Polypharmacy and Cytochromes in Primary Care:

A Case Based Approach

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Disclosures

I have no relevant disclosures.

Overview

- Objectives
- WHO Global Patient Safety Challenge: Medication Without Harm
- Review polypharmacy to include definition, prevalence, and implications
- Role of cytochromes and the CYP 450 enzymatic system in polypharmacy
- Medication mapping

(World Health Organization; 2019)

Objectives

- Review polypharmacy and the patient-, provider- and system-related implications
- Discuss the relationship between cytochromes and medication metabolism
- Discuss the role of the Cytochrome P450 (CYP 450) system in polypharmacy
- Utilize a systematic approach to medication mapping to evaluate patient cases of polypharmacy related to the CYP 450 enzymatic system

WHO Global Patient Safety Challenge: Medication Without Harm

(World Health Organization; 2022)

Early Priority Action: Polypharmacy

- Polypharmacy as one of early priority actions to take to protect patients from harm (WHO, 2017)
- Definition:
  - Concurrent and routine use of five or more medications
  - Includes over-the-counter, prescription and/or traditional and complementary medicines used by a patient
- Prevalence: "True magnitude not known" (p.12).

(World Health Organization, 2017, 2019)

Implications of polypharmacy

- Patient-related
- Provider-related
- Systems-related

(World Health Organization; 2019)

