GERO-PSYCHO-PHARMACOLOGY UPDATE FOR PRIMARY CARE PROVIDERS

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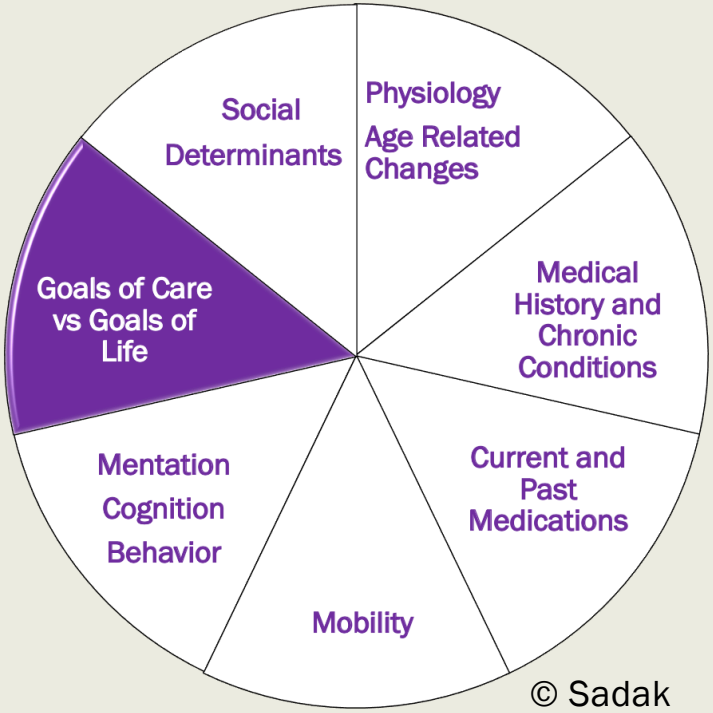
Objectives

Comprehensive Model for Guiding Prescribing Decisions in Geriatric Psychiatry



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Best Practices and Deprescribing

Case Study: Primary care follow-up for pneumonia

Patient - 75-year-old, African American man who had no chief complaint. “I am fine”

Family – Chief complaint: “He just sits on the couch and eats all day, refuses psychotherapy”

- On interview, patient reports:
  - *Being depressed, down, easily frustrated*
  - *Fatigued, has low motivation, does not feel like socializing*
  - Disinterested in hobbies and activities
  - Neglecting responsibilities and relationships
  - *Last week started hearing voices*
  - *No suicidal ideations*
  - *Forgetfulness, difficulty concentrating*
  - *Frustrated about recent decrease in libido*
  - *Frustrated about recent weight gain. 20 lb in past 3 months*
  - *Concerned about recent non-injury falls. Fearful of future falls*
  - *Sleeping “too much” 12-14 hrs. per night. Does not wake up rested*

Insurance: Medicare Part A (hospital), B (outpatient), D (prescriptions)

- Physical exam WNL. No history of mental illness or psychiatric admissions
- **Current diagnoses:** Osteoporosis. Peripheral Vascular Disease. Pre-Diabetes
- **History** of Hyponatremia and Hypogonadism
- Was robust and active until a recent episode of pneumonia
  - *Despite full recovery from pneumonia, seems to have low energy, depressed*
    - stooped posture, tearful, does not make eye contact
- Does not meet criteria for dementia or delirium
- Pre-diabetes and peripheral vascular disease (PVD) were controlled with diet and exercise
  - *A1C is now climbing (6), likely due to recently increased consumption of refined carbohydrates and inactivity*
  - *PVD is exacerbating, likely due to inactivity*
- Testosterone low, but WNL for his age (on supplementation for the past 12 months).
- All other laboratory values are normal
- CT, MRI, and positron emission tomography (PET) scans: generalized atrophy, but no activity difference among various brain areas. No metastasis, some subcortical infarcts
- **Current medications:**
  - Aspirin 81mg; Atorvastatin [Lipitor] 40mg; Cilostazol [Pletal] 100mg, Alendronate (Fosamax Plus D) 70-2800 mg (weekly); 7.5 g of 1% testosterone gel. Recently started on Metformin 500mg.

Patient is at risk for:

- Treatment resistant geriatric depression
- Worsened psychosis
- Worsened sexual dysfunction
- Continued weight gain
- Worsening of PVD and Osteoporosis
- Diabetes
- Hyponatremia
- Neurocognitive Disorder
  - Older adults with late-onset depression are more likely to have vascular risk factors
  - Depression is a predictor of progression to MCI and to dementia
    - Amnestic mild cognitive impairment and incident dementia and Alzheimer's disease in geriatric depression. Int Psychogeriatr. Steffens et al, 2014
- Accelerated frailty
    - Management of Frailty: A Systematic Review and Network Meta-analysis of Randomized Controlled Trials. J Am Med Dir Assoc. Negm et al, 2019

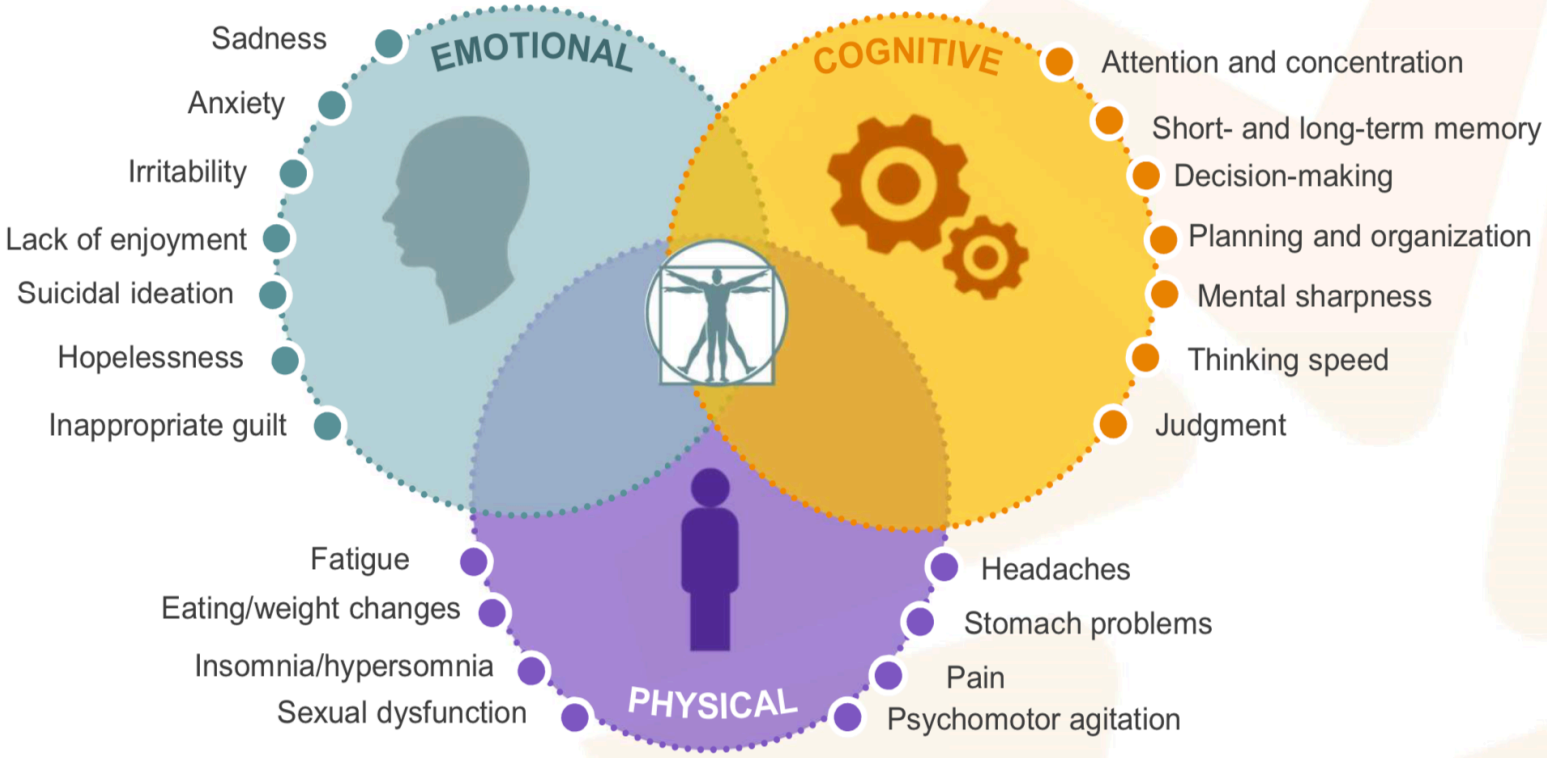
- Start an SSRI
  - *(e.g. fluoxetine [Prozac], or Vortioxetine [Trintellix])*
- Start an SNRI (e.g. venlafaxine [Effexor])
- Start an NDRI (e.g. bupropion [Wellbutrin])
- Start an NaSSA (e.g. mirtazapine [Remeron])
- Start a stimulant salt or Modafinil [Provigil]
- Start an antipsychotic (e.g. aripiprazole [Abilify])
- Increase Testosterone
- Start a combination of medications
- Refer to psychotherapy
- Initiate referral to physical therapy
- Consider ECT or TMS

Consider Diagnosis: Geriatric Depression

- ~ 52% of patients have their first onset of depression at age 60 or older
- Depression prevalence:
  - *4.6%–9.3% in patients older than 75 years*
  - *27% in those older than 85 years*
- **Early and late onset depression in old age**: different etiologies, same phenomenology
- **Most common symptoms are atypical**
  - Insomnia or hypersomnia; anorexia or weight gain
  - Treatment-resistant pain symptoms, headache and fatigue
  - Frequent office visits or use of medical services
  - Unexplained gastrointestinal symptoms
  - Signs of social isolation and increased dependency
- Elderly individuals may dismiss depression as a response to life stressors or a normal part of aging and not seek help
  - *Mental health stigma is highly prevalent*

Depression in older adults. Annu Rev Clin Psychol. Fiske et al., 2009.
J Affect Disord. Brodaty et al., 2001. The prevalence of mental disorders in older people in Western countries—a meta-analysis. Ageing Res Rev. Volkert et al., 2013
Diagnosing and Treating Depression in Patients with Alzheimer's Disease. Neurology and Therapy. Burke et al., 2019

MDD Has 3 Sets of Symptom Domains – Emotional, Physical, and Cognitive



MDD = major depressive disorder.

