PGx Marks the Spot – Clinical Applications and Implementation of Pharmacogenomics to Support Patient-Centered Care

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Disclosure Statement

- Mark Zangardi has no relevant financial relationship(s) with ineligible companies to disclose.

- None of the planners for this activity have relevant financial relationships with ineligible companies to disclose.

Learning Objectives

At the completion of this activity, the participant will be able to:

1. Outline key elements of pharmacogenomics
2. Identify resources that support interpretation and application of pharmacogenomics information in patient care
3. Describe evidence-based uses of pharmacogenomics in current clinical practice
4. Employ pharmacogenomics information when creating patient-specific medication plans

PHARMACOGENOMICS – INTRODUCTION, TERMINOLOGY, CONCEPTS

Pharmacogenomics (PGx)

- Drug effect/response differs between individuals

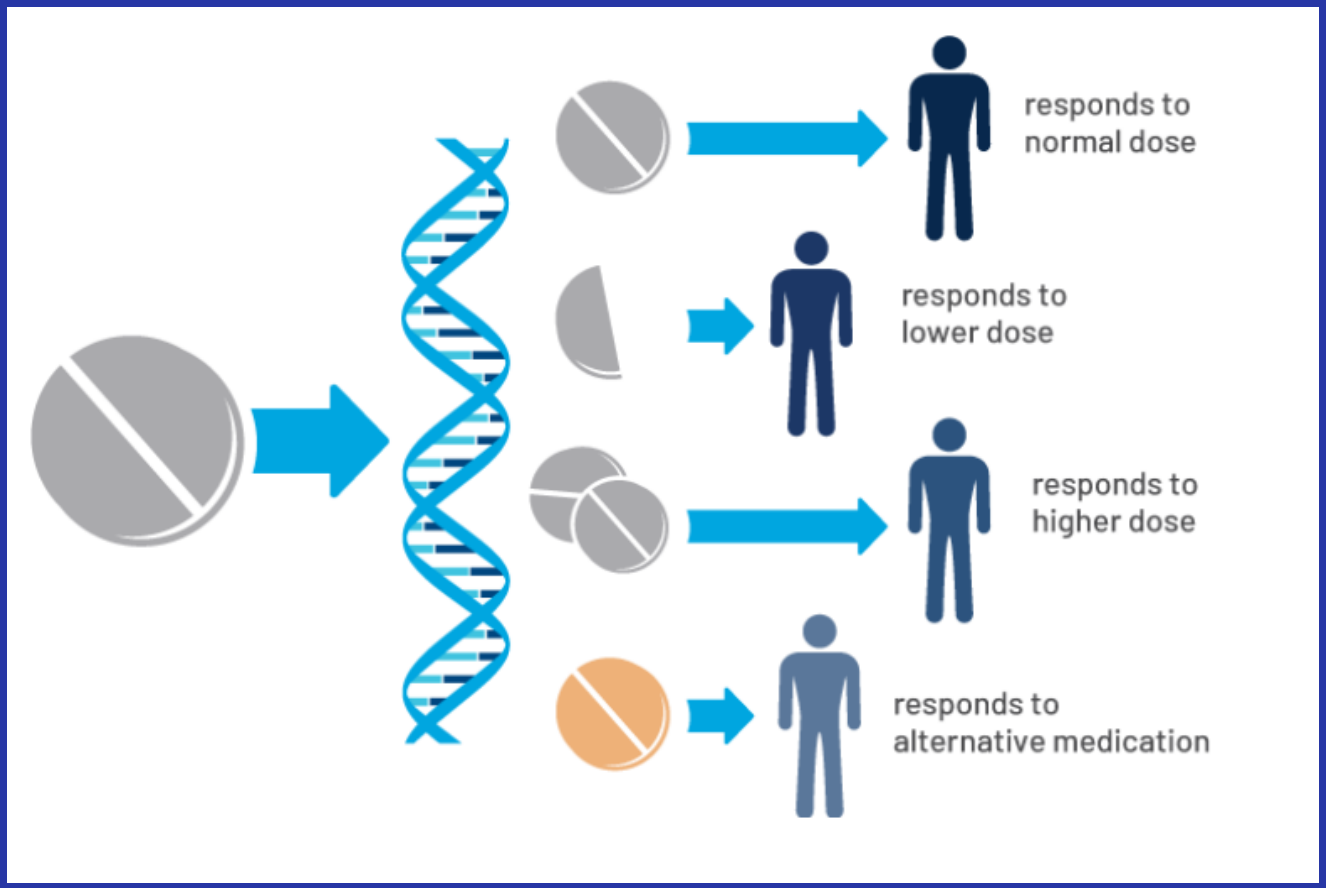
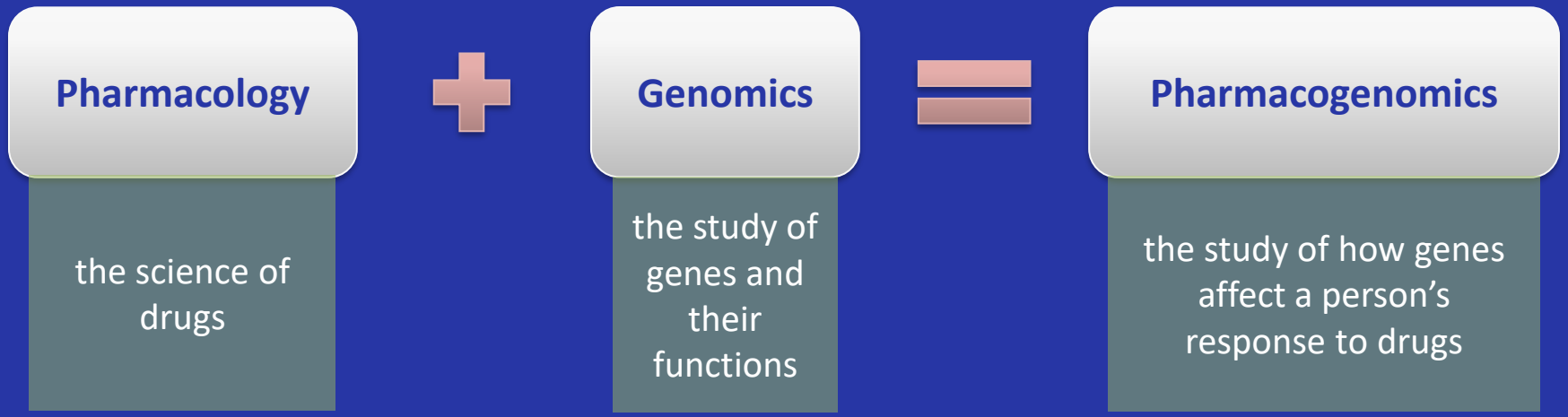


Image credit: https://www.genelex.com/test-menu/

Pharmacogenomics (PGx)

