ANTIDEPRESSANT SAFETY & USE IN SPECIAL POPULATIONS

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Learning Objectives

- Recognize common and serious drug interactions of antidepressants
- Formulate recommendations to avoid or minimize drug interactions
- Identify characteristics that influence the safety and efficacy of depression treatment in individual patients.
- Select an initial antidepressant regimen for an individual patient diagnosed with a depressive episode.

Additional materials to review

- Wisner KL, Oberlander TF, Huybrechts KF. The association between antidepressant exposure and birth defects—are we there yet? JAMA Psychiatry. Online ahead of print Aug 5, 2020.
  - Learning objective: Understand factors that guide the decision of whether an antidepressant is started or continued during pregnancy.

- Brent DA. Antidepressants and suicidality. Psychiatr Clin N Am. 2016;39:503-512. *Focus most closely on those sections highlighted in yellow.
  - Learning objective: Explain the antidepressant black box warning for increased risk of suicidal ideation in patient friendly terms
  - Learning objective: Describe how the risk for suicidal ideation with antidepressant use can be minimized

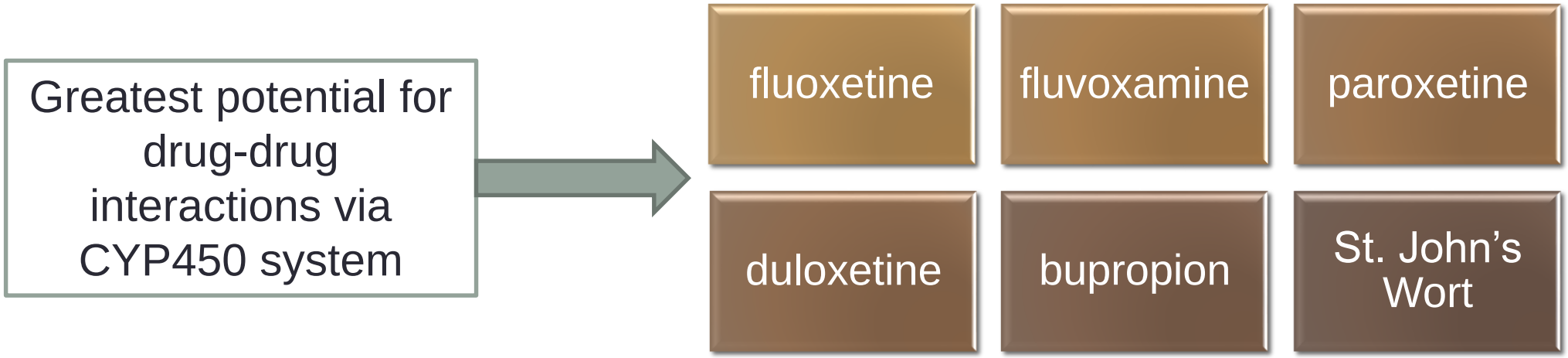
Interactions: MAO-Is

- MOA: irreversible inhibition of MAO-A & B, resulting in increased levels of 5HT, NE, and dopamine

- Risk of serotonin syndrome and/or hypertensive crisis when used concurrently with other drugs
- Concomitant use contraindicated:
  - Other antidepressants
    - Start SSRI or other antidepressant 14 days after stopping MAOI
    - 5 half-life wash out of previous antidepressant before starting MAOI
  - Buspirone
  - Dextromethorphan
  - Sympathomimetic drugs (amphetamine, cocaine, methylphenidate, epinephrine, phenylephrine, etc)
  - Foods high in tyramine

Pharmacokinetic Interactions (CYP450)

- Most antidepressant metabolized to some degree via CYP450 enzymes
- Some antidepressants are moderate to potent inhibitor of CYP450 enzymes
  - **2D6**, 2C19 most frequently implicated
- St. John's Wort is potent inducer of 1A2, 2C19, 2C9, 3A4