American Psychiatric Association. *Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition.* Arlington, VA: American Psychiatric Association; 2013. Marazziti D, et al. *Eur J Pharmacol*. 2010;626(1):83-86. Hammar A, et al. *Front Hum Neurosci*. 2009;3:26. Fehnel SE, et al. *CNS Spectr*. 2016;21(1):43-52.

Consider Diagnosis:
Geriatric Depression With Psychotic Feature

- **Common psychotic features**
  - *Delusions – False, fixed beliefs*
  - *Hallucinations – False sensory perceptions, usually auditory*
    - These symptoms are often missed
- Antidepressant medication should be given with an antipsychotic
  - *Risperidone, 0.75–2.25 mg/day*
  - *Olanzapine [Zyprexa], 5–10 mg/day*
  - *Quetiapine [Seroquel], 50–200 mg/day*
    - Recommended for psychosis and agitation
  - *Aripiprazole [Abilify], 5-20 mg/day*
    - Recommended for psychosis and vegetative symptoms
- If initial treatment fails, treatment of choice is ECT

Using antipsychotic agents in older patients. J Clin Psychiatry, Alexopoulos, 2004

Geriatric Treatment Resistant Depression

- At least 50% of older people fail to respond adequately to first-line antidepressant pharmacotherapy
- Treatment-resistant late-life depression (TRLLD) increases risk for:
  - *early relapse*
  - *undermines adherence to treatment for coexisting medical disorders*
  - *amplifies disability and cognitive impairment*
  - *imposes greater burden on family caregivers*
  - *increases the risk for early mortality, including suicide.*

Getting to and sustaining remission is the primary goal of treatment, yet there is a paucity of empirical data on how best to manage TRLLD.

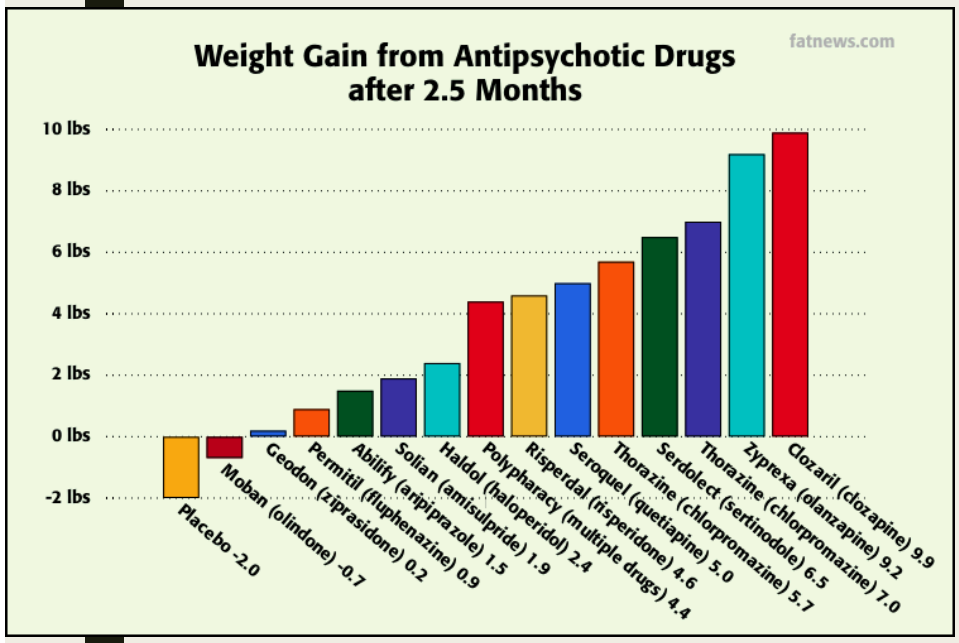
Treatment-resistant Late-life Depression: Challenges and Perspectives. Curr Neuropharmacol. Knochel et al., 2015

TRLLD Augmentation

- **Exercise**
  - *Significant reduction in depressive and cognitive symptoms*
- **Psychotherapy**
  - *Following modalities have strong evidence of effectiveness*
    - Cognitive & behavioral therapies (CBT)
    - Interpersonal therapy (IPT)
    - Problem-solving therapy (PST)
- **Aripiprazole [Abilify]**
  - *Full remission 50%*
- **Lithium**
  - *Full remission 50%*
  - *Partial response 20%*
- Stimulants – insufficient evidence
- Testosterone – insufficient evidence

Treatment-resistant Late-life Depression: Challenges and Perspectives. Curr Neuropharmacol. Knochel et al., 2015

aripiprazole [Abilify]



Abilify is not associated with significant:

- Weight gain
- Sedation
- Increased prolactin
- QTC prolongation

- Approved Adjunct for Major Depression
  - *2-10mg when used as adjunct*
- Dose adjustment generally not necessary in elderly patients
- No agent has been approved for treatment of elderly patients with dementia-related psychosis
  - *increased risk of death and cerebrovascular events compared to placebo*
- **Dose** in the am
  - *Use with caution if patient is anxious*
  - ***Reduce Abilify** by ½ when combining with Prozac, Paxil, Beta Blockers*
  - *Increase Abilify dose by ½ when combining with Carbamazepine or antacids*

Side Effects

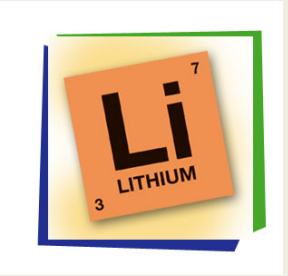
- *Dizziness, insomnia, akathisia, activation*
- *Nausea, vomiting*
- *Orthostatic hypotension, occasionally during initial dosing*
- *Constipation*

Table 3–7. Suggested schedule for monitoring adverse effects of antipsychotic treatment

	Baseline	4 weeks	8 weeks	12 weeks	Quarterly	Every 6 months	Annually	Every 5 years
Abnormal Involuntary Movement Scale	x	x	x			x		
Blood pressure and pulse (orthostatics)	x	x	x	x			x	
Electrocardiogram	x							
Fasting plasma glucose	x			x			x	
Fasting lipid profile	x			x				x
Liver function tests	x					x		
White blood cell count with differential	x	x				x		
Waist circumference	x						x	
Weight and height (body mass index calculation)	x	x	x	x	x			

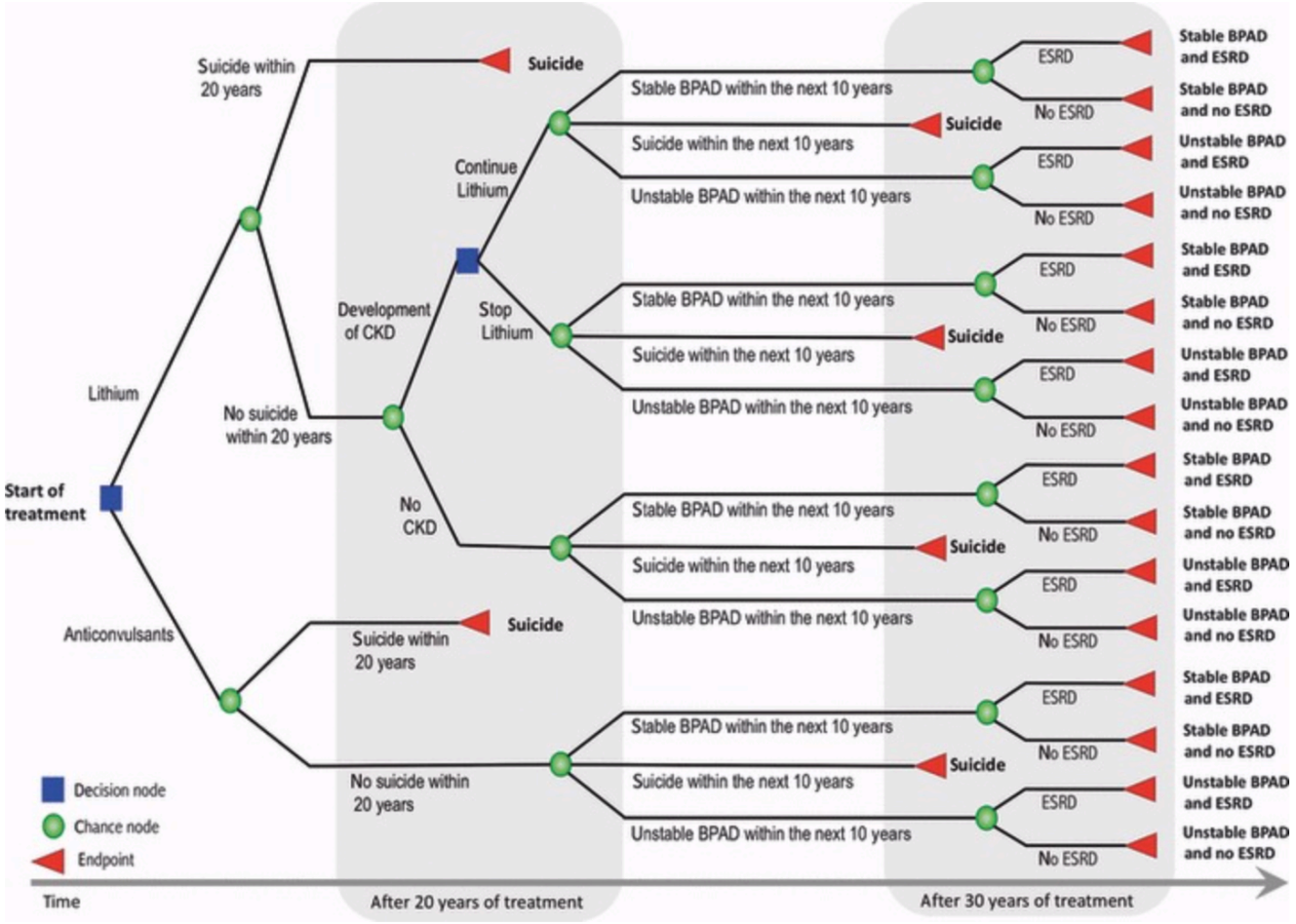
Lithium

- Absorption is relatively unchanged, distribution and clearance are both affected by aging duet to:
  - *relative decrease in total body water*
  - *increase in adipose tissue*
  - *decrease in glomerular filtration*
- **Elimination half-life** in elderly 28-36 hrs. vs. 24 hrs. in younger people
- **Plasma levels:** Recommended plasma levels 0.4 - 0.8
  - *Clearance declines with age. Can still be neurotoxic, e.g. delirium*
  - *Check serum 7 days after each dose change, monitor every 3 months*



- Single nightly dose of short acting Lithium allows for kidney recovery between doses
- Long-term (6-10 years) lithium treatment associated with gradual decline of renal functioning (eGFR) by about 30% more than that was associated with aging alone
- **Risks**
  - *Comorbid chronic kidney disease, diabetes, hypertension, heart failure*
  - *Anticonvulsants, antipsychotics, angiotensin-converting enzyme inhibitors or nonsteroidal anti-inflammatory*
  - *Multiple times a day dosing*
  - *Dietary changes (ex. low salt regiment)*
  - *Dehydration, diarrhea*
- May decrease suicide and suicide attempts

Psychiatric and physical outcomes of long-term use of lithium in older adults with bipolar disorder and major depressive disorder: A cross-sectional multicenter study. J Affect Dis. Morlet, et al., 2019; Long-term lithium treatment in bipolar disorder: effects on glomerular filtration rate and other metabolic parameters. Int J Bipolar Dis. Tondo et al., 2017; Werneke U, Ott M, Renberg ES, Taylor D, Stegmayr B. A decision analysis of long-term lithium treatment and the risk of renal failure. Acta Psychiatr Scand 2012; 126:186–97.



