Psych Congress MasterClass

Antidepressants for Older Adults with MDD: Integrating Clinical and Real-World Evidence with Patient-Specific Considerations to Optimize Outcomes

Supported by an independent educational grant from Takeda Pharmaceuticals, U.S.A

Faculty

Greg Mattingly, MD

Associate Clinical Professor
Washington University in St. Louis
President, Midwest Research Group
Co-Chair, Psych Congress
President, American Professional Society for ADHD and Related Disorders

Kevin N. Williams, MS, MPAS, PA-C

CEO and Lead Clinician
OnPoint Behavioral Health

Jennifer Brashear, MA pending LPC-A

Patient Advocate

Faculty Disclosures

Greg Mattingly, MD

Consultant – AbbVie, Acadia, Akilli, Alkermes, Angelini, Axsome, Aytu, Biogen, BMS, Boehringer Ingelheim, Cerevel, Corium, Eisai, Intracellular, Ironshore, Johnson & Johnson, Liva Nova, Lumos Labs, Lundbeck, Neurocrine, Noven, Otsuka, Redax, Relmada, Revibe, Roche, Sage, Sirona, Sky Therapeutics, Sunovion, Supernus, Takeda, Teva, and Tris Pharma; Research – AbbVie, Acadia, Alkermes, Akilli, Alto Therapeutics, Avanir, Axsome, BMS, Boehringer Ingelheim, Cingulate, Click Therapeutics, Corium, Emalex, Idorsia, Intracellular, Johnson & Johnson, Karuna, Lumos Labs, Medgenics, Neurocrine, NLS Pharma, Redax, Relmada, Roche, Sage, Sirtsei, Sumitomo, Sunovion, Supernus, Takeda, and Teva; Speakers Bureau – AbbVie, Alkermes, Angelini, Axsome, BMS, Corium, Intracellular, Ironshore, Johnson & Johnson, Lundbeck, Neurocrine, Noven, Otsuka, Sunovion, Supernus, Takeda, and Tris Pharma

Kevin N. Williams, MS, MPAS, PA-C

Advisory Board—Biogen/Sage, Myriad, Neurocrine, Supernus Pharmaceuticals, Teva Pharmaceuticals; Speakers Bureau—Abbvie, Alkermes, Myriad, Neurocrine, Teva Pharmaceuticals

Jennifer Brashear, pending LPC-A

has disclosed no relevant financial relationship with any ineligible company (commercial interest)

Disclosure

- The faculty have been informed of their responsibility to disclose to the audience if they will be discussing off-label or investigational use(s) of drugs, products, and/or devices (any use not approved by the US Food and Drug Administration)

- Applicable CME staff have no relationships to disclose relating to the subject matter of this activity

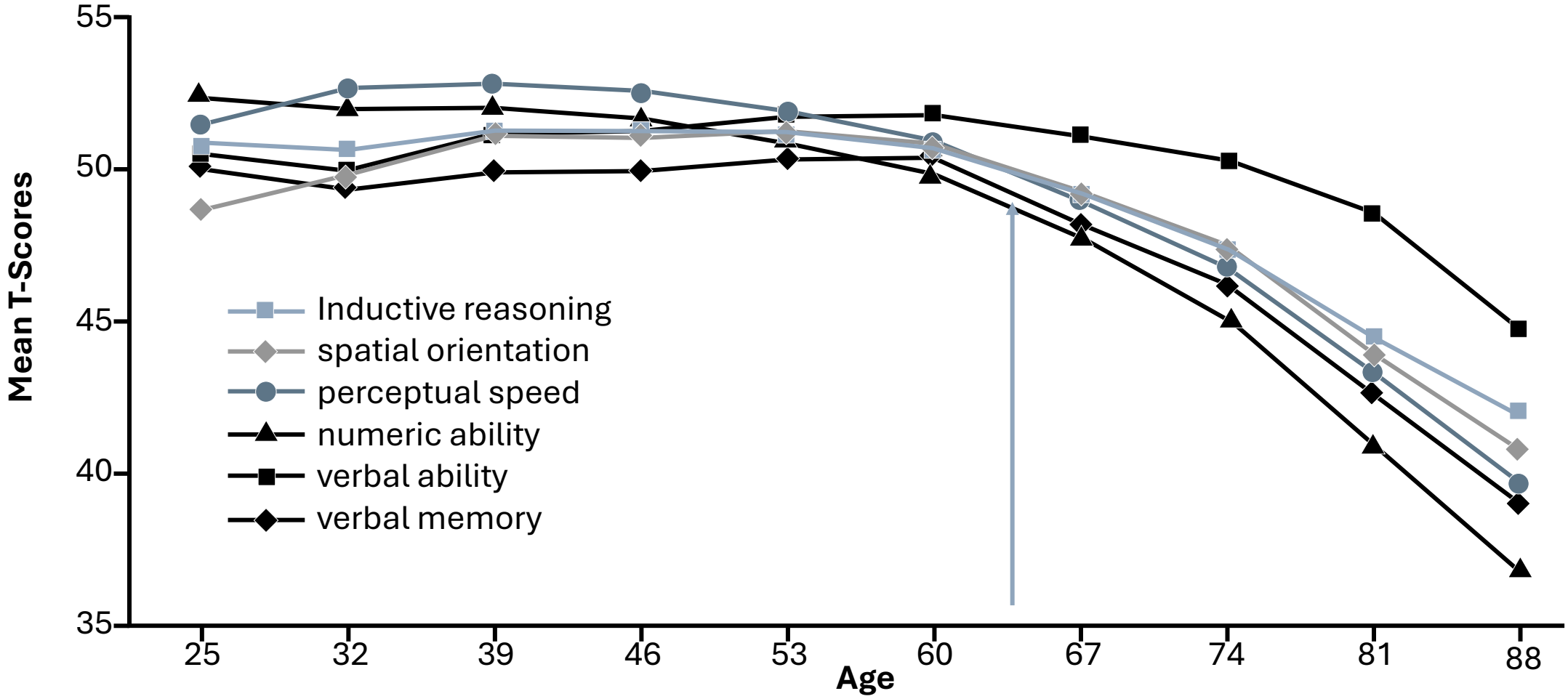
- This activity has been independently reviewed for balance

Learning Objectives

1. Describe factors associated with the under recognition of MDD among older adults and the importance of managing the disorder in these patients
2. Assess the ongoing challenges of managing MDD in older adults, including age-related biological changes and complex comorbidities
3. Evaluate the latest clinical and real-world evidence associated with conventional antidepressants and newer multimodal agents for older patients with MDD
4. Implement patient-centered treatment planning strategies for older adults with MDD, including shared decision-making with patients and caregivers

MDD = major depressive disorder.

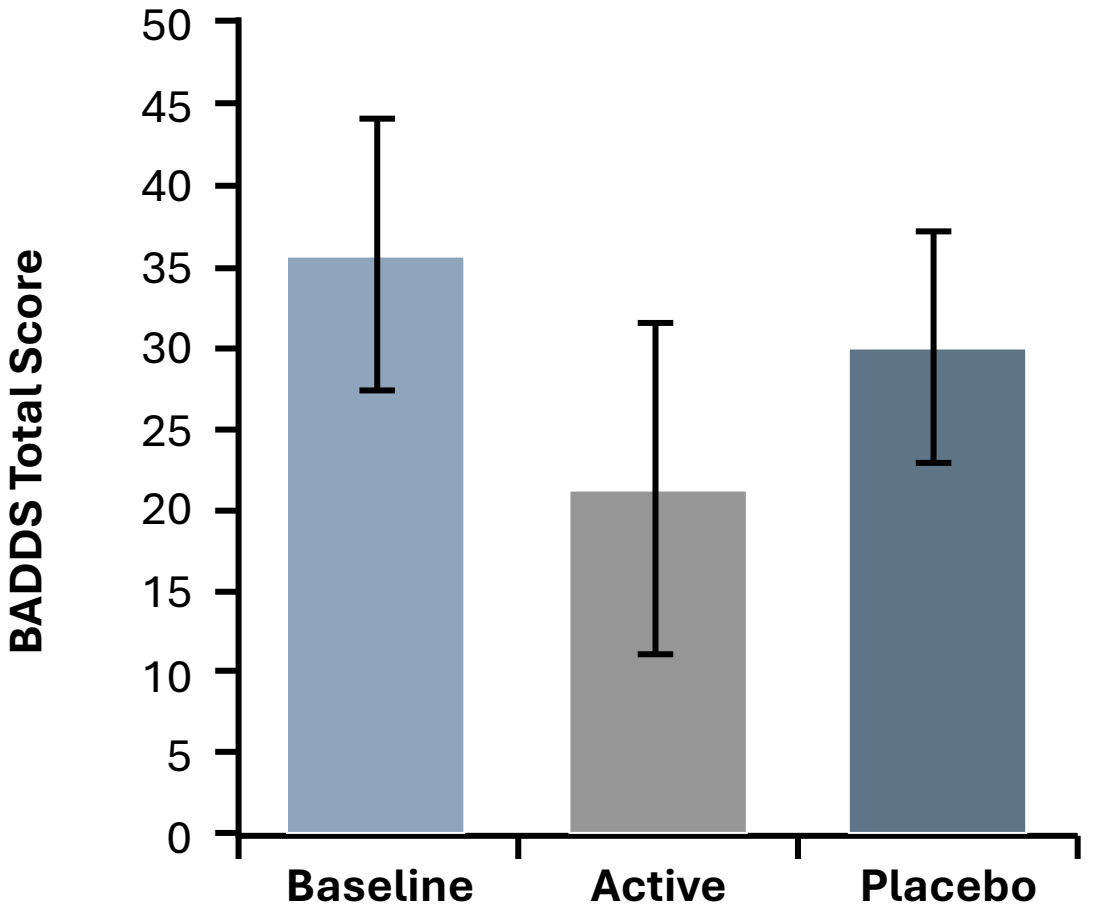
How About Memory and Aging?



Schaie et al. *Neuropsychol Dev Cogn B Aging Neuropsychol Cogn*. 2004;11:304.

Other Groups With Executive Function Deficits?

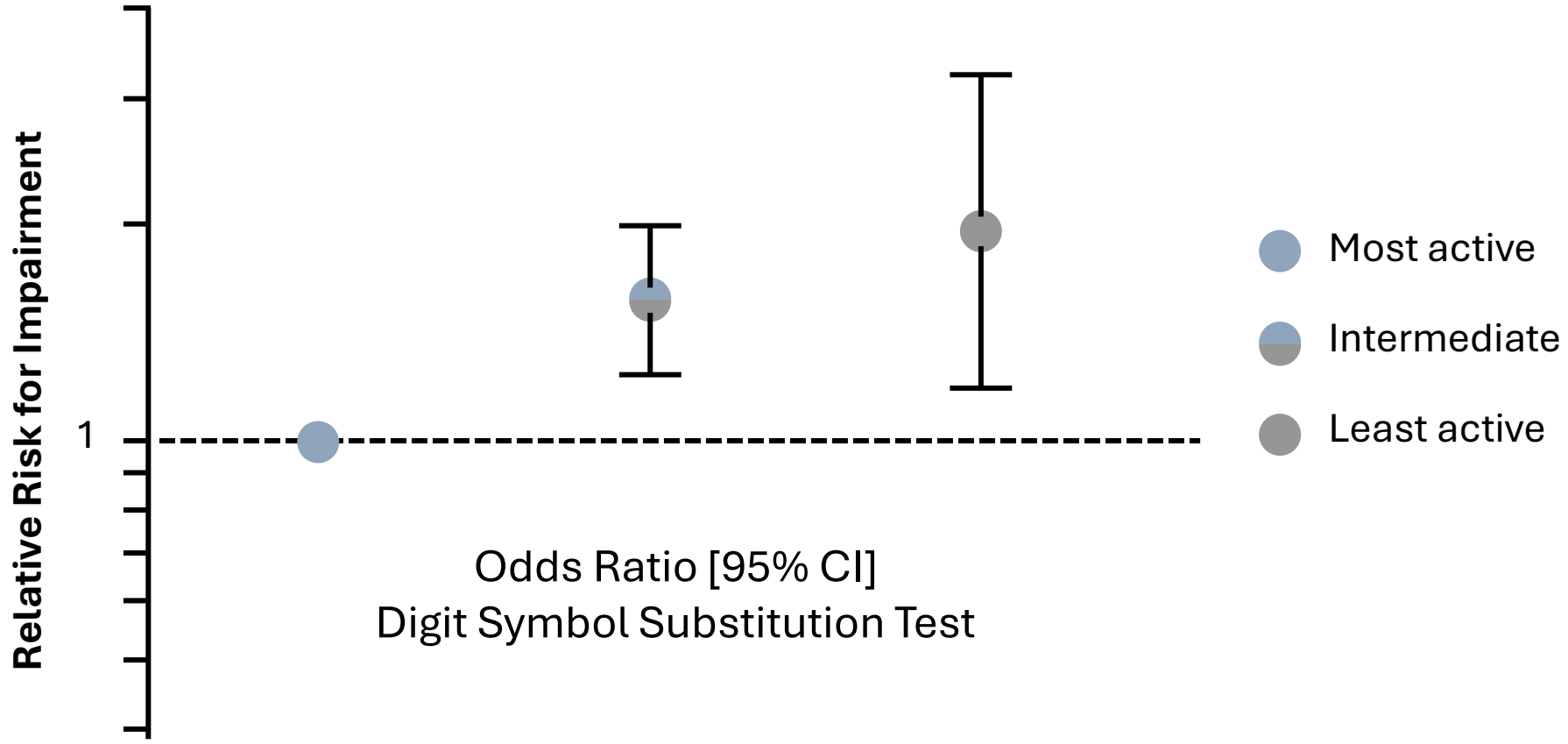
New onset executive function difficulties at menopause: a possible role for lisdexamfetamine



Epperson CN, et al. *Psychopharmacology*. 2015;232:3091.