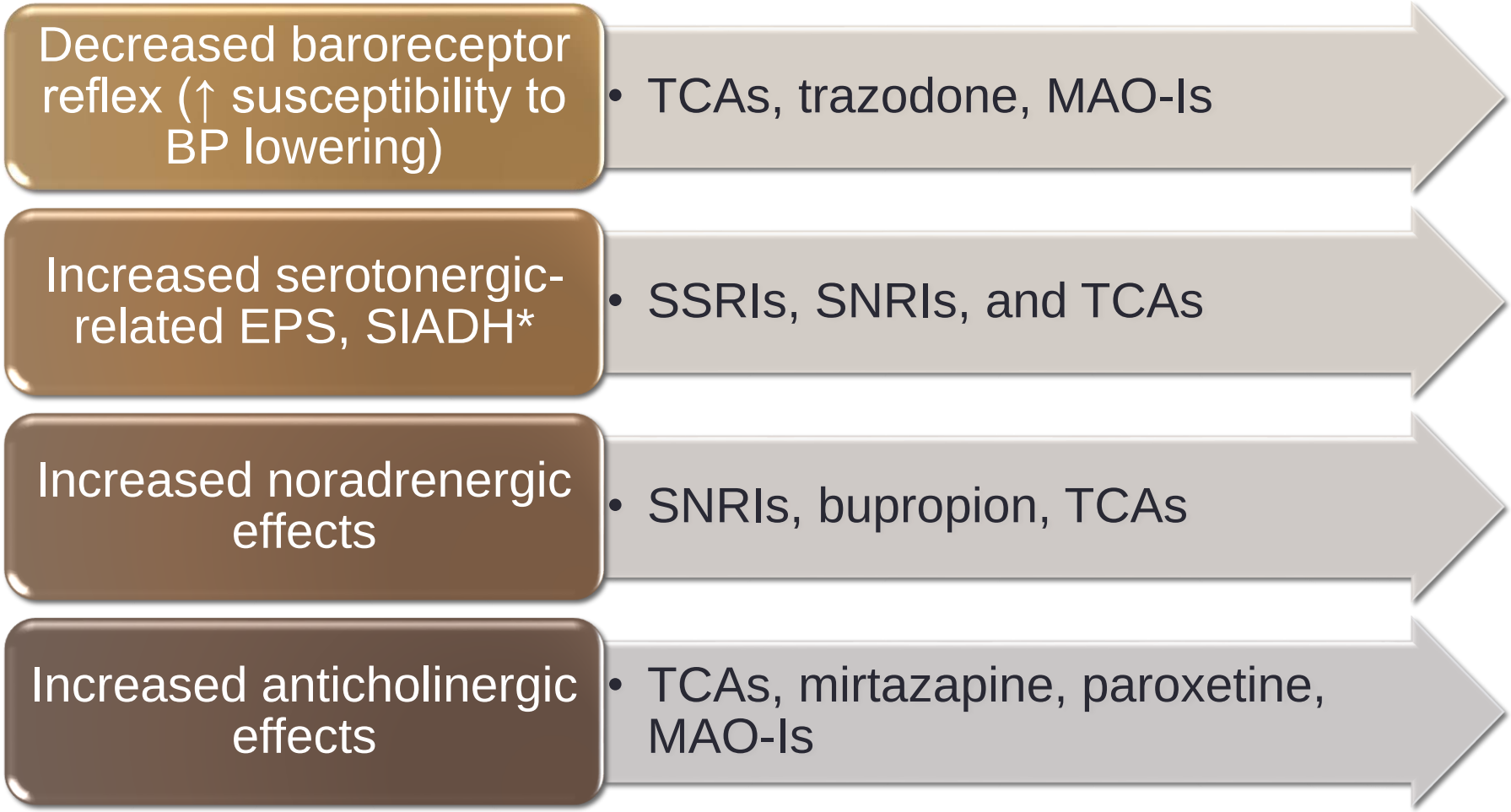
Pharmacodynamic Drug Interactions

Interacting agents (+ antidepressant)	Outcome	Management
NSAIDs, aspirin, anticoagulants, antiplatelet	Theoretical increased bleed risk (hemorrhagic stroke, GI bleed)	Ensure both anticoagulant/antiplatelet and antidepressant are indicated medications. Monitor for s/sx bruising and bleeding. Avoid concurrent use in high risk pts (i.e. current ulcer).
CNS depressants** *(e.g. sleep aids, benzos, opioids, antipsychotics, AEDs, etc.)*	Increased CNS depressive effects (excessive sedation, fall risk)	Caution use, if deemed necessary start low dose and titrate slowly, avoid tasks requiring mental concentration
Alcohol	Worsened depression, increased CNS depressive effects	Minimize alcohol intake
Serotonergic medications	Serotonin syndrome (excessive serotonergic activity in CNS & PNS)	Minimize serotonergic medication burden, always avoid concurrent use with MAO-I, lowest effective dose, educate patients

**Most problematic with highly sedating antidepressants (i.e. TCAs, mirtazapine, trazodone)

Antidepressant Use in Older Adults

Use of antidepressants in late-life depression. Drugs Aging. 2008;25:841-853.



*resulting in hyponatremia

SIADH (syndrome of inappropriate antidiuretic hormone) EPS (extrapyramidal symptoms)