Decision tree. CKD, chronic kidney disease; ESRD, end stage renal disease; BPAD, bipolar affective disorder.

Werneke U, Ott M, Renberg ES, Taylor D, Stegmayr B. A decision analysis of long-term lithium treatment and the risk of renal failure. Acta Psychiatr Scand 2012; 126:186–97

Treatment Resistant Depression + Suicidality = Use Lithium in Chronic And End Stage Kidney Disease

Testosterone

- Emerging as an augmentation therapy for depression in hypogonadal (total testosterone 345.82 ng/dL or less) and eugonadal men
- Not yet recommended as an antidepressant treatment by clinical practice guidelines
  - *National Institute for Health and Care Excellence or by Endocrine Society*
    - Randomized placebo-controlled clinical trials (RCTs) for Major Depression yielded inconsistent results
      - Most beneficial for men with low testosterone and comorbid:
        - Dysthymic disorder
        - Treatment-resistant depression
        - HIV
    - Higher doses
      - *M*ore effective for improving mood
        - After 6 weeks, maximum effect 18-30 weeks, effect demonstrated up to 36 months
- Similar effectiveness in older and younger men
  - Improves:
    - Lean muscle mass, muscle strengths and function; Body composition; Bone mineral density; Sexual function; Mood
  - Dose not improve
    - Cognition
  - Increased risks of Cardiovascular events

Association of Testosterone Treatment With Alleviation of Depressive Symptoms in Men: A Systematic Review and Meta-analysis. JAMA Psychiatry. Walther et al., 2019

Modafinil [Provigil]

Pharmacological actions distinct from those of conventional amphetamine - like psychostimulants.

- *Blocks the reuptake of norepinephrine and dopamine and promotes their neuronal release*
- Acts in the hypothalamus by stimulating wake-promoting areas

- Risk of abuse, withdrawal, or side effects is smaller
- Positive effects mainly on fatigue and sleepiness
- Meta-analysis show significant effect of modafinil augmentation compared to placebo on fatigue and other core depressive symptoms.
- Usual Dosage Range
  - *100-400 mg daily, I only go to 200 in the elderly*
  - Dividing doses and giving a second dose at noon does not appear to affect sleep architecture
- Side effects:
  - *Transient ECG changes have been reported in patients with preexisting heart disease*
  - *Rare psychiatric reactions (activation of mania, anxiety)*
- Other considerations
  - *Cost ~$37 with Medicare insurance*
  - *Have to meet criteria for hypersomnia, narcolepsy, hypopnea with obstructive sleep apnea, fatigue in MS*

Efficacy of off-label augmentation in unipolar depression: A systematic review of the evidence. European Neuropsychopharmacology. Kleeblatt et al., 2017

SLEEPINESS SCALE

EPWORTH SLEEPINESS SCALE

Name: _____ DOB: _____ Date: _____

This questionnaire was developed to determine the level of daytime sleepiness in individuals. It has become one of the most frequently used methods for determining a person's average level of daytime sleepiness.

Please rate how likely you are to doze or fall asleep in the following situations by selecting the response that best applies. If you have not done some of these activities recently, select what would most likely happen if you were in that situation.

0 Would ***never*** doze

1 ***Slight*** chance of dozing

2 ***Moderate*** chance of dozing

3 ***High*** chance of dozing

	Chance of Dozing			
Sitting and reading	0	1	2	3
Watching television	0	1	2	3
Sitting inactive in a public place (eg, a theater or a meeting)	0	1	2	3
As a passenger in a car for an hour without a break	0	1	2	3
Lying down to rest in the afternoon when circumstances permit	0	1	2	3
Sitting and talking to someone	0	1	2	3
Sitting quietly after a lunch without alcohol	0	1	2	3
In a car, while stopped for a few minutes in traffic	0	1	2	3
			Total Score:	

Interpreting Epworth Sleepiness Scale Scores[1,2]		
Normal	EDS*	High Levels of EDS*
0-10	>10	>16

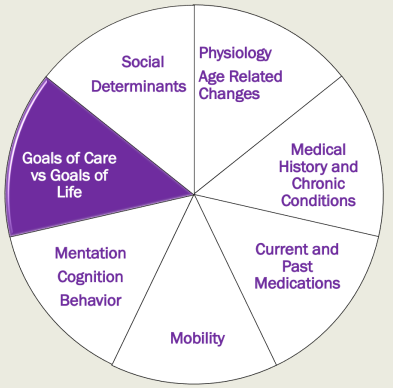
Sources: **1.** Johns M, Hocking B. Excessive daytime sleepiness: daytime sleepiness and sleep habits of Australian workers. *Sleep*. 1997;20(10):844-849. **2.** Johns MW. A new method for measuring daytime sleepiness: the Epworth sleepiness scale. *Sleep*. 1991;14(6): 540-545.

*Excessive daytime sleepiness.

What MATTERS
Goals of Care vs Goals of Life

"Frustrated about recent decrease in libido
Frustrated about recent weight gain. 20 lb in past 3 months
Concerned about recent non-injury falls. Fearful of future falls
Sleeping "too much" 12-14 hrs. per night. Does not wake up rested"

Consider
Patient
and
Family



Goals of Care – Goals of Life. E.g. Sexuality

Most Common Antidepressant Related Treatment-Emergent Sexual Dysfunction (TESD)

- 54% males and females experience decreased libido, 36% difficulty achieving orgasm
- 37% males erectile dysfunction

Antidepressants and TESD

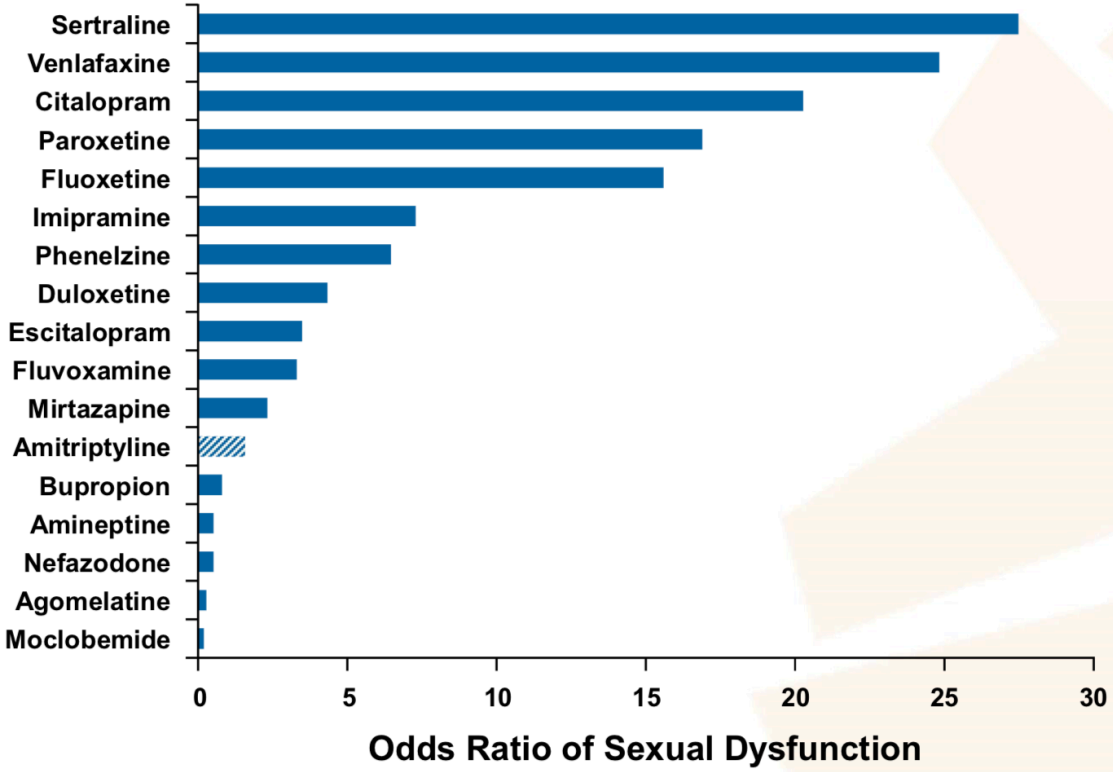
- SSRIs and SNRIs ~ 60 %
- Mirtazapine [Remeron] ~ 25 %
- Vortioxetine [Trintellix] ~ 10 %
- Bupropion [Wellbutrin] ~ 10 %

TESD Expert Advice

- Wait 2-6 weeks
  - *If depression/anxiety remission is achieved, try decreasing antidepressant dose*
  - *If partial response to the initial dose or exacerbation when dose is decreased, consider adjunct*
    - Males - phosphodiesterase-5 inhibitors [sildenafil (Viagra), tadalafil (Cialis), and vardenafil (Levitra)]
    - Males and females - Bupropion [Wellbutrin] or Buspirone [Buspar]
  - *If therapeutic effect of the initial high dose antidepressant is marginal, consider switching*
    - ~ 80% improvement in sexual dysfunction when switched from SSRI to Bupropion [Wellbutrin]

Sexual dysfunction caused by selective serotonin reuptake inhibitors (SSRIs): Management. UpToDate. Hirsh et. al., 2019

Recent Data Continues to Highlight Risk of Sexual Dysfunction with Antidepressants



A total of 14 publications, including 8 qualified randomized clinical trials, were eligible. The frequency of SD in overall, male and female patients was 5.7%, 11.9%, and 1.7%, respectively. SD was six-fold higher in men than women.