Patient-related implications

Decreased

Quality of life

Medication adherence

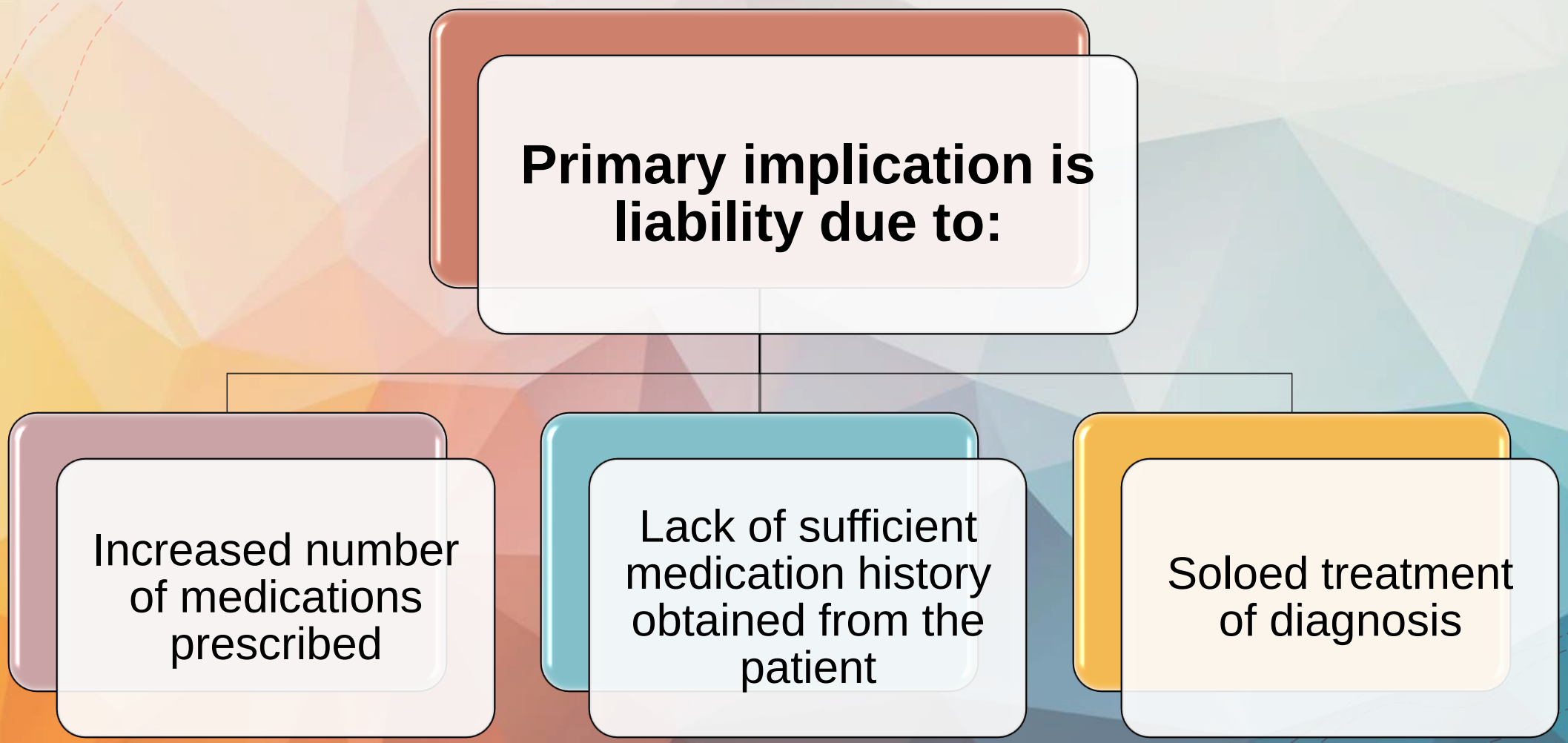
Increased

Financial burden

Risk for adverse drug events/ reactions

(World Health Organization; 2019)

Provider-related implications



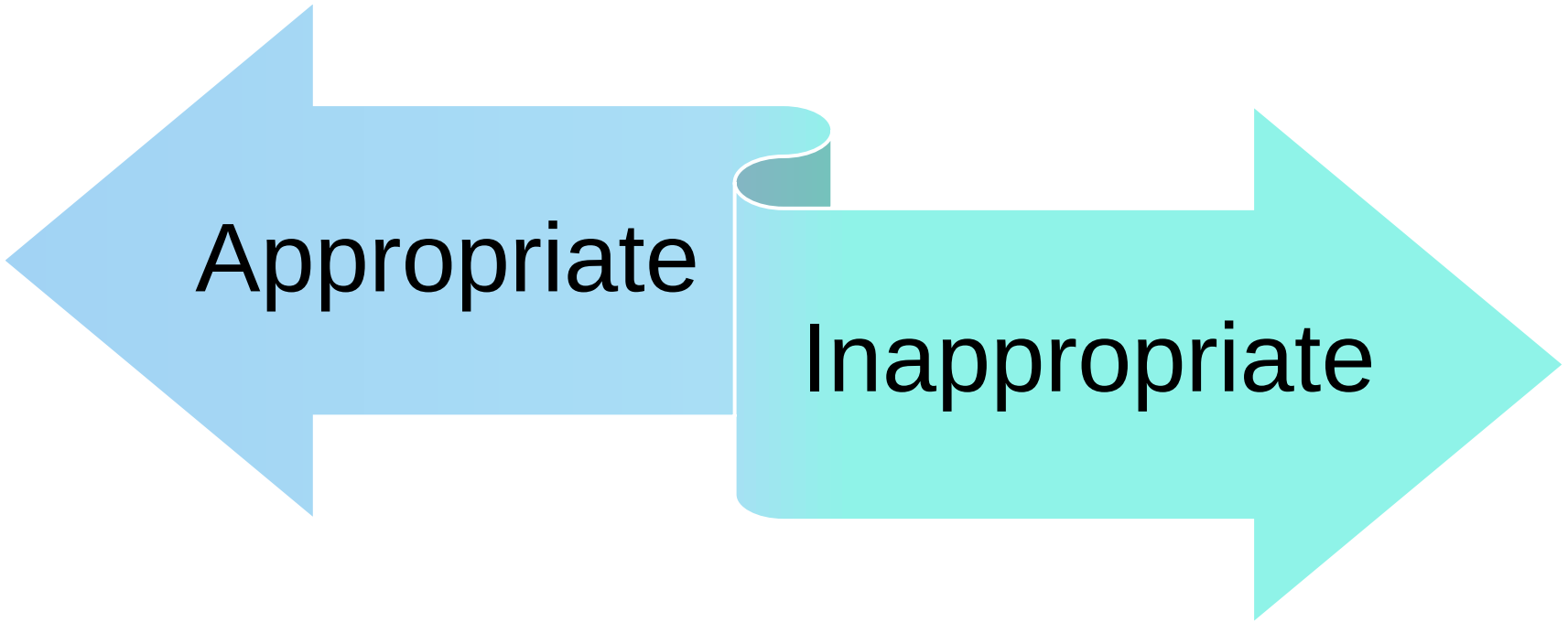
(World Health Organization; 2019)