Risk of Cognitive Impairment

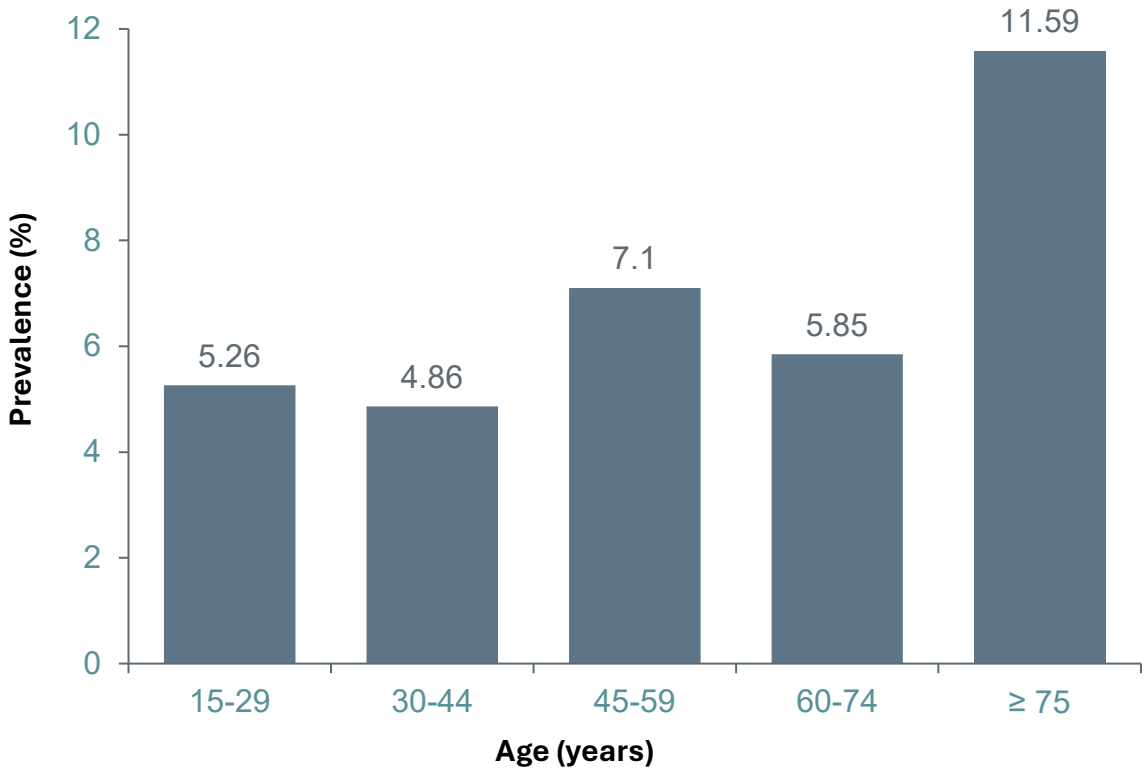
Impact of Television and Exercise After 25 Years



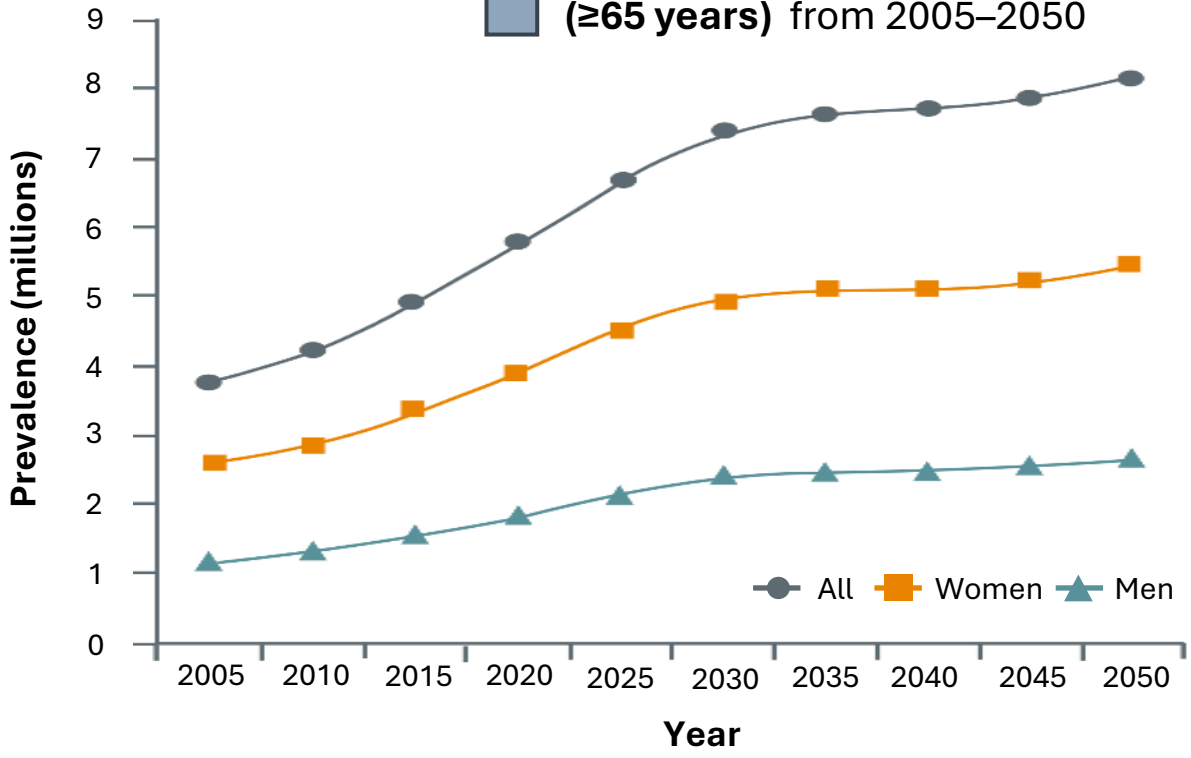
Hoang TD, et al. *JAMA Psychiatry*. 2016;73:73.

The Prevalence of MDD Increases with Advancing Age

The prevalence of **MDD was found to be highest among patients 75 years of age or older***



117% projected **increase of MDD in the older population (≥65 years)** from 2005–2050



BRFSS = Behavioural Risk Factor Surveillance Survey.

Arias-de la Torre J, et al. *Lancet Public Health*. 2021;6(10):e729-e738. Heo M, et al. *Int J Geriatr Psychiatry*. 2008;23:1266–1270.

Adding the Caregiver Perspective

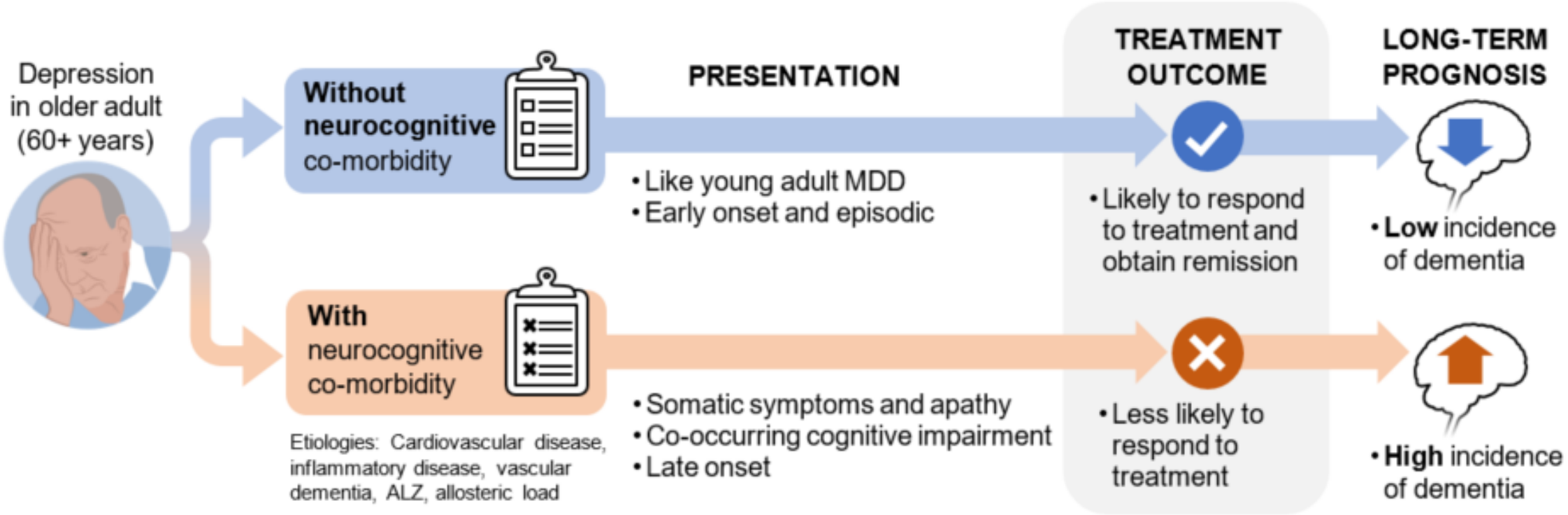
Jennifer Brashear

Psych Care Has Become More Complicated

- Many treatments are available
  - A lot of these treatments are complex
  - Choosing one is complex
- Concurrent medications need to be dealt with
  - Patients are taking a lot of medications
  - Self-medicating with EtOH, substances, OTC meds, and supplements

Srifuengfung M, et al. *Ther Adv Psychopharmacol*. 2023;13:1-14.

Aging and Two Types of Depression



Subramanian S, et al. *Psychiatr Clin North Am*. 2023;46(2);371-389.

Untreated Hearing Loss and Dementia Risk

- 2953 patients from the Framingham Study
- Average age 68.9 years
- 583 (20%) developed dementia
- Of these 245 (42%) developed hearing loss (HL) before age 70

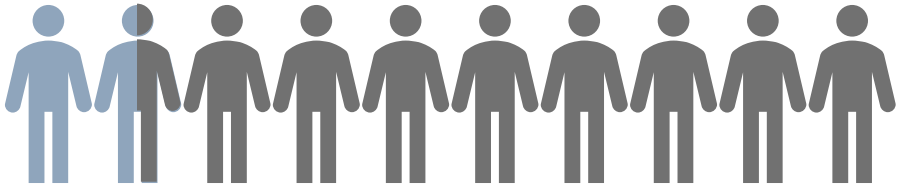
Participants with HL prescribed hearing aids had a 61% lower risk for incident all-cause dementia!
(Compared with participants with HL without hearing aids)

Francis L, et al. *JAMA Neurol*. 2025 Aug 18:e252713.

MDD is Commonly Comorbid with Other Neurological Conditions Prevalent in the Elderly Population

In a meta-analysis,

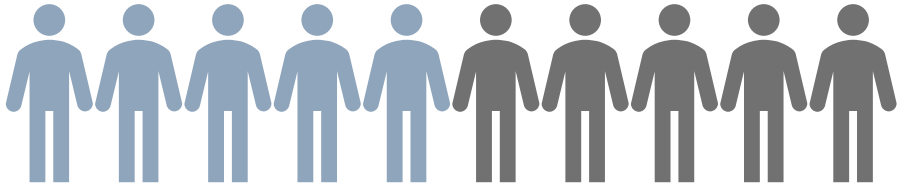
15%



of patients with **Alzheimer's disease** had MDD

MDD is present in

40–50%



of patients with **Parkinson's disease**

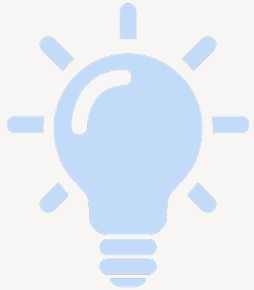
Depression may be **underdiagnosed** in neurological conditions due to **overlapping symptoms**

Asmer MS, et al. *J Clin Psychiatry*. 2018;79(5);17r11772. American Psychiatric Association. Practice Guideline for the Treatment of Patients With Major Depressive Disorder. 3rd ed. Arlington, VA; 2010. Conroy S, et al. *Focus (Am Psychiatr Publ)*. 2020;18:150–161. Rickards H. *J Neurol Neurosurg Psychiatry*. 2005;76(Suppl 1):i48–i52. Agrawal N, Rickards H. *J Neurol Neurosurg Psychiatry*. 2011;82(8):828–829.

Adding the Caregiver Perspective

Jennifer Brashear

Key Learning Points



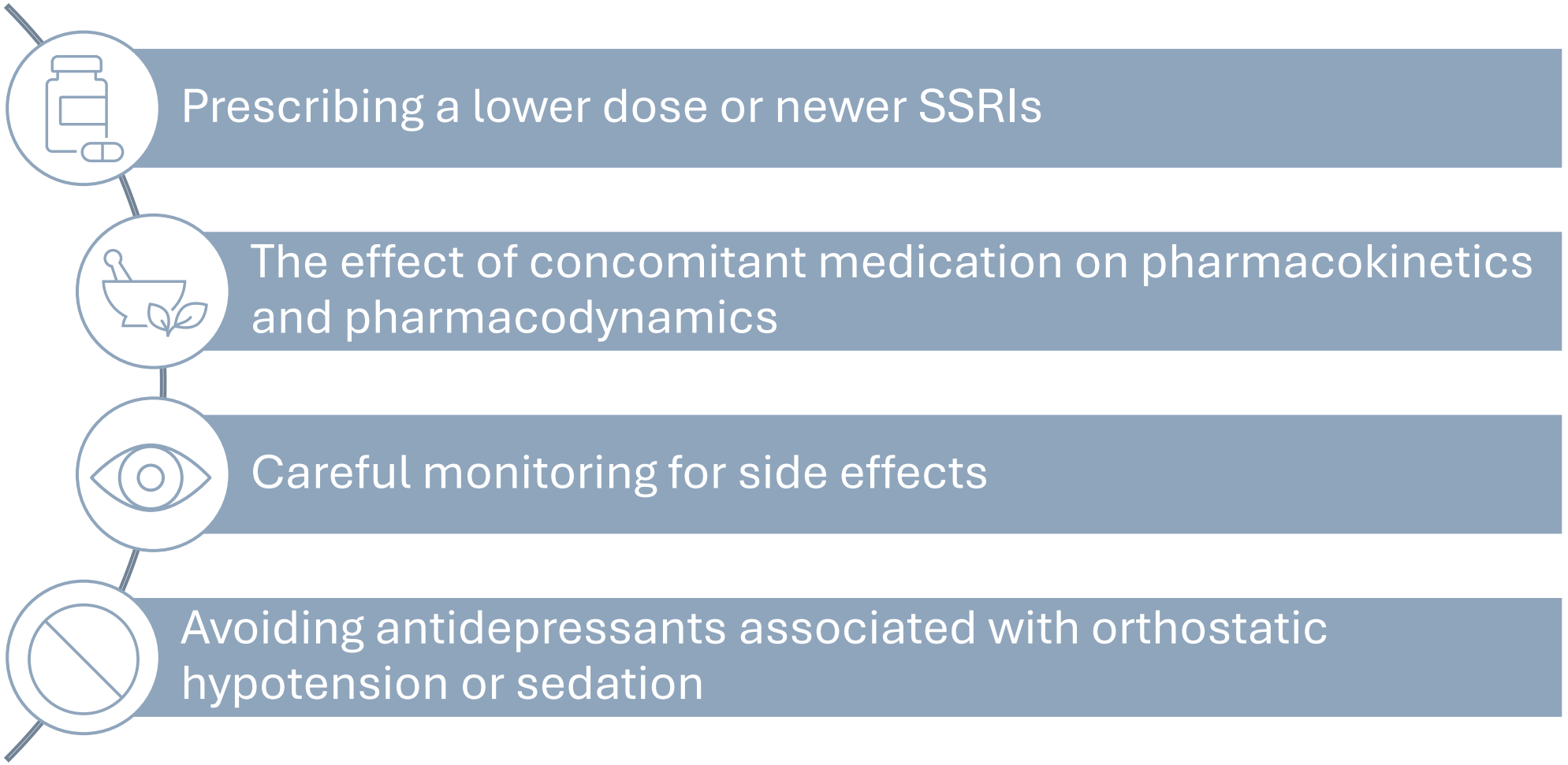
- The prevalence of major depressive disorder (MDD) **increases substantially with advancing age**, particularly in individuals ≥75 years.
- **Cognitive impairment and executive dysfunction** often emerge in older adults, complicating recognition and management of MDD.
- **MDD frequently coexists with neurological conditions** such as Alzheimer's disease and Parkinson's disease, making accurate diagnosis difficult due to overlapping symptoms.
- **Inclusion of caregiver perspectives is essential**, as they provide critical insights into symptom monitoring, treatment complexity, and patient functioning

Why Did You Choose That Treatment

References

Treatment Considerations for MDD in the Elderly Population

WFSBP Guidelines



SSRI = selective serotonin reuptake inhibitor; WFSBP = World Federation of Societies of Biological Psychiatry.