SD = sexual dysfunction.

Chen LW, et al. *Am J Mens Health*. 2018;12(2):370-379. Serretti A, et al. *J Clin Psychopharmacol*. 2009;29(3):259-266.

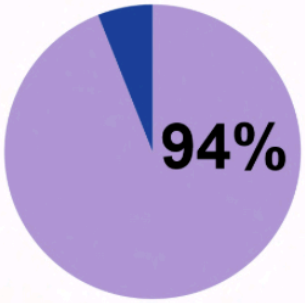
Goals of Care –Goals of Life. E.g. Cognition

Cognitive Symptoms in Depression

Cognitive symptoms in depression are highly prevalent and persistent – *even after* treatment

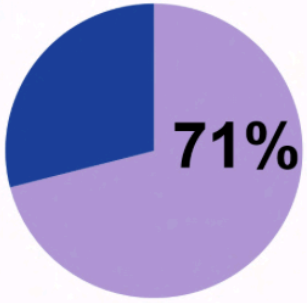
ACUTE

In one study, cognitive problems dominated and were **present for up to 94% of the time** during depressive episodes



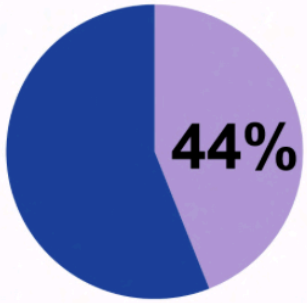
RESPONSE

Another study showed that **71% of patients who responded to treatments** still had cognitive symptoms



REMISSION

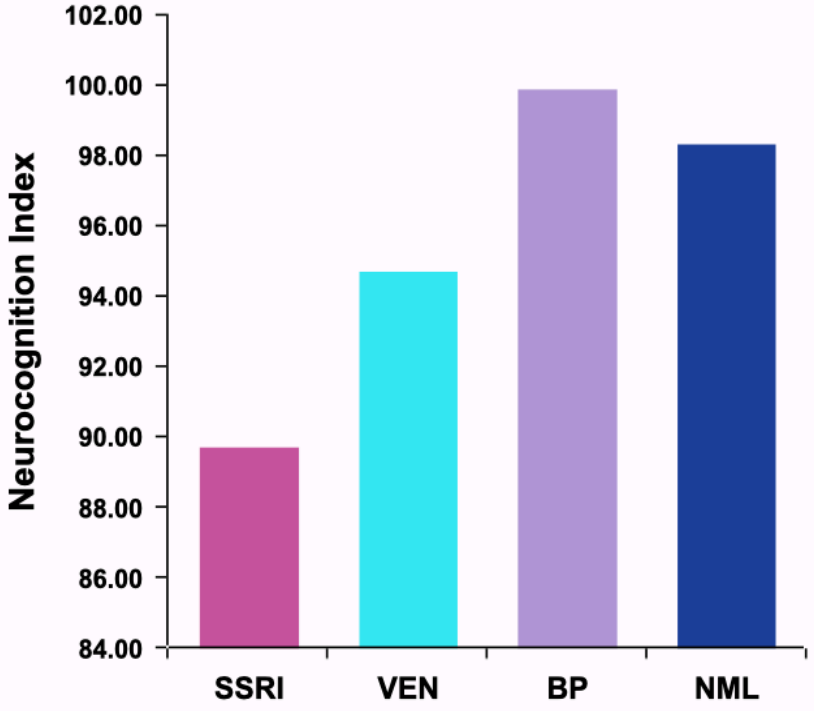
Even in patients thought to be in remission, cognitive symptoms were shown to be **present in patients with depression for an average of 44% of the time** during periods of remission



Conradi HJ, et al. *Psychol Med*. 2011;41(6):1165-1174. McClintock SM, et al. *J Clin Psychopharmacol*. 2011;31(2):180-186.

Antidepressants Have a Differential Impact on Cognition in Patients with MDD

- N=81 patients with MDD were treated with a stable dose of medication for at least 4 weeks (bupropion=27; venlafaxine=27; SSRIs=27). N=27 controls were randomly selected from the CNS Vital Signs normal database
- Patients were tested with the CNS Vital Signs (CNSVS) battery at the North Carolina Neuropsychiatry Clinics
- CNSVS is a PC-based neurocognitive screening battery that comprises 7 familiar neuropsychological tests: verbal memory (VBM); visual memory (VIM); finger tapping (FTT); symbol-digit coding (SDC); the Stroop test (ST); the shifting attention test (SAT); and the continuous performance test (CPT)

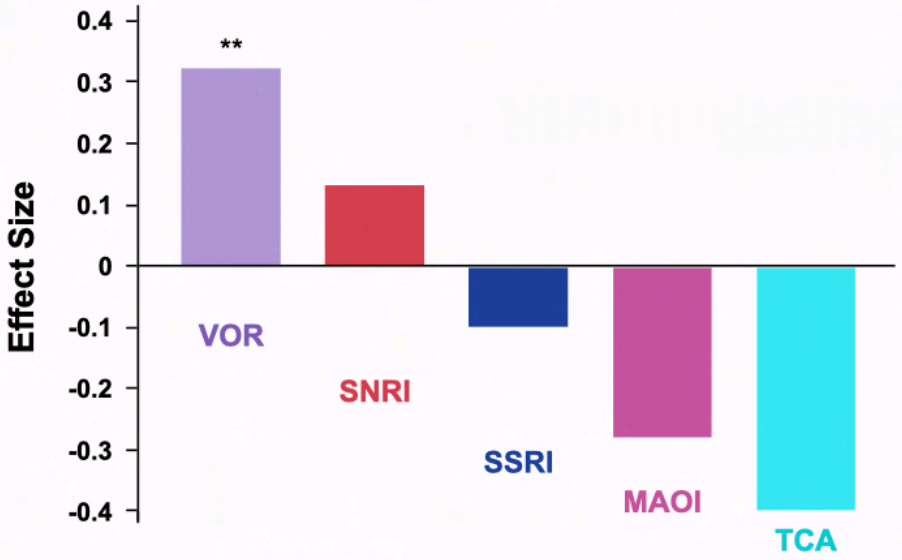


The SSRI group scored significantly below controls in tests of psychomotor speed, cognitive flexibility, and reaction time. The venlafaxine group scored more poorly than controls in reaction time, a measure of information processing speed derived from the Stroop test. The bupropion group did not differ from controls in any of the cognitive domains.

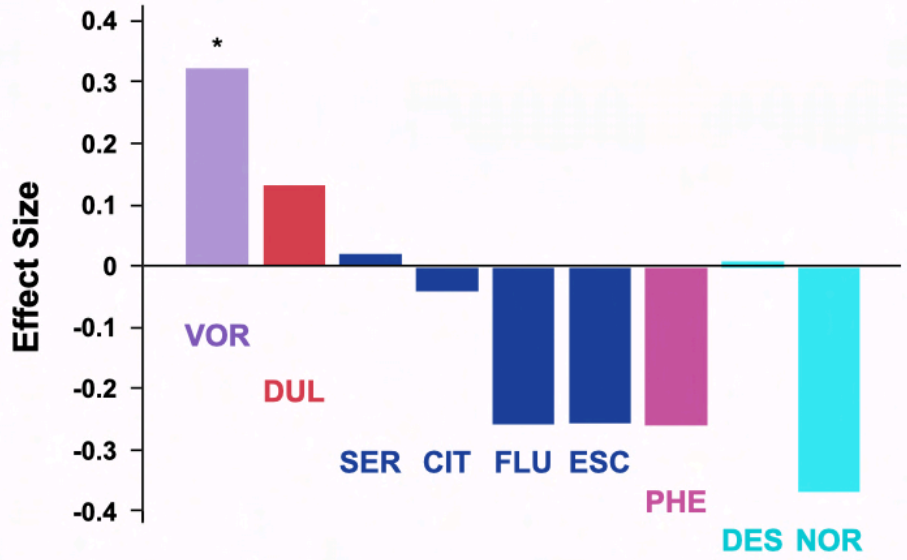
Gualtieri CT, et al. *MedGenMed*. 2007;9(1):22.

Improvement in Cognitive Dysfunction in MDD as Assessed by the DSST

Standardized Effect Size Relative to Placebo by Antidepressant Therapeutic Classes



Standardized Effect Size Relative to Placebo by Individual Antidepressants



As of May 2018, US Prescribing Information for vortioxetine shows data on a positive effect on processing speed, an aspect of cognitive function that is impaired in many patients with MDD.

****P*<.05; ***P*<.01. CIT = citalopram; DES = desipramine; DUL = duloxetine; ESC = escitalopram; FLU = fluoxetine; NOR = nortriptyline; PHE = phenelzine; SER = sertraline; VOR = vortioxetine.**

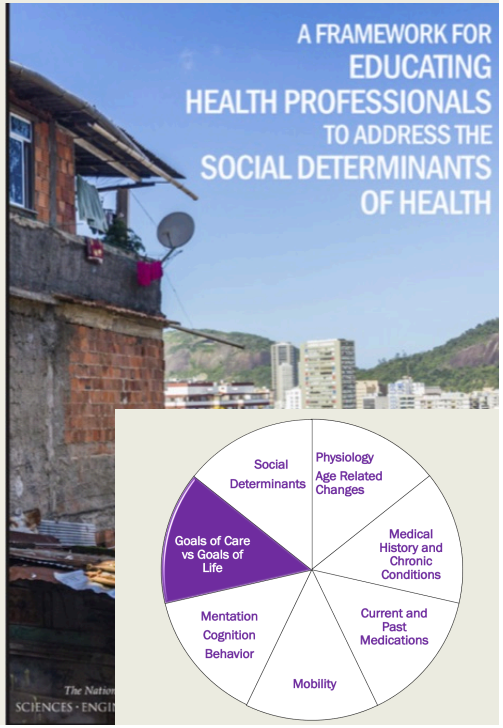
Baune BT, et al. *Int J Neuropsychopharmacol*. 2018;21(2):97-107.

