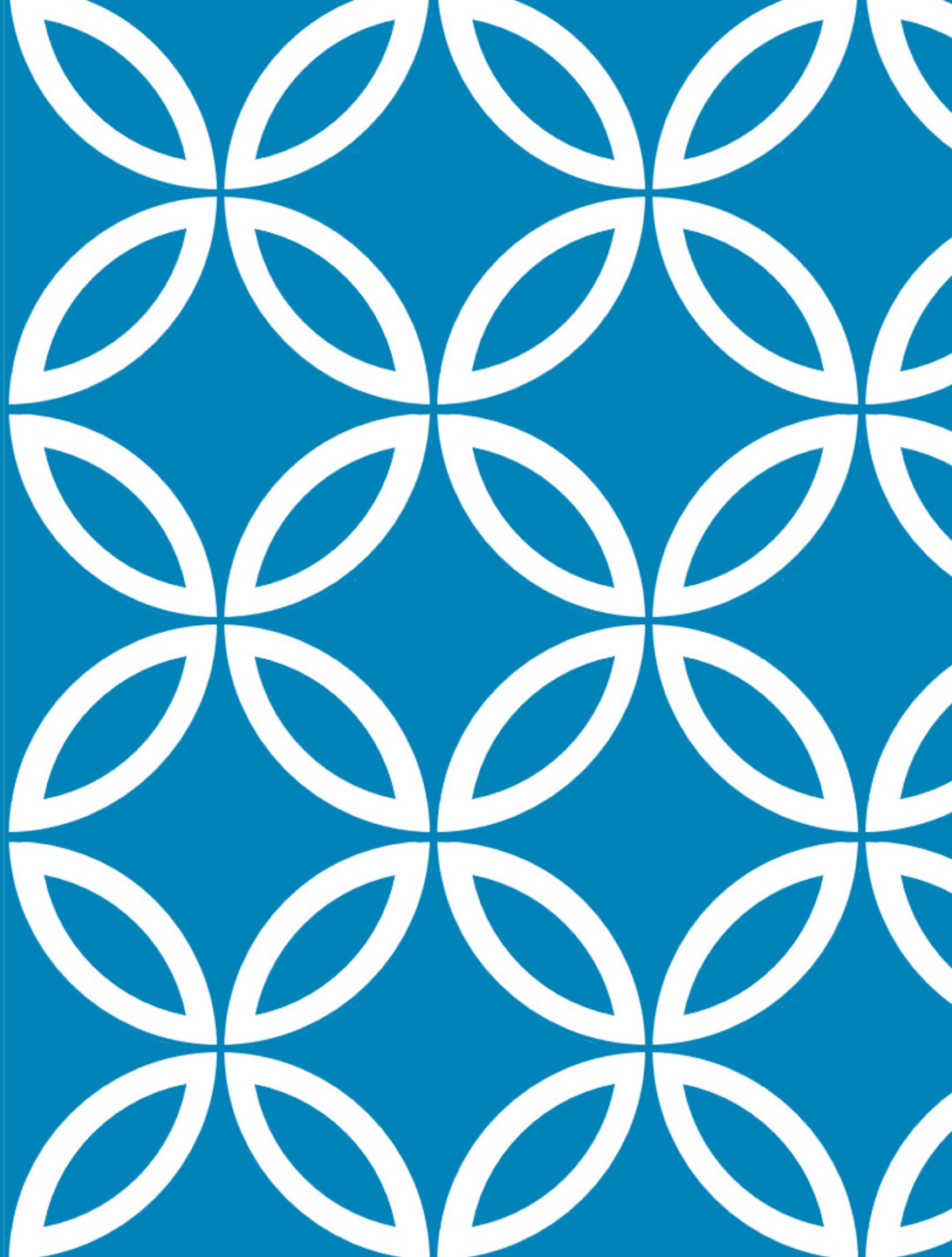
# GERIATRICS

Essentials in Evaluation and Treatment of Late-Life Depression



# DISCLOSURES

I have the following relevant financial relationship with a commercial interest to disclose:

