

- Pharmacology of Pain
 - Pain Urgencies and Emergencies or how patients can make things interesting
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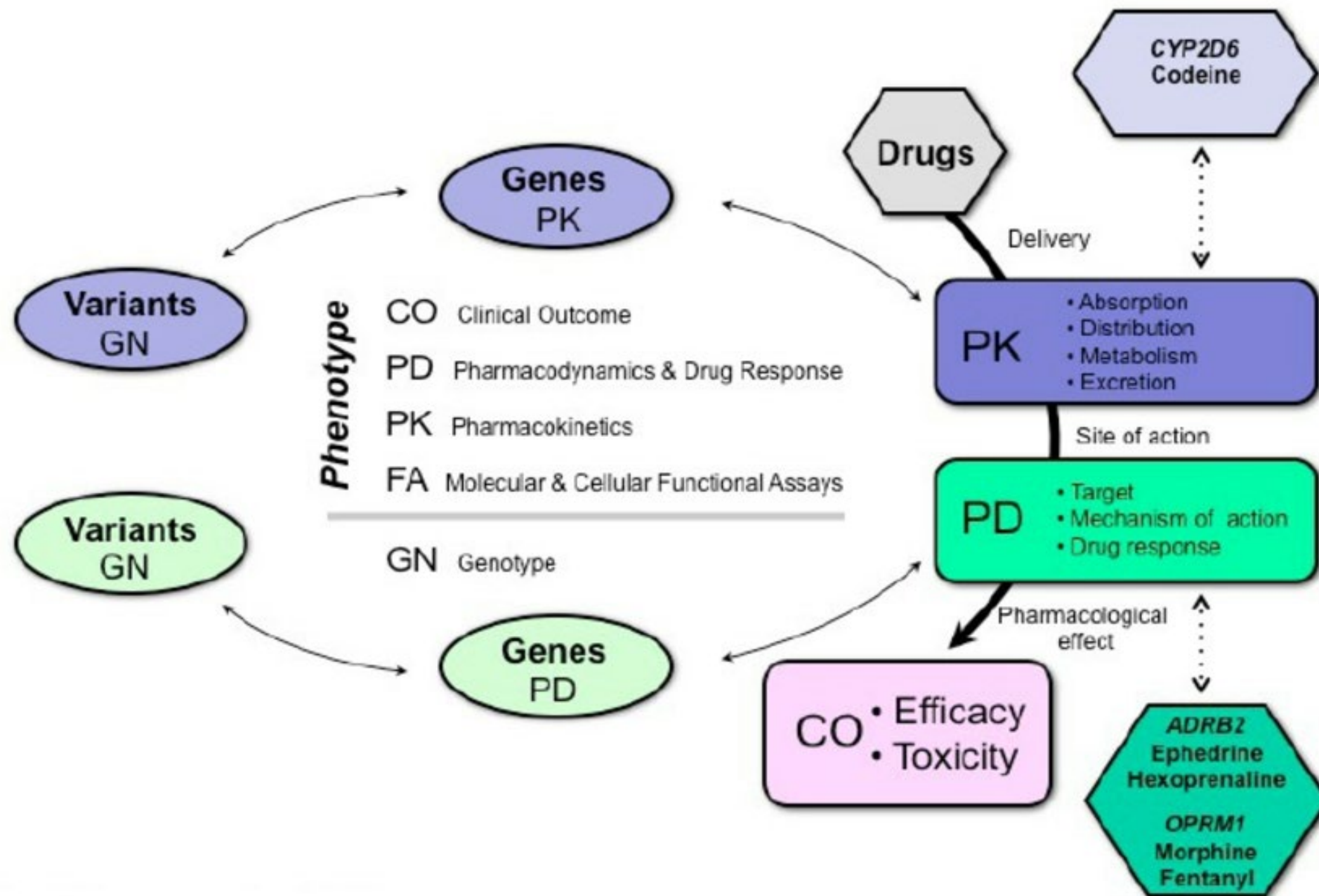
Disclosures....