Dodd S, et al. *World J Biol Psychiatry*. 2017;19(5):330–348.

Treatment Choices for Depression

- Numerous SSRIs (eg, fluoxetine)
- Numerous SNRIs
- Mirtazapine
- Bupropion (IR, SR, XL)
- Vortioxetine
- Vilazodone
- MAOIs (pills, patch)
- TCAs
- Neuromodulation: rTMS, ECT, VNS
- Ketamine, esketamine, bupropion/dextromethorphan, psychedelics

AND AUGMENTATION

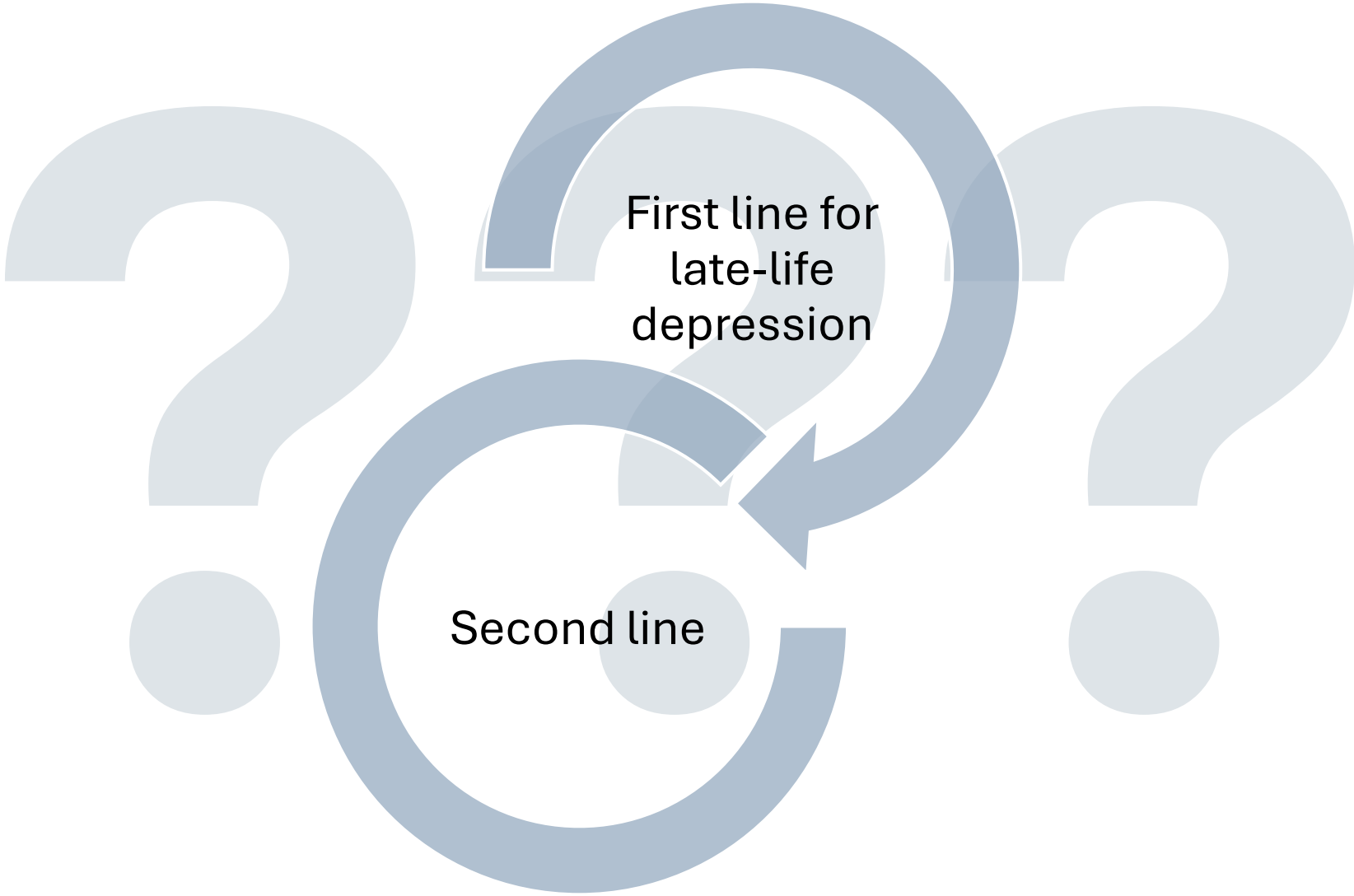
- Second antidepressant
- Antipsychotic
- Lithium
- (Es)ketamine
- Liothyronine
- Lamotrigine

And psychotherapy!

SNRIs = serotonin-norepinephrine reuptake inhibitors; MAOIs = monoamine oxidase inhibitors; TCAs = tricyclic antidepressants; rTMS = repetitive transcranial magnetic stimulation; ECT = electroconvulsive therapy; VNS = vagus nerve stimulation.

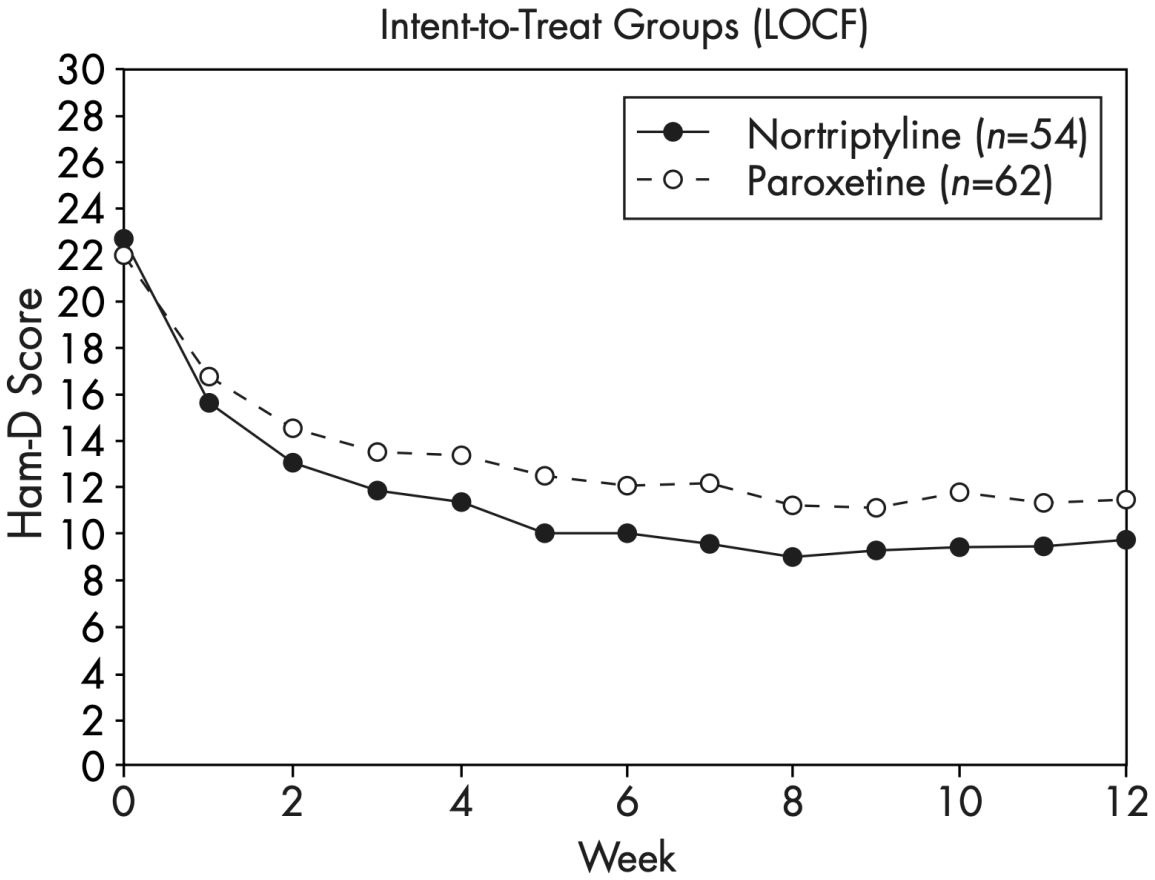
In the Face of This Complexity:

Care Algorithms Are Needed to Maximize Benefits and Minimize Risks

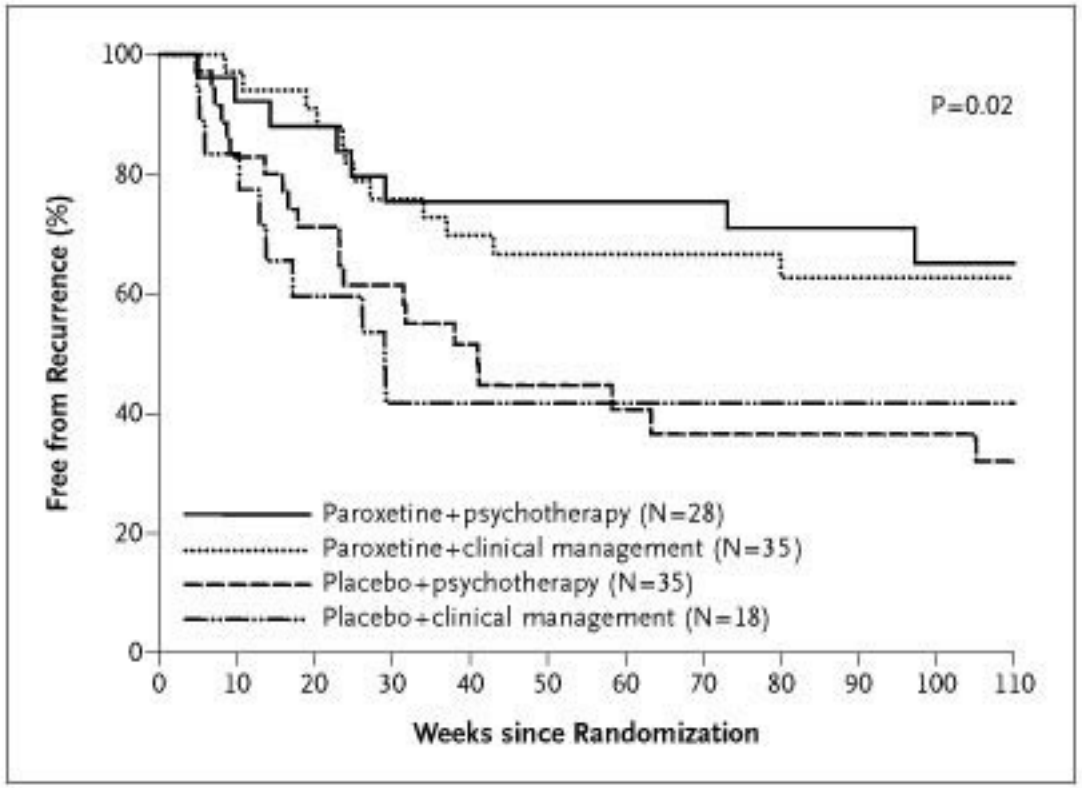


The Road to Evidence-Based Care in Late Life Depression

TCA vs SSRI



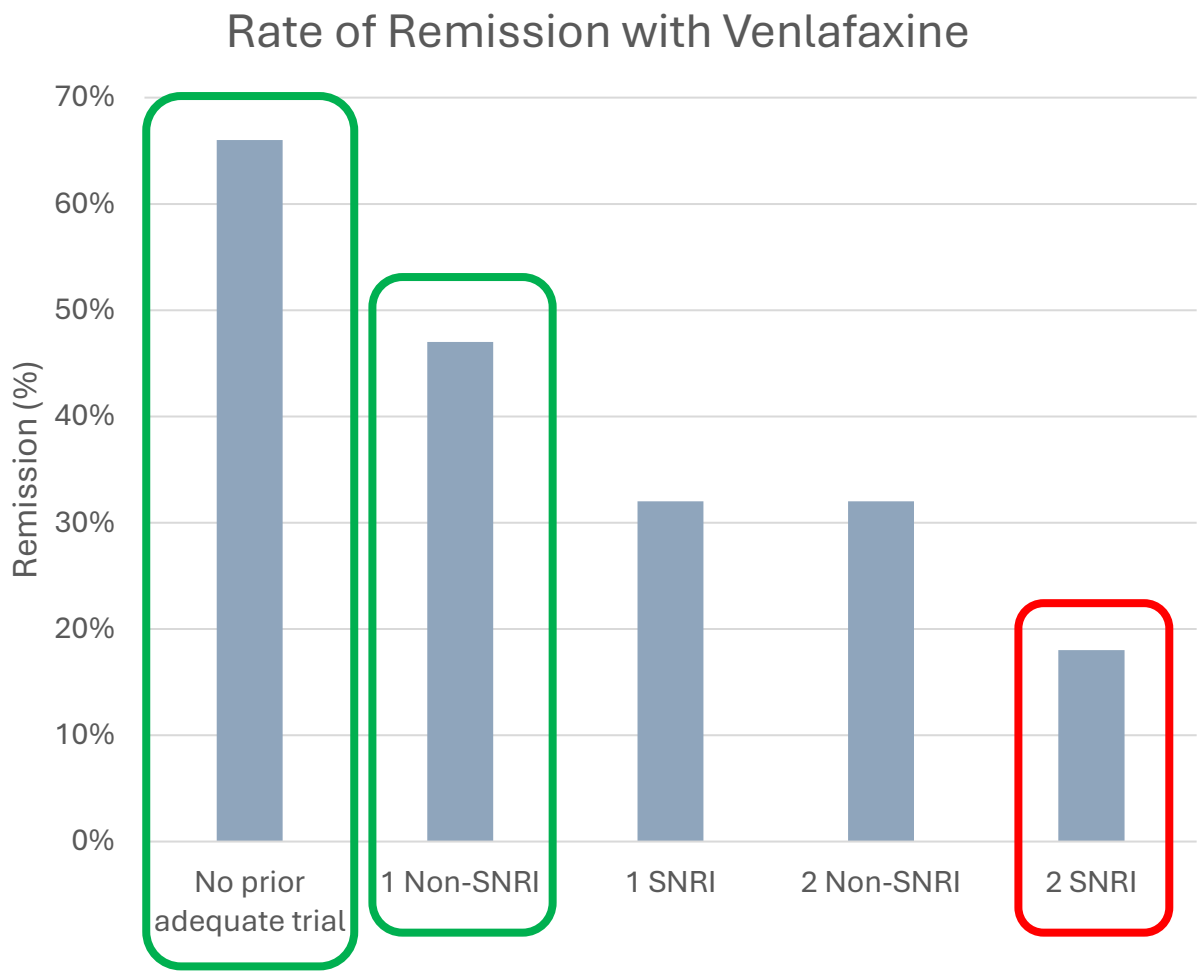
Maintenance of SSRI prevents depression from recurring



Mulsant B, et al. *Am J Geriatr Psychiatry*. 2001;9(4):406-414. Reynolds C, et al. *N Engl J Med*. 2006;354(11):1130-1138.