Springer Publishing; Book Royalties, for book on late-life depression prevention

# TOPIC AREAS

- Nosology
- Risk factors
- Special aspects of depression in older adults
- Prevalence, epidemiology
- Psychopharmacology and treatment approaches

# COMMON MYTHS IN LATE-LIFE DEPRESSION

- Getting depressed is a “normal” part of aging
- LLD can’t be treated, or treatment doesn’t matter (if other major illnesses or dementia is present)
- Older adults do not want treatments for depression

# NOSOLOGY OF LATE-LIFE DEPRESSION

- Clinical syndromes
  - Major depressive disorder
  - Dysthymia/Persistent Depressive Disorder (DSM-5)
  - Others (e.g., bipolar depression)

# NOSOLOGY OF LATE-LIFE DEPRESSION

- Sub-clinical depressions
  - Minor depression
    - 2 or more weeks of depressed/anhedonic mood without full complement of other symptoms (but at least two)
  - Sub-syndromal depressive symptoms
    - 2 or more symptoms present

APA, *DSM-IV-TR*, 2000; Pincus et al., 1999

# NOSOLOGY OF LATE-LIFE DEPRESSION

- Sub-clinical vs. Clinical Depression: does it make a difference in late-life?
- Clinical and sub-clinical depression in late-life differ little from each other with regard to:
  - poorer functional outcomes
  - degree of health impairment
  - increased ED and physician visits
  - health costs (ED and outpatient charges)

Lyness et al., 2007; Lyness et al., 2006; Lebowitz et al., 1997

# KEY FEATURES IN LATE-LIFE DEPRESSION

- Cognitive deficits: more prominent memory, concentration and decision-making problems (often effort-dependent)

- Early-onset vs. Late-onset depression:
  - Greater likelihood of dementia at follow-up
  - Lower likelihood of family history of mood disorder

- Behavioral changes: anger, aggression, irritability, anxiety, social withdrawal, regressive behaviors