- Component of precision medicine
- Variability in drug response – genetic factors
- Aim to tailor drug therapy to each person or group of people



National Cancer Institute. NCI Dictionary of Genetics Terms. https://www.cancer.gov/publications/dictionaries/genetics-dictionary
CDC. Genomics & Precision Health. Pharmacogenomics: What dose it mean for your health? https://www.cdc.gov/genomics/disease/pharma.htm

Categories of Genetic Variability Affecting Drug Response

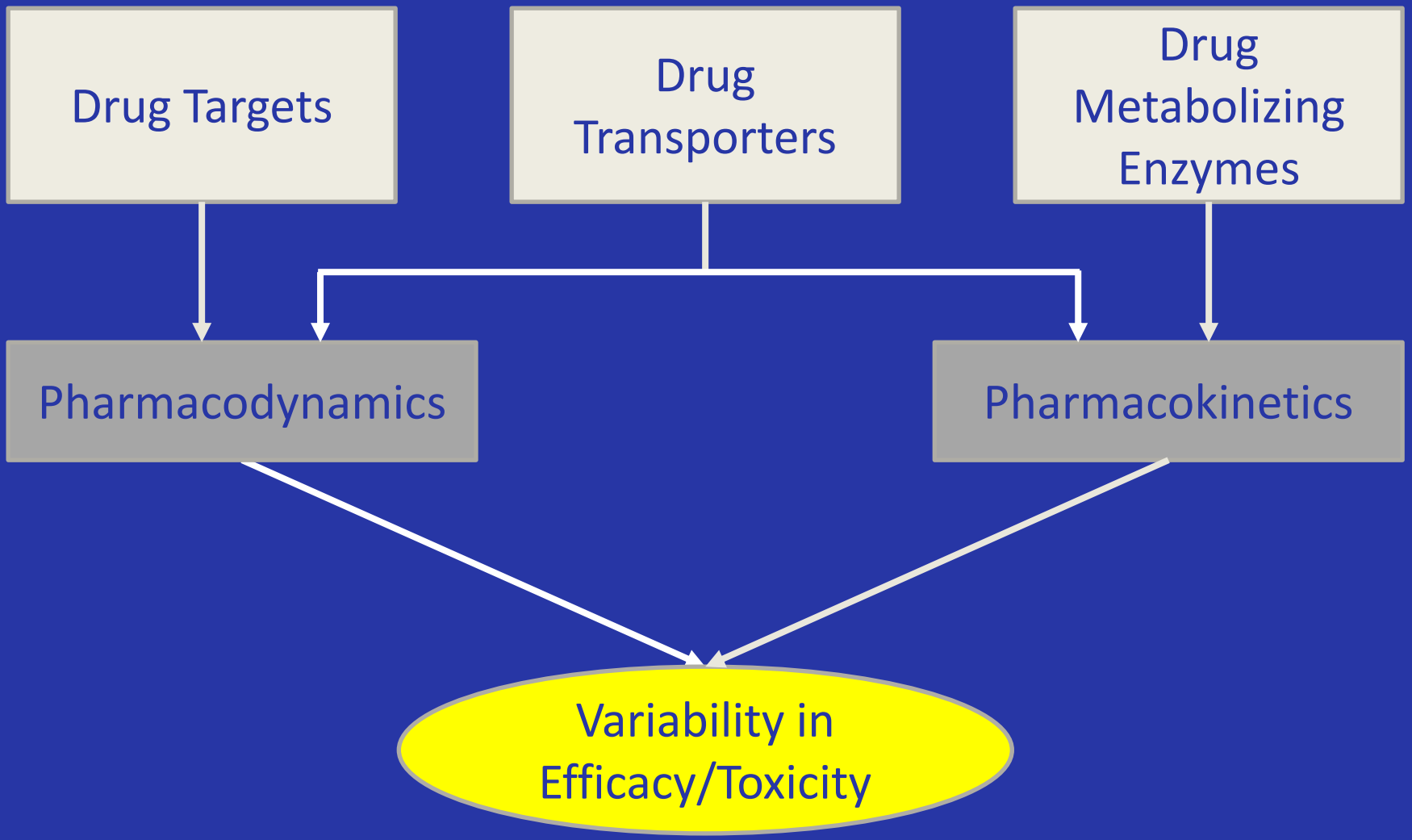


Figure used with permission from Emily J. Cicali, PharmD, BCPS

PGx Testing – Logistics and Considerations

- Sample: blood, saliva, or buccal (cheek) swab

- Various test types and methods
  - May be performed “in-house” or send-out
  - Lab Developed Test (LDT) vs. FDA-approved/cleared
  - National Institutes of Health (NIH) Genetic Testing Registry (https://www.ncbi.nlm.nih.gov/gtr/)

- Turnaround time = hours to days to weeks

PGx Testing – Logistics and Considerations

- Single gene vs. multigene (panel)
- Reactive vs. preemptive testing
- Costs, billing, reimbursement
- Integration in electronic health record (EHR) and clinical decision support (CDS)

Potential Benefits of PGx-Guided Pharmacotherapy

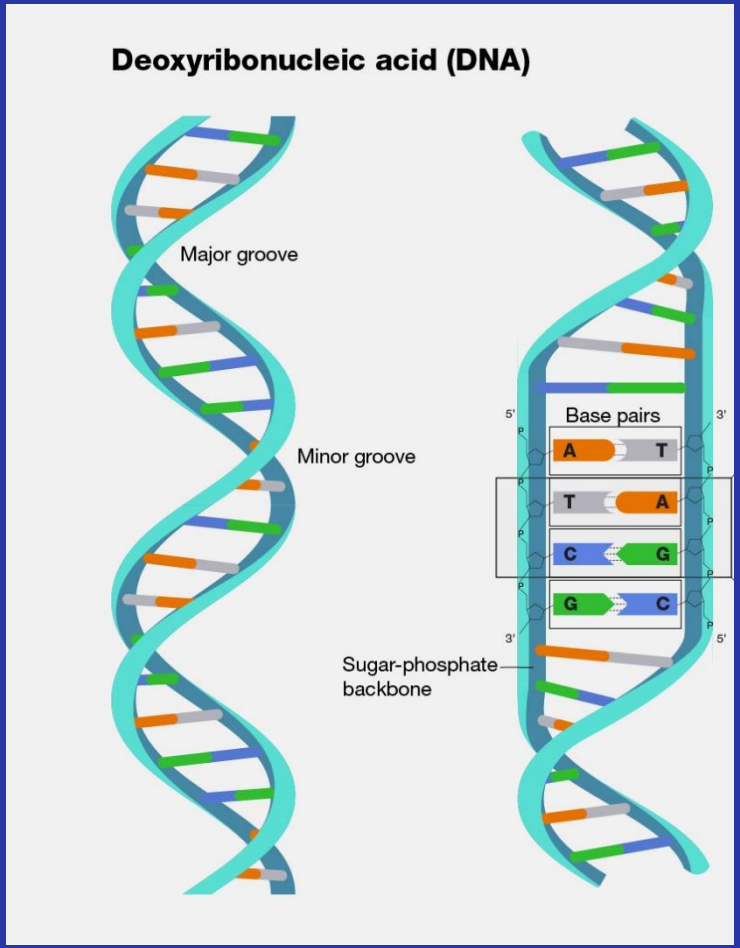
- Use of PGx testing has the potential to:
  - Improve selection of appropriate therapies
  - Optimize drug dosing
  - Reduce the risk of adverse drug reactions (ADRs)
  - Increase patient and provider satisfaction
  - Reduce overall cost of care

- One tool – not a silver bullet

Hockings JK et al. *Cleve Clin J Med* 2020;87(2):91-99.