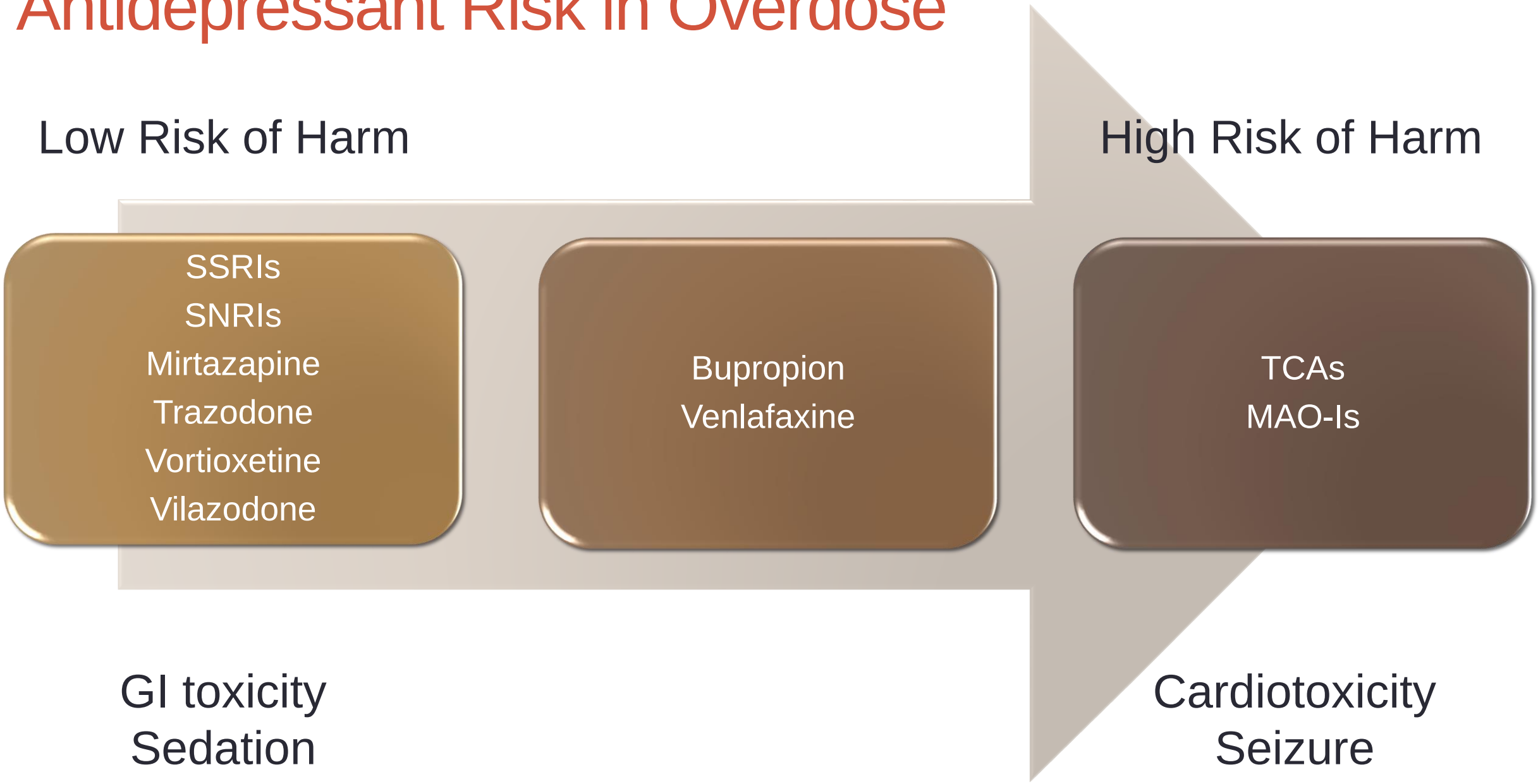
Antidepressants & Fall Risk

Antidepressant Class	No. of events	Falls Adjusted HR (95% CI)
No antidepressant	5208	1.00
TCA	1704	1.30 (1.23-1.38)
SSRI	3575	1.66 (1.58-1.73)
Misc antidepressant	631	1.39 (1.28-1.52)
Cohort study of patients ≥65 yo with diagnosis of depression (n=60,746)		

- Antidepressants associated with increased fall risk (greatest evidence for TCAs and SSRIs)
- Patients at high risk for falls should have fall risk assessment conducted prior to antidepressant initiation to reduce risk

Antidepressant use and risk of adverse outcomes in older people: population based cohort study. BMJ. 2011;343.
Pharmacologic treatment of depression in the elderly. Can Fam Physician. 2014;60:121-126.