# KEY FEATURES IN LATE-LIFE DEPRESSION

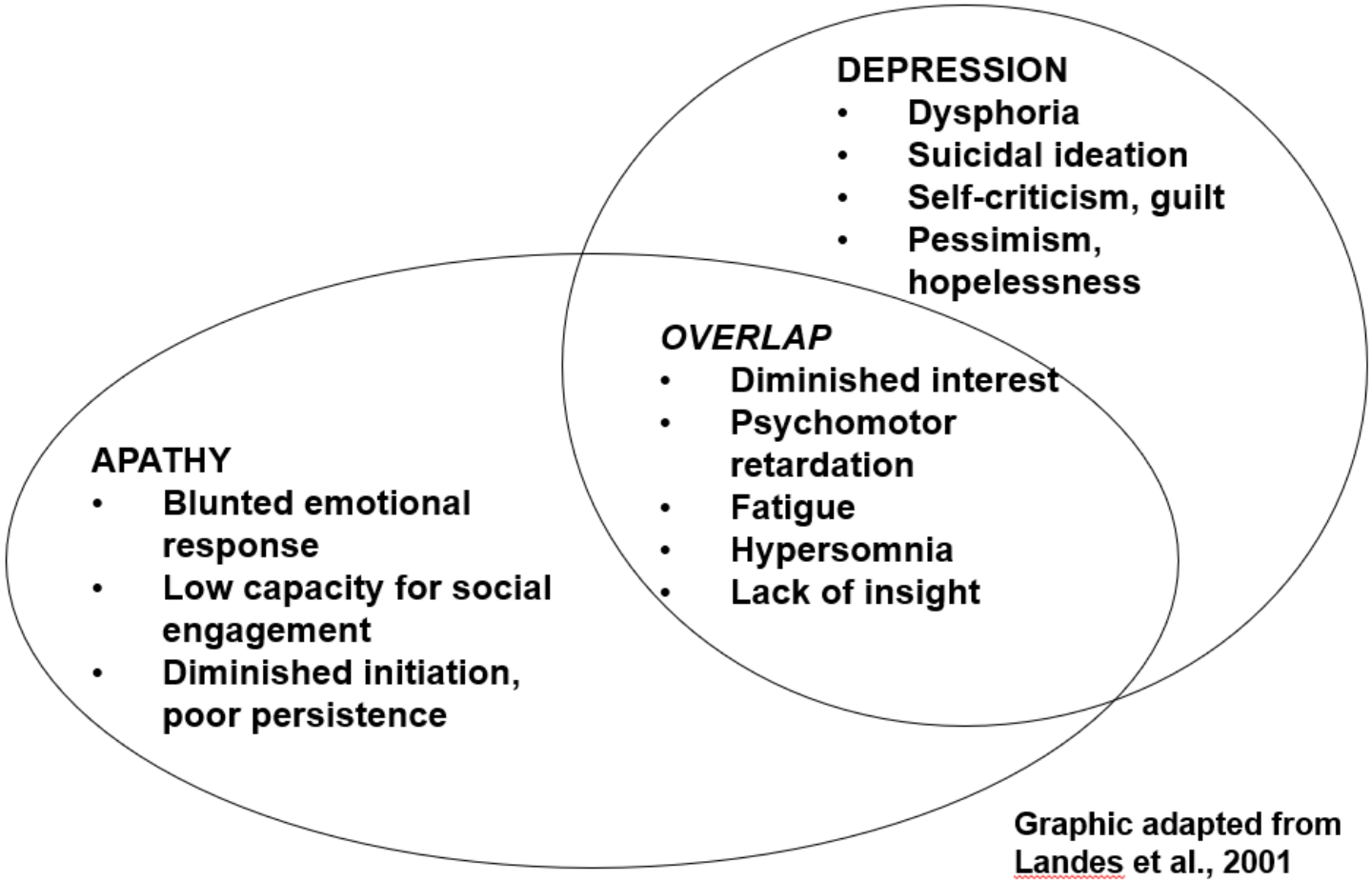
- Less subjective sadness, more anhedonia and helpless feelings → “Depression without sadness” (Gallo J, 1999)
- Symptom replacement with somatic preoccupation
- Psychotic symptoms: proportion increases with age
- Impaired self-care, increased falls, incontinence, anorexia → “failure-to-thrive”
- “Vascular” depression

# VASCULAR DEPRESSION

- Bi-directionality:
  - Appears to be independently related to risk of stroke
  - Can lead to worsening of vascular risk parameters (e.g., diabetes, overweight/obesity, hypertension, smoking)
  - May have shared etiology with vascular disease (e.g., inflammation, immune activation, hyperhomocysteinemia)

Kales et al., 2005; Pan et al., JAMA, 2011

# DISTINGUISHING DEPRESSION FROM APATHY




Graphic adapted from Landes et al., 2001

# DISTINGUISHING DEPRESSION FROM ALZHEIMER DISEASE (AD)

| **Feature** | **Depression** | **AD** |
|---|---|---|
| Prior psychiatric history | Usual | Unusual |
| **Symptom duration** | Short | Long |
| **Memory complaints** | Frequent | Variable |
| **Effort on tasks** | Poor | Good |
| **Prompting** | More helpful | Less helpful |
| **Recognition memory** | More intact | Impaired |
| Neurologic exam | Normal | Abnormal |
| Worse at night | Less typical | More typical |

Depression as prodromal manifestation? (Almeida et al, Transl Psych, 2017; Gillis et al., IJGP, 2017)

# IMPACTS OF LATE-LIFE DEPRESSION

- Common, serious and disabling in older adults
- When co-morbid with medical illness can:
  - Increase functional disabilities associated with illness
  - Increase use of resources: 12-month cost difference ranges from $4,800-15,000 across all levels of medical co-morbidity
  - Reduce effectiveness of rehabilitation for common conditions (e.g., post-stroke, or Parkinson, coronary and lung diseases)
- High suicide rate among persons aged 65+
  - Among those 75+, rate is 10-fold higher for men vs. women
  - 75% of older adults who died by suicide had seen their PCP in the last month of life, and a third in the last week
  - Depression is not sole factor, but remains a key driver