System-related implications

- Mismanaged polypharmacy + suboptimal medication use = 4% of the world's total avoidable cost
- Medication errors = ~$42 billion globally each year
- Preventable polypharmacy = savings of ~$18 billion in unnecessary healthcare expenditures

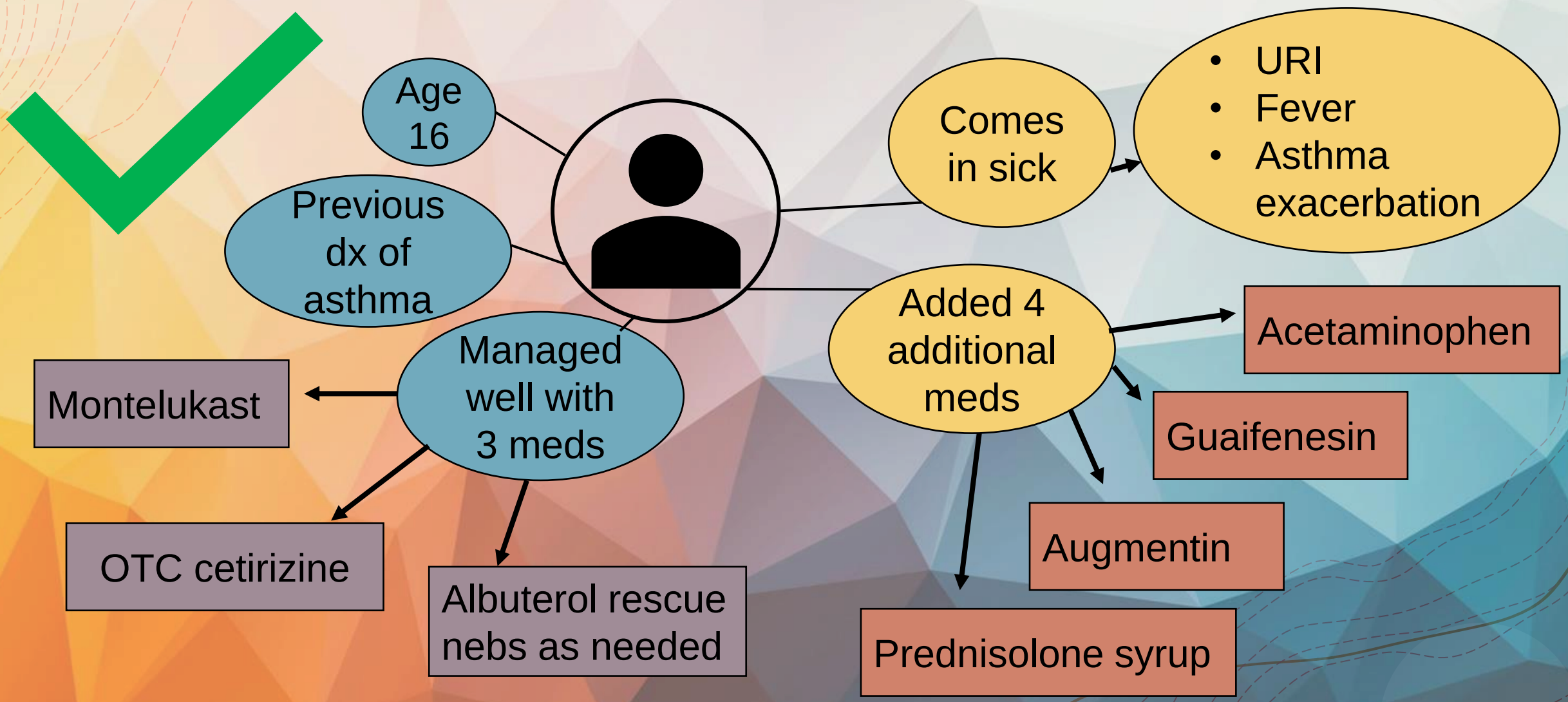
(World Health Organization, 2017, 2019)