Medicare Part D Prescription Coverage

Racial and ethnic minority elders often experience:

- Greater burden of unmet mental health needs
- Greater stigma within their cultural groups
- Under-prescribing of psychiatric medications
- Fewer referrals to psychotherapy

Mental Health Issues in Racial and Ethnic Minority Elderly. Current Psychiatry Reports. Nhi-Na et all., 2019



STUDIED IN ELDERLY POPULATION

- Improves processing speed and cognitive function. Fast onset 2-4 weeks

Mechanism of Action:

- Increases release of serotonin, norepinephrine, dopamine, glutamate, acetylcholine, histamine. Reduces release of GABA

USE:

- Depression +anxiety, depression+ cognitive dulling, GAD, depression + sexual dysfunction, those who did not respond to other antidepressants

CAUTION:

- History of seizures
- Co-administration with Bupropion results in 2x increase in serum levels of Trintellix

Common SE ~9% :

- Nausea, Dizziness, Dry mouth

Dosing:

- 5 mg to 20 mg daily
- Elderly 5 – 10mg daily

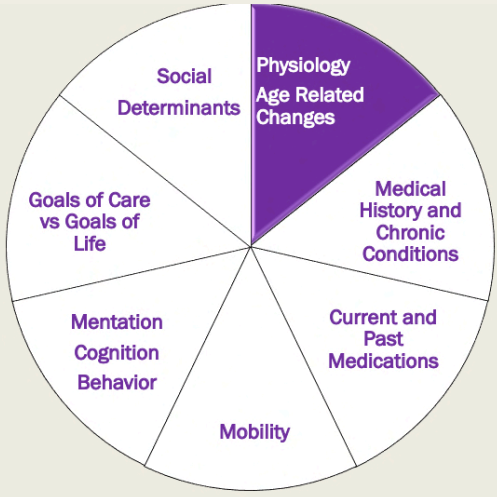
COST ~ $410 per month

With persistence and prior authorization can reduce to ~$58 for Medicare Part D

Managed Care Plans with Co-insurance ~ $179 per month.

Manufacturer sponsored financial assistance programs for patients are only available for commercial insurances

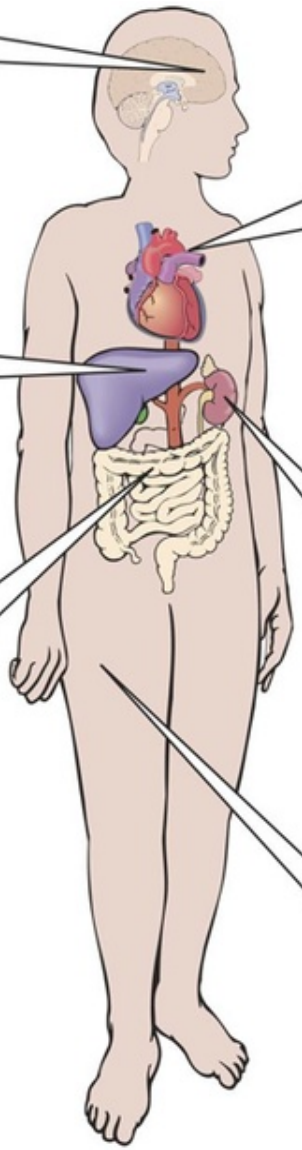
Consider Age Related Changes



Drug-receptor interaction
Brain receptors become more sensitive, making psychoactive drugs very potent.

Metabolism
Liver mass shrinks.
Hepatic blood flow and enzyme activity decline.
Metabolism drops to 1/2 to 2/3 the rate of young adults.
Enzymes lose ability to process some drugs, thus prolonging drug half-life.

Absorption
Gastric emptying rate and gastrointestinal motility slow.
Absorption capacity of cells and active transport mechanism decline.



Circulation
Vascular nerve control is less stable.
Antihypertensives, for example, may overshoot, dropping blood pressure too low.
Digoxin, for example, may slow the heart rate too much.

Excretion
In kidneys, renal blood flow, glomerular filtration rate, renal tubular secretion and reabsorption, and number of functional nephrons decline.
Blood flow and waste removal slow.
Age-related changes lengthen half-life for renally excreted drugs.
Oral antidiabetic drugs, among others, stay in the body longer.

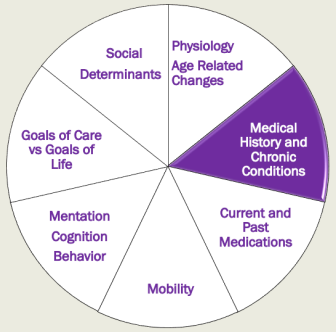
Distribution
Lean body mass falls.
Adipose stores increase.
Total body water declines, raising the concentration of water-soluble drugs, such as digoxin, which can cause heart dysfunction.
Plasma protein diminishes, reducing sites available for protein-bound drugs and raises blood levels of free drug.

Medical History: Hyponatremia

- Monitor serum Na concentrations at baseline and 1 to 2 weeks after initiation of therapy

PREVALENCE:

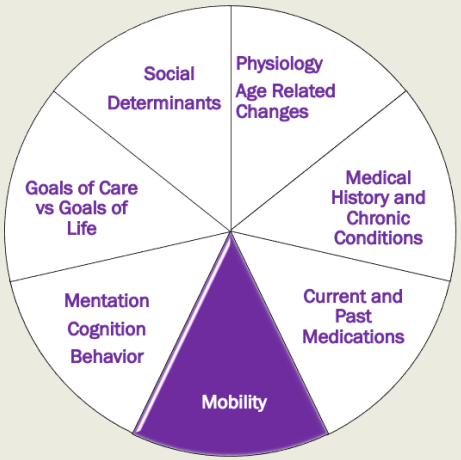
- Tricyclic antidepressants, 16% -33%
- SSRIs, up to 40%
  - Significantly increased risk with fluoxetine, citalopram, and escitalopram
  - Lower risk with paroxetine and sertraline
- SNRIs
  - 20–70% for venlafaxine [Effexor]
  - 11% for duloxetine [Cymbalta]
- **Relative safety of use for mirtazapine [Remeron] and bupropion [Wellbutrin] in patients who developed hyponatremia with SSRIs**
- Some reports with typical antipsychotics, less common with atypical



Hyponatremia and psychotropics. Geriatric mental Health. Sahoo et al., 2016
Bupropion induced hyponatremia: A review of literature. European Psychiatry. Arts et al., 2017

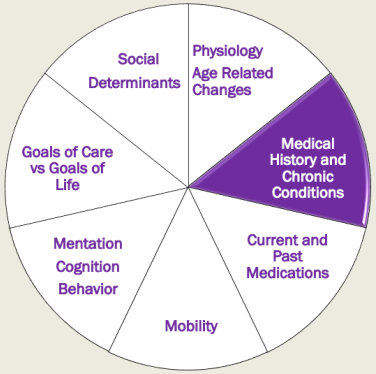
MOBILITY: Falls

- 20 to 30% of elderly experience at least one fall annually
- Falls account for 85% of seniors' injury-related hospitalizations and over 30% of subsequent admissions to long-term care
- **Highest Risk medications:**
  - Long acting benzodiazepines and sedative-hypnotics
  - MAOIs, SSRIs, TCAs
  - Anticonvulsants
  - Anxiolytics
  - Antipsychotics
  - Anti - arrhythmic, antihypertensives and digoxin
- Beta blockers are NOT associated with increased risk of falling



Relationship between the use of benzodiazepines and falls in older adults: A systematic review. Diaz-Gutierrez et al., 2017. Antidepressant Use and Recurrent Falls in Community-Dwelling Older Adults: Findings From the Health ABC Study. Ann Pharmacother., Markum., 2016. A Systematic Review and Meta-Analyses of the Association Between Anti-Hypertensive Classes and the Risk of Falls Among Older Adults. Drugs and Aging. Ang., 2018

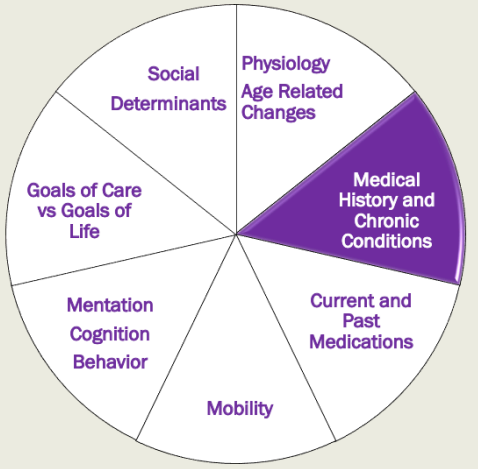
Chronic Conditions: Osteoporosis



- ~200 million people are affected by osteoporosis world-wide
- ~ 9 million fractures caused by osteoporosis annually
- ~ 20% of older males and 30% of older females will experience osteoporotic fractures
- In the USA, the number of hip fractures is estimated to triple by 2040
- One of the major factors governing the progression of secondary osteoporosis are long-term usage of:
  - Corticosteroid, anticancer
  - Anticonvulsants, Mood Stabilizers
    - Lithium may be protective for bone health; 20% reduction in fracture risk
    - Lamotrigine has the lowest negative effect on bone health
    - Valproate Acid (Depakote) has the strongest negative effect on bone health
      - *An update on the problem of osteoporosis in people with epilepsy taking antiepileptic drugs. Expert opinion on drug safety. Miziak et al., 2019*
  - Antidepressants
  - Antipsychotics
    - Aripiprazole [Abilify] and Quetiapine [Seroquel] has the lowest negative effect on bone health
    - All first-generation antipsychotics, second-generation- risperidone/paliperidone have strongest negative effect
      - *Relationship between antipsychotic medication, serum prolactin levels and osteoporosis/osteoporotic fractures in patients with schizophrenia: a critical literature review. Expert Opin Drug Saf. De Hert et al., 2016.*
  - Benzodiazepines

Chronic Conditions: PVD

- 1/3 of patients with PVD experience depression
- Depressive symptoms in PVD have been associated with:
  - Worse claudication
  - Decreased patency after peripheral revascularization
  - Increased incidence of major amputation
  - Adverse cardiac events
  - Mortality
- Possible pathophysiological mechanisms:
  - *Increased inflammation*
  - Dysregulate the metabolic system and coagulation pathway
- Increased risk of depression in PVD patients who are:
  - Female
  - African Americans
  - Have poor physical function
- Depression exerts a negative influence on walking ability and physical function independently of peripheral arterial disease