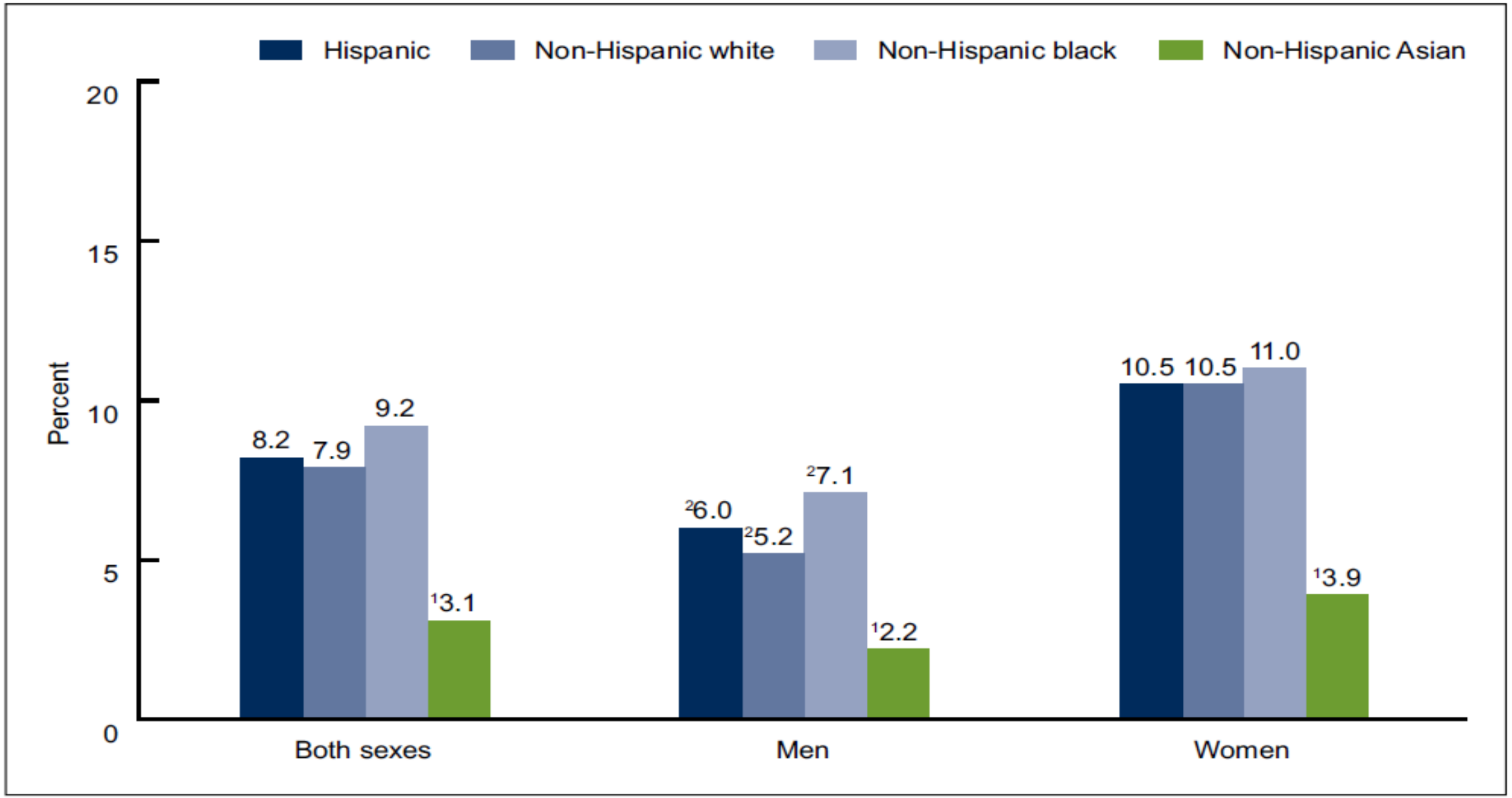
Antidepressant Risk in Overdose



Additional Antidepressant Indications

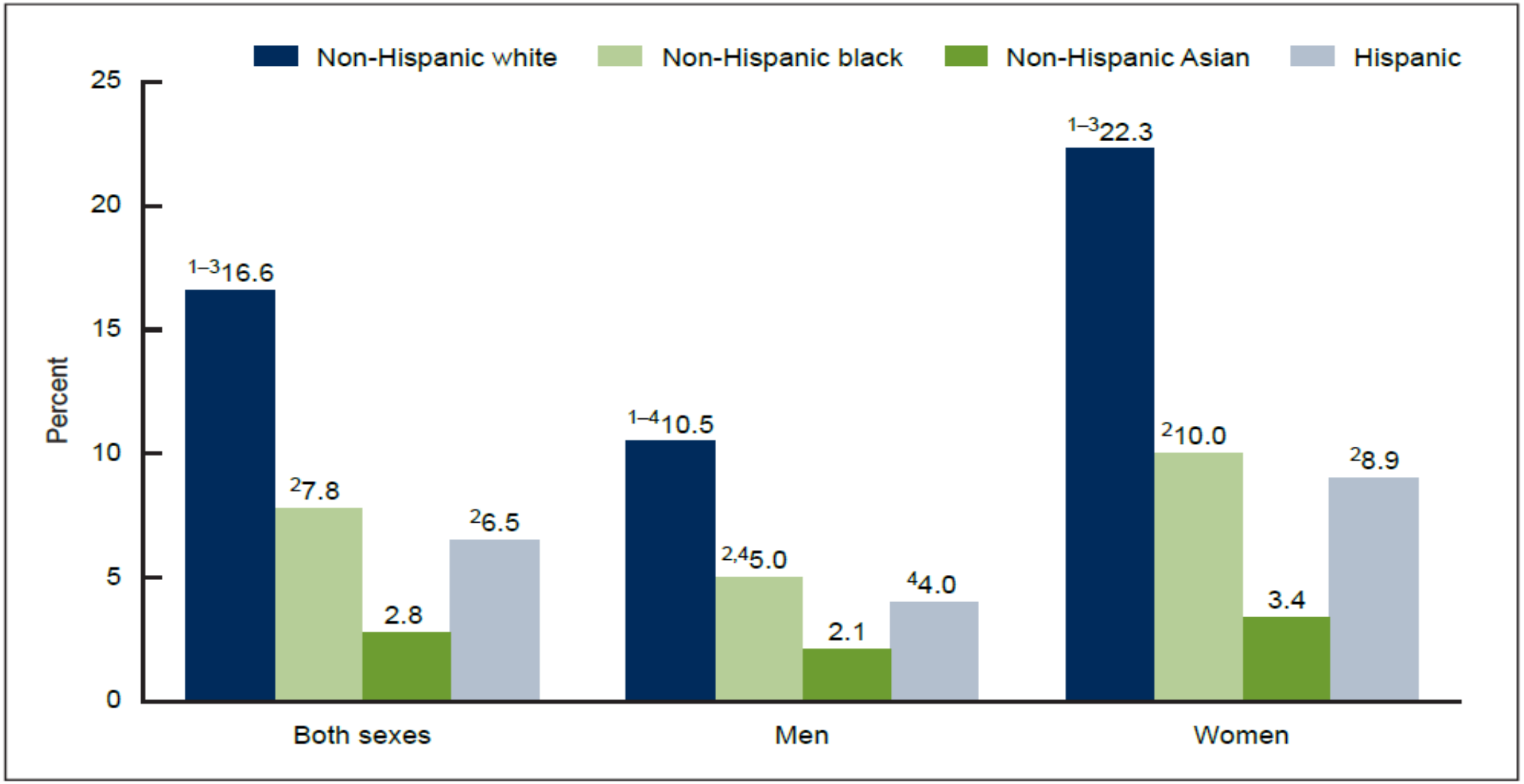
Smoking cessation	• bupropion
Migraine	• venlafaxine, amitriptyline
Anxiety	• SSRIs, SNRIs
ADHD	• bupropion, TCAs
Insomnia	• mirtazapine, trazodone, TCAs
Neuropathic pain	• TCAs, duloxetine

Figure 2. Percentage of persons aged 20 and over with depression, by race and Hispanic origin and sex: United States, 2013–2016



[1]Significantly lower than Hispanic, non-Hispanic white, and non-Hispanic black.
[2]Significantly lower than women of the same race and Hispanic-origin group.
NOTES: Depression was defined as a score greater than or equal to 10 on the Patient Health Questionnaire. Access data table for Figure 2 at: https://www.cdc.gov/nchs/data/databriefs/db303_table.pdf#2.
SOURCE: NCHS, National Health and Nutrition Examination Survey, 2013–2016.

Figure 2. Percentage of adults aged 18 and over who used antidepressant medication over past 30 days, by race and Hispanic origin and sex: United States, 2015–2018