Polypharmacy



(National Institute on Aging, 2021;
World Health Organization; 2019)

Appropriate polypharmacy case example



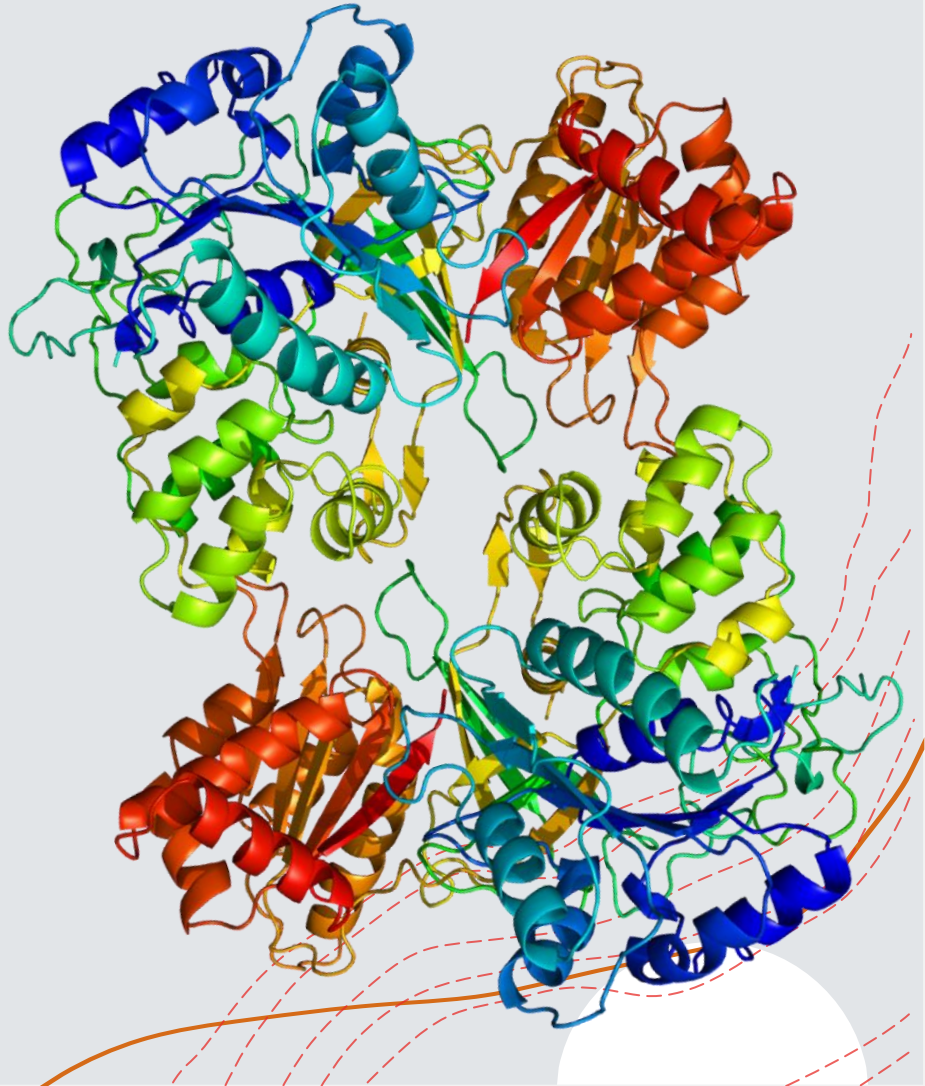
The role of CYPs in polypharmacy

- Medication Without Harm challenge, polypharmacy, and the cytochrome P450 enzymatic system
- Increased knowledge is the first step in understanding how the CYPs must be mapped against the patient's medication regimen to reduce polypharmacy
- Important questions