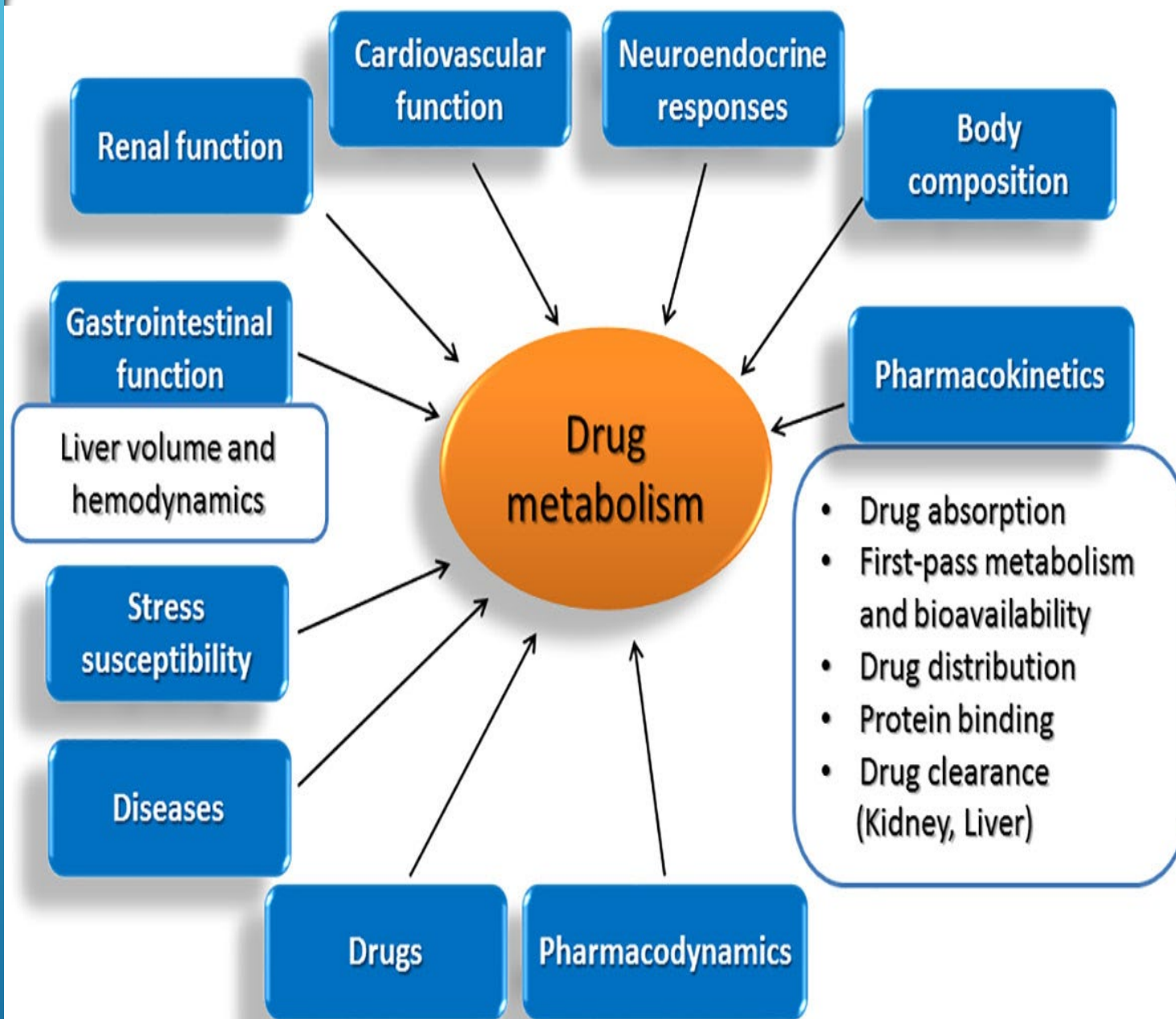
None

- ▶ Terminology
- ▶ **Genetics** – the study of individual genes , heredity, and genetic variations
- ▶ **Genomics** – The study of an organism's entire genome. Looks at how genes interact with one another, and the environments' role on affecting them
- ▶ **Pheno-conversion-** the phenomenon where an individual's drug metabolism (their actual ability to metabolize drugs) differs from what is predicted based upon their genotype(UM,IM,PM) – This is due to non genetic factors – smoking , other medications, lifestyle choices

- ▶ **Pharmacogenomics**- The study of how a person's genes affect their response to a drug. Allows the prescriber to move away from “one size fits all” approach to a more personalized approach.
- ▶ **Pharmacodynamics**- Focuses on what a drug does to the body. It investigates biochemical ,physiological and molecular effects of drugs on living systems. Looks at drug –receptor interaction ,Dose –response relationships, Mechanism of action , and factors influencing responses – aging , diseases, and **other drugs**

TERMINOLOGY CONTINUED





- Metabolism of Opiates and all the ways to mess it up.