SNRIs: Remission Rate is High as First or Second Line, Low After That

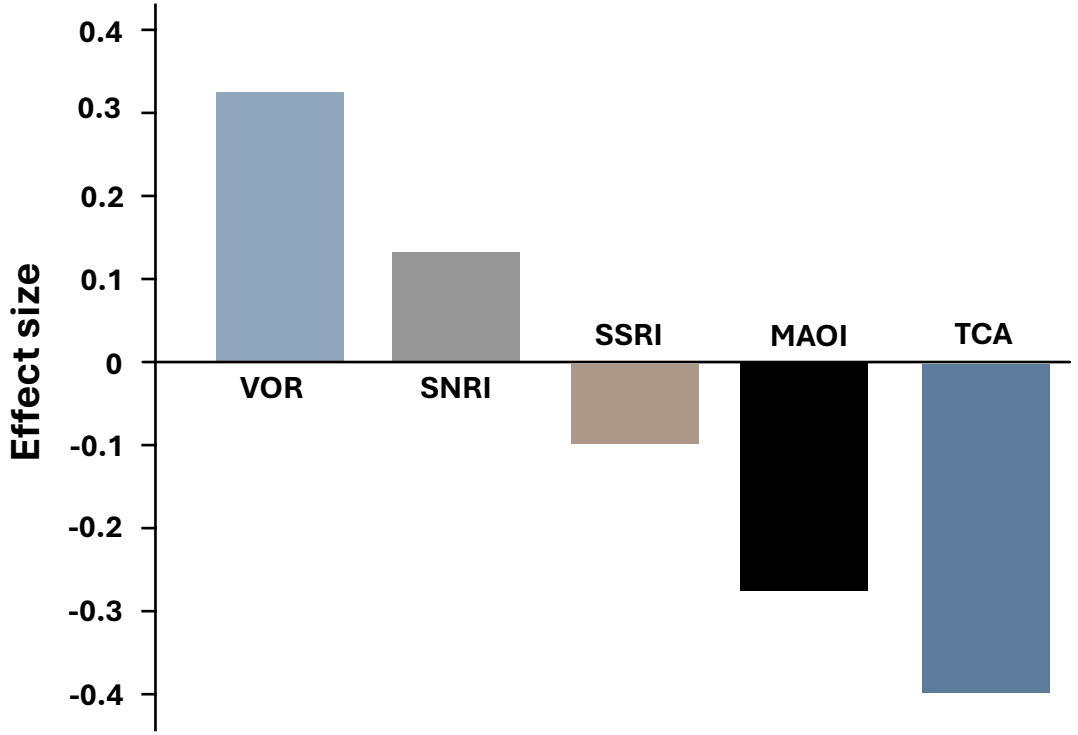
- 500 older adults with depression
- Venlafaxine extended release for 12 weeks
- Higher doses of venlafaxine were more likely to be required to achieve remission in patients with prior adequate trials



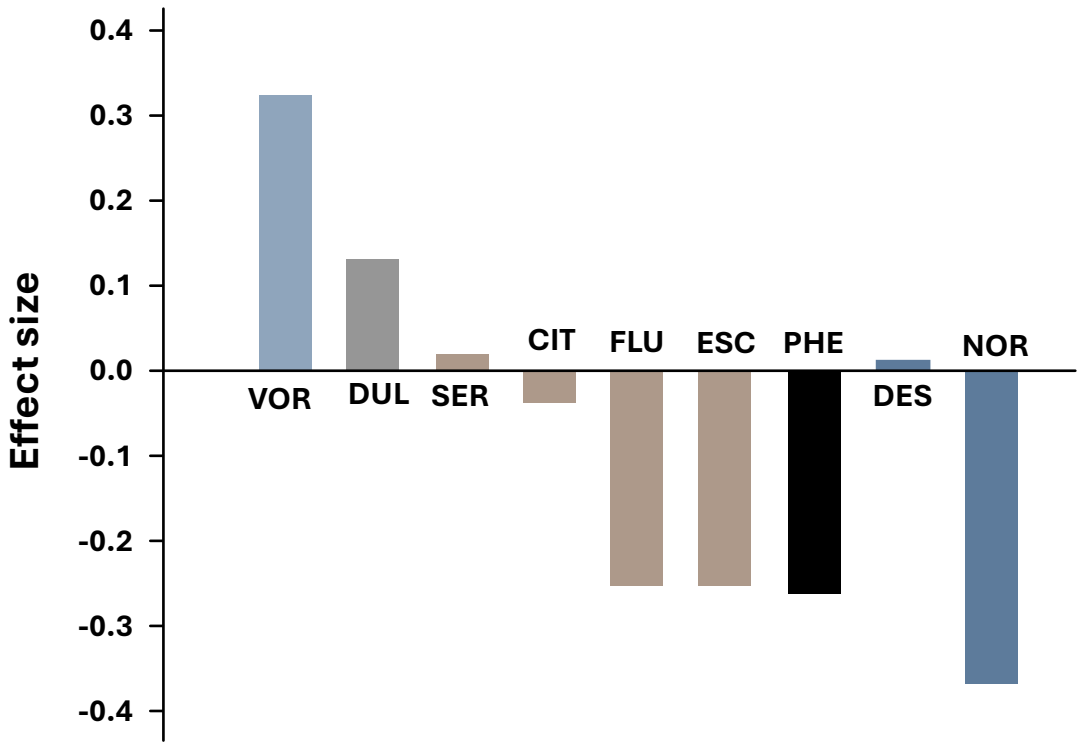
Buchalter E, et al. *J Clin Psychiatry*. 2019;80(6).

Comparing Effects of Antidepressants on Cognition Improvement in Processing Speed on DSST

Standardized effect size relative to placebo by antidepressant therapeutic classes



Standardized effect size relative to placebo by individual antidepressants

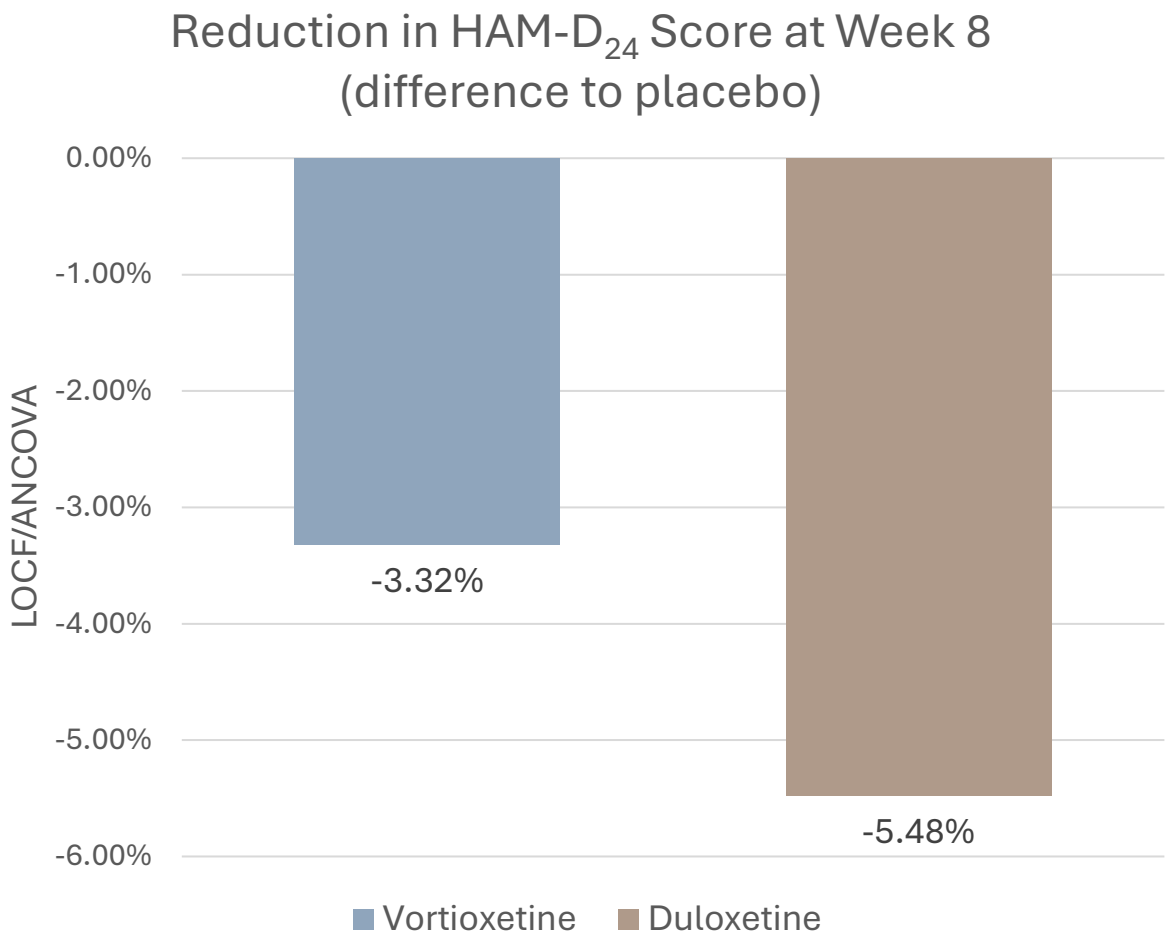


DSST = Digit Symbol Substitution Test.

Mattingly GW et al. *Postgraduate Medicine*. 2016;8:665. Baune BT, et al. *Int J Neuropsychopharmacol*. 2018;21:97. Mattingly GW et al. Front Psychiatry. 2022;13:824-831.

Vortioxetine (5 mg) Improved Cognitive Performance in Older Patients with Recurrent MDD

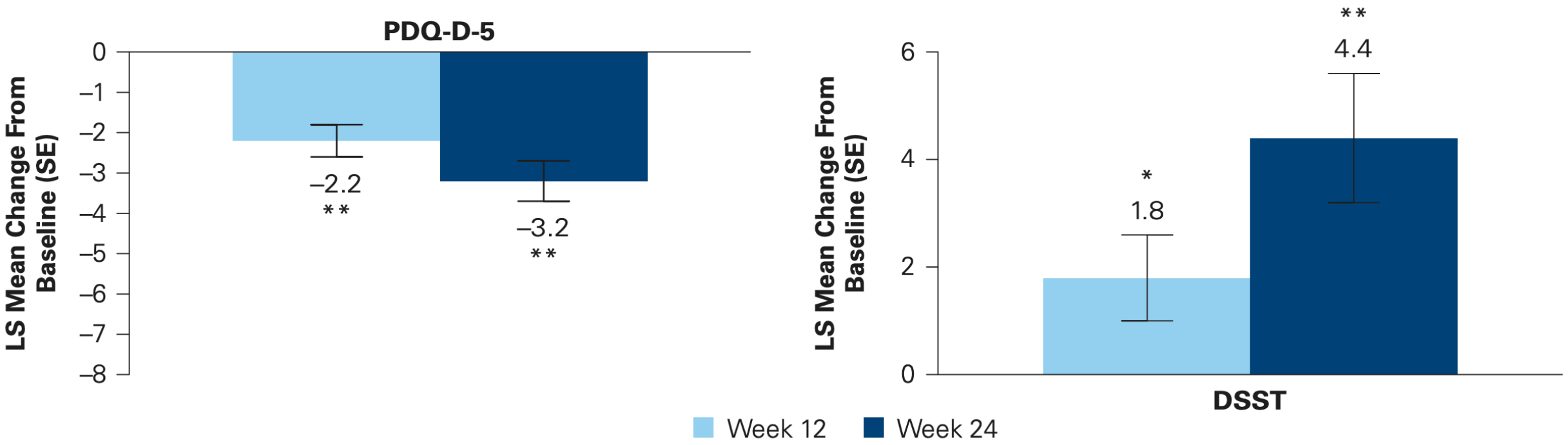
- 452 patients with a mean age of 70.6 years
- 8-week, double-blind study of vortioxetine (5mg), duloxetine (60mg) as active reference, and placebo
- Primary efficacy endpoint was change in HAM-D_{24} total score
- Mean HAM-D_{24} score at start of trial was 29.0



Katona C, et al. *Int Clin Psychopharmacol*. 2012;27:215–223.

Improvements in Cognitive Performance and Cognitive Symptoms in Elderly Patients with MDD (Vortioxetine 5–20 mg/day)

Cognitive Function: Adjusted LS Mean Change (SE) From Baseline



*P< 0.05. **P< 0.01.