PGx Terminology

- Deoxyribonucleic acid (DNA): carries genetic information
  - Two linked strands – "double helix"
  - Backbone of alternating sugar and phosphate groups
  - One of fours bases is attached to each sugar
    - **A** (adenine), **T** (thymine), **C** (cytosine), **G** (guanine)



Courtesy: National Human Genome Research Institute

NIH. National Human Genome Research Institute. Talking Glossary of Genomic and Genetic Terms. https://www.genome.gov/genetics-glossary

PGx Terminology

- Gene: the basic unit of inheritance
  - Contain information needed to specify traits
    - Physical and biological
  - Coding genes provide instructions for specific proteins

NIH. National Human Genome Research Institute. Talking Glossary of Genomic and Genetic Terms. https://www.genome.gov/genetics-glossary

PGx Terminology

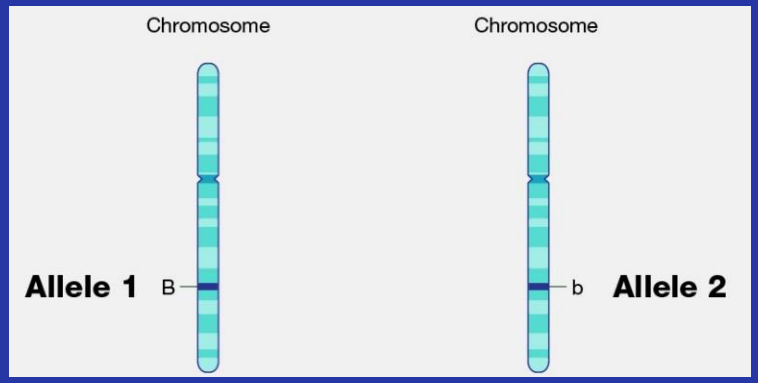
- Polymorphism: a variation in DNA sequence
  - Various types
    - **Most common is single nucleotide polymorphism (SNP)**
  - May or may not have functional consequences

Courtesy: National Human Genome Research Institute

https://www.genome.gov/genetics-glossary

PGx Terminology

- Allele: one of two or more versions of DNA sequence at a given genomic location (locus)
  - Humans are diploid organisms → 2 alleles
  - A given allele may contain a combination of genetic variants (e.g., SNPs, insertions/deletions, etc)
    - May be referred to as *haplotype*



Courtesy: National Human Genome Research Institute

https://www.genome.gov/genetics-glossary

He Y, Hoskins JM, McLeod HL. *Trends Mol Med* 2011;17(5):244-51.

PGx Terminology

- In PGx, alleles are generally characterized by functional status

Allele Terminology	Functional Definition
Increased function	Function greater than normal function
Normal function	Fully functional/wild-type
Decreased function	Function less than normal function
No function	Nonfunctional
Unknown function	No literature describing the function or the allele is novel
Uncertain function	Literature supporting function is conflicting or weak

https://www.genome.gov/genetics-glossary

Caudle KE et al. *Genet Med* 2017;19(2):215-223.

PGx Terminology

- Allele nomenclature
  - Basic nomenclature
    - Gene Position Allele
    - Example: *CYP2C19* 681 G **OR** *CYP2C19* 681 A
  - Reference SNP (rs) nomenclature
    - Each SNP is assigned an rs number
    - Example: *CYP2C19* 681 G>A → rs4244285

PGx Terminology

- "Star" nomenclature in PGx
  - Gene * Allele Number
  - Example: *CYP2C19* * 1 **OR** *CYP2C19* * 2

Kalman LV et al. *Clin Pharmacol Ther* 2016;99(2):172-185.

PGx Terminology

- Some notes about “star” nomenclature in PGx
  - *1 generally denotes the default reference allele (“wild-type”)
    - Generally considered fully functional
    - Usually based on the initial population studied
    - Absence of known variant alleles that were tested for

Kalman LV et al. *Clin Pharmacol Ther* 2016;99(2):172-185.
Clinical Pharmacogenetics Implementation Consortium. Alleles. https://cpicpgx.org/alleles/

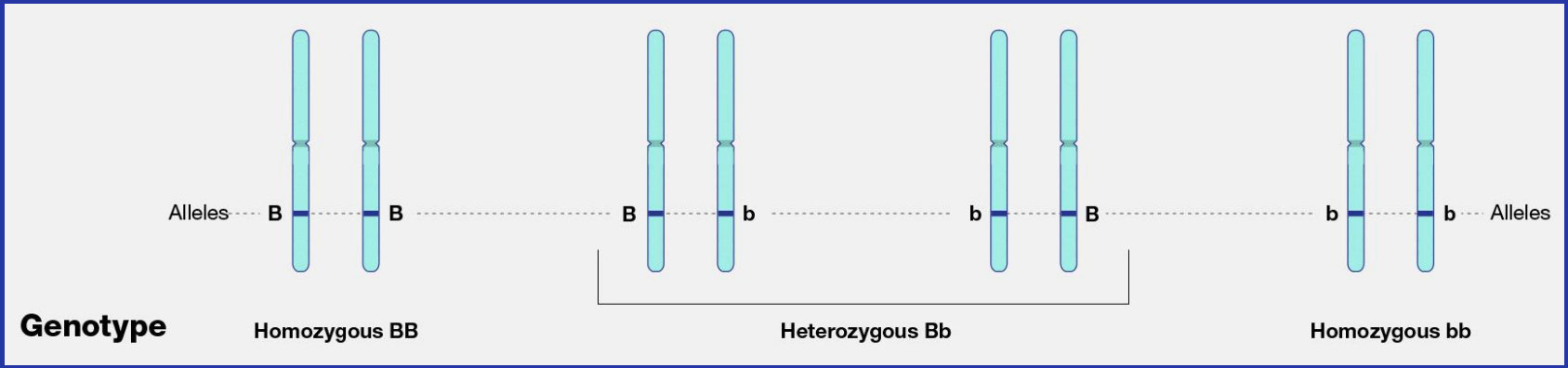
PGx Terminology

- Some notes about “star” nomenclature in PGx
  - The same “star” number does not always reflect the same functional effect
    - *CYP2C9**2 = decreased function
    - *CYP2D6**2 = normal function