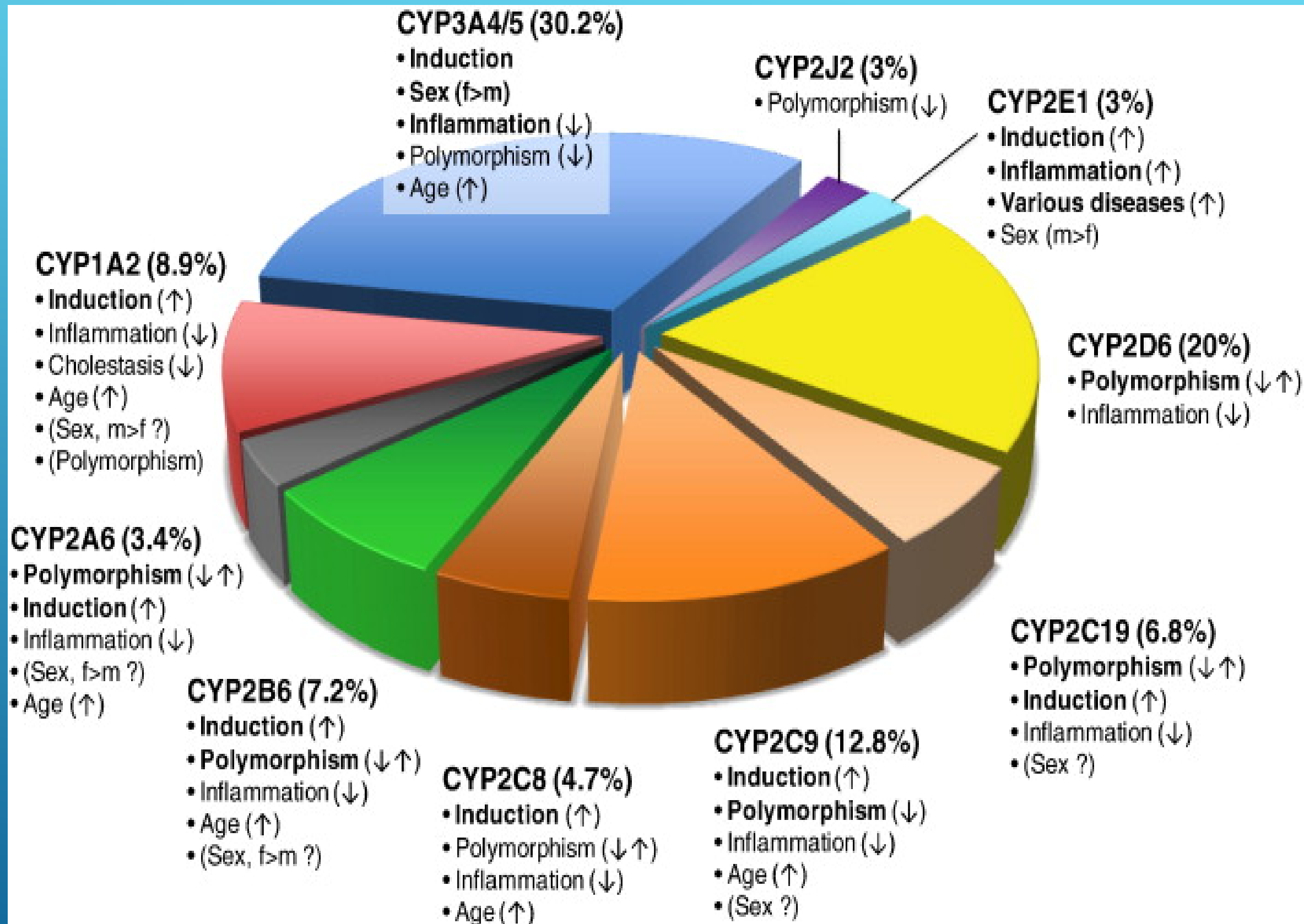


Table 1

Inhibitory Effect of SSRIs on CYP-450 Isoenzymes

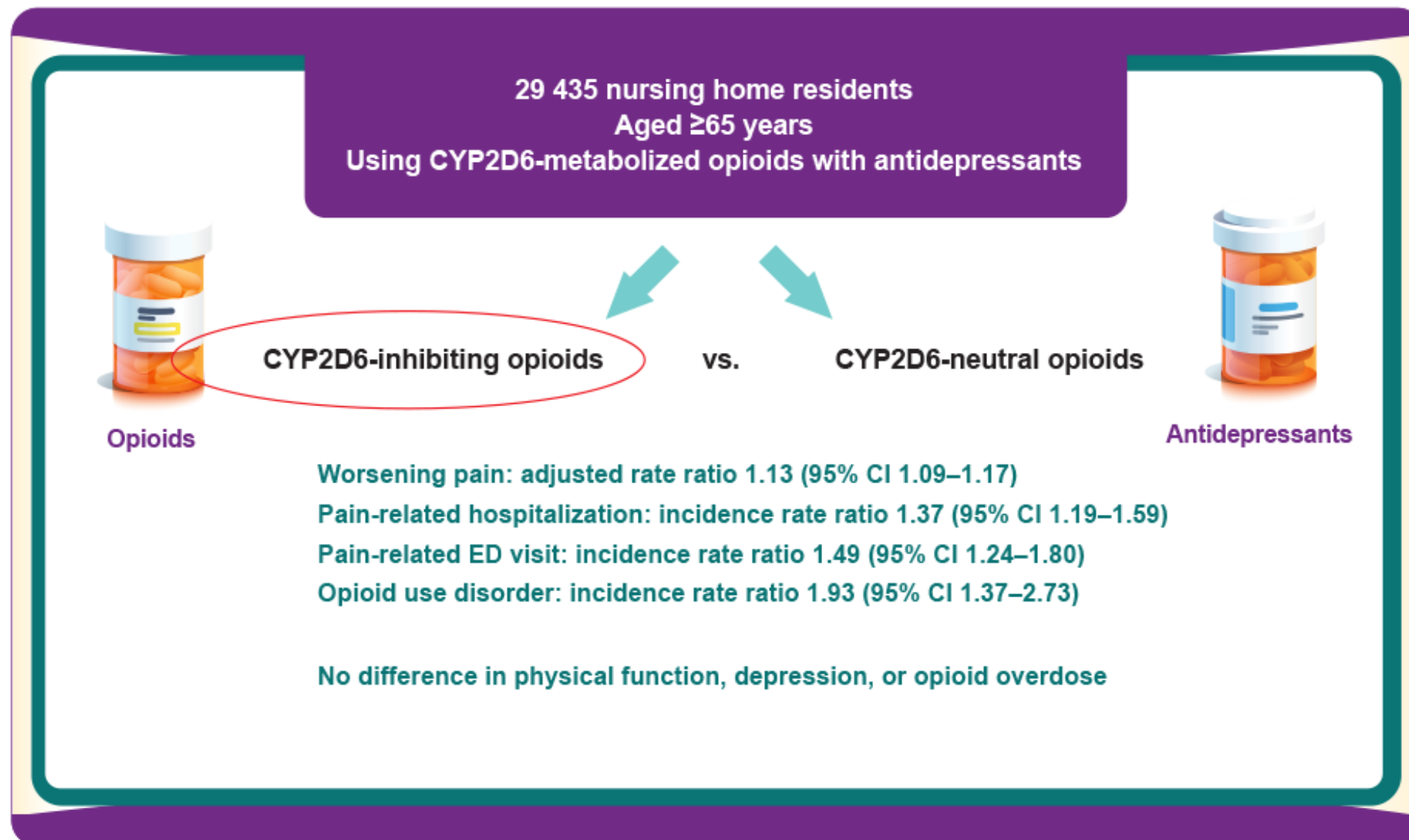
Agent	CYP-450 Isoenzymes				
	CYP-1A2	CYP-2C9	CYP-2C19	CYP-2D6	CYP-3A4
Citalopram	0	0	0	+	0
Fluoxetine	+	++	+ / ++	+++	+ / ++
Fluvoxamine	+++	++	+++	+	++
Mirtazapine	0	0	0	+	0
Nefazodone	0	0	0	+	+++
Paroxetine	+	+	+	+++	+
Sertraline	+	+	+	+ / ++	+
Venlafaxine	0	0	0	+	+

SSRI: selective serotonin reuptake inhibitor; CYP: cytochrome P; 0: minimal/no inhibition; +: mild inhibition; ++: moderate inhibition; +++: potent inhibition.