Cytochrome P450 (CYP) enzymatic system overview

- Heme protein (oxygen)
- Required for the metabolism of many drugs
- Primarily in the liver
- Catalyst for oxidation in Phase I of metabolism
- Enzymatically converts lipid-soluble compounds to more water-soluble compounds during the oxidation process

(McDonnell & Dang, 2013; Zhao et al., 2021)



Key Terms

Precision medicine

Inhibitor

Substrate

Inducer

Xenobiotics

Pharmacogenomics

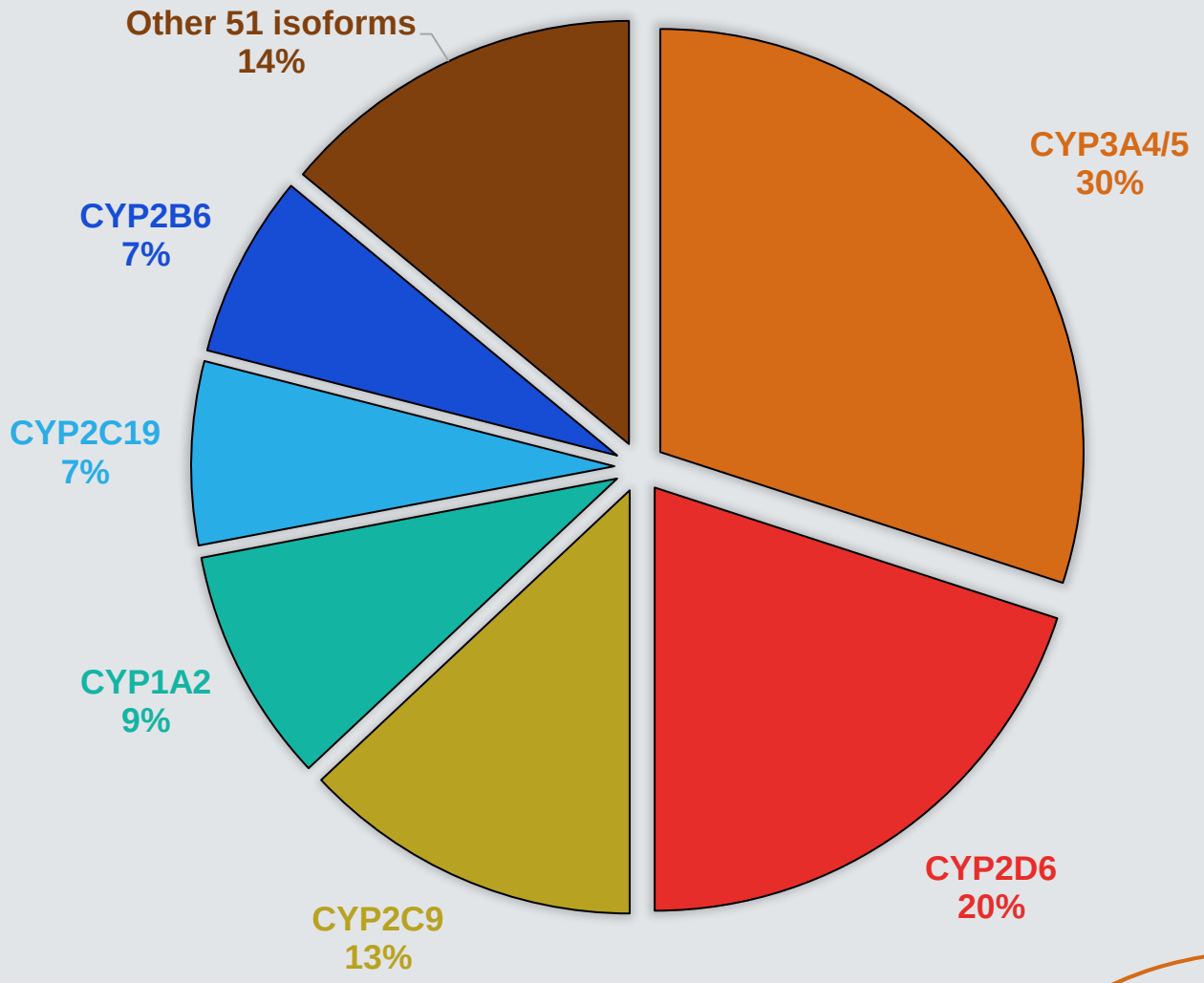
Airborne View of US Highway System in Seattle City. (2008). *Kathiresan R.* [Photograph]. Flickr. https://www.flickr.com/photos/denalinps/8639280606/