Kalman LV et al. *Clin Pharmacol Ther* 2016;99(2):172-185.
Clinical Pharmacogenetics Implementation Consortium. Alleles. https://cpicpgx.org/alleles/

PGx Terminology

- Genotype: genetic constitution of an individual
  - Set of alleles present at one or more specific loci
  - May be referred to as *diplotype*



Courtesy: National Human Genome Research Institute

https://www.genome.gov/genetics-glossary

https://www.cancer.gov/publications/dictionaries/genetics-dictionary/

PGx Terminology

- Phenotype: an individual's observable traits
  - In PGx, often refers to "metabolizer status" of drug metabolizing enzymes

Metabolizer Status (phenotype)	Functional Definition
Ultrarapid metabolizer (UM)	Increased enzyme activity compared to rapid metabolizers
Rapid metabolizer (RM)	Increased enzyme activity compared to normal metabolizers, but less than ultrarapid metabolizers
Normal metabolizer (NM)	Fully functional enzyme activity
Intermediate metabolizer (IM)	Decreased enzyme activity
Poor metabolizer (PM)	Little to no enzyme activity

https://www.genome.gov/genetics-glossary

Caudle KE et al. *Genet Med* 2017;19(2):215-223.

PGx Terminology

- Putting it together…
  - "Star" nomenclature for PGx
    - Gene * Allele Number/* Allele Number = PHENOTYPE
    - Examples
      - *CYP2C19* *1/*1 = normal enzyme activity
        - » Normal metabolizer
      - *CYP2C19* *1/*2 = reduced enzyme activity
        - » Intermediate metabolizer
      - *CYP2C19* *2/*2 = no enzyme activity
        - » Poor metabolizer

Additional PGx Concepts

- Activity value of alleles
  - Utilized for several genes that encode drug metabolizing enzymes (e.g., *CYP2C9*, *CYP2D6, DPYD*)
  - For each diplotype, calculate the activity score (AS)
    - AS = activity value [allele 1] + activity value [allele 2]

Allele functional status	Activity value	Example *CYP2C9* alleles
Normal function	1.0	*1, *9
Decreased function	0.5	*2, *5, *8
No function	0	*3, *6

Theken KN et al. *Clin Pharmacol Ther* 2020;108(2):191-200.

Additional PGx Concepts

- CYP2C9 phenotype assignment based on AS

Likely phenotype	Activity score	Genotypes	Examples of diplotypes
Normal metabolizer	2	Two normal function alleles	*1/*1
Intermediate metabolizer	1.5 1	-One normal function allele + one decreased function allele **OR** -One normal function allele + one no function allele **OR** -Two decreased function alleles	*1/*2 *1/*3 *2/*2
Poor metabolizer	0.5 0	-One no function allele + one decreased function allele **OR** -Two no function alleles	*2/*3 *3/*3
Indeterminate	N/A	Allele combinations with uncertain and/or unknown function alleles	

Theken KN et al. *Clin Pharmacol Ther* 2020;108(2):191-200.

PATIENT CASE

- DJ is a 77 year old female that underwent PGx testing of *CYP2C9,* revealing *1/*2 diplotype.
  - What is DJ's activity score?
    - *CYP2C9*1* activity value = 1.0
    - *CYP2C9*2* activity value = 0.5
    - **Activity score = 1.0 + 0.5 = 1.5**
  - What is DJ's likely CYP2C9 phenotype?
    - **Intermediate metabolizer**

Additional PGx Concepts

- Copy number variation
  - More or less than two copies of a gene (for humans)
  - *CYP2D6* is subject to gene deletion, duplication, multiplication
    - *CYP2D6*5* = gene deletion (no function allele)
    - Duplication/multiplication is denoted as "xN"
      - xN = number of *CYP2D6* gene copies of the specific alleles
      - Example: *CYP2D6*1/*2xN*
        - » One copy of *CYP2D6*1*, two copies of *CYP2D6*2*

He Y, Hoskins JM, McLeod HL. *Trends Mol Med* 2011;17(5):244-51.

Goetz MP, et al. *Clin Pharmacol Ther* 2018;103(5):770-777.

Additional PGx Concepts

- Phenoconversion
  - Clinical phenotype does not match the genotype-based phenotype due to drug interaction
    - Drug-Drug-Gene Interaction
  - Example
    - Patient has a genotype-based CYP2D6 normal metabolizer phenotype
    - Patient also takes bupropion (strong CYP2D6 inhibitor)
    - Patient is converted to CYP2D6 poor metabolizer

Cicali EJ et al. *Clin Pharmacol Ther* 2021;110(3):677-687.

Additional PGx Concepts

- Having a variant “pharmacogene” does not guarantee the outcome at risk
- Frequency of allele variants differs between populations (ancestral, geographic)
- Impact may be substrate (drug) specific

Additional PGx Concepts

- Context matters
  - Indication
  - Drug dose, duration of therapy, therapeutic index
  - Concurrent therapies
  - Alternative metabolic pathways

PGx Resources Summary

Resource	Explanation/Uses
PharmGKB (www.pharmgkb.org)	-Knowledge base for PGx -Curated PK/PD/ADR pathways -Variant and clinical annotations -Clinical guideline and drug label annotations

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FDA	-Table of Pharmacogenomic Biomarkers in Drug Labeling -List of therapeutic products with PGx in drug labeling

Abbreviations: PGx, pharmacogenomics; PK, pharmacokinetics; PD, pharmacodynamics; ADR, adverse drug reaction; CPIC, Clinical Pharmacogenetics Implementation Consortium; FDA, Food and Drug Administration