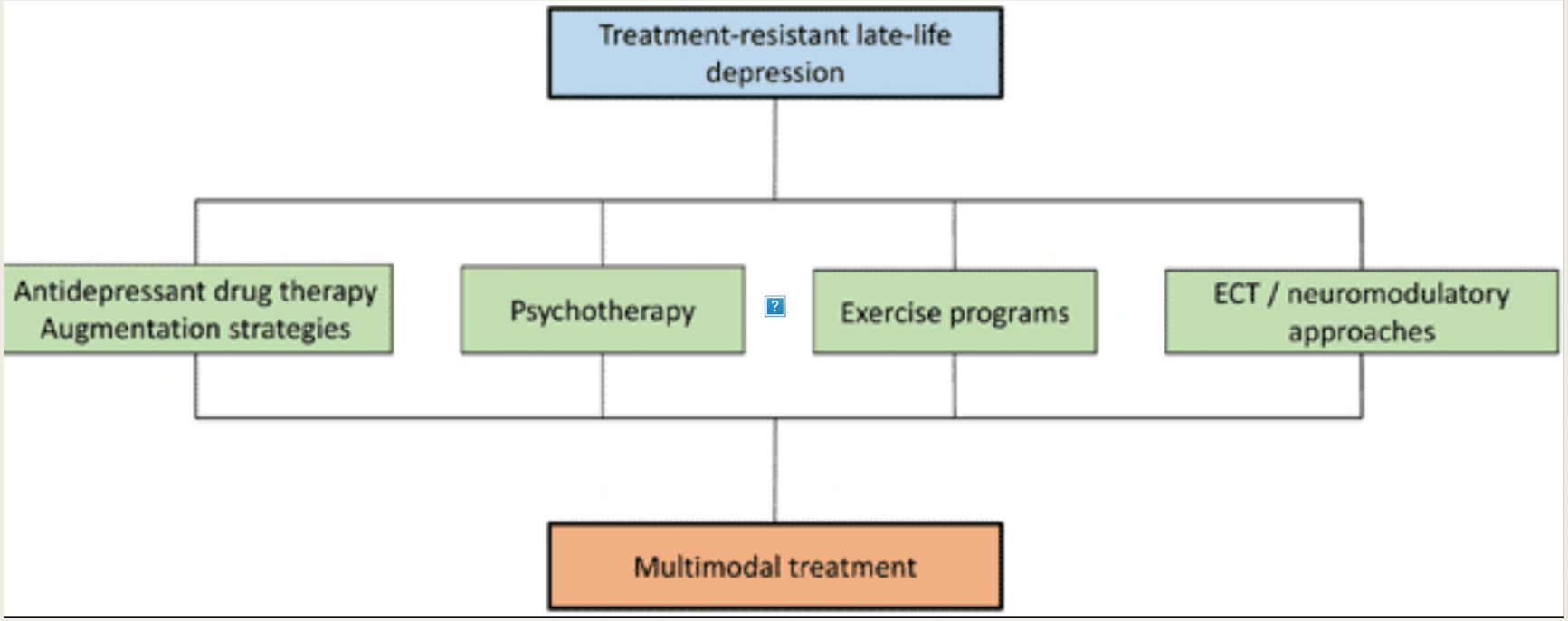


Depression and peripheral arterial disease: A call to action. Vascular News. Ramirez et al., 2019

Anxiety and depression in patients with peripheral arterial disease admitted to a tertiary hospital. J Vasc Bras. Aragao et al., 2019

Depression in patients with peripheral arterial disease: A systematic review. Eur J of Card Nurs. Brostov et al., 2017

BEST PRACTICE TRLLD



Treatment-resistant Late-life Depression: Challenges and Perspectives. Curr Neuropharmacol. Knochel et al., 2015

What initial affordable medication will you choose to treat depression and apathy and mitigate worsening of sexual dysfunction, weight gain and future risks of hyponatremia?

- Start an SSRI (e.g. fluoxetine [Prozac])
- Start an SNRI (e.g. venlafaxine [Effexor])
- Start an NDRI (e.g. bupropion [Wellbutrin]) GOOD CHOICE
- Start an NaSSA (e.g. mirtazapine [Remeron])
- Start a stimulant salt or Modafinil [Provigil]
- Start an antipsychotic (e.g. aripiprazole [Abilify]) GOOD CHOICE
- Start a combination of medications
- Refer to psychotherapy
- Initiate referral to physical therapy
- Consider ECT or TMS GOOD CHOICE

5 weeks follow-up

Patient's depression/apathy had partial response to bupropion [Wellbutrin], but he is still gaining weight, hearing voices, and has very low energy. What is an appropriate augmentation?

10 week follow-up

Partial, but incomplete response. Patient states "I can not live like this anymore." What is your next step?

ECT in Depression

- Response rates by age:
  - *< 59 : 54%*
  - *60 - 74 : 73%*
  - *>75 -- 67%*
- No differences in tolerance even though older patients had more baseline cognitive impairment and medical problems
- Predictors of good response:
  - Psychotic symptoms
  - Neuro-vegetative symptoms (eg. catatonia, disturbance in sleep and appetite)
- Predictors of poor response:
  - Physical illness during the index episode
  - Higher number of longer lifetime depressive episodes
- Response to ECT and TMS is comparable in depressed patients without psychotic symptoms
- Never a first line treatment
- **High risk in** increased intracranial pressure, recent myocardial infarction, recent cerebral hemorrhage or stroke, vascular aneurysm, retinal detachment and pheocromocytoma

Electroconvulsive therapy in the elderly. Geriatric Mental Health. Grover et al., 2017

ECT or TMS

ECT

- Efficacy – 70%-90% (APA, 2010)
- Memory Effects are more prominent
- Mostly covered by third-party payers -Insurance, Medicare, etc

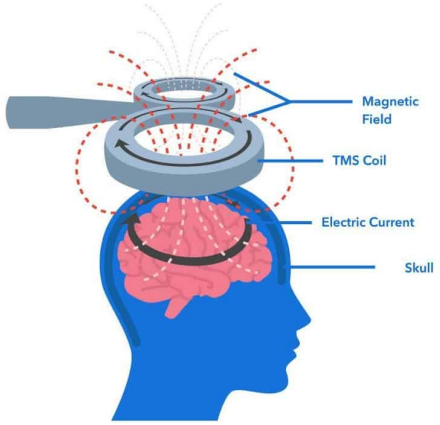
TMS

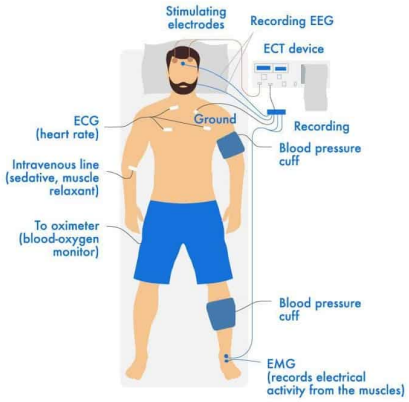
- Preliminary studies indicate that ECT is more effective than repetitive transcranial magnetic stimulation. (NICE-UK)
  - LCOH date: 40% Efficacy
- No significant memory impairment
- Limited third-party coverage

Lindner Center of HOPE

University of Cincinnati

TMS vs. ECT



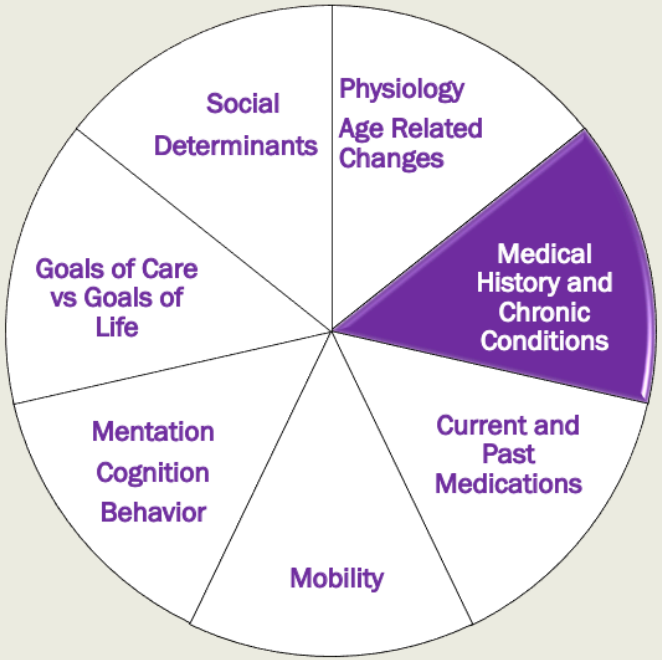


rTMS vs. ECT

	rTMS	ECT
Seizure Induced	No	Yes
Anesthesia Required	No	Yes
Current Reaches Deep Structures	No	Yes
Psychosocial Impact	Can drive from treatments and can work the same day	Can't drive from treatments or work the same day
Direction of Induced Current	Tangential	Radial
After-Effects	None. Pro-cognitive	Mild memory loss

MULTIMORBIDITY:

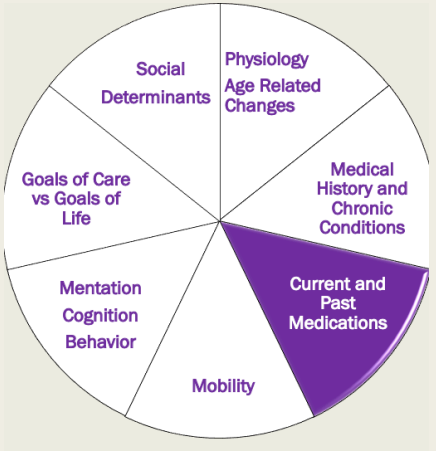
- 50% of older adults have at least two chronic conditions that require management
- **Most prevalent:**
  - *Hypertension*
  - *Arthritis*
  - *Cardiovascular disease*
  - *Diabetes*
  - *Depression*
- Multimorbidity is associated with:
  - *Poor health outcomes*
  - *Increased healthcare utilization*
  - *Disability, institutionalization and mortality*
- Somatic conditions + depression = most disabling



Associations between prevalent multimorbidity combinations and prospective disability and self-rated health among older adults in Europe. BMC Geriatrics. Sheridan eat al., 2019

Multimorbidity combinations and disability in Older adults. J Gerontol Ser A Biol Med Sci. Quiñones ., 2016.

