europe (common) vs US (less common)

Dose-response curve across antipsychotic drugs converted to risperidone equivalents



Leucht S. Am J Psychiatry 2020. PMID: 31838873
Schoretsanitis G. J Clin Psychiatry 2020. PMID: 32433836

Scope of work: overarching workflow

Define scope of guideline

Drugs: All currently approved antipsychotics

Genes (*CYP2D6*, *CYP2C19*, *CYP3A4, CYP2A5, CYP1A2)*

Structured literature review = 1,185 total publications

CYP2D6 = 645

CYP2C19 = 107

CYP3A4/5 = 433

CYP1A2 = 

Major Finding Statements (MFs) extracted from 373 publications

Individual study quality assessed

MFs collated

Strength of evidence for each MF
(High, Moderate, Weak)

MFs used to develop prescribing recommendations and assign CPIC Level of Evidence (i.e., A, B, C, or D)

Scope of work: antipsychotic selection

- **Goal**: inclusive, comprehensive, contemporary
- **39 drugs** included in literature search

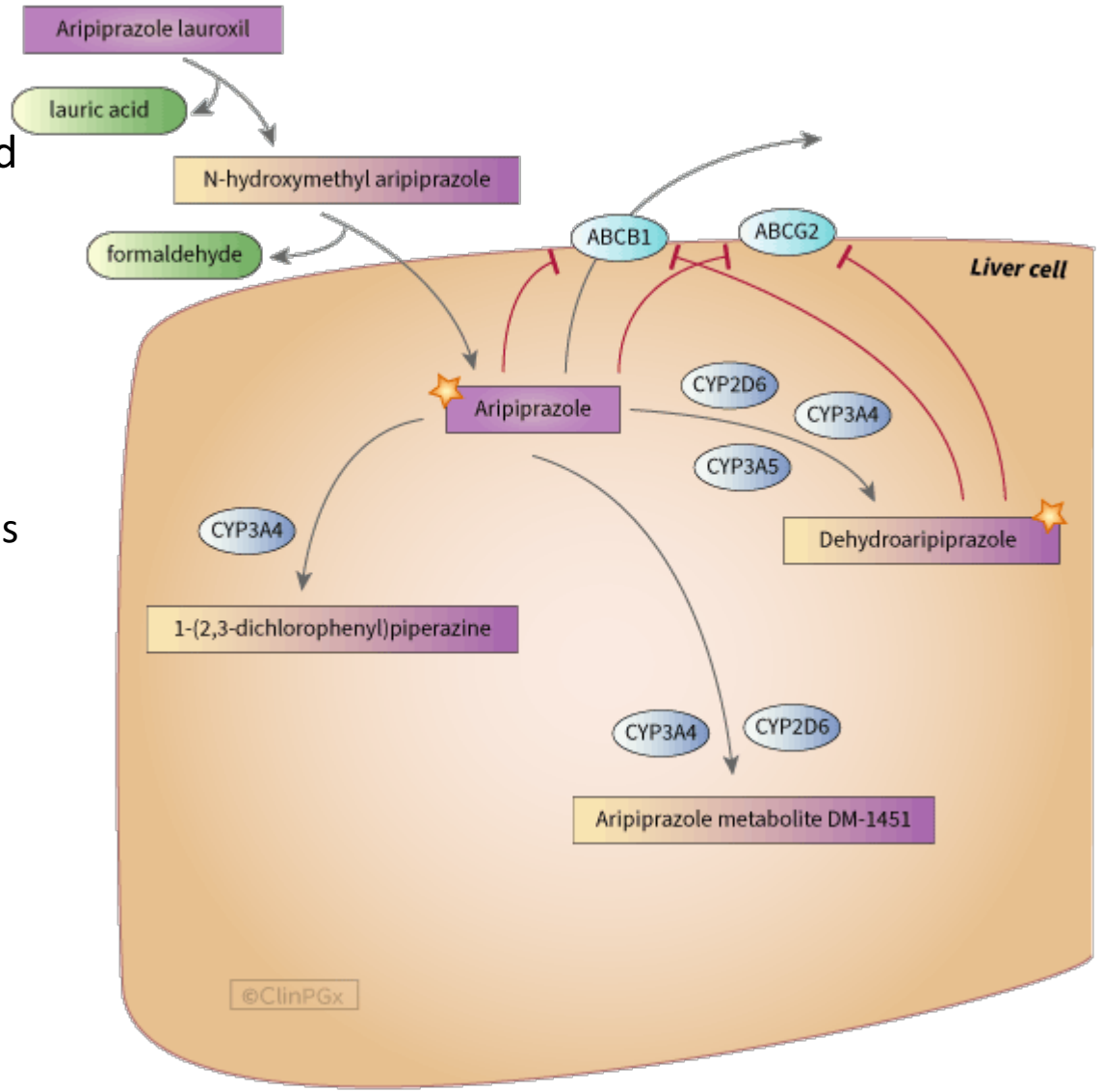
Amisulpride	Iloperidone	Prochlorperazine
Aripiprazole	Levomepromazine	Quetiapine
Asenapine	Loxapine	Risperidone
Blonanserin	Lumateperone	Sertindole
Brexpiprazole	Lurasidone	Sulpride
Bromperidol	Melperone	Thioproperazine
Cariprazine	Molindone	Thioridazine
Chlorpromazine	Olanzapine	Thiothixene
Chlorprothixene	Paliperidone	Trifluoperazine
Clozapine	Periciazine	Xanomeline/Trospium
Flupentixol	Perphenazine	Ziprasidone
Fluphenazine	Pimavanserin	Zotepine
Haloperidol	Pimozide	Zuclopenthixol

Scope of work: gene selection

- **Pharmacokinetic genes:** *CYP1A2,* ***CYP2C19, CYP2D6, CYP3A4/5*** involved with metabolism of many antipsychotics
  - Commonly reported relationships on many commercial tests
  - *CYP1A2*:
    - No standardized haplotype definitions and phenotype assignment frameworks
    - Some variants may confer increased expression, but only in the context of smoking
    - Lack of consistency in SNPs assessed and other variables considered in existing literature
    - Author group concluded not to conduct comprehensive literature review but include discussion of challenges
  - *ABCB1* (P-glycoprotein): not ready/out of scope
    - No standardized genotype>phenotype
    - Substrate specificity important and not comprehensively defined
- **Pharmacodynamic genes:** not ready/out of scope
  - *DRD2/ANKK1, HTR2A, HTR2C, MC4R*
    - Many studies exploring efficacy and tolerability
    - No standardized genotype>phenotype, allelic variation across populations, many class/subclass studies (vs. drug specific studies)