di Nicola, M et al. Poster presented at Psych Congress. Poster 68. 2023

Treatment Resistant Depression

World Psychiatr

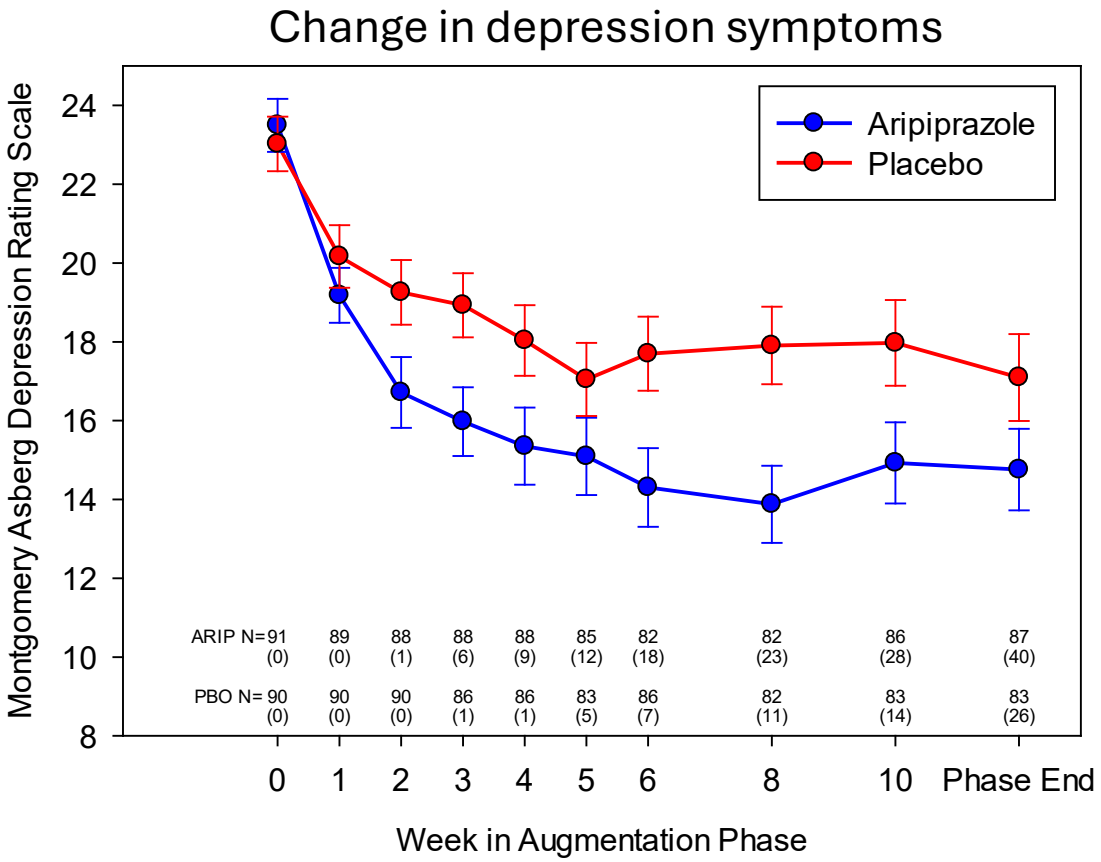
OFFICIAL JOURNAL OF THE WORLD PSYCHIATRIC ASSOCIA

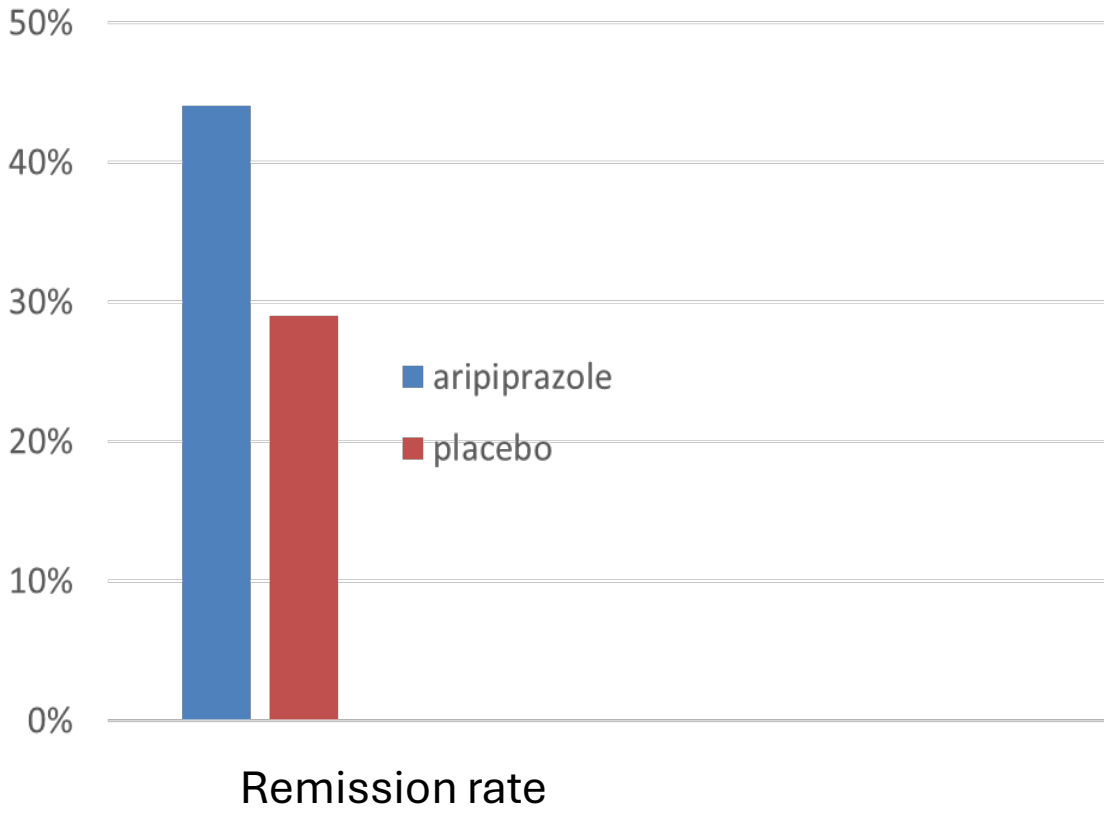
Volume 22, Number 3 *October 2023*

TRD: Major depressive episode that is persistent despite 2 adequate antidepressant trials

TRD= treatment-resistant depression.

Aripiprazole for TRD in Patients 60 Years of Age and Older





Lenze EJ, et al. *Lancet*. 2015;386(10011):2404-2412.

Safety of Aripiprazole for Late-Life Depression

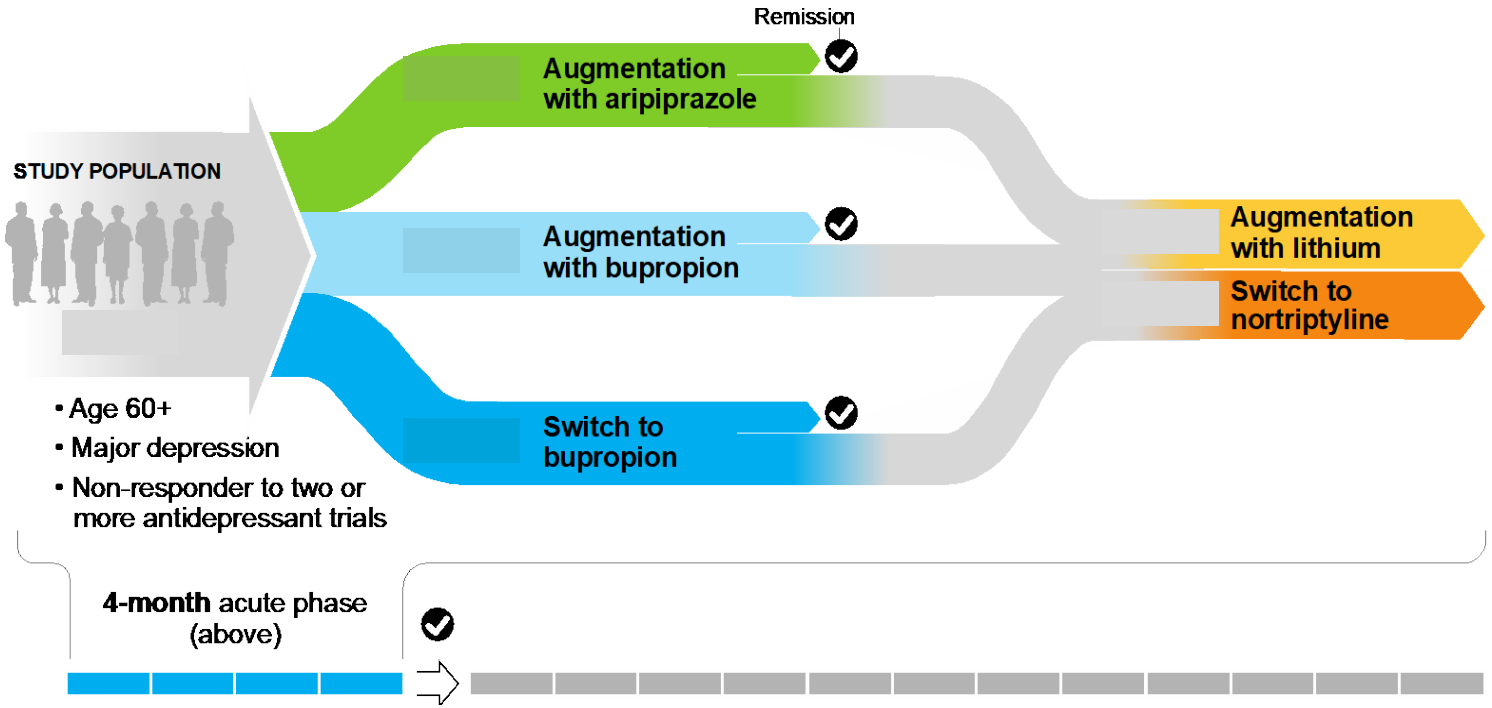
- Akathisia and Parkinson's
  - Yes, but usually mild and often self-limited
- Increased body fat and insulin resistance?
  - Minimal to none
- ECG changes: QTc prolongation?
  - None (venlafaxine and/or aripiprazole)

Lenze EJ, et al. *Lancet*. 2015;386(10011):2404-2412.

OPTIMUM Study Design

1 **Step 1** (for 10 wks): Patient is prescribed **augmentation with aripiprazole or bupropion,** or **switched to bupropion**

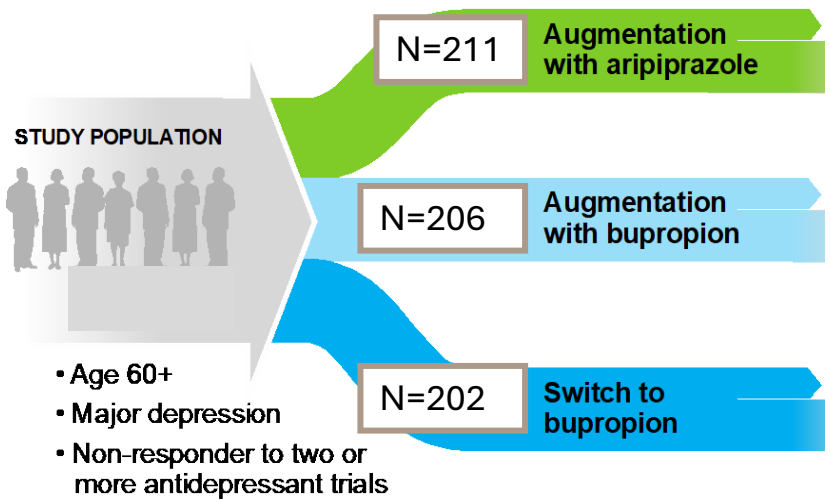
2 **Step 2** (for 10 wks): Those who do not improve in Step 1 receive **lithium augmentation** or **switched to nortriptyline**



Cristancho P, et al. *Am J Geriatr Psychiatry*. 2019;27(10):1138-1152.

Improvement in Psychological Well-Being

1 **Step 1** (for 10 wks): Patient is prescribed **augmentation with aripiprazole or bupropion,** or **switched to bupropion**



Change in psychological well-being (SD 10)

+4.8

+4.3

+2.0

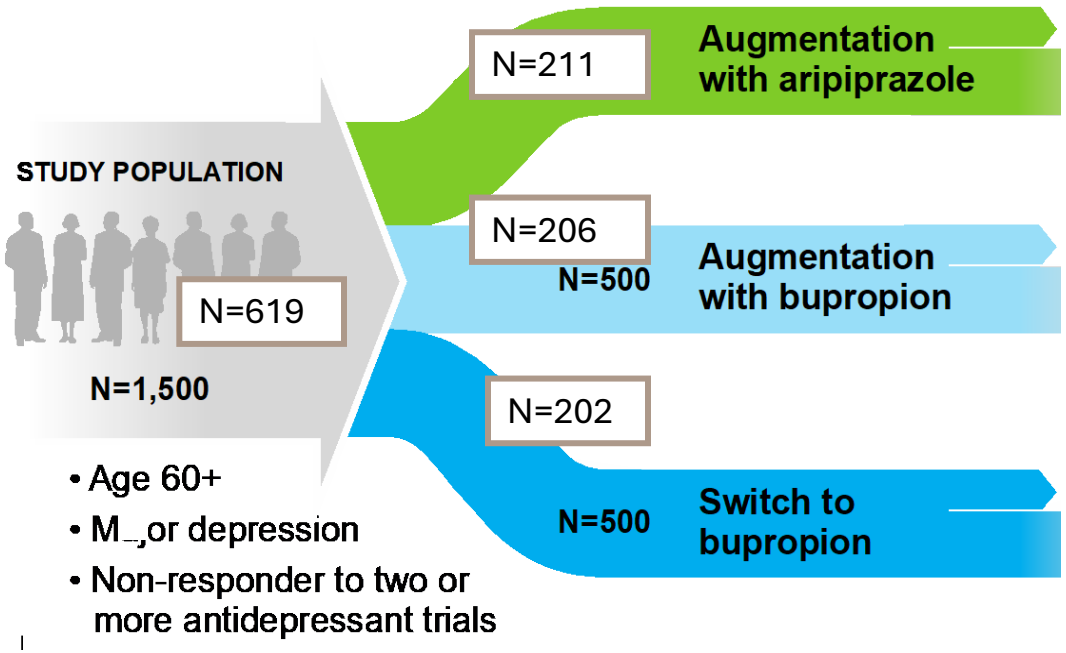
P = .014

Conclusion: Augmentation approaches beat switching.

Cristancho P, et al. *Am J Geriatr Psychiatry*. 2019;27(10):1138-1152. Lenze EJ, et al. *N Engl J Med*. 2023;388(12):1067-1079.

Fall Rates

1 **Step 1** (for 10 wks): Patient is prescribed **augmentation with aripiprazole or bupropion,** or **switched to bupropion**



Fall rate
(during 10 wks of treatment):

0.33

0.55

***P* =.02**

0.38

Bupropion augmentation has a higher rate than aripiprazole augmentation.

Cristancho P, et al. *Am J Geriatr Psychiatry*. 2019;27(10):1138-1152. Lenze EJ, et al. *N Engl J Med*. 2023;388(12):1067-1079.

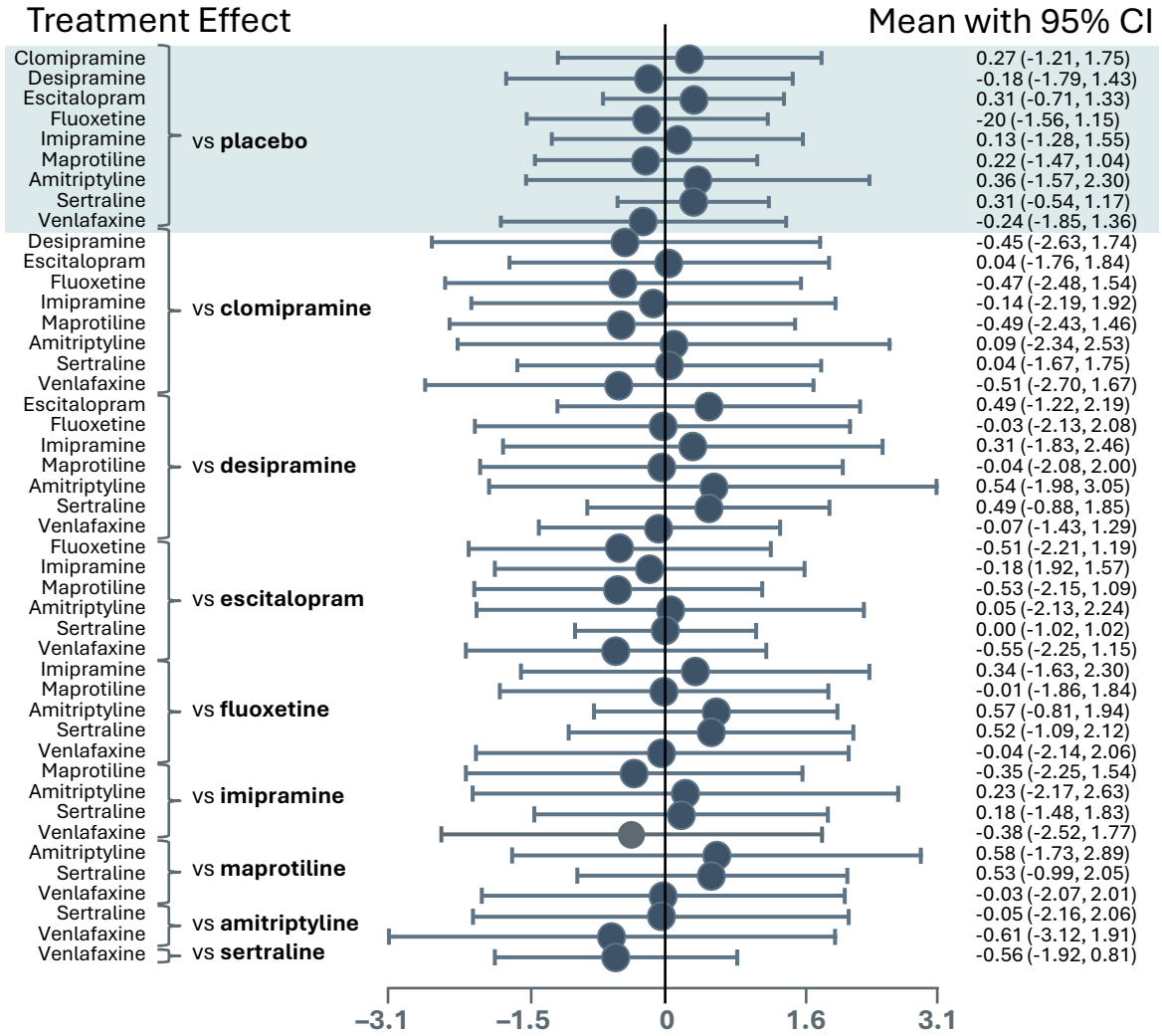
Falls With Bupropion: Why?