CYP Classification

- Family
- Subfamily
- Isoform or individual enzyme
- Example:
- CYP2D6
  - Family: CYP2
  - Subfamily: D
  - Isoform/enzyme: 6

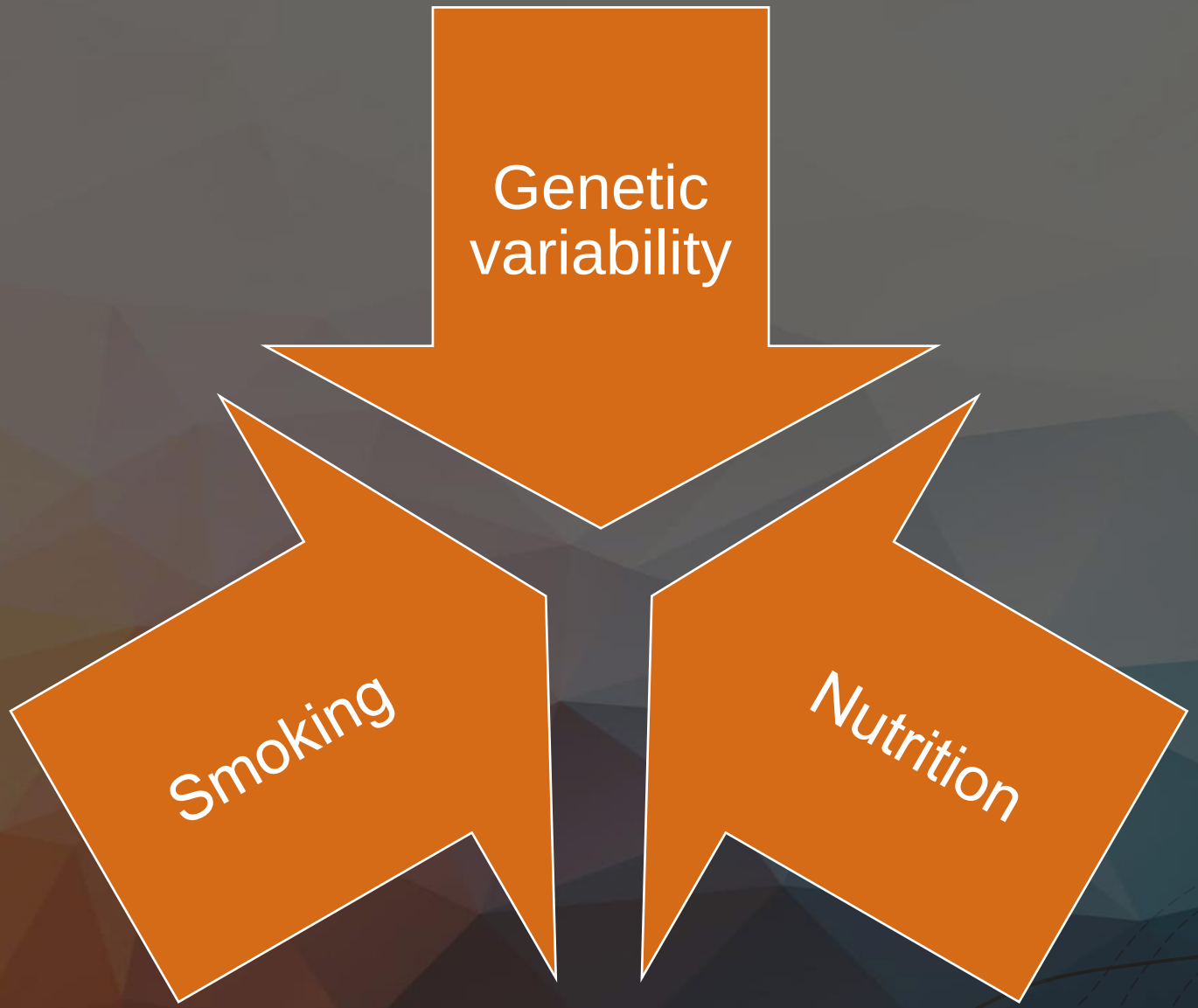
(Mitchell, 2019)