Aripiprazole and *CYP2D6*

- Second generation antipsychotic with active metabolite, and relatively longer half-life (~75hr parent, ~94hr metabolite)
- Parent+metabolite = active moiety
- 50 studies
- PK evidence:
  - Continuous association of 2D6 AS x PK phenotypes
  - NM vs IM: ↓metabolism in Ims with variable effect size across studies
  - NM vs PM: moderate/high (~50% ↑PM)
  - Similarities between PO and LAI
- Clinical evidence:
  - Dose relationships (PMs)
  - Increased discontinuation (PM+UM) or trend (PM and UM separate)
- Discussion points:
  - UM recommendation (vs no rec)
  - Differences in TDM perspectives
  - Whether to lump/split LAI vs PO



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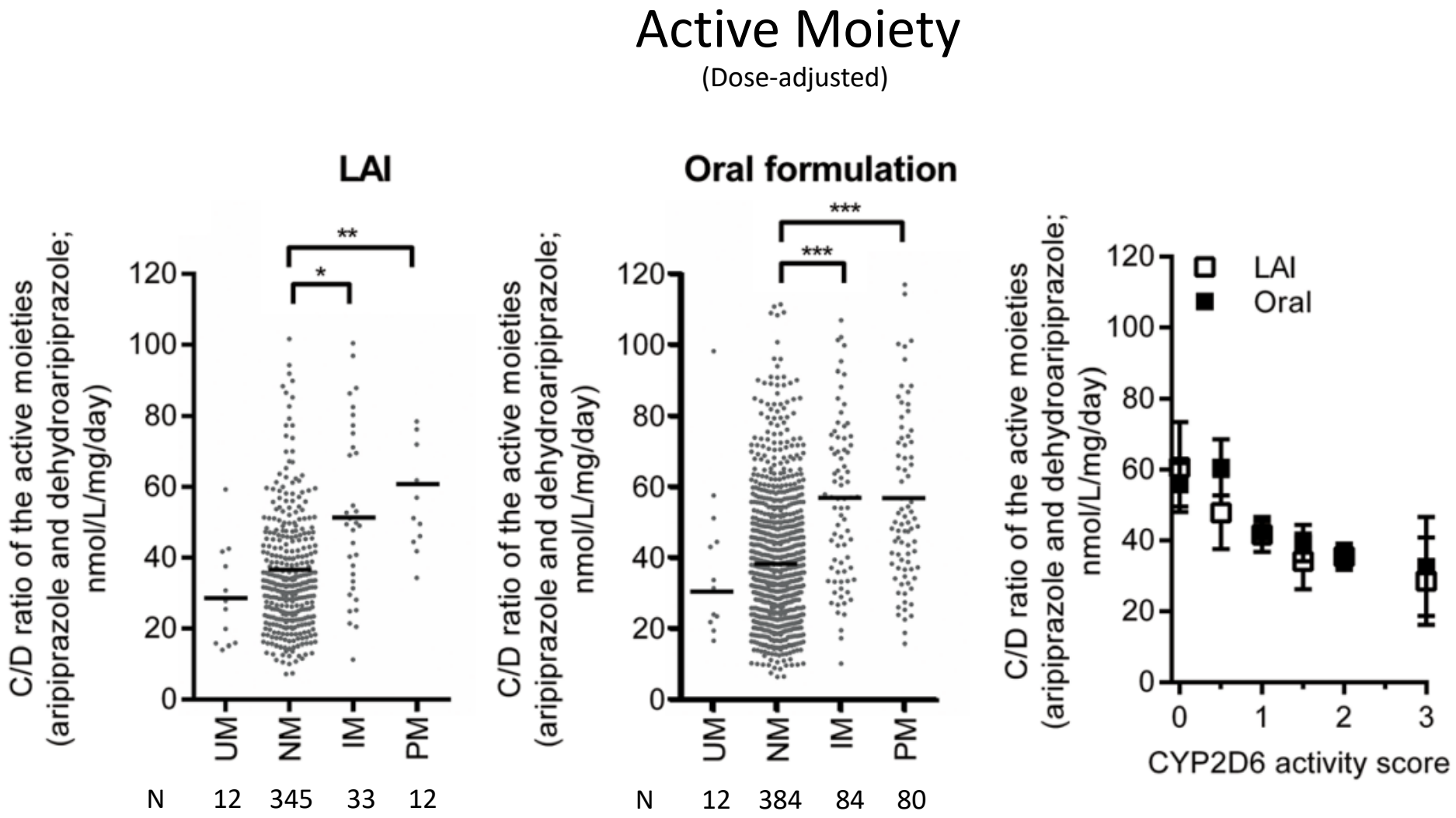
Aripiprazole x CYP2D6 LAI vs Oral formulation example