Polypharmacy in Multiple Chronic Conditions



- Polypharmacy = Potentially Inappropriate Prescribing (PIP)
  - High prevalence in MCC
- 51% of older adults take 11+ prescription medications
  - Odds of PIP increase by 10% with each additional medication
- Medication related problems are more frequent in people with:
  - *Diabetes*
  - *Congestive heart failure*
  - *End-stage renal disease*
  - *Respiratory conditions*
  - *Hypertension*
  - Depression
- Polypharmacy Increases risk of:
  - Adverse drug reactions
  - Healthcare utilization
  - Morbidity
  - Mortality

Associations Between Chronic Disease, Polypharmacy, and Medication-Related Problems Among Medicare Beneficiaries. J Managed Care. Almadovar eta al., 2019

MEDICATIONS

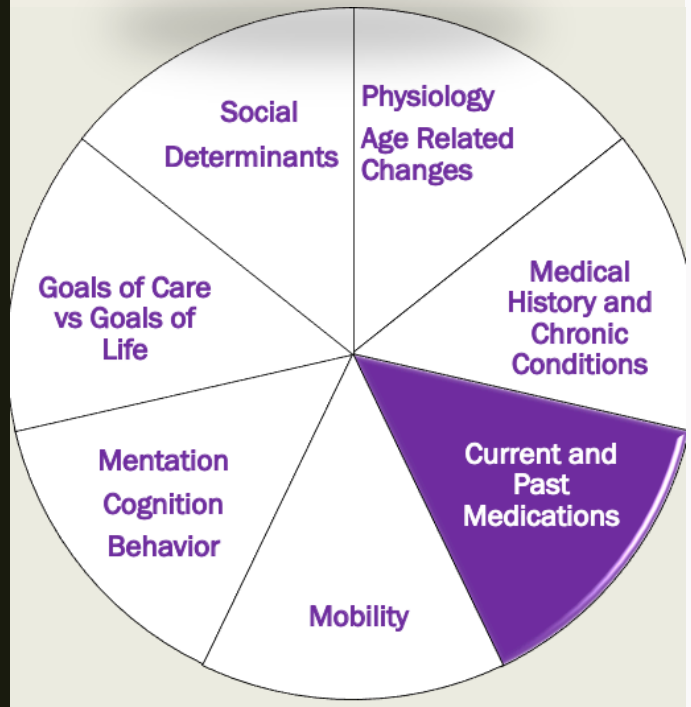
"In diseases of the mind…it is an art of no little importance to administer medicines properly;

But, it is an art of much greater importance and more difficult acquisition to know when to suspend or altogether omit them."

(Phillipe Pinel, physician 1806)

Best measures must account for:

- Drug-drug interactions
- Disease-disease interactions
- Disease-drug interactions



Monitor Closely

aspirin + cilostazol

aspirin, cilostazol. Either increases toxicity of the other by pharmacodynamic synergism. Use Caution/Monitor. The need for simultaneous use of low-dose aspirin and anticoagulant or antiplatelet agents are common for patients with cardiovascular disease; monitor closely.

bupropion + aripiprazole

bupropion will increase the level or effect of aripiprazole by affecting hepatic enzyme CYP2D6 metabolism. Use Caution/Monitor.

aripiprazole + metformin

aripiprazole, metformin. Other (see comment). Use Caution/Monitor. Comment: Atypical antipsychotics have been associated with hyperglycemia that may alter blood glucose control; monitor glucose levels closely.

bupropion + metformin

bupropion increases levels of metformin by Other (see comment). Use Caution/Monitor. Comment: Bupropion may inhibit OCT2 mediated renal excretion of metformin.

Minor

testosterone + metformin

testosterone increases effects of metformin by pharmacodynamic synergism. Minor/Significance Unknown.

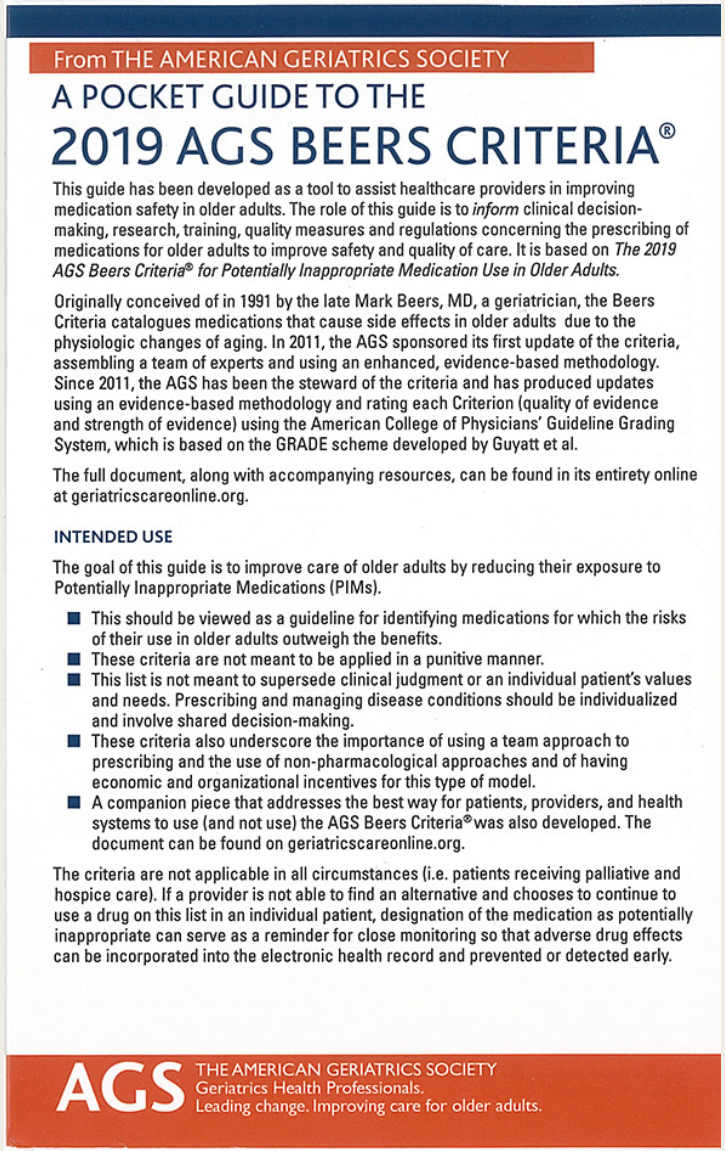
aspirin + alendronate

aspirin, alendronate. Either increases toxicity of the other by pharmacodynamic synergism. Minor/Significance Unknown. Increased risk of GI ulceration.

Reducing Potentially Inappropriate Prescribing (PIP)

The 2019 American Geriatrics Society Updated Beers Criteria® for Potentially Inappropriate Medication Use in Older Adults

- https://consultgeri.org/try-this/general-assessment/issue-16



From THE AMERICAN GERIATRICS SOCIETY

A POCKET GUIDE TO THE

2019 AGS BEERS CRITERIA®

This guide has been developed as a tool to assist healthcare providers in improving medication safety in older adults. The role of this guide is to *inform* clinical decision-making, research, training, quality measures and regulations concerning the prescribing of medications for older adults to improve safety and quality of care. It is based on *The 2019 AGS Beers Criteria® for Potentially Inappropriate Medication Use in Older Adults.*

Originally conceived of in 1991 by the late Mark Beers, MD, a geriatrician, the Beers Criteria catalogues medications that cause side effects in older adults due to the physiologic changes of aging. In 2011, the AGS sponsored its first update of the criteria, assembling a team of experts and using an enhanced, evidence-based methodology. Since 2011, the AGS has been the steward of the criteria and has produced updates using an evidence-based methodology and rating each Criterion (quality of evidence and strength of evidence) using the American College of Physicians' Guideline Grading System, which is based on the GRADE scheme developed by Guyatt et al.

The full document, along with accompanying resources, can be found in its entirety online at geriatricscareonline.org.

INTENDED USE

The goal of this guide is to improve care of older adults by reducing their exposure to Potentially Inappropriate Medications (PIMs).

- This should be viewed as a guideline for identifying medications for which the risks of their use in older adults outweigh the benefits.
- These criteria are not meant to be applied in a punitive manner.
- This list is not meant to supersede clinical judgment or an individual patient's values and needs. Prescribing and managing disease conditions should be individualized and involve shared decision-making.
- These criteria also underscore the importance of using a team approach to prescribing and the use of non-pharmacological approaches and of having economic and organizational incentives for this type of model.
- A companion piece that addresses the best way for patients, providers, and health systems to use (and not use) the AGS Beers Criteria®was also developed. The document can be found on geriatricscareonline.org.

The criteria are not applicable in all circumstances (i.e. patients receiving palliative and hospice care). If a provider is not able to find an alternative and chooses to continue to use a drug on this list in an individual patient, designation of the medication as potentially inappropriate can serve as a reminder for close monitoring so that adverse drug effects can be incorporated into the electronic health record and prevented or detected early.

AGS THE AMERICAN GERIATRICS SOCIETY
Geriatrics Health Professionals.
Leading change. Improving care for older adults.

STOPP START Toolkit Supporting Medication Review

https://www.herefordshireccg.nhs.uk/your-services/medicines-optimisation/prescribing-guidelines/deprescribing/748-stopp-start-herefordshire-october-2016/file

STOPP & START

STOPP

- Screening Tool of Older Person's Prescriptions
- Addresses potentially inappropriate medications
- 65 rules or criteria
- Each criteria given concise explanation
- Most criteria related to drug-drug or drug-disease interactions
- Sets maximum doses for digoxin (125 mcg) and aspirin (150 mg)
- Other criteria address: indication, place in therapy, duration of use,
- Defines renal failure as GFR 20-50 mL/min

START

- Screening Tool to Alert doctors to the Right Treatment
- Addresses potential errors of omission or underutilization
- 22 rules or criteria
- Lists medication therapy that should be utilized in patients with specific medical conditions

Gallagher et al. *Clin Pharm Ther* 2011;89:845-854
Gallagher et al. *Int J Clin Pharm Ther* 2008;45:72-83
Rynn et al. *Ann Pharmacother* 2009;43M157e1-3

BNF Chapter 4. Nervous System

STOP:

Tricyclic antidepressants (TCA) (particularly Dosulepin):

- with dementia *(risk of worsening cognitive impairment).*
- with glaucoma *(likely to exacerbate glaucoma).*
- with cardiac conductive abnormalities *(pro-arrhythmic effects).*
- with constipation or medication likely to exacerbate constipation, following review *(likely to worsen constipation).*
- with prostatism or prior history of urinary retention *(risk of urinary retention).*

Benzodiazepines or hypnotics:

- with acute or chronic respiratory failure i.e. pO_2 less than 8.0 kPa and/ or pCO_2 greater than 6.5 kPa (*risk of exacerbation of respiratory failure*).
- if fallen in past 3 months.
- for longer than 4 weeks (*no indication for longer treatment; risk of prolonged sedation, confusion, impaired balance, falls, road traffic accidents; all*

STOPP START Toolkit Supporting Medication Review

BNF Chapter 4. Nervous System

START:

Levodopa or dopamine agonist in idiopathic Parkinson's disease with definite functional impairment and resultant disability.