Unutzer et al, 2009; Lebowitz et al., 1997; Alexopoulos et al., 2009; Conwell, 2009; Bruce et al., 2004

# PREVALENCE OF LATE-LIFE DEPRESSION

- Major depression
  - Total range 0.4 – 10.2%
  - All but one < 5%
  - 13 of 16 < 3%
  - Weighted mean = 1.8%
- Minor depression
  - Total range 2.4 – 14.3%
  - 5 of 6 > 8%
  - Weighted mean = 10.2%
- Combined major and minor depression
  - Weighted mean from 28 studies (n=46,075) = 13.3%
  - Sex/gender ratio ~2:1 (female/women)

Beekman et al., 1999

# PREVALENCE OF LATE-LIFE DEPRESSION

- **Differences Across Ethnic/Racial Minority Groups**
  - Still relatively understudied area
  - Blazer et al. (1998) found no differences in current prevalence comparing African-Americans and Whites (Duke EPESE)
  - Lower lifetime prevalence of depression for older adults of African descent also reported by Ford et al., 2007
  - Higher current prevalence of depressive symptoms reported in other cohorts reported by Barry et al., 2014
  - Higher symptom levels, item-level symptom burden (Vyas et al., 2020)
  - Racial/ethnic differences may be influenced by US region (Vyas et al., 2022)
  - Black and Latino adults appear to have disparities of under-diagnosis and under-treatment of depression (Neighbors et al., 2008), despite greater symptom severity (Xu et al., 2010) and role dysfunction when depression occurs (Williams et al., 2007)

# KEY FACTORS IN LATE-LIFE DEPRESSION RISK

## RISK FACTORS

- Substance Use
  - Heavy drinking
  - Current smoking
- Ill-caregiving burden
- Social isolation
- Physical problems
  - Sleep problems
  - Pain
  - Medical Conditions
  - Disability/limitations

## PROTECTIVE FACTORS

- Good social network/stronger social ties
- Psychosocial support
- Higher social standing (in community)
- Exercise/Physical Activity
- Time spent caregiving for children or grand-children
- Religious service attendance
- Caffeine/coffee, Flavonoids, Mediterranean diet, Omega-3

**Temporal or cohort factors (recession, COVID-19 pandemic)**

**CASE EXAMPLE #1: LLD and PT for pain and mobility issues**

Lucas et al., 2011; Lucas et al., 2011; Pan et al., 2012; Mekary et al., 2013; Lucas et al., 2014; Chang et al., 2016; Chang et al., 2016; Li et al., 2016

# PSYCHOTHERAPIES IN LATE-LIFE DEPRESSION

- Psychotherapy approaches
  - CBT, IPT, PST are all evidence-based, indicated options for treatment of depression
  - Combined treatment can greatly increase efficacy
  - Primary care vs. specialty referral-based

- Key factors in geriatric psychotherapy:
  - Adaptations to sensory or physical impairments
  - Adjustments for age-related cognitive and working memory changes: more sessions, more time, cue and review, family members, case mgt
  - Emerging evidence areas: psychotherapy in older adults with immigrant status, minority status, MCI

# SOMATIC THERAPIES IN LATE-LIFE DEPRESSION

- **ECT (Electroconvulsive therapy)**
- Efficacy: still the most effective single antidepressant treatment (~80%); safety profile (mortality ~ 1/10,000 or 0.01%)
- Often suggested by:
  - Older age
  - History of prior response
  - Delusions, malnutrition/dehydration, severe self-neglect
- Memory loss: recent retrograde amnesia more common, not remote; usually improves rapidly within several weeks after course; cognition may actually *improve* in some severe cases
- Disproportionate fear and stigma; need to counter distortions
- Cardiovascular AEs are the primary cause of mortality

- **rTMS (repetitive transcranial magnetic stimulation)**
  - FDA approval in documented mild treatment-resistant depression
  - Consider for vascular depression (Taylor et al., 2018)