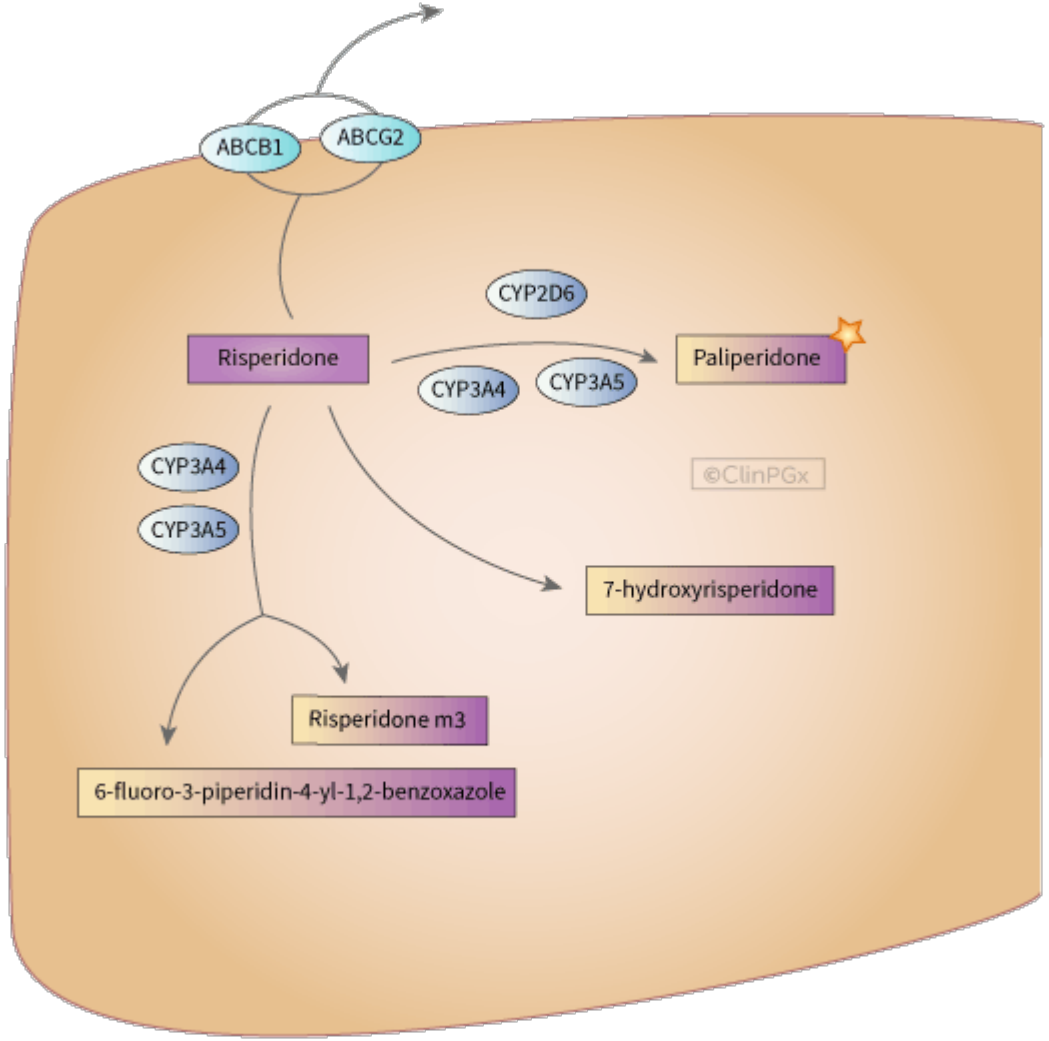
Tveito et al 2020, PMID: 31637453

Phene	Implication (abridged)	Therapeutic Recommendation	Strength
CYP2D6 UM	Increased metabolism of aripiprazole...may increase the likelihood of lower concentrations, lower overall exposure to aripiprazole and active moiety…clinical relevance of these relationships remains inconclusive.	Initiate therapy with recommended starting dose and titrate to maintenance dose based on effectiveness and tolerability. **Due to the uncertain impact of UMs on effectiveness and safety outcomes, use therapeutic drug monitoring to guide dosing.**	Optional
CYP2D6 IM	Reduced metabolism…may increase the likelihood of dose related side effects. **Differences between intermediate metabolizers and normal metabolizers varies across studies for both oral and long-acting injectable formulations**.	**Reduce starting dose and maintenance dose (oral or long-acting injectable formulation) by 25-50%.**	**Moderate**
CYP2D6 PM	Greatly reduced metabolism…evident in both oral and long-acting injectable formulations…**increases the likelihood of dose-related side-effects and may increase the likelihood of treatment discontinuation.**	**Reduce starting and maintenance dose by 50% for oral formulations or by 25-50% for long-acting injectable formulations.**	**Strong**

Considerations: Drug-drug interactions (e.g., CYP3A4 and CYP2D6 inducers and inhibitors), therapeutic drug monitoring, and other patient characteristics (e.g., age, BMI, diet, renal function, liver function, and diagnosis) should be considered when adjusting dose or selecting an alternative therapy.

Risperidone and *CYP2D6*

- Second generation antipsychotic with active metabolite
- Parent+metabolite = active moiety
  - Some potential clinical differences in risperidone vs 9-OH risperidone
- 113 studies
- PK evidence:
  - Continuous association of 2D6 AS x PK phenotypes
  - UM vs NM – ↓ in UMs but variable effect sizes
  - NM vs IM – variable effect size across studies
  - NM vs PM – moderate/high (~50% ↑PM)
  - Similarities between PO and LAI
- Clinical evidence:
  - Dose relationships (UMs and PMs)
  - Increased discontinuation (PM and UM) – stronger than aripiprazole
  - Tolerability>efficacy/effectiveness
- Discussion points:
  - Whether to lump/split LAI vs PO
  - Evolving substrate specificity – E.g., *17 may behave like UM and *29 closer to PM – review ongoing and action TBD