CLINICALLY RELEVANT USES OF PGX

CYP-Mediated Drug Metabolism

Fraction of Clinically Used Drugs Metabolized by P450 isoforms

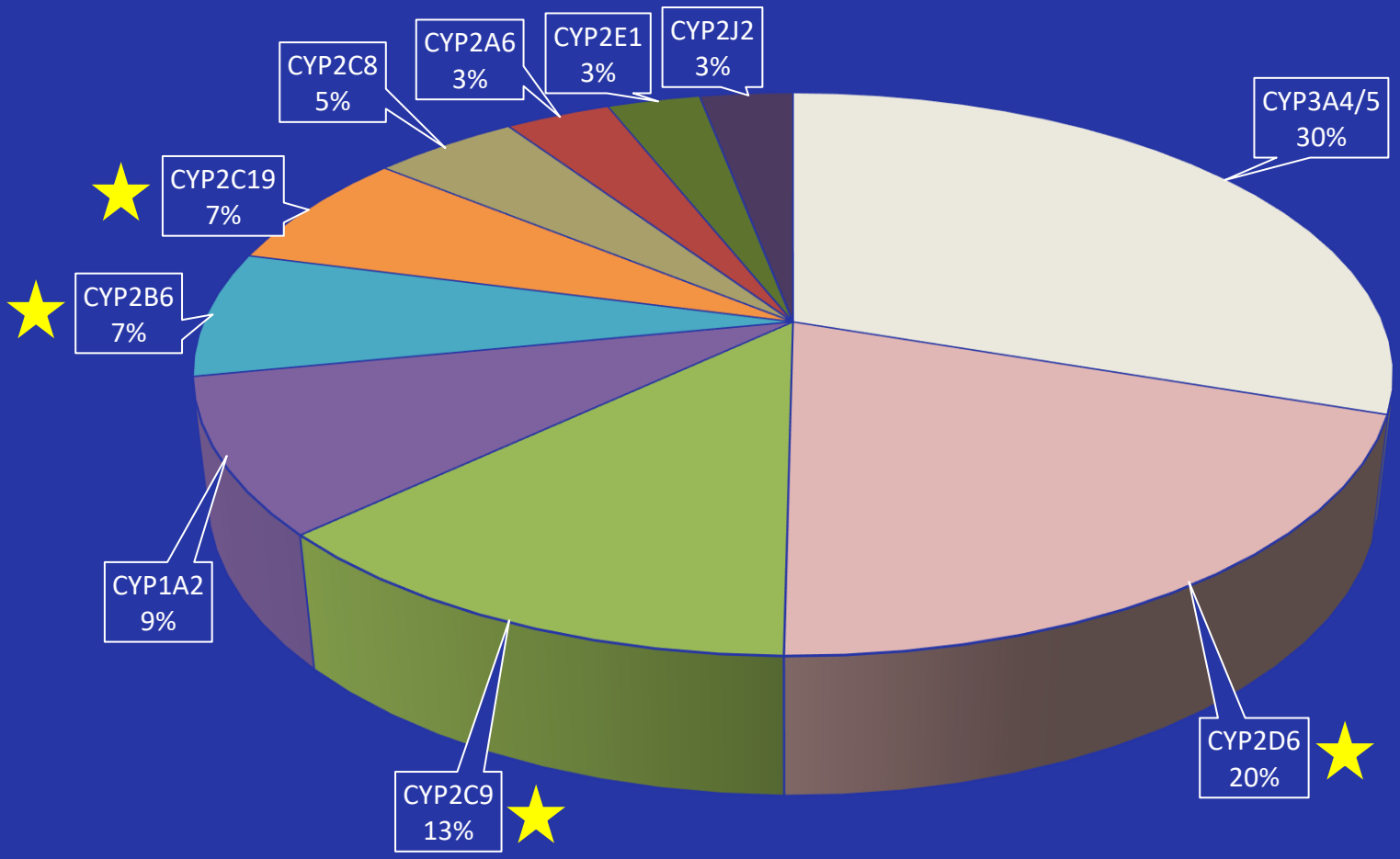
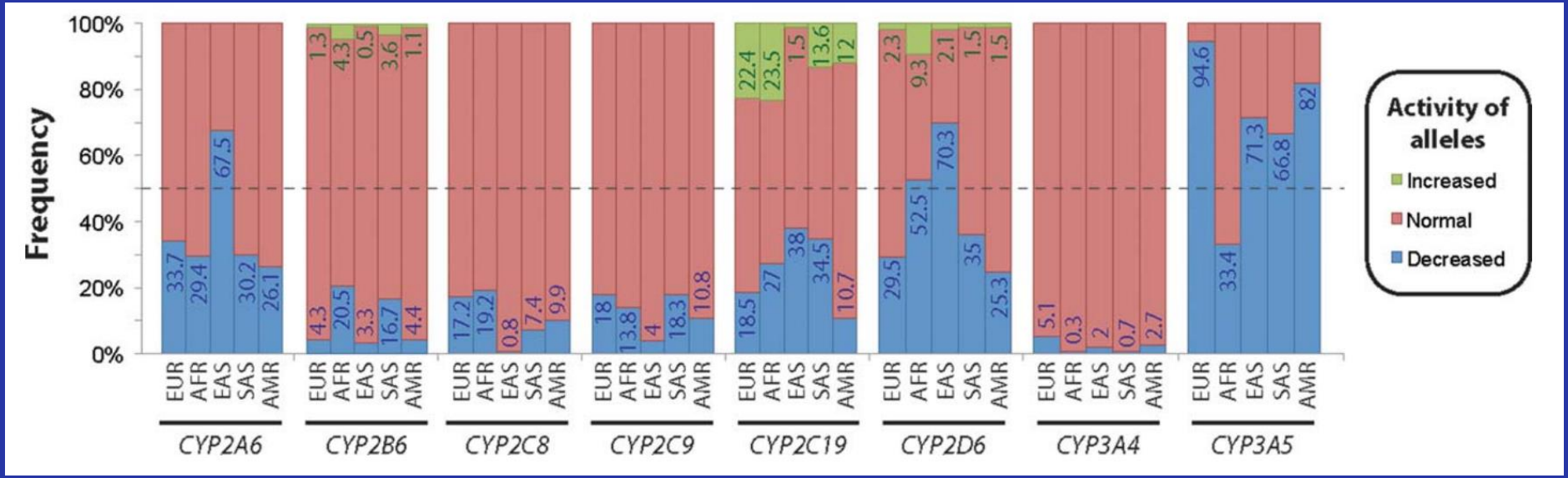


Figure adopted from: Zanger UM, Schwab M. *Pharmacol Ther* 2013;138(1):103-41.

PGx of CYP-Mediated Drug Metabolism

- Several CYP enzymes are subject to genetic variation
  - Frequency ranges widely between populations



Abbreviations: EUR, Europeans; AFR, Africans; EAS, East Asians; SAS, South Asians; AMR, admixed Americans

Zhou Y, Ingelman-Sundberg, Lauschke VM. *Clin Pharmcol Ther* 2017;102(4):688-700.