Breakdown of CYP isoform activity by percentage



(Zhao et al., 2021)

Factors impacting CYP enzymatic action



(Zhao et al., 2021)

Medication mapping (aka reviews)

- Medication mapping/reviews
  - Structured evaluation of patient's medications
  - Aim: optimize medication use and improve outcomes
  - Requires identification of possible adverse drug reactions and development of a corrective action plan

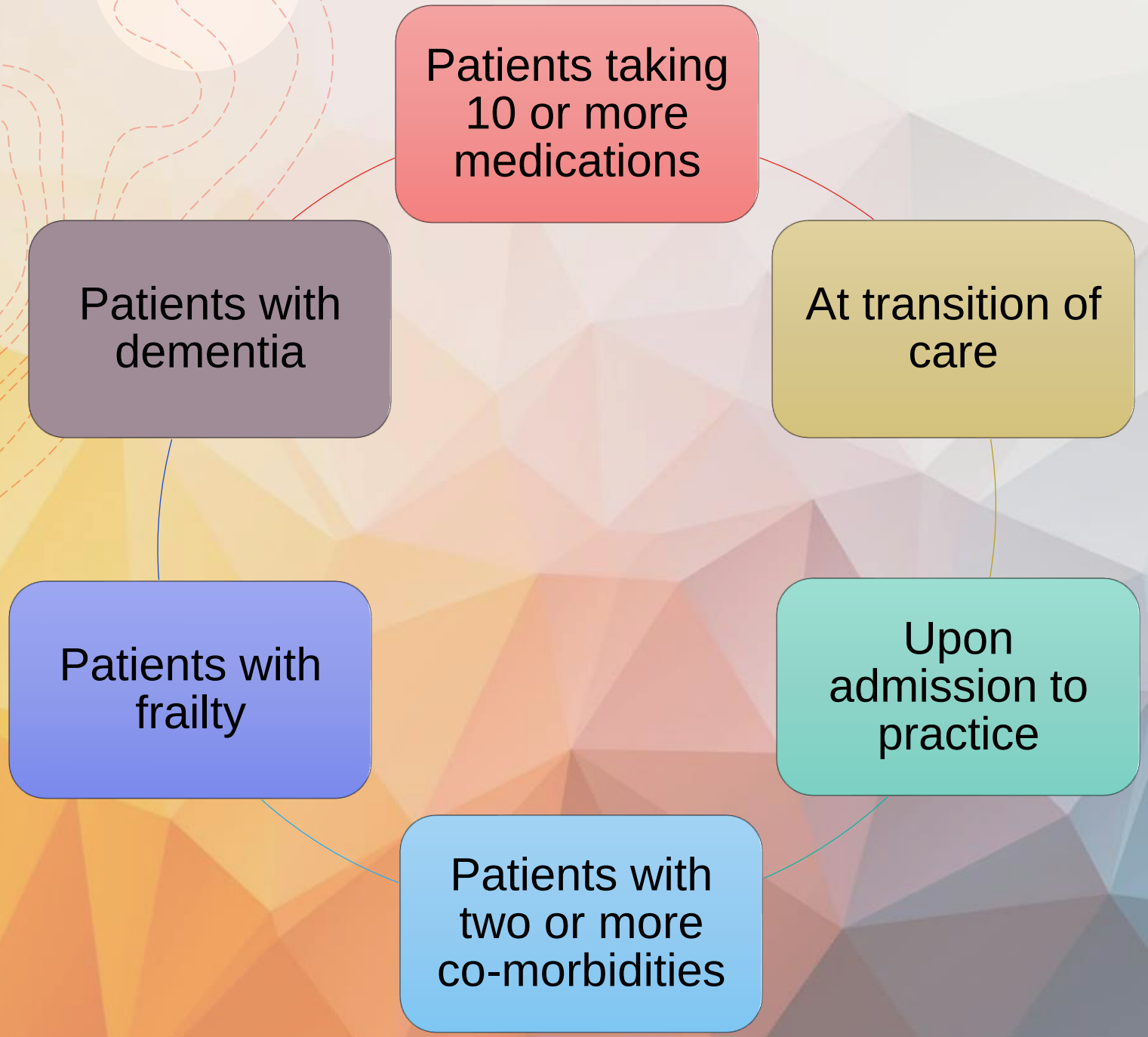
- Although deprescribing may be a critical part of the corrective action plan, medication mapping is not intended for the purpose of simply discontinuing medication.