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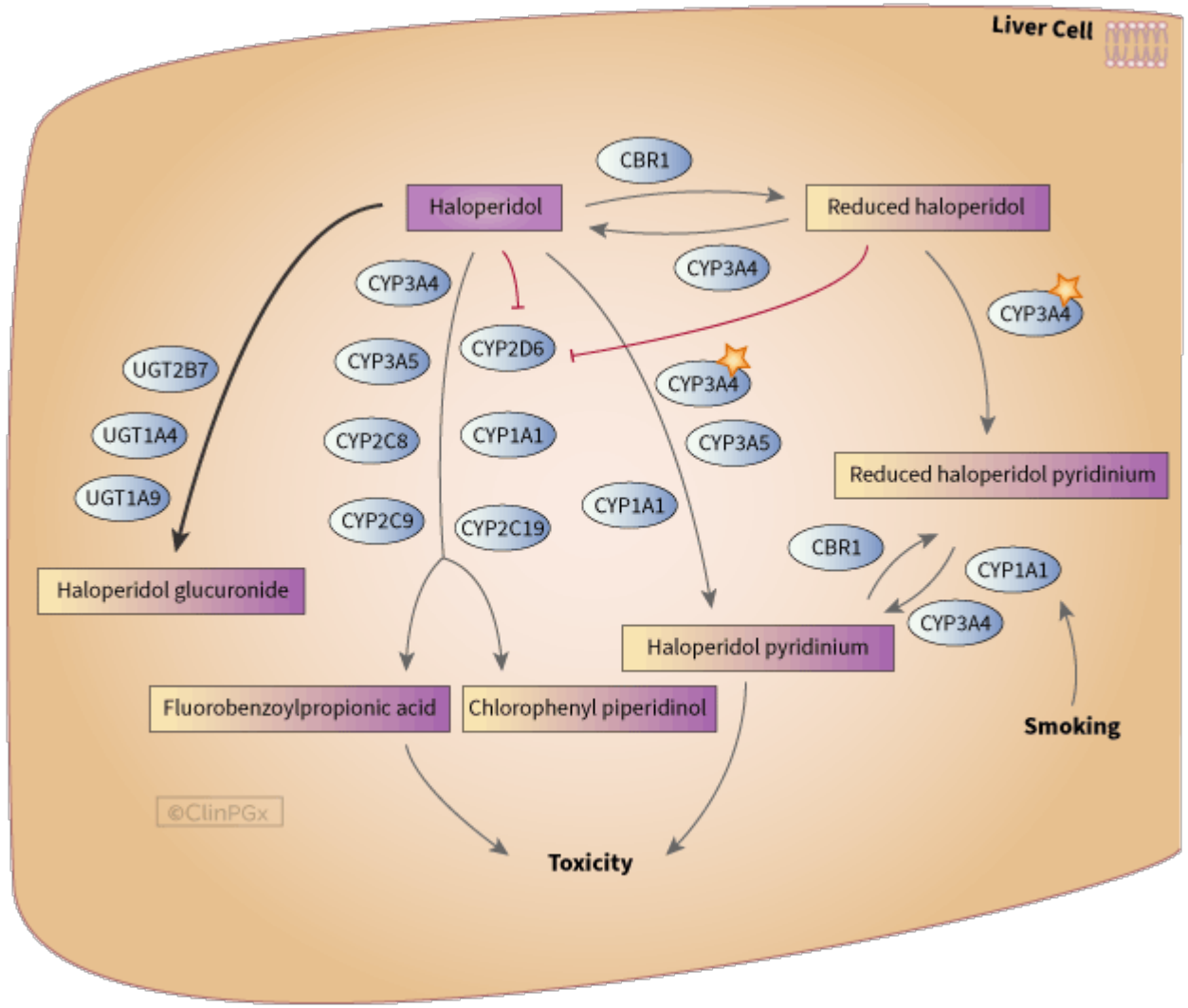
Phene	Implication (abridged)	Therapeutic recommendation	Strength
CYP2D6 UM	Increased metabolism of risperidone…may increase the likelihood of lower concentrations, lower overall exposure…**and increase the likelihood of inadequate treatment response and discontinuation**.	**Select a clinically appropriate alternative medication**. If risperidone use is warranted, initiate therapy with recommended starting dose. Increasing the target maintenance dose may be needed. **Due to the uncertain impact of UMs on effectiveness and safety outcomes, use therapeutic drug monitoring to guide dosing.**	Optional
CYP2D6 IM	Reduced metabolism…Higher concentrations and exposure…**may increase the likelihood of dose related side effects**.	**Reduce starting dose and maintenance dose (oral or long-acting injectable formulation) by 25%.**	Optional
CYP2D6 PM	Greatly reduced metabolism…Higher concentrations and exposure…are evident in both oral and long-acting injectable formulations. **This increases the likelihood of dose-related side-effects and the likelihood of treatment discontinuation**	**Reduce starting and maintenance dose by 25-50%** for oral formulations or long-acting injectable formulations. If dose-related complications persist, **consider selecting a clinically appropriate alternative** medication.	Moderate

Considerations: Drug interactions, therapeutic drug monitoring, and other patient characteristics (e.g., age, BMI, diet, renal function, liver function, and diagnosis) should be considered when adjusting dose or selecting an alternative therapy.

Caveats: new data summarizing substrate specific effects of *17 and *29 currently in review to determine next steps.

Haloperidol and *CYP2D6*

- First generation high potency antipsychotic
- High doses strongly associated with movement disorders
- Parent drug active
- 46 studies
- PK evidence:
  - UM vs NM – small “n” with signal of effect but variable impact
  - NM vs IM – similar
  - NM vs PM – moderate/high (~25-50% ↑PM)
  - PO vs LAI x 2D6 lacking
- Clinical evidence:
  - Tolerability>efficacy/effectiveness
- Discussion points:
  - UM recommendation
  - TDM relevance
  - Evolving dosing strategies over time and impact on data (e.g., lower dosing used now vs in past)