Source: References 12, 13, 14.

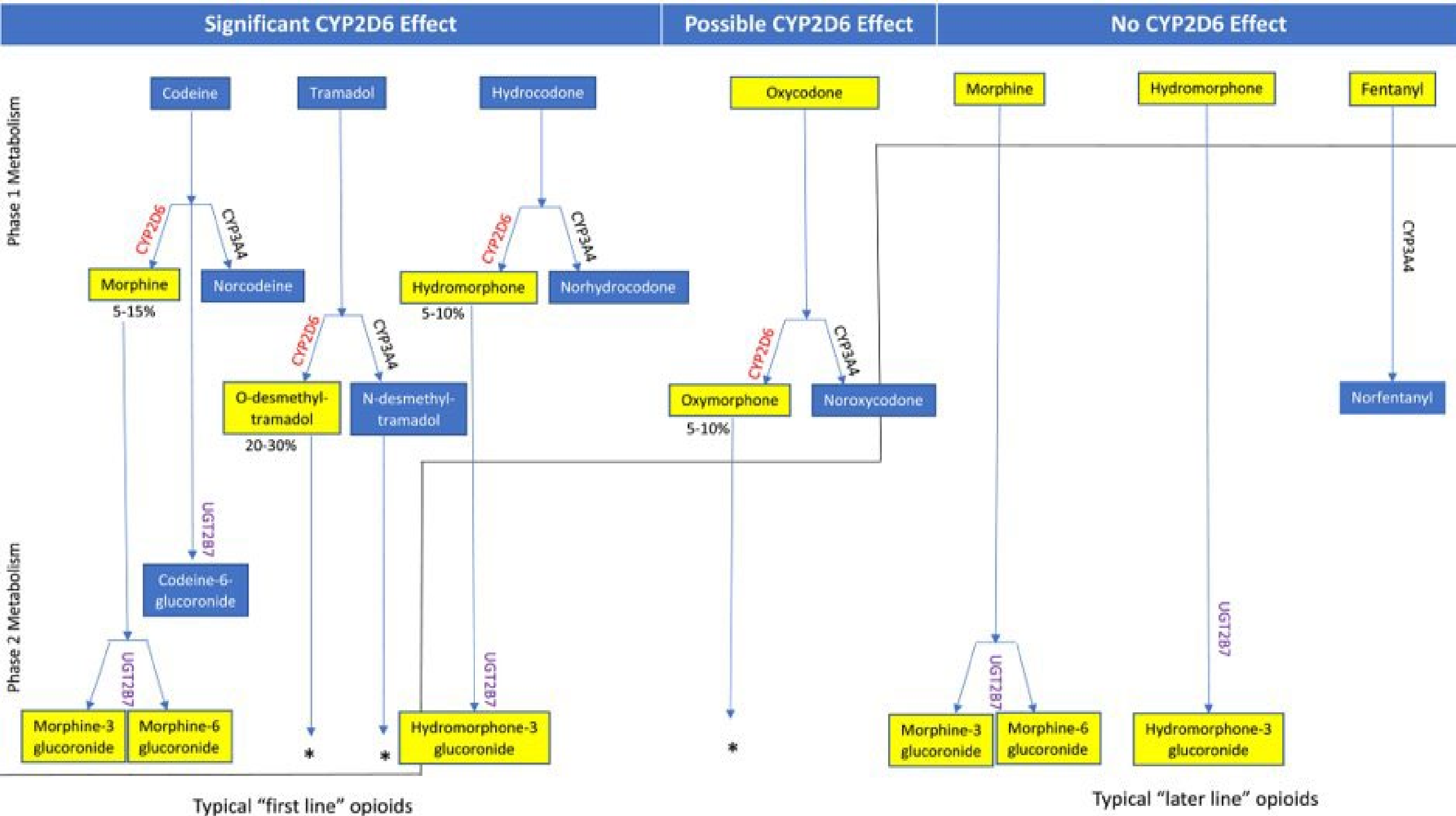
- ▶ What does this mean
- ▶ Concept of **phenoconversion** – As noted earlier but worth repeating : The phenomenon where an individual's drug metabolism phenotype (their actual ability to metabolize a drug) differs from their genotype (UM, IM, PM) due to non-genetic factors (medications, lifestyle choices, health)

Is use of CYP2D6-metabolized opioids with antidepressants associated with clinical outcomes?