PGx of CYP-Mediated Drug Metabolism

- Drugs that may have altered metabolic activity due to variant alleles encoding CYP enzymes

CYP enzyme	Selected examples of potentially affected drugs
CYP2B6	Bupropion, efavirenz*, methadone
CYP2C9	Erdafitinib, fluvastatin*, phenytoin*, NSAIDs*, warfarin*
CYP2C19	Clopidogrel*, diazepam, PPIs*, SSRIs*, TCAs*, voriconazole*
CYP2D6	Aripiprazole, atomoxetine*, carvedilol, duloxetine, metoprolol, ondansetron*, opioids*, risperidone, SSRIs*, tamoxifen*, tamsulosin, TCAs*
CYP3A5	Tacrolimus*
CYP4F2	Warfarin*

Abbreviations: NSAIDs, nonsteroidal anti-inflammatory drugs; PPIs, proton pump inhibitors; SSRIs, selective serotonin reuptake inhibitors; TCAs, tricyclic antidepressants
*CPIC guideline available

Clinical Pharmacogenetics Implementation Consortium. Genes-Drugs. https://cpicpgx.org/genes-drugs/

DPYD PGx

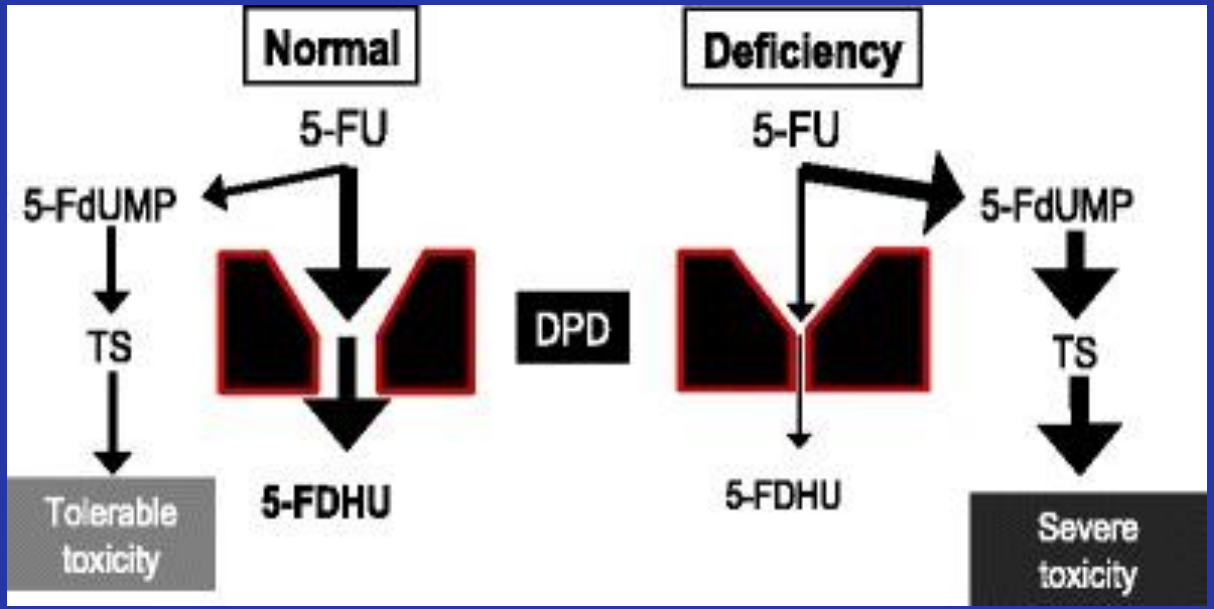
- *DPYD*: encodes dihydropyrimidine dehydrogenase (DPD)
  - Rate-limiting enzymes for breakdown of fluoropyrimidines
    - 5-fluorouracil (5-FU) and capecitabine
  - Certain *DPYD* variants → reduced or absent DPD activity
    - Partial deficiency estimated in 2-8% of individuals
    - Increased risk of toxicity with fluoropyrimidine-based chemotherapy

Del Re M et al. *EPMA J* 2010;1(3):495-502.

Amstutz U et al. *Clin Pharmacol Ther* 2018;103(2):210-216.

DPYD PGx

- Role of DPD in fluoropyrimidine catabolism



Del Re M et al. *EPMA J* 2010;1(3):495-502.

Phase II Drug Metabolism

- Conjugation reactions
- Phase II drug metabolizing enzymes
  - UDP-glucuronosyltransferases (UGTs)
  - Sulfotransferases (SULTs)
  - *N*-acetyltransferases (NATs)
  - Glutathione S-transferases (GSTs)
  - Thiopurine S-methyltransferases (TPMTs)
  - Catechol O-methyltransferases (COMTs)

Almazroo OA, Miah MK, Venkataramanan R. *Clin Liver Dis* 21(1):1-20.

PGx of Phase II Drug Metabolism

- Phase II drug metabolizing enzymes impacted by genetic variation

Enzyme	Selected examples of potentially affected drugs
COMT	Citalopram, opioids
GSTM1	Cisplatin, oxaliplatin
GSTP1	Cyclophosphamide, epirubicin, fluorouracil, oxaliplatin
NAT2	Hydralazine, isoniazid, procainamide, SMZ/TMP, sulfasalazine
TPMT	6-mercaptopurine*, azathioprine*, thioguanine*
UGT1A1	Atazanavir*, dolutegravir, irinotecan, nilotinib, pazopanib, sacituzumab govitecan-hziy

Abbreviations: SMZ/TMP, sulfamethoxazole and trimethoprim
*CPIC guideline available

Clinical Pharmacogenetics Implementation Consortium. Genes-Drugs. https://cpicpgx.org/genes-drugs/

PGx of Drug Transporters

- Important role in absorption, distribution, metabolism, and elimination (ADME)
  - Endogenous and xenobiotics (i.e., drugs)

- Two main superfamilies
  - ATP-binding cassette (ABC) transporters
    - Efflux transporters
  - Solute carrier (SLC) transporters
    - Uptake of small molecules into cells

Nigam SK. *Nat Rev Drug Discov* 2015;14(1):29-44.

PGx of Drug Transporters

- Drug transporter enzymes impacted by genetic variability

Gene	Selected examples of potentially affected drugs
ABCB1	Digoxin, fentanyl, methotrexate, ondansetron, simvastatin
ABCG2	Allopurinol, rosuvastatin*
★ *SLCO1B1*	Methotrexate, statins*
SLC6A	Citalopram, escitalopram
SLC28A3	Daunorubicin, doxorubicin

*CPIC guideline available

Clinical Pharmacogenetics Implementation Consortium. Genes-Drugs. https://cpicpgx.org/genes-drugs/

PGx of Drug Hypersensitivity

- Human Leukocyte Antigen (HLA)
  - Part of the human major histocompatibility complex (MHC)
    - Class I: *HLA-A*, *HLA-B*, and *HLA-C*
      - Encode proteins that present intracellular antigens to the immune system
      - Among the most highly polymorphic genes in humans

Kloypan C et al. *Pharmaceuticals (Basel)* 2021;14(11):1077.