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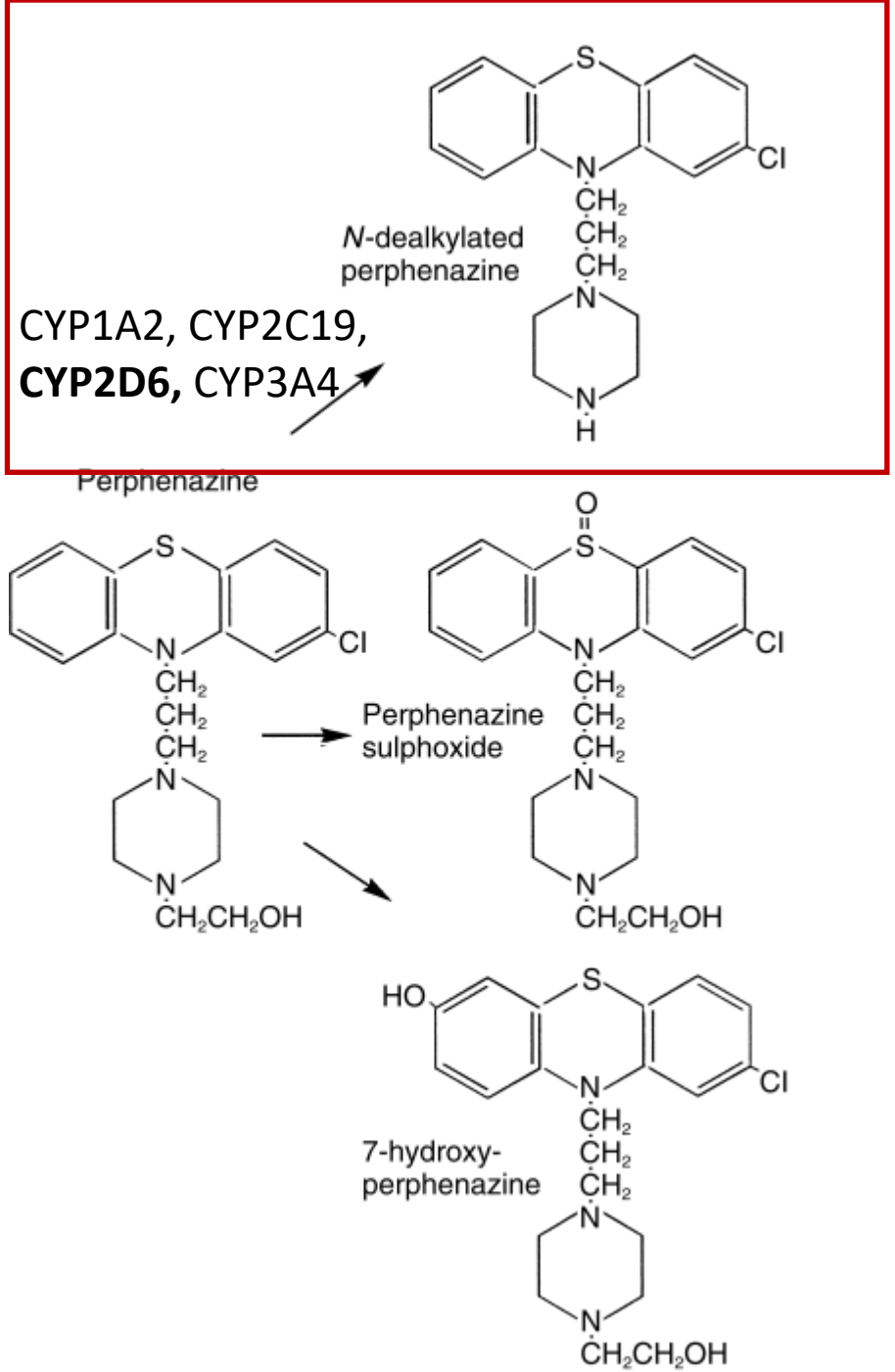
Phene	Implication (abridged)	Therapeutic recommendation	Level
CYP2D6 UM	Increased metabolism of haloperidol…may increase the likelihood of lower concentrations and lower overall exposure to haloperidol and increase the likelihood of inadequate treatment response...**magnitude of this effect and clinical relevance is unclear due to the small number of CYP2D6 ultrarapid metabolizers characterized in the literature**.	Initiate therapy with recommended starting dose and titrate to maintenance dose based on effectiveness and tolerability. Due to the uncertain impact of UMs on effectiveness and safety outcomes, **use therapeutic drug monitoring to guide dosing**.	Optional
CYP2D6 IM	Reduced metabolism…may increase the likelihood of dose related side effects. The magnitude of this effect and clinical relevance are unclear due to variability…across studies.	Initiate therapy with recommended starting dose and titrate to maintenance dose based on effectiveness and tolerability.	**Moderate**
CYP2D6 PM	Moderate to greatly reduced metabolism…Higher concentrations and exposure…characterized in persons taking oral formulations, while the impact on short or long-acting intramuscular formulations is unclear. **Increased exposures in CYP2D6 poor metabolizers taking oral formulations increases the likelihood of dose-related side-effects.**	**Reduce starting and maintenance dose by 25-50% for oral formulations**. If dose-related complications persist, **consider selecting a clinically appropriate alternative medication**.	**Strong**

Considerations: Drug interactions, therapeutic drug monitoring, and other patient characteristics (e.g., age, BMI, diet, smoking, renal function, liver function, QTc interval, serum potassium, and diagnosis) should be considered when adjusting dose or selecting an alternative therapy.

Perphenazine and *CYP2D6*

- First generation medium potency antipsychotic
- Dose-related
- Parent drug active
- 6 studies
- PK evidence:
  - UM vs NM – no data
  - NM vs IM – 1.5-3x higher exposure IMs
  - NM vs PM – 3-4x higher exposure PMs
- Clinical evidence:
  - Dosing (PMs)
- Discussion points:
  - UM recommendation with no UMs in literature?
  - Translating effect sizes in IMs/PMs to dose adjustments – this contributed to consider alternative language



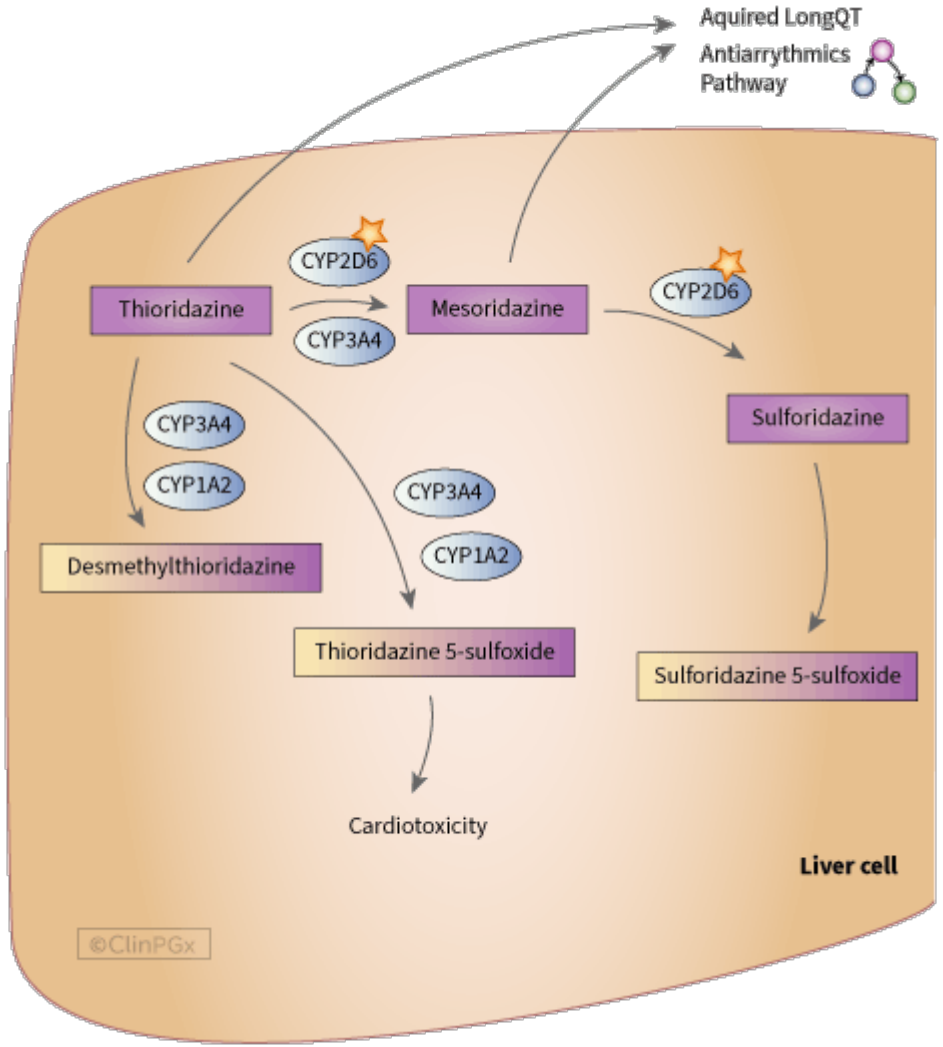
Olesen and Linnet. Br. J Clin Pharmacol. 2000. PMID: 11136295