- ▶ Original Research
- ▶ 23 July 2024
- ▶ **Clinical and Adverse Outcomes Associated With Concomitant Use of CYP2D6-Metabolized Opioids With Antidepressants in Older Nursing Home Residents: A Target Trial Emulation Study**
- ▶ **Authors:** Yu-Jung Jenny Wei, PhD <https://orcid.org/0000-0001-8861-6907>, Almut G. Winterstein, PhD <https://orcid.org/0000-0002-6518-5961>, Siegfried Schmidt, MD, PhD <https://orcid.org/0000-0001-5941-6009>, Roger B. Fillingim, PhD, Michael J. Daniels, ScD, Steven T. DeKosky, MD <https://orcid.org/0000-0003-3743-2758>, **Publication:** Annals of Internal Medicine
- ▶ Volume 177, Number 8
- ▶ <https://doi.org/10.7326/M23-3109>

- ▶ Results:
- ▶ Among 29 435 identified residents, use of CYP2D6-metabolized opioids concomitantly with CYP2D6-inhibiting (vs. CYP2D6-neutral) antidepressants was associated with a higher adjusted rate ratio of worsening pain (1.13 [95% CI, 1.09 to 1.17]) and higher adjusted incidence rate ratios of pain-related hospitalization (1.37 [CI, 1.19 to 1.59]), pain-related ED visit (1.49 [CI, 1.24 to 1.80]), and OUD (1.93 [CI, 1.37 to 2.73]), with no difference in physical function, depression, and opioid overdose.



- ▶ Real life examples
- ▶ Case 1 – 78-year-old female status post ORIF with CMN for intertrochanteric hip fracture with subtrochanteric extension
- ▶ Construct is stable post op and patient is WBAT
- ▶ Pain is 10/10 post operative and non-responsive to hydrocodone at 5 to 10 mg Q 4 dosing prn pain.
- ▶ She is changed to Oxycodone 5-10 mg Q 4 prn pain with slight improvement in pain score to 8-9/10
- ▶ She is admitted to rehab for acute rehab services, and pain control.

- ▶ Case 2 – Acute care hospitals and patient families can make for entertaining times.
- ▶ 72-year-old female with longstanding chronic pain. History of multiple lumbar spine surgeries with instrumentation for chronic back pain. Patient is on chronic opiates for her chronic pain.
- ▶ Admitted to rehab after a 3 day stay in an acute care hospital for encephalopathy – work upon presentation to the acute care hospital revealed UTI with impending sepsis – antibiotics initiated, and patient cleared cognitively

- ▶ On presentation to rehab- patient was noted to complain of back pain 10/10 – her chronic Oxycodone at home was 10 mg 4x/day with prn Tramadol /Tylenol Q 6. Pain control per the patient and family was suboptimal. An interesting combination, but people are on interesting combinations. Keeps Doctors young and curious
- ▶ Pain poorly controlled on above cocktail. Oxycodone increased from 10 mg Q4 to 15 mg Q4 as patients' family demanded increase as mom is very tolerant of pain medications (a potential canary in the coal mine)
- ▶ After 3 days on high dose opiates at the rehab hospital the patient suddenly became obtunded with hyperventilation – required Narcan x 2

- ▶ Meds
- ▶ Amlodipine, Metformin, Simvastatin
- ▶ **Wellbutrin** at home- It was stopped at the acute care hospital and was never restarted and no mention made on the DC summary (active metabolite half life is greater than 2 days)
- ▶ Wellbutrin is a very potent inhibitor of CYP2D – when it finally cleared her system, she garnered the full effects of the opiate. Had this been Prozac, the same thing would have occurred only much later at **home**. Drugs will get you into trouble and sometimes stopping them can be a problem.

Neuropathic Pain

- Or it burns, stings, buzzes tingles and sometimes feels like someone is ripping my arm/leg off.
- Neurotransmitters and ion channels implicated in pain modulation
- Acetylcholine / Serotonin / Norepinephrine
- CGRP / GABA
- Na⁺ and Ca²⁺ ion channels
- Just to name a few. Good news and bad news: Lots of options- good / bad ?