- Bupropion has complex pharmacokinetics
  - CYP2D6 inhibitor, CYP2B6 substrate
  - Multiple active metabolites
- When to pay close attention?
  - High dose (400+ mg) as augmentation
  - Interactions with “-oxetine”
  - Especially in patients with a history of falls

Joo J, et al. *J Clin Psychiatry*. 2002;63(10):936-941.

What Evidence Do We Have to Guide Our Treatment of MDD in Elderly Patients with Neurological Comorbidities?

Standard Antidepressants Showed No Statistically Significant Difference in Cognitive Function in Patients with MDD and Alzheimer's Disease Compared with Placebo



MMSE = Mini-Mental State Examination.

He Y, et al. *J Psychopharmacol*. 2021;35(8):901–909.

DDIs Can Reduce Efficacy and Increase Adverse Effects

- Selected antidepressants, including SSRI and SNRIs, can have pharmacokinetic and/or pharmacodynamic interactions
- Clinically relevant DDIs are usually caused by potent CYP inhibitors, including fluoxetine, paroxetine, and fluvoxamine
- Plasma drug concentrations should be monitored when CYP inhibitors are combined with drugs that are metabolised by the same CYP isoenzymes
- **CANMAT and RANZCP guidelines recommend**:
  - **Comprehensive and collaborative treatment** that focusses on psychiatric illness and comorbidity
  - **Close monitoring of medications and lifestyle factors**, with ongoing education and encouragement

CANMAT = Canadian Network for Mood and Anxiety Treatments; CYP = cytochrome; RANZCP = The Royal Australian & New Zealand College of Psychiatrists.

Kennedy SH, et al. *Can J Psychiatry*. 2016;61:540–60. Chen G, et al. *Clin Pharmacokinet*. 2018;57:673–686. Bauer M, et al. *World J Biol Psychiatry*. 2013;14:334–385. Malhi GS, et al. *Aust N Z J Psychiatry*. 2021;55(1):7–117. Bauer M, et al. *World J Biol Psychiatry*. 2013;14:334–385. Ramasubbu R, et al. *Ann Clin Psychiatry*. 2012;24(1):82–90.

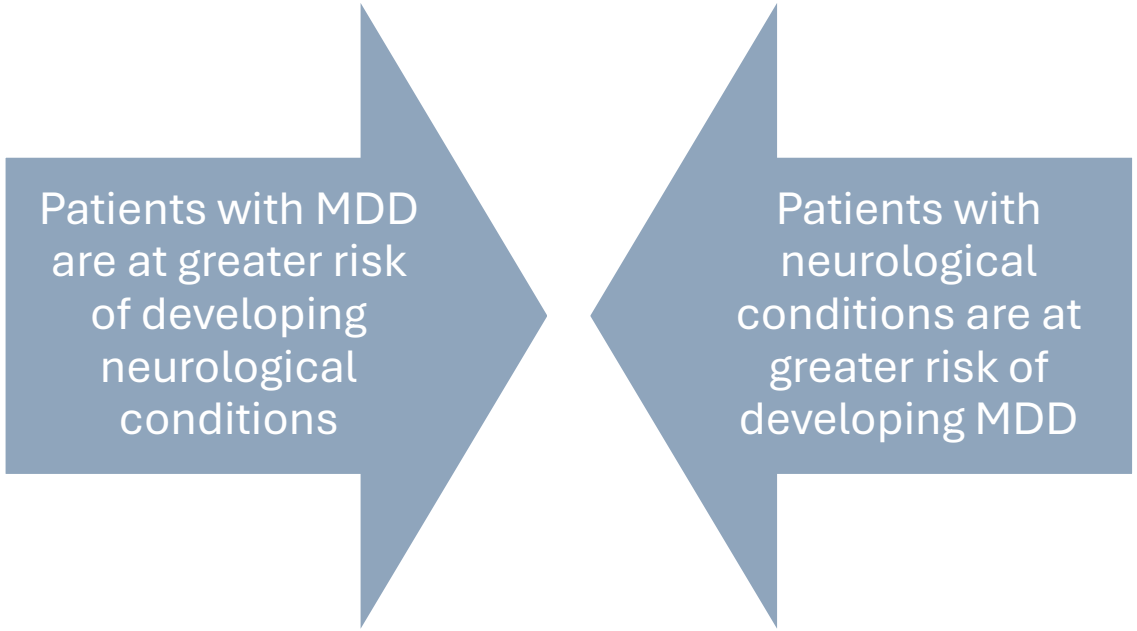
Know Your Medication

	AMITRIPTYLINE	DESVENLAFAXINE
Main mechanism	SNRI	SNRI
Side effects	Somnolence, confusion, dry everything	Usually mild and self-limited
Drug interactions	Watch out for 2D6 and 2C19 inhibitors and oral contraceptives	None
Off-target pharmacodynamics	Anticholinergic, antihistaminergic, alpha-1 adrenergic blockade	None
Active metabolites	Nortriptyline	None
Toxicity	YES – watch levels and ECG, avoid in cardiac patients	No

Winner!

Comorbid MDD Can Negatively Impact Neurological Conditions in Older Patients

The relationship between MDD and neurological conditions is bidirectional



Comorbid MDD in patients with Alzheimer's disease is associated with further decline in cognitive function

- In patients with all-cause dementia, cognitive function declined by 13.7 points (as measured by MMSE) over 3 years
- The presence of depression led to an **additional decline of 2.7 points**

Kanner, A. Depression in neurological disorders: comorbidity or another clinical manifestation? In: Strain JJ , Blumenfield M (eds.) Depression as a Systemic Illness. Oxford University Press. 2018;123-143. Rapp MA, et al. *Am J Geriatr Psychiatry*. 2011;19:357–363.

Presentation of Depression Symptoms May Vary in Patients with Neurological Conditions

- In patients with MDD and either Alzheimer's disease or Parkinson's disease, symptoms often overlap
  - Apathy is frequently observed in both Alzheimer's disease and Parkinson's disease
  - Distinguishing apathy from depression is challenging because of shared symptoms (eg, anhedonia) and their frequent co-occurrence
  - Clear differentiation between apathy and depression is critical, as selective serotonin reuptake inhibitors (SSRIs) have been linked to higher rates of apathy
- A recent Delphi consensus reported that 97% of panelists agreed that anhedonia is a prominent feature of depression in Parkinson's disease
- In another Delphi consensus, 67% of panelists agreed that anhedonia is a prominent feature of depression in Alzheimer's disease

Pagonabarraga J, et al. *Lancet Neurol*. 2015;14(5):518–531. Leung D, et al. *Int J Geriatr Psychiatry*. 2021;36(9):1330–1344. Connors H, et al. *Aust N Z J Psychiatry*. 2023;57(6):884–894. Stocchi F, et al. *Neurol Sci*. 2023;44(9):3123–3131. Padovani A, et al. *Neurol Sci*. 2023 Dec;44(12):4323-4332.

The Importance of Addressing Depressive Symptoms of MDD in Patients with Neurological Comorbidities

Depressive symptoms in this population are associated with:

- Poor QOL
- Daily function impairment
- Acceleration of disease progression
- Earlier institutionalization
- Caregiver stress
- Higher cost of care
- Earlier pharmacotherapy initiation
- Increased mortality

Burke A, et al. *Neurol Ther*. 2019;8:325–350. Marsh L. *Curr Neurol Neurosci Rep*. 2013;13(12):409.

Several subdomains of goal-directed behaviour can contribute to apathy via separate neural pathways

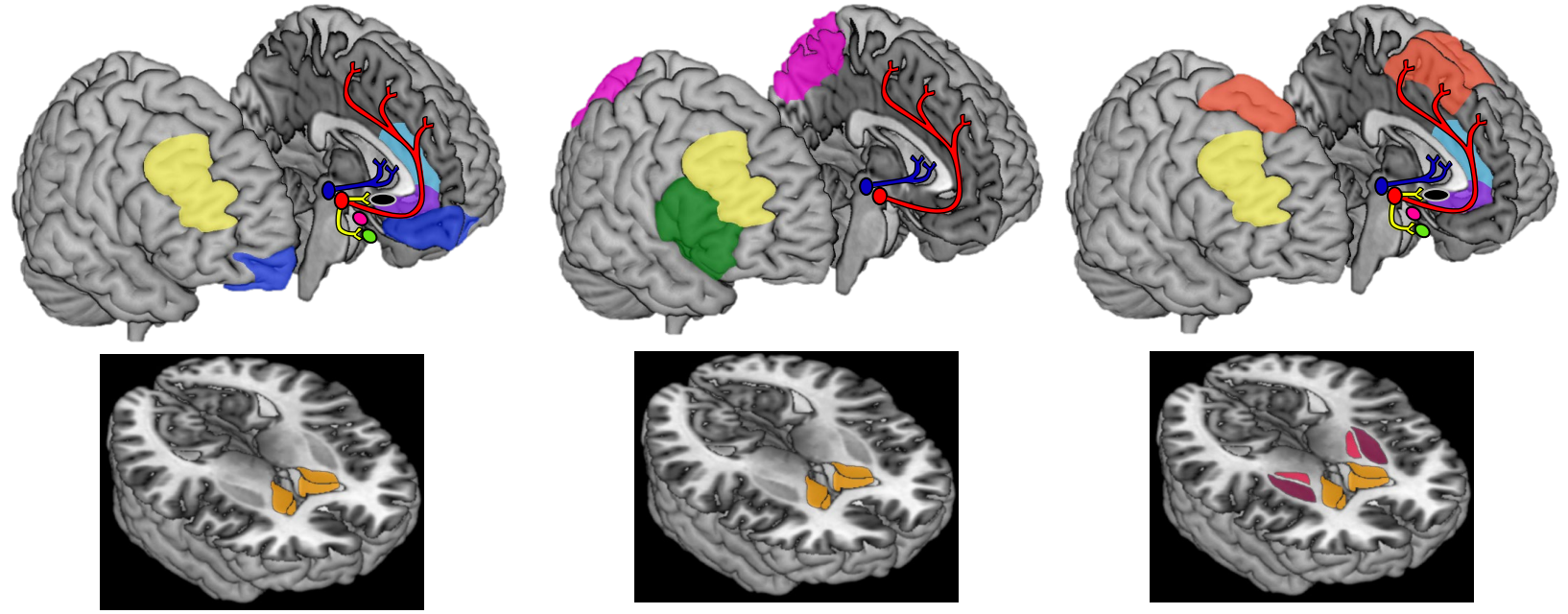
Apathy subdomains

Reward deficiency syndrome	Emotional distress	Executive function	Auto-activation deficit (psychic akinesia, athymhormia)
Emotional blunting, diminished emotional resonance	Negative affect (sadness, hopelessness)	Cognitive inertia	Lack of self-initiated behaviours, reversed by external stimuli
Orbitomedial or ventromedial prefrontal cortex ↕ Anterior cingulate cortex ↕ Amygdala and ventral striatum ↕ Substantia nigra pars compacta–ventral tegmental area	Increased activity in subgenual cingulate cortex (BA25) + decreased activity in dorsolateral prefrontal cortex and dorsal anterior cingulate cortex (BA24b)	Lateral prefrontal cortex–lateral caudate and putamen–anterior cingulate cortex	Substantia nigra pars compacta–ventral tegmental area, caudate, globus pallidus pars interna, mediodorsal and anterior thalamus, dorsal–medial prefrontal cortex (supplementary motor area, anterior cingulate cortex)
Dopamine receptor agonists, methylphenidate, bupropion	Antidepressants (SNRIs, bupropion, tetracyclic antidepressants, tricyclic antidepressants)	Acetylcholinesterase inhibitors	Dopamine receptor agonists

Blunted Emotional Response and Athymhormia
(Auto-Activation Deficit, Self-Psychic Akinesia)

Cognitive Apathy

Depressive Apathy



- Mesocortical pathway
- Mesolimbic pathway
- Nigrostriatal pathway
- VTA
- Hypothalamus
- Amygdala
- Nucleus Accumbens
- DLPFC
- VMPFC
- OFC
- PPC
- SMA
- Subgenual Cingulate
- Dorsal Cingulate
- Caudate Nucleus
- Putamen
- Globus Pallidus

DLPFC = dorsolateral prefrontal cortex; OFC = orbitofrontal cortex; PPC = posterior parietal cortex; SMA = supplementary motor area; VMPFC = ventromedial prefrontal cordex.

Pagonabarraga J, et al. *Lancet Neurol*. 2015;14(5):518–531.