Phene	Implication (abridged)	Therapeutic recommendation	Level
CYP2D6 UM	Potential increased metabolism of perphenazine…may increase the likelihood of lower concentrations and lower overall exposure…clinical relevance is unclear due to **no published data characterizing CYP2D6 ultrarapid metabolizers receiving perphenazine**.	**Insufficient data to make dose or drug selection recommendation based on genotype.** Therapeutic drug monitoring may be helpful in guiding dose adjustments.	No Rec
CYP2D6 IM	Reduced metabolism…may increase the likelihood of dose related side effects. The magnitude of this effect and clinical relevance are unclear due to variability observed across studies.	**Reduce starting and maintenance dose by 25-50%.**	**Moderate**
CYP2D6 PM	Greatly reduced metabolism...Higher concentrations and exposure…**increases the likelihood of dose-related side-effects**.	**Reduce starting and maintenance dose by 50-75% or consider selecting a clinically appropriate alternative** medication.	**Moderate**

Considerations: Drug interactions, therapeutic drug monitoring, and other patient characteristics (e.g., age, BMI, diet, smoking, renal function, liver function, QTc interval, serum potassium, and diagnosis) should be considered when adjusting dose or selecting an alternative therapy.

Thioridazine and *CYP2D6*

- First generation low potency antipsychotic
- Strong dose/exposure relationships with QTc prolongation
- Active metabolite (mesoridazine)
- Product labeling for contraindication in “reduced metabolizers”
- 7 studies
- PK studies
  - Strong AS/metabolizer status relationships with exposure/PK parameters.
  - Few UMs in published literature
- Clinical studies
  - Reproducible relationships of CYP2D6 metabolizer status and exposure and QT interval outcomes
- Discussion points
  - UM recommendation given small n in published literature, uncertainties of active metabolite, “TDM” vs noting specific metabolites
  - IM/PM recommendations for naïve vs non-naïve patients
  - Level of additional detail needed in the “considerations” column given unique safety risks



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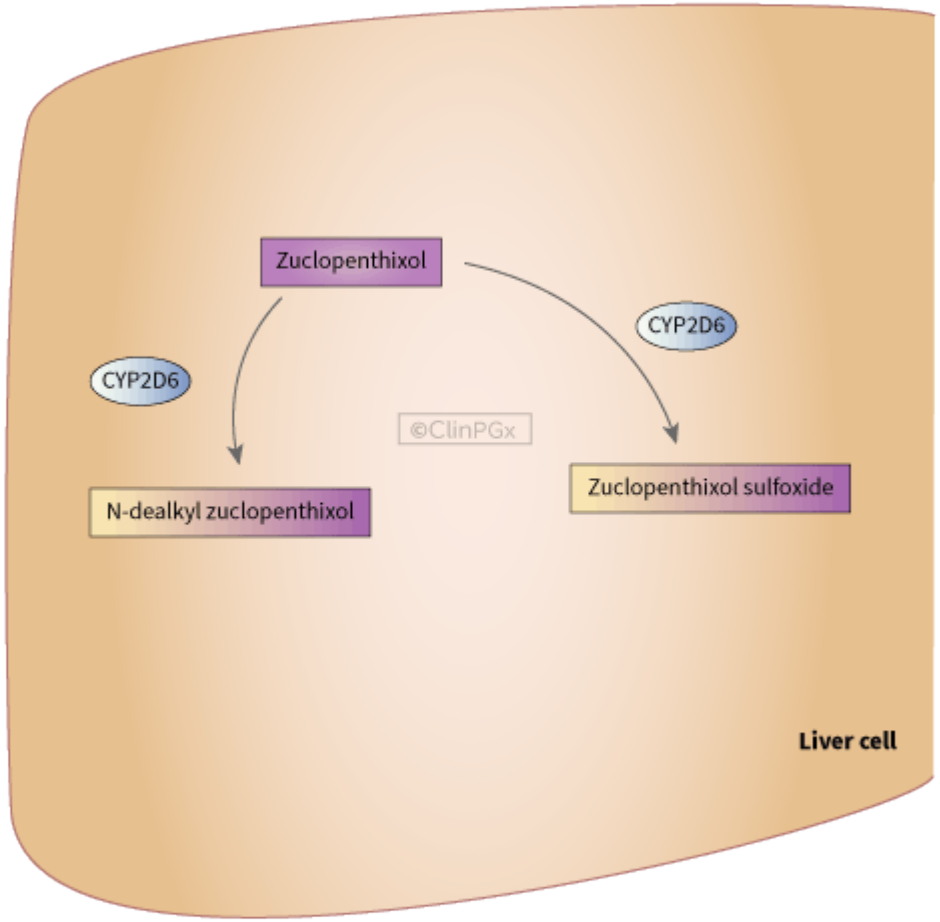
Phene	Implication (abridged)	Therapeutic recommendation	Level
CYP2D6 UM	Increased metabolism of thioridazine…may increase the likelihood of lower concentrations and lower overall exposure...The magnitude of the effects of increased thioridazine metabolism to the active metabolite mesoridazine on clinical outcomes is unclear due to the small number of CYP2D6 ultrarapid metabolizers characterized in the literature.	Initiate therapy with recommended starting dose. Due to the uncertain impact of UMs on effectiveness and safety outcomes, **use therapeutic drug monitoring of thioridazine and metabolites to guide dosing**.	**Moderate**
CYP2D6 IM	Reduced metabolism...Higher concentrations and…may increase the likelihood of dose related side-effects, including life threatening cardiac rhythm abnormalities.	**Do not use in thioridazine naïve patients.** Select a clinically appropriate alternative medication.	**Moderate**
CYP2D6 PM	Moderate to greatly reduced metabolism…Increased exposures in CYP2D6 poor metabolizers increases the likelihood of dose-related side-effects including life threatening cardiac rhythm abnormalities.	**Do not use in thioridazine naïve patients.** Select a clinically appropriate alternative medication.	**Strong**

Considerations: Thioridazine is contraindicated in known CYP2D6 reduced/poor metabolizers. Drug interactions, therapeutic drug monitoring, and other patient characteristics (e.g., age, BMI, diet, smoking, renal function, liver function, ECG/QTc interval, serum potassium, and diagnosis) should be considered when selecting an alternative therapy.