PGx of Drug Hypersensitivity

- Genetic variants in *HLA* genes
  - Associated with increased risk of severe cutaneous adverse drug reactions (SCARs) with several drugs

Gene	Selected examples of potentially affected drugs
HLA-A	Allopurinol, carbamazepine*, oxcarbazepine
HLA-B	Abacavir*, allopurinol*, carbamazepine*, fosphenytoin*, oxcarbazepine*, phenytoin*
HLA-C	Allopurinol, methazolamide

*CPIC guideline available

Kloypan C et al. *Pharmaceuticals (Basel)* 2021;14(11):1077.
Clinical Pharmacogenetics Implementation Consortium. Genes-Drugs. https://cpicpgx.org/genes-drugs/

G6PD PGx

- G6PD converts glucose-6-phosphate to 6-phosphogluconolactone
  - First step in the pentose phosphate pathway
  - Source of NADPH for erythrocytes
    - Protection from oxidative stress

- G6PD deficiency can increase the risk of erythrocyte lysis → acute hemolytic anemia (AHA)
  - Drug-induced
  - Concurrent illnesses (e.g., infection)
  - Dietary stressors (e.g., fava beans)

Gammal RS et al. *Clin Pharmacol Ther* 2022 Sep 1

G6PD PGx

- Drugs that can trigger AHA in G6PD deficiency
  - Therapeutic recommendations according to CPIC

Drug	Risk	Classification of Recommendation
Dapsone	High	Strong
Methylene blue	High	Moderate
Pegloticase	High	Strong
Primaquine (standard dose)[#]	High	Strong
Primaquine (medium dose)^	Medium	Strong
Rasburicase	High	Strong
Nitrofurantoin	Medium	Optional

[#]standard dose primaquine = 0.25-0.5 mg/kg daily for 14 days
^medium dose primaquine = 0.75 mg/kg or 45 mg once weekly for 8 weeks

Gammal RS et al. *Clin Pharmacol Ther* 2022 Sep 1

PATIENT CASE

- ER is a 59 year old male presenting to clinic to discuss management of depression. The patient has previously completed panel-based PGx testing.
  - The clinician asks you which genes may be relevant to help guide decisions around selection of an appropriate antidepressant.
  - What is your response to the clinician?

PATIENT CASE

CYP enzyme	Selected examples of potentially affected drugs
CYP2B6	Bupropion, efavirenz*, methadone
CYP2C9	Erdafitinib, fluvastatin*, phenytoin*, NSAIDs*, warfarin*
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Abbreviations: NSAIDs, nonsteroidal anti-inflammatory drugs; PPIs, proton pump inhibitors; SSRIs, selective serotonin reuptake inhibitors; TCAs, tricyclic antidepressants

*CPIC guideline available

CLINICAL APPLICATIONS OF PGX – SELECTED EXAMPLES

CYP2C19 – clopidogrel

- Clopidogrel: antiplatelet agent ($P2Y_{12}$ inhibitor)
  - Reduce risk of myocardial infarction and stroke
    - Patients with acute coronary syndrome (ACS) and/or following percutaneous coronary intervention (PCI)
  - Prodrug → requires hepatic biotransformation to an active metabolite
    - Two step process involving multiple CYP450 enzymes
      - **Most important: CYP2C19**

Lee CR et al. *Clin Pharmacol Ther* 2022;112(5):959-967.

CYP2C19 – clopidogrel

- *CYP2C19* is highly polymorphic
  - Frequency of reduced function CYP2C19 phenotypes

Population	Intermediate Metabolizer	Poor Metabolizer
African American/ Afro-Caribbean	31.4%	4%
American	21.4%	1.5%
Central/South Asian	40.8%	8.2%
East Asian	45.9%	13%
European	26%	2.4%
Latino	19%	1.1%
Near Eastern	23.5%	1.9%
Oceanian	36.9%	57%
Sub-Saharan African	30%	3.7%

Lee CR et al. *Clin Pharmacol Ther* 2022;112(5):959-967.

CYP2C19 – clopidogrel

Predicted CYP2C19 phenotype	*CYP2C19* Genotype	Examples of *CYP2C19* diplotypes
Ultrarapid metabolizer	Two increased function alleles	*17/*17
Rapid metabolizer	One normal function allele + one increased function allele	*1/*17
Normal metabolizer	Two normal function alleles	*1/*1
Likely intermediate metabolizer[b]	-One normal function allele + one decreased function allele -One increased function allele + one decreased function allele -Two decreased function alleles	*1/*9, *9/*17, *9/*9
Intermediate metabolizer	-One normal function allele + one no function allele -One increased function allele + one no function allele	*1/*2, *1/*3, *2/*17, *3/*17
Likely poor metabolizer[b]	One decreased function allele + one no function allele	*2/*9, *3/*9
Poor metabolizer	An individual carrying two no function alleles	*2/*2, *3/*3, *2/*3
Indeterminate metabolizer	One or two uncertain function alleles	*1/*12, *2/*12, *12/*14

[b] There are limited data to characterize the function of decreased function alleles

Lee CR et al. *Clin Pharmacol Ther* 2022;112(5):959-967.

CYP2C19 – clopidogrel

- CYP2C19 intermediate and poor metabolizers
  - Reduced formation of clopidogrel active metabolites
  - Higher rates of major adverse cardiovascular events
- Knowledge of *CYP2C19* genotype can guide antiplatelet selection
  - Clopidogrel vs. prasugrel or ticagrelor
  - May reduce the risk of cardiovascular events and bleeding

Lee CR et al. *Clin Pharmacol Ther* 2022;112(5):959-967.

CYP2C19 – clopidogrel

- CPIC recommendations
  - Antiplatelet therapy for ACS and/or PCI

CYP2C19 phenotype	Therapeutic recommendation	Classification of recommendation
Ultrarapid metabolizer	If considering clopidogrel, use at standard dose (75 mg/day)	Strong
Rapid metabolizer	If considering clopidogrel, use at standard dose (75 mg/day)	Strong
Normal metabolizer	If considering clopidogrel, use at standard dose (75 mg/day)	Strong
Intermediate metabolizer, or likely intermediate	Avoid standard dose clopidogrel (75 mg) if possible. Use prasugrel or ticagrelor at standard dose if no contraindication	Strong
Poor metabolizer, or likely poor	Avoid clopidogrel if possible. Use prasugrel or ticagrelor at standard dose if no contraindication	Strong

Lee CR et al. *Clin Pharmacol Ther* 2022;112(5):959-967.

PATIENT CASE

- PW is a 64 year old Asian male undergoing PCI after myocardial infarction. PW completes *CYP2C19* genotyping/PGx testing. His *CYP2C19* diplotype is *2/*2.

- What is PW's predicted CYP2C19 metabolizer status?
  a. Normal metabolizer
  b. Intermediate metabolizer
  c. Indeterminate metabolizer
  d. Poor metabolizer

PATIENT CASE

- PW is a 64 year old Asian male undergoing PCI after myocardial infarction. PW completes *CYP2C19* genotyping/PGx testing. His *CYP2C19* diplotype is *2/*2.

- Based on PW's *CYP2C19* diplotype and predicted metabolizer status, clopidogrel is the preferred antiplatelet agent to use post-PCI.
  1. True
  2. False

Preemptive PGx Panel Testing

- PREPARE study – open-label, multicenter, randomized crossover implementation study
  - Evaluated the clinical utility of preemptive PGx panel testing
    - 12-gene PGx panel (*CYP2B6*, *CYP2C9*, *CYP2C19*, *CYP2D6*, *CYP3A5*, *DPYD*, *F5*, *HLA-B*, *SLCO1B1*, *TPMT*, *UGT1A1*, *VKORC1*)
  - Block randomized by country, then crossed over
    - Study group: start with genotype-guided drug prescribing
    - Control group: standard clinical care

Swen JJ et al. *Lancet* 2023;401(10374):347-356.