# KEY CHALLENGES IN GERIATRIC PSYCHOPHARMACOLOGY

- More history to gather re: co-morbidities, concurrent meds, reconciling meds
- Knowing what the drug-free baseline looks like
- Setting treatment expectations, providing extensive education
- Assessing which medications are still needed, de-prescribing
- Longer time-to-treatment response
- Higher sensitivity to side effects, more potential interactions
- Pill-taking and adherence issues, especially if cognitive impairment present
- PK and PD changes associated with normal physiologic aging

# PHARMACOKINETICS

How the **body affects** antidepressant **medications** in aging

**Absorption**

**Distribution**

**Metabolism**

**Elimination**

# ABSORPTION CHANGES

- Rate is slowed in normal aging
- Extent tends to be unaffected

# DISTRIBUTION CHANGES

- Changes in aging that affect drug distribution
  - ↑ Fat stores
  - ↓ Lean body mass
  - ↑ Volume of distribution for lipophilic drugs
  - ↓ Albumin levels

- Consequences
  - Drugs accumulate in fat stores → longer half-life
  - IM injections may be more painful due to decreased muscle mass
  - Less drug in systemic circulation immediately available
  - More unbound drug may reach brain due to decreased albumin

# METABOLISM CHANGES

- ☐ PHASE 1 - CYP 1A2 and 3A4 are most affected by aging
- ☐ PHASE 2 - Not typically affected by aging

# ELIMINATION CHANGES

## Elimination determines:

- Time to reach steady-state
- Time to drug elimination – ie, how quickly to titrate the drug

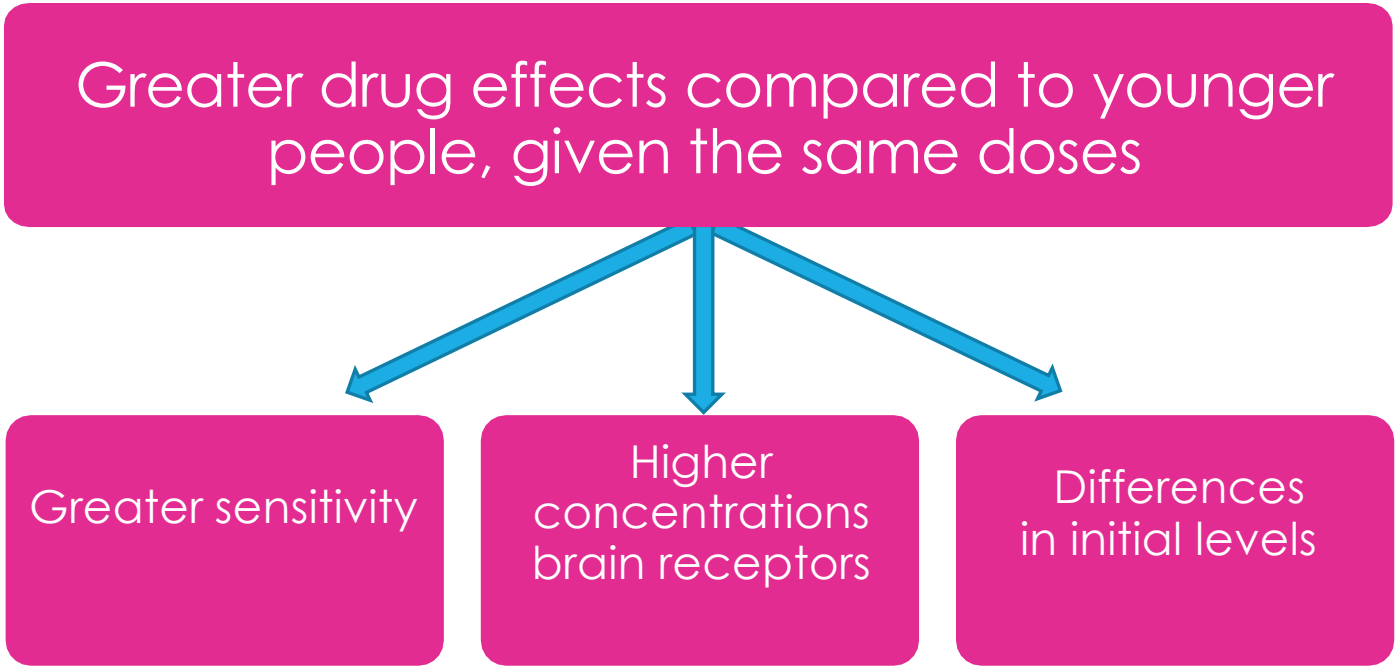
## Reduced hepatic blood flow and renal clearance