Zuclopenthixol and *CYP2D6*

- First generation high potency antipsychotic
  - International use, not approved in US
- 7 studies
- PK evidence:
  - UM vs NM – small n but lower exposure
  - NM vs IM – (~25-35% ↑IM)
  - NM vs PM – moderate/high (~45-70% ↑PM)
  - PO vs LAI x 2D6 relationships similar effect sizes but more variability in IMs
- Clinical evidence:
  - Fewer studies, less data
- Discussion points:
  - UM recommendation
  - TDM relevance
  - Lumping vs splitting LAI recommendation



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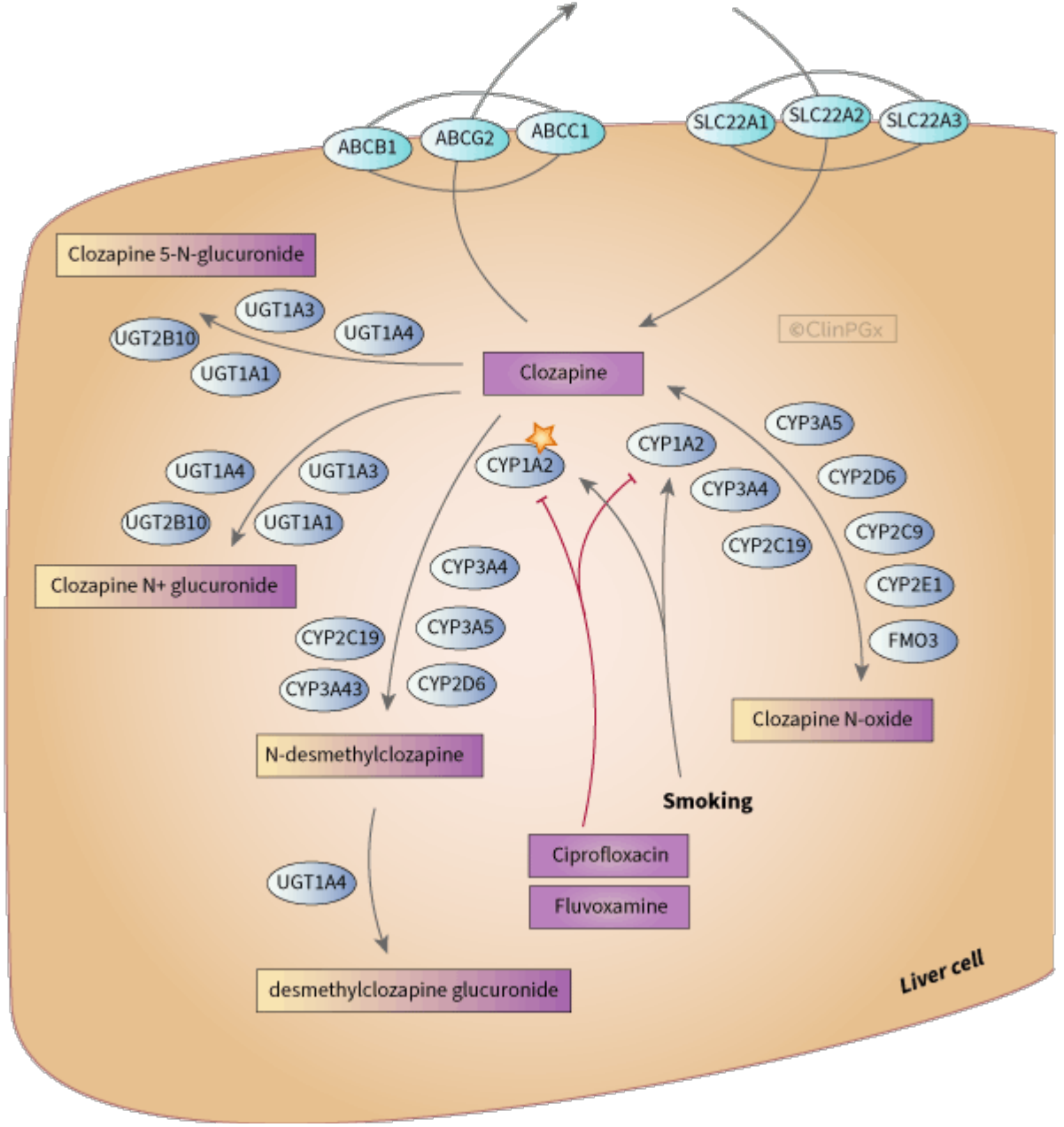
Phene	Implication (abridged)	Therapeutic recommendation	Level
CYP2D6 UM	Increased metabolism of zuclopenthixol…may increase the likelihood of lower concentrations and lower overall…**The magnitude of the effects of increased zuclopenthixol metabolism to the inactive metabolites on clinical outcomes is unclear due to the small number of CYP2D6 ultrarapid metabolizers characterized in the literature.**	Initiate therapy with recommended starting dose and titrate to maintenance dose based on effectiveness and tolerability. **Due to the uncertain impact of UMs on effectiveness and safety outcomes, use therapeutic drug monitoring to guide dosing**.	Optional
CYP2D6 IM	Reduced metabolism...Higher concentrations and…may **increase the likelihood of dose related side-effects. Effect sizes of increased zuclopenthixol concentrations in intermediate metabolizers were similar in oral and long-acting injectable (LAI) formulations, but more variable in LAIs.**	**Reduce starting and maintenance dose by 25%.**	**Moderate**
CYP2D6 PM	Moderate to greatly reduced metabolism when compared to CYP2D6 normal metabolizers. Increased exposures in CYP2D6 poor metabolizers **may increase the likelihood of dose-related side-effects**. **Effect sizes of increased zuclopenthixol concentrations in poor metabolizers were similar in oral and long-acting injectable (LAI) formulations, but more variable in LAIs.**	**Reduce starting and maintenance dose by 50%.**	**Moderate**

Considerations: Drug interactions, therapeutic drug monitoring, and other patient characteristics (e.g., age, BMI, diet, smoking, renal function, liver function, QTc interval, serum potassium, and diagnosis) should be considered when adjusting dose or selecting an alternative therapy.