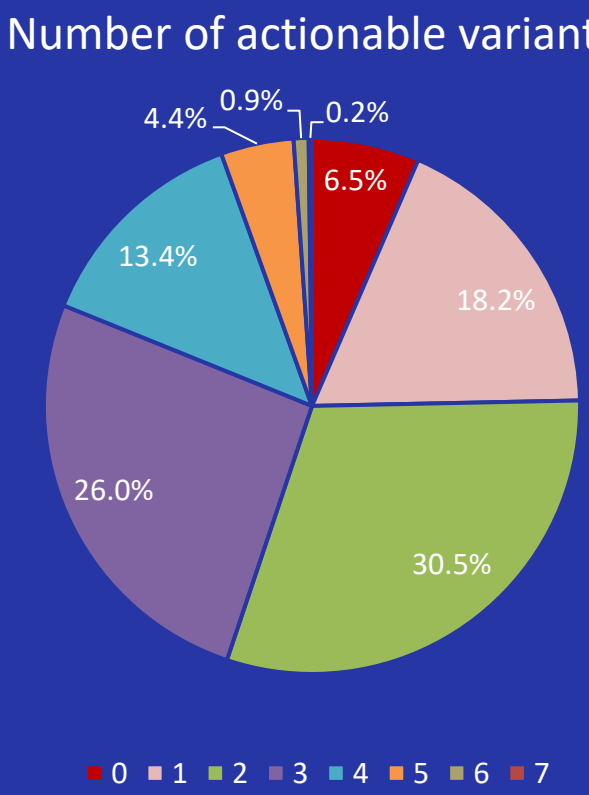
Preemptive PGx Panel Testing

- PREPARE study
  - Seven European countries
  - Patients (n=6944) receiving a first prescription for a drug with actionable PGx recommendation
  - Primary outcome: incidence of causal and clinically relevant ADRs within the 12 week follow-up period

Swen JJ et al. *Lancet* 2023;401(10374):347-356.

Preemptive PGx Panel Testing

- PREPARE study – results
  - 93.5% of patients carried ≥1 actionable variant



Swen JJ et al. *Lancet* 2023;401(10374):347-356.

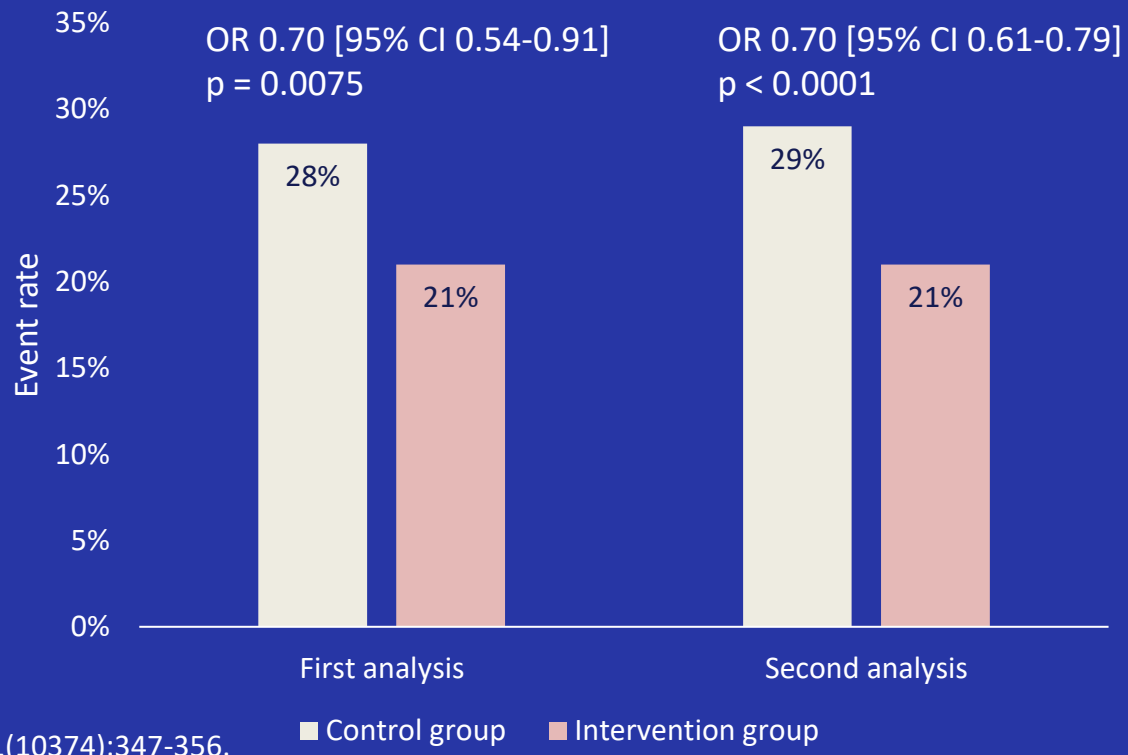
Preemptive PGx Panel Testing

- PREPARE study – results
  - 25.2% of patients carried an actionable variant for their index drug
    - Atorvastatin: 204/716 (28.5%)
    - Tramadol: 183/379 (48.3%)
    - Clopidogrel: 172/619 (27.8%)
  - Approximately 70% of recommendations were accepted

Swen JJ et al. *Lancet* 2023;401(10374):347-356.

Preemptive PGx Panel Testing

- PREPARE study – results
  - Frequency of causal clinically relevant ADRs in patients with an actionable result



Swen JJ et al. *Lancet* 2023;401(10374):347-356.

Abbreviations:
OR, odds ratio;
CI, confidence interval

Preemptive PGx Panel Testing

- PREPARE study – discussion and conclusions
  - 12-gene PGx panel significantly reduced the incidence of clinical relevant ADRs
  - Did not address drug efficacy
  - Cost-effective analysis is being conducted
  - Supports large-scale implementation of panel-based PGx testing
    - PGx-guided decision making at the point of care

Swen JJ et al. *Lancet* 2023;401(10374):347-356.

CLOSING THOUGHTS

Barriers to PGx Adoption and Implementation

- Education – patients, providers, pharmacists
- Evidence on clinical utility
- Guideline support for testing
  - Professional organizations and societies
- Costs, billing, reimbursement
- Information technology (IT) needs
  - EHR integration, CDS alerts

Summary and Conclusions

- PGx is a widely available tool to support safe and effective medication use
- PGx resources are freely available online
- Pharmacists are well-positioned to be leaders in PGx practice
- Ongoing education, research, funding, and resources are needed to support broad implementation of PGx in clinical practice

References

Noted on slides throughout presentation

Need More Information?

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