(World Health Organization; 2019)

Benefits of medication mapping/ review

- Reduced emergency department visits
- Reduced admissions
- Reduced medication-related problems
- Improved patient outcomes

(World Health Organization; 2019)



Prioritization of medication reviews

(World Health Organization; 2019)

Case studies
&
Medication Mapping

Acceptable polypharmacy mapping

Patient Name:	16 yo with asthma								
Date of Review:	3/1/23								
Name of Medication:	**CYP450 Yes/No**	**CYP3A4/5**	**CYP2D6**	**CYP2C9**	**CYP1A2**	**CYP2C19**	**CYP2B6**	**OTHER**	**Note:**
	Yes	Substrate		Substrate				Substrate: CYP2C8	
	Unknown								Only know 8-10% of drug is metabolized using the CYP450 enzyme system; medication not impacted by known inhibitors or inducers
albuterol	No								
acetaminophen	Yes							CYP2E1	
guaifenesin	No								Guaifenesin is not known to interfere with the cytochrome P450 (CYP) system, nor is it an inhibitor or inducer of this system.
Augmentin	No								
prednisolone	Yes					Inhibitor			

Inappropriate polypharmacy

Patient Name:	24 yo female								
Date of Review:	3/1/23								
Name of Medication:	**CYP450 Yes/No**	**CYP3A4/5**	**CYP2D6**	**CYP2C9**	**CYP1A2**	**CYP2C19**	**CYP2B6**	**OTHER**	**Note:**
sertraline	Yes						Substrate		
olanzapine	Yes				SubstrateM				
clopidogrel	Yes						**Inhibitor**		
apixaban	Yes	Substrate		SubstrateM	SubstrateM			CYP2J2M	
Patient changed:									
prasugrel		Substrate		Substrate			Substrate		Weak inhibitor of CYP2B6, but sertraline is stronger

Concurrent use with a CYP1A2 inhibitor or inducer (e.g., smoking) can result in clinically significant interactions.

PDR.net

- My choice for identification of CYP450 interactions
- Reference sheet provided
- Information is transferred to provided worksheet

Resources

- https://www.pdr.net/
- https://drug-interactions.medicine.iu.edu/MainTable.aspx
- https://www.mayocliniclabs.com/~/media/it-mmfiles/special-instructions/Pharmacogenomic_Associations_Tables.pdf

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