Clozapine and *CYP2D6*

- Second generation antipsychotic
  - Unique indications for treatment resistance and suicidal ideation schizophrenia
- Highly efficacious but requires significant monitoring
- FDA labeling and Section 1 of FDA Table of PGx Associations
  - “Dose reduction may be necessary in patients who are CYP2D6 poor metabolizers. Clozapine concentrations may be increased in these patients…”
- 23 studies reviewed including recent large studies of n~900 and ~10K sampling measurements (PMID: 40971654)
- Convincing data that CYP2D6 genotype does **NOT** meaningfully impact clozapine disposition and clinical outcomes
- No genotype recommendation from the committee



https://www.clinpgx.org/pathway/PA166163661

Drugs with *CYP2D6* based dosing in labeling but no/little published data

Iloperidone: **CYP2D6 poor metabolizer**	Although the FDA label for iloperidone recommends a maximum daily dose of 12 mg for CYP2D6 PMs and slower titration with strong CYP2D6 inhibitors, based on pharmacokinetic data and QTc prolongation concerns, there is insufficient clinical evidence to support a genotype- guided prescribing recommendation	**No recommendation** for therapy due to insufficient or no evidence regarding drug exposure and clinical effectiveness	**Clinicians should remain aware of FDA labeling and use clinical judgment when incorporating CYP2D6 genotyping into iloperidone** prescribing, particularly in patients at higher QTc risk.
Iloperidone context: only looked at 2 individual SNPs corresponding to *10 and *4. Published data (2 studies) available assessed as not convincing.			
Pimozide: **CYP2D6 poor metabolizer**	Although the FDA label for pimozide includes a recommendation that individuals known to be CYP2D6 PMs not exceed a total daily dose of 4 mg based on pharmacokinetic modeling and concerns regarding QTc prolongation, there is insufficient clinical evidence to support genotype-guided prescribing based on this CPIC review.	**No recommendation** for therapy due to insufficient or no evidence regarding drug exposure and clinical effectiveness	**Clinicians should remain aware of FDA labeling and use clinical judgment when incorporating CYP2D6 genotyping into pimozide prescribing,** particularly in patients at higher QTc risk. See the guideline text for additional details.
Pimozide context: FDA labeling based on simulation data only with little published CYP2D6 data (3 studies, one case report). Other PK and drug interaction studies suggest CYP3A4 activity potentially more relevant.			

Drugs with *CY2D6* based dosing in labeling but no/little published data

Brexpiprazole: CYP2D6 poor metabolizer	Although the FDA and EMA labels for brexpiprazole include recommendations that individuals identified as CYP2D6 poor metabolizers should have their standard dosage reduced by 50%, there is insufficient clinical evidence to support genotype-guided prescribing based on this CPIC review.	No recommendation for therapy due to insufficient or no evidence regarding drug exposure and clinical effectiveness	**Clinicians should remain aware of FDA labeling and use clinical judgment when incorporating CYP2D6 genotyping into brexpiprazole prescribing**.
Brexpiprazole context: Published data available (4 studies) either did not support actionable genotype-driven effect sizes or were noted to have significant weaknesses/caveats that precluded a CPIC recommendation.			
Sertindole: CYP2D6 poor metabolizer	Although the Swiss drug label for sertindole indicates normal metabolism via CYP2D6 and CYP3A and reports 2-3 times higher plasma concentrations in CYP2D6 poor metabolizers due to reduced clearance, there is insufficient published evidence to support a genotype-guided dosing or prescribing recommendation for sertindole based on this evidence review.	No recommendation for therapy due to insufficient or no evidence regarding drug exposure and clinical effectiveness	**Prescribers should remain aware of labeling warnings and apply clinical judgment,** including ECG monitoring as clinically appropriate.
Sertindole context: Published data available limited to 1 study primarily investigating effects of renal impairment (n=24 with n=2 *4/*4) was not sufficient to support a CPIC recommendation.			

CYP2C19 and *CYP3A4/5*

- Search conducted for all antipsychotics
- *CYP3A*: search included *CYP3A4*, *CYP3A5*, *CYP3A*, *CYP3A4/5*
- Current data do not support drug-gene pair recommendations
- **Quetiapine:** The DPWG provides a recommendation for genotype-based guidance, whereas the CPIC committee concluded that the current evidence does not meet the threshold required to support genotype-based clinical recommendations

Additional considerations and deliberations

- Diagnostic specificity and relevance of drug-gene relationships
- Pediatrics
  - Aripiprazole and risperidone have sufficient data
  - Other drugs – extrapolation at discretion of prescriber
- How/if to include TDM language in recommendations
- CYP2D6 ultrarapid metabolizer language
  - Small “n” in publications, effect signals with variability, potential applicability of TDM
- Evolving risperidone *17 and *29 literature
- Comprehensiveness of caveats and other clinical considerations
- What to do with the drugs with FDA labeling but lack of available data for CPIC-framework assessment

Summary of Recommendations

CYP2D6 Phenotype	Aripiprazole	Risperidone	Haloperidol	Perphenazine	Thioridazine	Zuclopenthixol
Ultrarapid	TDM	⊘	TDM	TDM	TDM	TDM
Intermediate	⚠	⚠	-	-	⊘	⚠
Poor	⚠	⚠ ⊘	⚠ ⊘	⚠ ⊘	⊘	⚠

⚠ Dose adjustment may be required

⊘ Consider alternative medication

TDM: Therapeutic Drug Monitoring

Conclusions and next steps

- This CPIC antipsychotic guideline includes recommendations based on CYP2D6 genotypes for:
  - Aripiprazole, risperidone, haloperidol, perphenazine, thioridazine, and zuclopenthixol
- Most comprehensive guideline assessment to date of drugs and drug metabolizing enzyme genes
- Notable surprises:
  - Strength of CYP2D6 findings in long-acting injectable formulations
  - Lack of published data to support some drugs with CYP2D6-related product labeling
  - New substrate specificity data for risperidone – stay tuned
- Finalizing evidence tables and impact of late-breaking publications
- Manuscript and supplemental materials drafts in progress

Thank you!

Any questions?