- Cr may not be an accurate indicator of renal clearance

**Can offset these changes by reducing dosing rate. This is the reason to "*start low and go slow*".**

# PHARMACODYNAMIC CHANGES

How the antidepressant **medication affects the body** in aging



# PHARMACODYNAMIC CHANGES

- In aging, there may be a decrease in ability to up-regulate or down-regulate postsynaptic receptors

- *Decreased* acetylcholinesterase activity with increasing aging, but there is also *increased* sensitivity to anticholinergic properties of drugs (e.g., TCAs, paroxetine)

**Overall:** Older adults are at much higher risk of having pharmacodynamic drug-drug interactions due to polypharmacy (ie, multiple drugs affecting same neurotransmitters/receptors)

# OVERVIEW: GENERAL TIPS

- ☐ Start low, go slow
- ☐ Make just one change at a time – and explain importance of this to patients/family
- ☐ Re-evaluate need for each drug *at each visit*
  - ☐ Adherence problems increase with the number of prescriptions
  - ☐ Always screen carefully for potential drug-drug interactions
- ☐ Simplify wherever possible
  - ☐ Once daily is optimal (*imagine* how patient will take the meds)
  - ☐ Choose dose strengths that reduce burden of taking the pills (eg, pill sizes, how easy to cut)
  - ☐ Choose liquid formulations/sprinkles/capsules that can be emptied, if swallowing difficult

# ANTIDEPRESSANTS

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- TCA
  - Nortriptyline 10-150 mg/d
  - Desipramine 10-250 mg/d
  - Common side effects: mildly anti-cholinergic, minimal orthostasis, needs blood levels, toxicity in overdose

- SSRI
  - Fluoxetine 5-40 mg/d
  - Sertraline 25-200 mg/d
  - Paroxetine* 5-40 mg/d
  - Fluvoxamine 25-250 mg/d
  - Citalopram 5-20 mg/d
  - Escitalopram 5-20 mg/d
  - Common side effects: anxiety/ sedation, agitation, restlessness, GI complaints, headache, rash, sexual dysfunction

    *weakly anti-cholinergic, may lower dosing options

# ANTIDEPRESSANTS

- Serotonin/Norepinephrine Reuptake Inhibitors (SNRI)
  - Venlafaxine XR 37.5-225 mg/d
    side effects: increase in BP, confusion, lightheadedness
  - Duloxetine 30-120 mg/d
    side effects: GI, dry mouth, dizziness, sweating, decreased appetite

- Alpha 2 antagonist/Selective Serotonin
  - Mirtazapine 7.5-45 mg/d
    side effects: sedation, weight gain

- Atypical/Other Antidepressants
  - Trazodone 25-250 mg/d
    side effects: sedation, orthostasis, priapism in males (rare)
  - Bupropion 37.5-450 mg/d
    side effects: insomnia (avoid after 4 pm), anxiety, seizures (rare)
  - Vortioxetine 5-20 mg/d
    side effects: N/V, GI, dry mouth, dizziness, caution with CYP 2D6 poor metabolizers (↓ dose)
  - Vilazodone 5-20 mg/d
    side effects: N/V, GI, dry mouth, dizziness, caution with CYP 3A4 inhibitors (↓ dose)