Antidepressant (non TCA) in the presence of moderate-severe depressive symptoms lasting at least three months (*higher risk of adverse drug reactions with TCAs than with SSRIs or SNRIs).*

SSRI (or SNRI if SSRI is contra-indicated) for persistent severe anxiety that interferes with independent functioning, or for social anxiety disorder where patient declines cognitive behavioural therapy.

Dopamine agonist (ropinirole or pramipexole or rotigotine) for moderate-severe Restless Legs Syndrome, once iron deficiency and severe renal failure have been excluded and in conjunction with lifestyle measures.

Nervous system prescribing resources.

NICE guidance:

- CG26 Post-traumatic stress disorder: management, March 2005
- CG42 Dementia: supporting people with dementia and their carers in health and social care, November 2006.
- CG90 Depression in adults: recognition and management, October 2009.
- CG103 Delirium: prevention, diagnosis and management, July 2010.
- CG113 Generalised anxiety disorder and panic disorder in adults:
- management, January 2011.
- CG137 Epilepsies: diagnosis and management, January 2012.
- CG140 Palliative care for adults: strong pain relief, May 2012.
- CG159 Social anxiety disorder: recognition, assessment and treatment, May 2013

Deprescribing

- The process of withdrawal of an inappropriate medication supervised by a clinician.
- Guided by four Principles of biomedical ethics:
  - *Beneficence*
  - *Non-maleficence*
  - *Autonomy*
  - *Justice*
- People are rarely updated on the **altered risks and benefits** of their long-term medications **as they age**

Person-Centered Care Including Deprescribing for Older People Smith et all, 2019

Deprescribing Barriers

- Respecting the autonomy of older adults is complex:
  - they may not wish to be active in the decision-making process
  - they may have reduced cognitive function
  - family members may have to step in as surrogate decision-makers
- Iterative discussions of risks and benefits of long-term medications do not routinely take place
  - **Informed consent** is intended as **a process** of information giving and reflection, where **consent can be withdrawn at any time**
- Clinical guidelines are usually designed for single conditions
  - Evidence base for these is taken from clinical trials using younger people
  - People with multimorbidity and polypharmacy are routinely excluded
  - Patients with multimorbidity and severe frailty may obtain limited benefit from medicines treating a single condition

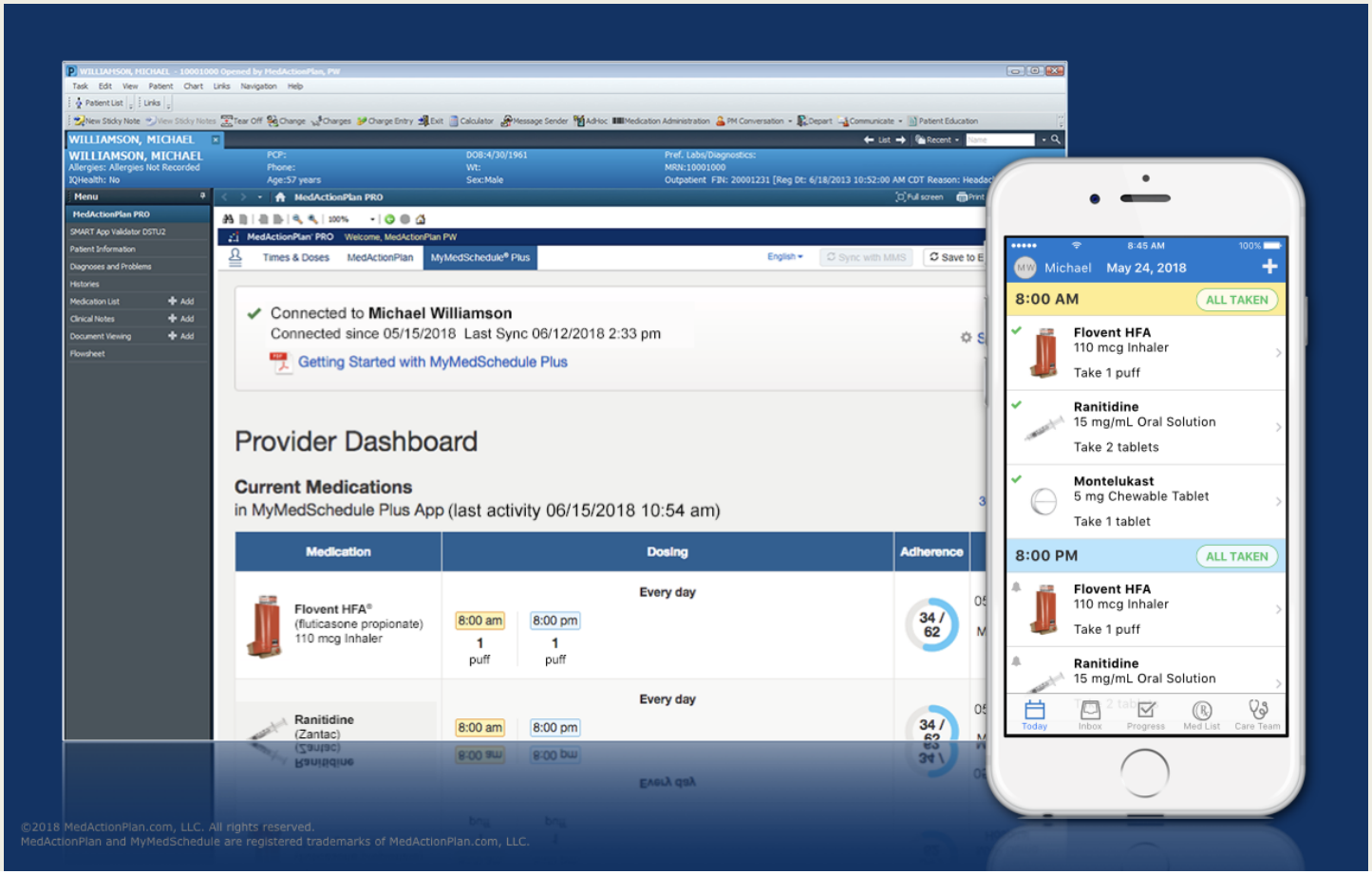
Person-Centered Care Including Deprescribing for Older People Smith et all, 2019

Foundations of Geriatric Drug Management:

- Medications reconciliation, including herbs and nonprescription drugs at each visit
- Avoid medications if benefit is marginal or if non-pharmacologic alternatives exist
- Consider the cost
- Start low, go slow, but get there!
  - *Initiate at half the normal adult dose*
  - ***Simplify the regimen***
  - *Evaluate for response frequently*
  - *Make dose changes only after steady-state achieved*
  - *Increase dose until benefit or toxicity*
  - *Reevaluate and taper as necessary*
  - ***Avoid under-treatment***
- Write instructions out clearly
- Assess for cognitive impairment frequently, status may change

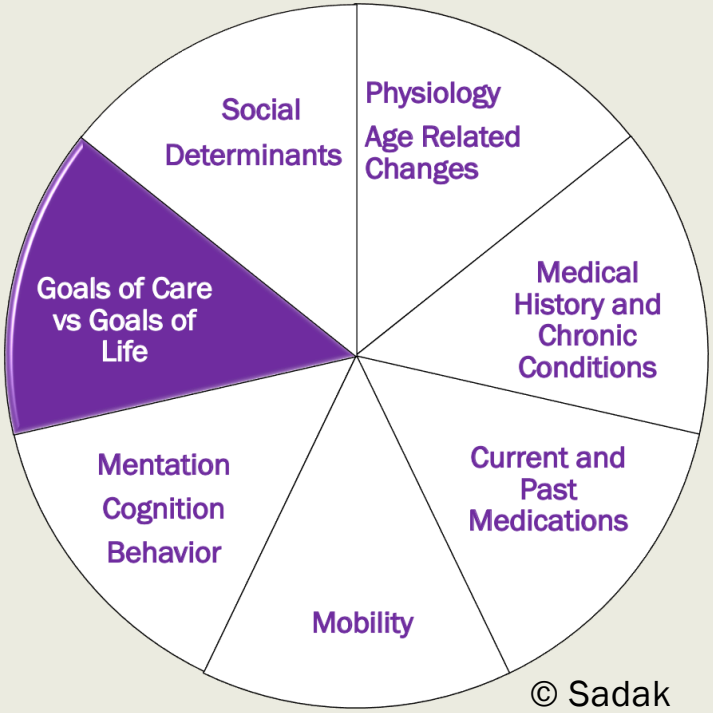
Encourage the use of Medi-Sets

Encourage the use of free apps: Eg. MedActionPlan



Summary

Comprehensive Model for Guiding Prescribing Decisions in Geriatric Psychiatry



Best Practices and Deprescribing

RESOURCES

- FREE Comprehensive Geriatric Assessment https://www.cgakit.com/cga---more
  - *Geriatric Physical Exam*
  - *Geriatric Prescribing Guidelines and Medications Review*
  - *Geriatric Syndromes*
    - Frailty, Falls, Incontinence, Pressure Ulcers, Sleep Disorders
  - *Proactive Care*
    - Personalized Care Planning
    - Nutrition
    - Exercises for older adults
  - *Thorny Issues*
    - Elder abuse assessment, Tough Conversations, Alcohol Assessment, Hoarding in late life, Driving
- STOPP/START
  - *https://www.kssahsn.net/what-we-do/our-news/events/Past%20events%202017/2016%20Stopp%20Start%20Cumbria.pdf*
- Psychiatric Medications Dosing for Elderly
  - Appropriate Use of Psychotropic Drugs in Nursing Homes. Am Fam Phys. Gurvich, 2000.
- Changes in Sexual Functioning Questionnaire Short Form (CSFQ-14)
  - https://www.dbsalliance.org/wp-content/uploads/2019/02/Restoring_Intimacy_CSFQ_Handout.pdf
- Monitor effectiveness using Epworth Sleepiness Scale
  - *https://www.edsandosa.com/tools-and-resources/screening/?utm_medium=cpc&utm_source=google&utm_campaign=tests&utm_content=epworthsleepinessscale&gclsrc=aw.ds&&gclid=EAIaIQobChMI2Mzerc2V5QIVXR-tBh3lXQu3EAAYAiAAEgK82fD_BwE*