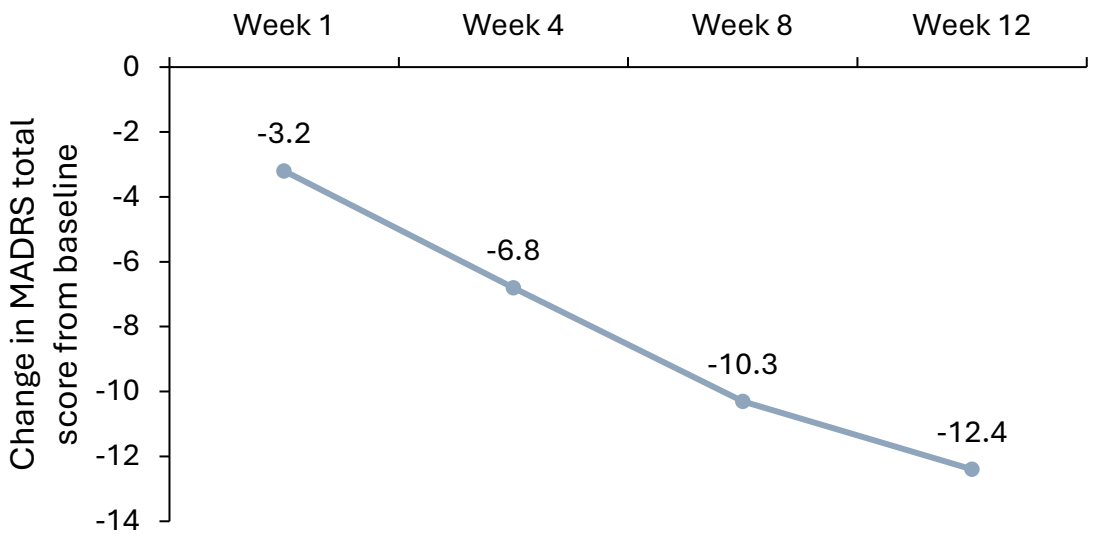
MEMORY Study: Effectiveness of Vortioxetine in Patients with MDD and Early-Stage Dementia

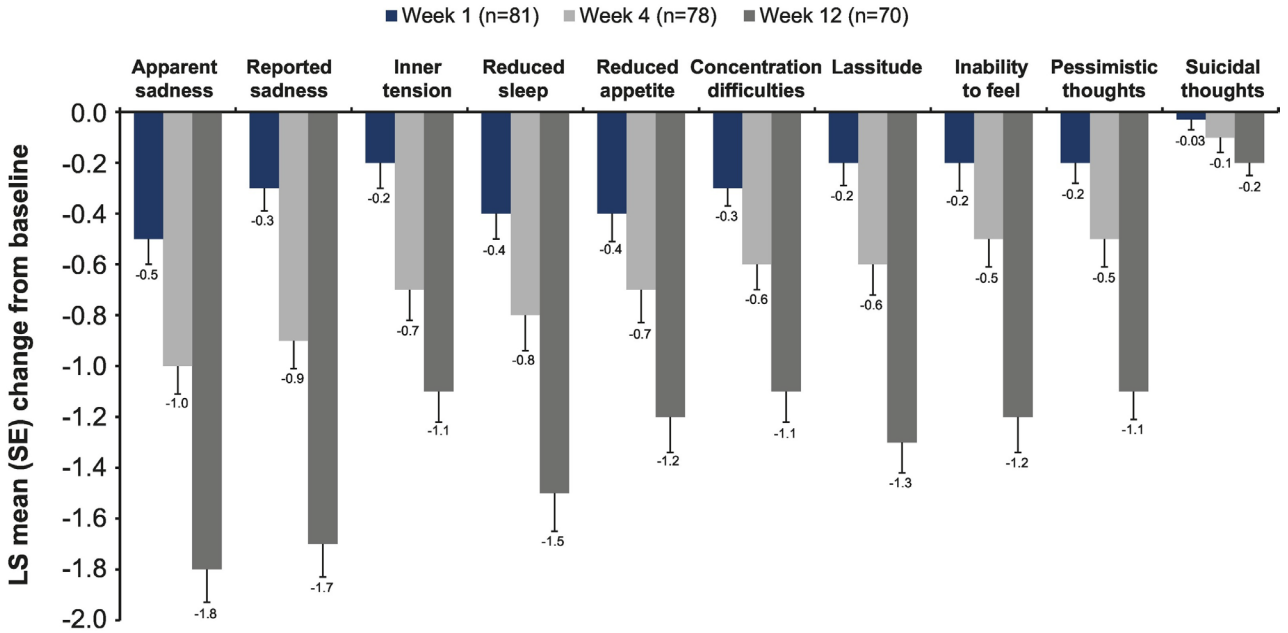
- 12-week, open-label trial assessing vortioxetine (5–20 mg/day) for depressive symptoms, cognition, memory, daily functioning, safety, and HRQoL in patients with MDD and early dementia.
- Primary endpoint was change in MADRS total score from baseline to Week 12
- Secondary endpoints included:
  - Change from baseline to Week 12 in DSST score, RAVLT score, IADL score, CGI-S score, CGI-I score and BASQID score
  - Response at Week 12 (≥50% decrease from baseline in MADRS total score)
  - Remission at Week 12 (MADRS ≤10)
- **Patient population (n=82):** Adults aged 55–85 years with recurrent MDD (onset <55 years), current major depressive episode <6 months, and MADRS ≥26
- **Comorbidity criteria:** Dementia diagnosed ≥6 months before screening (after MDD diagnosis) with MMSE-2 score 20–24

BASQID = Bath Assessment of Subjective Quality of Life in Dementia; CGI-I = Clinical Global Impression-Improvement; CGI-S = Clinical Global Impression-Severity; DSST = Digital-Symbol Substitution Test; HRQoL = health-related quality of life; IADL= Instrumental Activities on Daily Living; MADRS = Montgomery–Åsberg Depression Rating Scale; MDE = major depressive episode; MMSE-2 = Mini-Mental State Examination; 2nd Edition, Standard Version; RAVLT = Rey Auditory Verbal Learning Test.

Christensen MC, et al. *J Affect Disord*. 2023;338:432-431.

Improvement in Depressive Symptoms in Patients with MDD and Comorbid Early Dementia

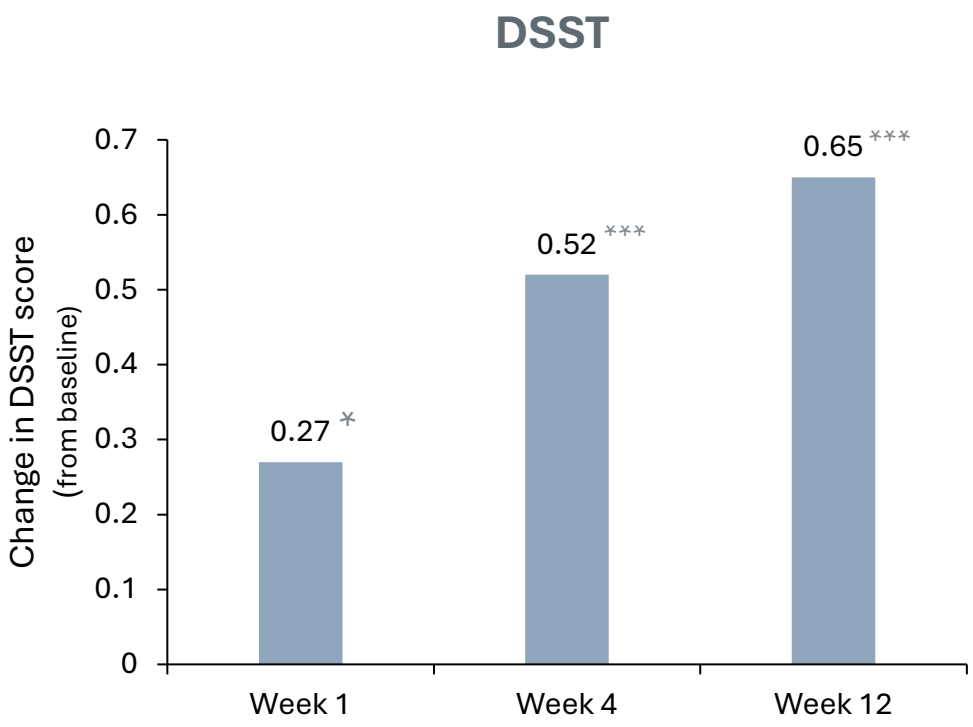


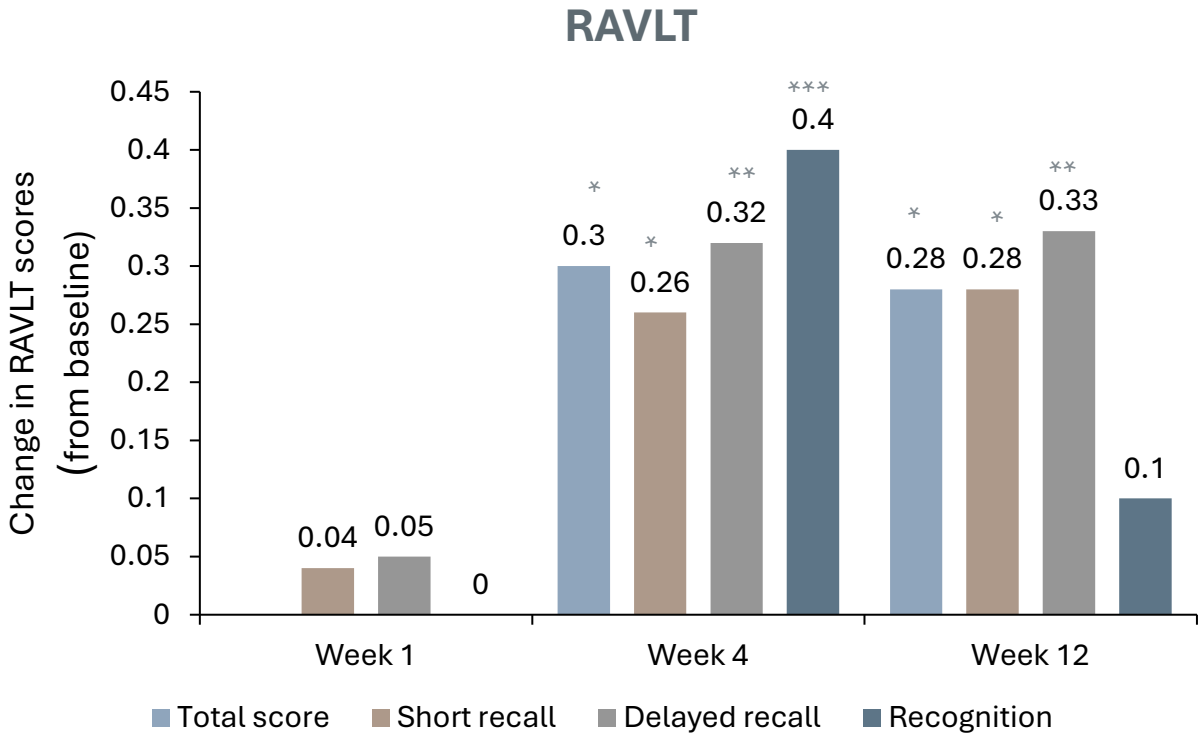


36% of patients showed a **response** with at least a 50% reduction in MADRS score **at Week 12**

Christensen MC, et al. *J Affect Disord*. 2023;338:432–431.

Improvement in Cognitive Performance and Verbal Learning and Memory in Patients with MDD and Comorbid Early Dementia

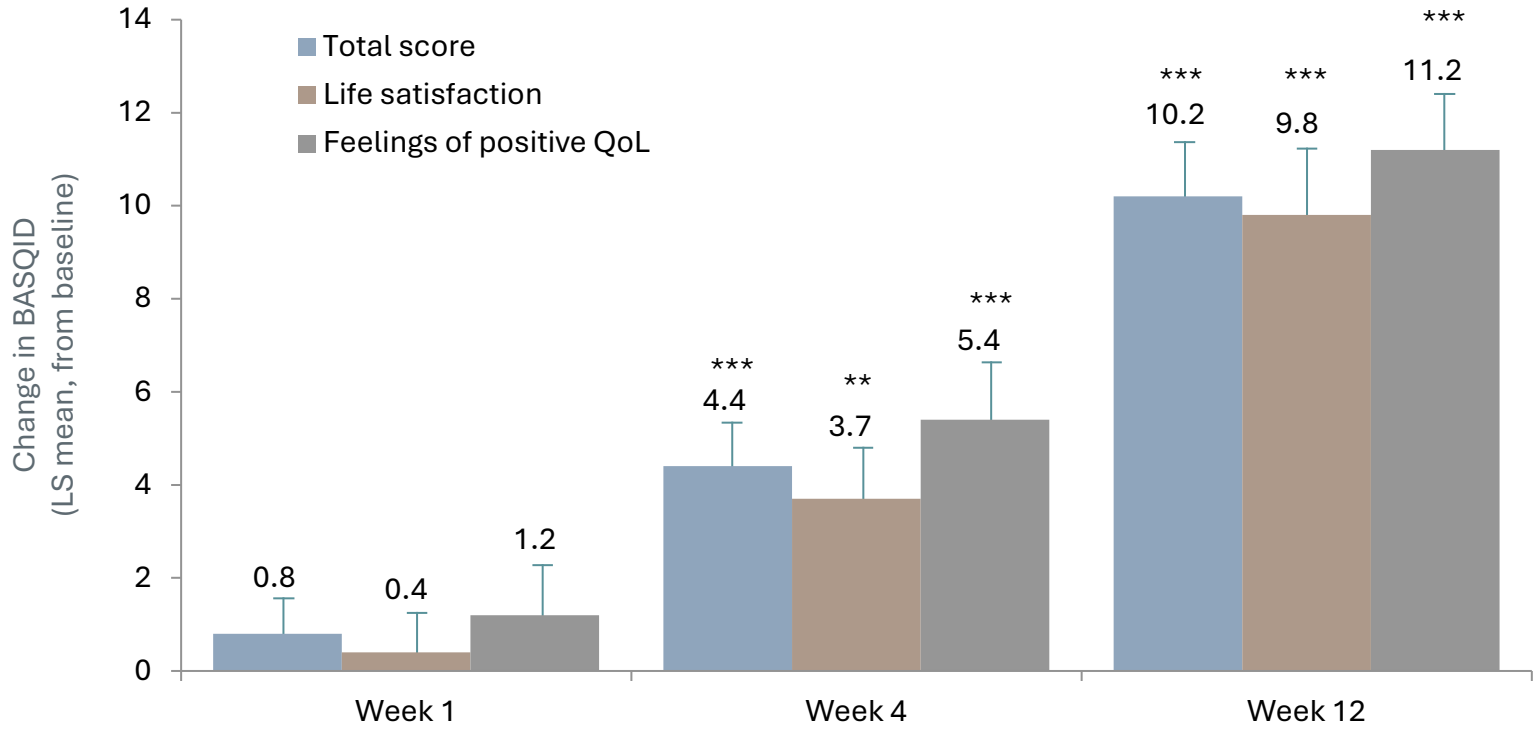




***p<0.05, **p<0.01, ***p<0.001.**

Christensen MC et al. *J Affect Disord*. 2023;338:432-431.

Improvement in HRQoL in Patients with MDD and comorbid Early Dementia



Improvements in MADRS total score were significantly correlated with improvements in HRQoL

****p<0.01, ***p<0.001.**

BASQID = Bath Assessment of Subjective Quality of Life in Dementia; HRQoL = health-related quality of life; IADL = Instrumental Activities of Daily Living; LS = least squares; QoL = quality of life.

Christensen MC, et al. *J Affect Disord*. 2023;338:432–431.