# ANTIDEPRESSANTS-PLUS

- Other agents
  - Monoamine oxidase inhibitors: phenelzine, tranylcypromine
  - Psychostimulants: dextroamphetamine, methylphenidate
  - Dopamine agonists: pramipexole, ropinerole
  - Non-amphetamine stimulant-like: modafinil, armodafinil
- Augmentation Strategies
  - Combining antidepressants (eg, SSRI+bupropion)
  - L-thyroxine, lithium, buspirone
  - Atypical antipsychotics

**CASE EXAMPLE #2: LLD and medical co-morbidity**

# ANTIPSYCHOTICS

- ☐ Document target symptoms and establish a time frame for assessment of results
- ☐ Evaluate:
  - ☐ History of metabolic disorder, stroke, coronary disease
  - ☐ History of extrapyramidal symptoms, Parkinson
- ☐ Lipid panel/A1c at baseline then annually or as indicated
- ☐ Use lowest doses necessary for the shortest time period
- ☐ Black box warning re: patients with dementia:
  - ☐ Typicals just as potentially hazardous as atypicals
- ☐ Educate health care agent/care partner about benefits, risks
- ☐ **Care coordination, low threshold for specialty referral**

# ANTIPSYCHOTICS: TYPICAL DOSE RANGES FOR OLDER ADULTS

| Atypical agents and characteristics | | |
|---|---|---|
| Name | Dose range | Common side effects, key features |
| Olanzapine | Start: 1.25-2.5 mg/d<br>Optimal: 5-10 mg/d | EPS, mildly anticholinergic, sedation, postural hypotension |
| Risperidone | Start: 0.25-0.5 mg/d<br>Optimal: 0.5-2 mg/d | EPS (dose-related), minimally anticholinergic, prolactin increase, orthostatic hypotension |
| Quetiapine | Start: 12.5-25 mg/d<br>Optimal: 50-100 mg/d | Lower rate of EPS, more sedation, orthostatic hypotension |
| Aripiprazole | Start:1-2 mg/d<br>Optimal: 5-10 mg/d | EPS can be significant, low risk of sedation, lower weight gain |
| Pimavanserin* | 10 mg/d tablet or 34 mg/d capsule | Nausea, constipation, confusion; 10-mg tablet if using with CYP 3A4 inhibitors (* PD psychosis approval) |
| All | | Follow ADA/APA consensus guidelines, check QTc, **Note: FDA Black Box warning** |

# MANAGING ADVERSE EFFECTS

- Understanding pharmacokinetics
  - Dosing once daily → higher peaks; peaks typically associated with the side effects for some meds
  - Splitting dose might reduce side effects (but weigh benefits with risk for nonadherence, especially if cognitive impairment is an issue)

- GI side effects, dizziness, sedation → give dose at bedtime
- Activation → give dose in the morning
- Tremor → use split dosing
- Sexual dysfunction → try switching medications or augmenting with bupropion

# MEDICATION TEACHING

- ☐ Use open-ended questions
  - ☐ Emphasize that there are no “bad” or “silly” questions
  - ☐ Identify biases/pre-conceptions about medications, major concerns
  - ☐ Identify and direct focus on target symptom(s)

- ☐ Use read-backs of instructions; print out or write out (easy to do now in EHRs)

- ☐ Include and educate family members whenever possible, but this is essential in cases of cognitive disorders

- ☐ Encourage patient and family to keep medication lists on them at all times and to use pill organizers/med-minders

# KNOW ABOUT THE BEERS CRITERIA

- ☐ Potentially Inappropriate Medication Use in Older Adults:
  - ☐ Anticholinergic medications (diphenhydramine, benztropine, TCAs, paroxetine)
  - ☐ Antihistamines (educate on OTC use!)
  - ☐ BZDs & z-drugs (zolpidem, zaleplon, eszopiclone)
  - ☐ Muscle relaxants (eg, cyclobenzaprine)
  - ☐ NSAIDs (increased GI bleeding risk with SRI drugs)

- ☐ Avoid ≥ 3 CNS-active drugs whenever possible due to increased risk for falls
  - ☐ Antidepressants
  - ☐ Antipsychotics
  - ☐ Opioids

Thank you