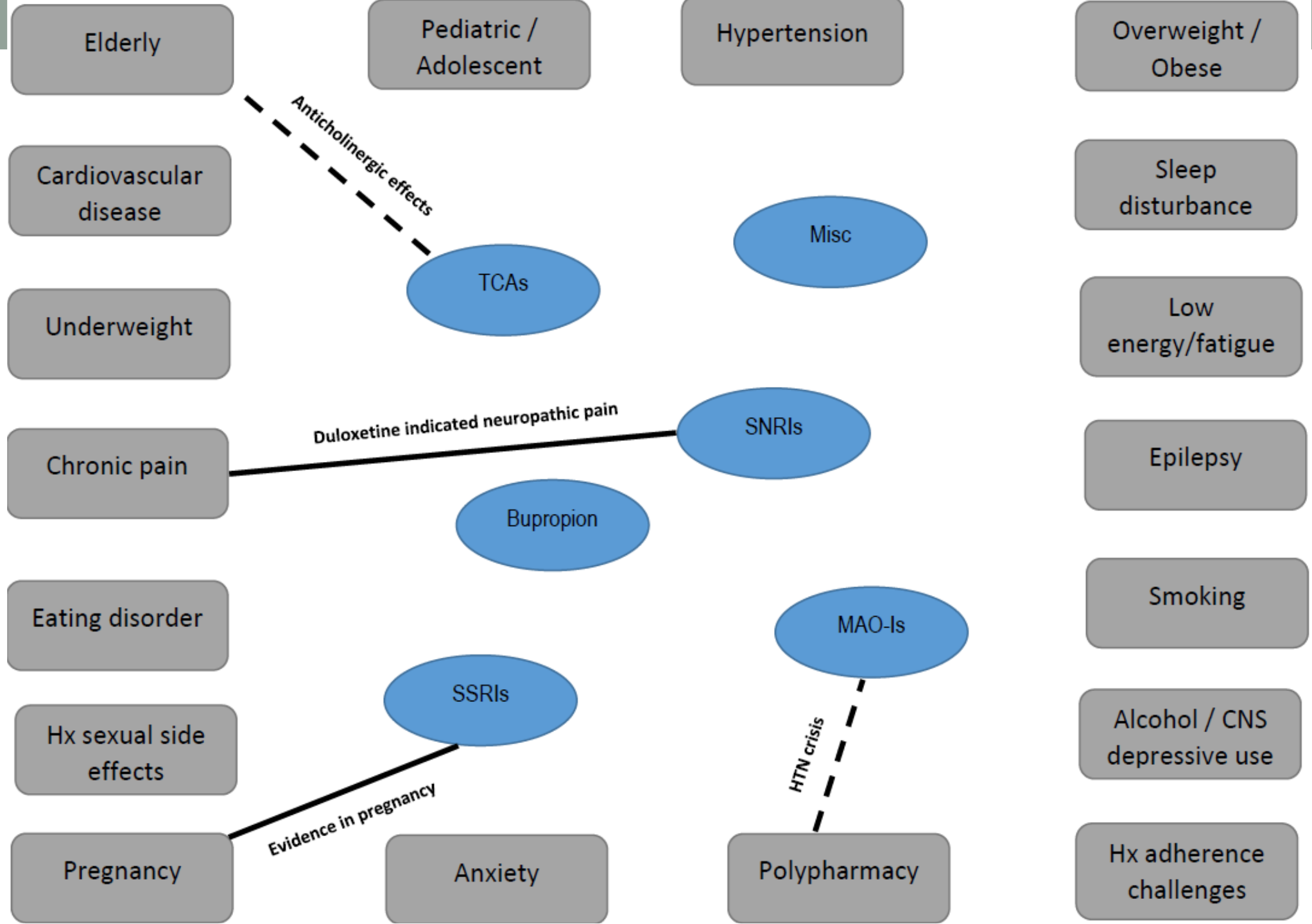


[1]Significantly higher than non-Hispanic black.
[2]Significantly higher than non-Hispanic Asian.
[3]Significantly higher than Hispanic.
[4]Significantly lower than women in same race or Hispanic-origin group.
NOTES: Persons who reported other race, or more than one race are not included in the figure. Access data table for Figure 2 at: https://www.cdc.gov/nchs/data/databriefs/db377-tables-508.pdf#2.
SOURCE: National Center for Health Statistics, National Health and Nutrition Examination Survey, 2015–2018.

Concept Map

Good choice

Poor choice



Questions??

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