Safety Outcomes

- No new safety signals were observed during the MEMORY study; vortioxetine was generally well tolerated
- During the study, 38 (46%) patients reported TEAEs, with few patients (n=6, 7.3%) withdrawing due to AEs
- The most commonly reported AEs were abdominal pain (n=9, 11%) and nausea (n=9, 11%)
- 51.4% (n=37/72) of patients remained on vortioxetine 20 mg/day until study end at Week 12

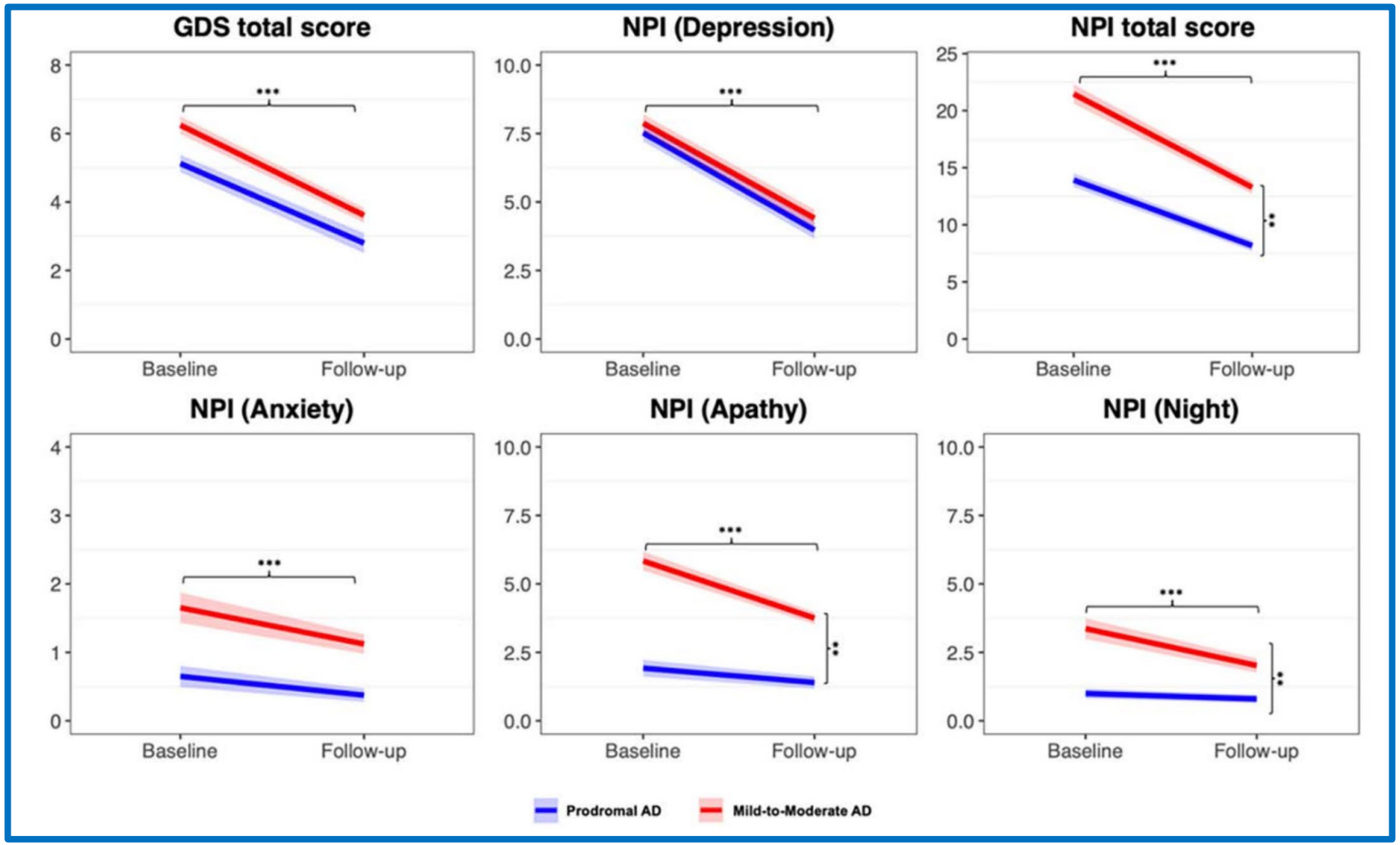
	No. of patients (%)	No. of events
Any TEAE	38 (46.3)	56
Serious TEAE	1 (1.2)	1
Withdrawal due to TEAE	6 (7.3)	8
TEAEs occurring in ≥2 patients		
Abdominal pain	9 (11.0)	9
Nausea	9 (11.0)	9
Headache	6 (7.3)	7
Diarrhea	3 (3.7)	3
Dizziness	3 (3.7)	3
Nasopharyngitis	3 (3.7)	3
Pruritus	3 (3.7)	3
Psychomotor hyperactivity	2 (2.4)	2
Somnolence	2 (2.4)	2
Spinal pain	2 (2.4)	2

AE = adverse event; SAE = serious adverse event; TEAEs = treatment emergent adverse events.

Christensen MC, et al. *J Affect Disord*. 2023;338:432-431.

Vortioxetine Treatment for Depression

Use in Prodromal vs Mild Alzheimer's Disease?



Padovani A, et al. *J Prev Alzheimers Dis*. 2024;11(2):375-381.

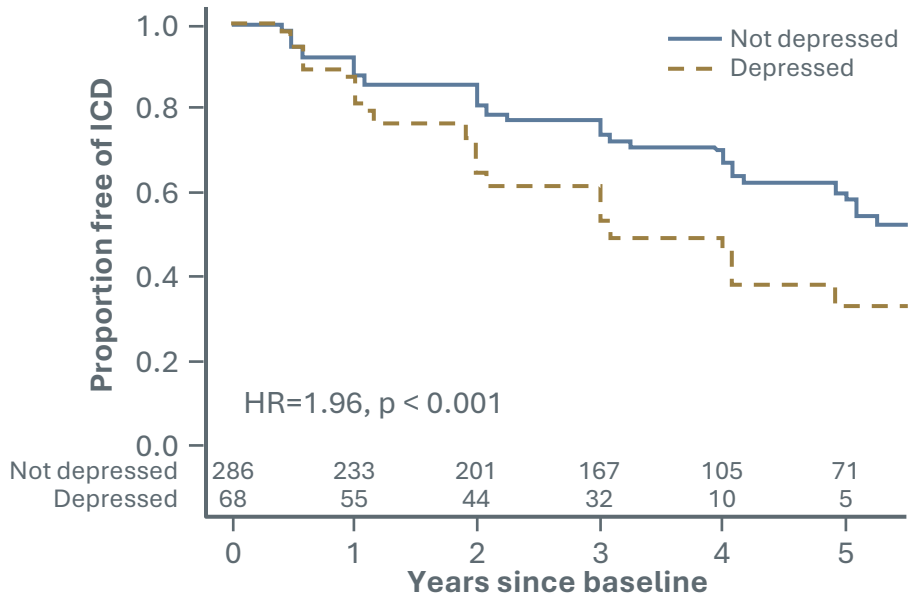
MDD and Parkinson's Disease: Core Symptoms

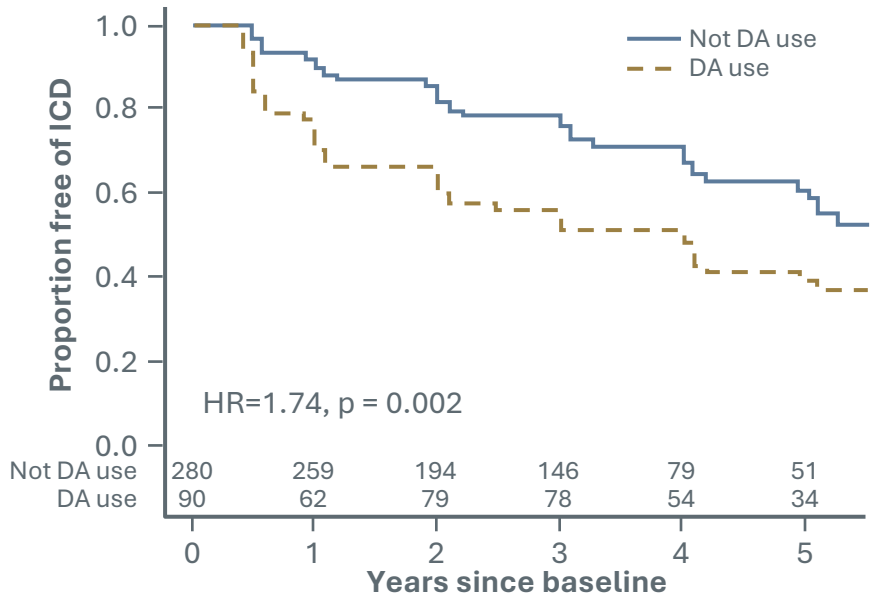
Depressive Mood	• Fearfulness toward life • Persistent negative ruminations and emotional bias toward negativity • Sadness • Low self-esteem accompanied by guilt • Diminished capacity for affection • Anhedonia across multiple domains
Deficits in Energy and Drive	• Clinophilia • Fatigue • Energy
Changes in circadian rhythms and sleep architecture	• Increased REM and decreased phase 4
Low Tolerance	• Pain • Stress

REM = rapid eye movement.

Marsh L, et al. *Mov Disord*. 2006;21(2):148-58. Bollu P and Sahota P. *Mo Med*. 2017;114(5):381-386. Leentjens, A. *J Geriatr Psychiatr and Neurol*. 2004;17(3):120-126.

Heightened Risk of Impulse Control Disorders with Depression or Dopamine Agonist Treatment





In Parkinson's disease, both depression and dopamine agonist initiation are independent and additive risk factors for impulse control disorders

DA = dopamine agonist; ICD = impulse control disorders; PD = Parkinson's disease.

Marín-Lahoz J, et al. *Ann Neurol*. 2019;86:762-769.

VOPARK Study: Effectiveness of Vortioxetine in Patients with MDD and Parkinson's Disease

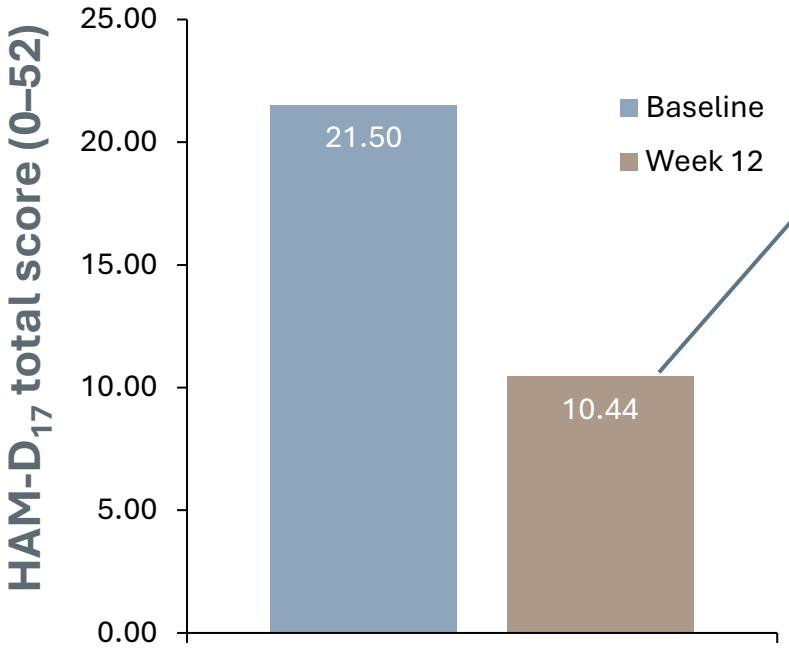
- 12-week, observational, prospective, open-label, single-arm study assessing vortioxetine (5–20 mg/day) for depressive symptoms, cognition, apathy, fatigue and HRQoL in patients with MDD and Parkinson's disease
- Primary endpoint was change in Change in HAM-D_{17} total score from baseline to Week 12
- Secondary endpoints included:
  - Change in apathy (AS), cognition (PD-CRS) and fatigue (FSS) scores from baseline to Week 12
  - Analysis of vortioxetine on QoL and functional capacity for daily living
- **Patient population (n=30):** Adults ≥40 years with MDD (DSM-5; HAM-D17 ≥16) and Parkinson's disease (UK Brain Bank criteria)
- **Treatment/stability criteria:** On stable dopaminergic therapy with no planned adjustments for 3 months; excluded if meeting dementia criteria

AS = Apathy Scale; DSM-5 = Diagnostic and Statistical Manual of Mental Health Disorders, Fifth Edition; FSS = Fatigue Severity Scale; HAM-D_{17} = 17-item Hamilton Depression Rating Scale; PD-CRS = Parkinson's Disease Cognitive Rating Scale.

Santos Garcia D, et al. *Brain Sci*. 2022;12(11):1466.

Improvement in Depressive Symptoms and HRQoL in Patients with MDD and Parkinson's Disease

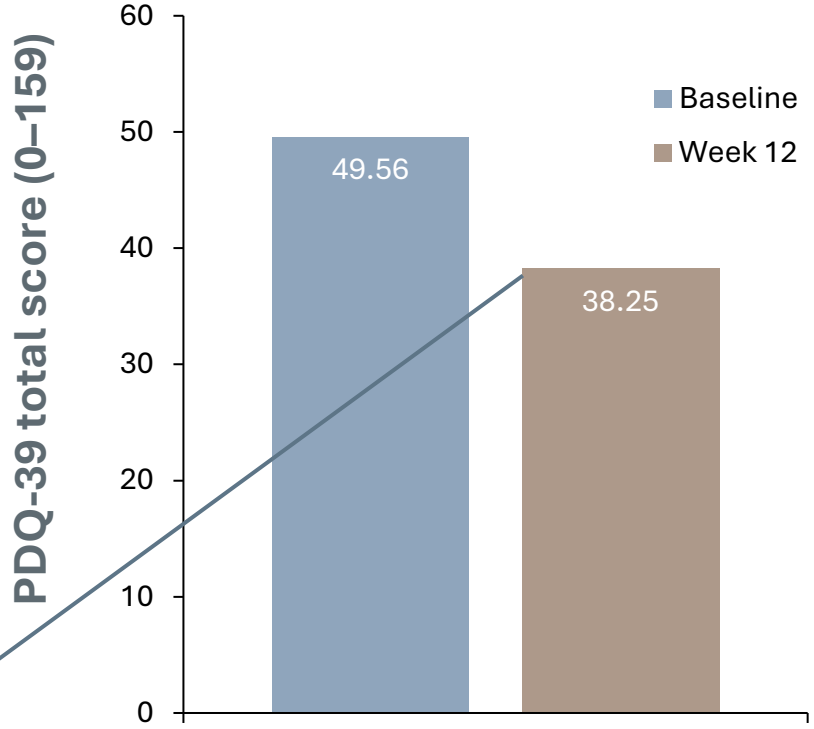
Mean change in HAM-D_{17} total score from baseline to Week 12



52.7% reduction in depressive symptoms

23.8% improvement in HRQoL

Mean change in PDQ-39 total score from baseline to Week 12



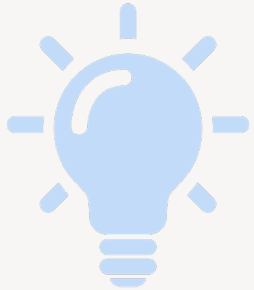
Santos Garcia D, et al. *Brain Sci*. 2022;12(11):1466.

Improvement in Non-Motor Symptoms in Patients with MDD and Parkinson's Disease Treated with Vortioxetine (5–20 mg/day)

AS	• Baseline: 17.6 ± 6.54 (1–31) • 12 Weeks: 11.29 ± 7.18 (1–26) • -35.10% change (*P*<0.0001)
PD-CRS	• Baseline: 80.66 ± 19.14 (29–116) • 12 Weeks: 86.81 ± 20.45 (38–127) • 7.94% change (*P*=0.007)
FSS	• Baseline: 38.7 ± 18.49 (9–76) • 12 Weeks: 29.04 ± 16.3 (9–60) • -27.90% change (*P*=0.014)

Santos Garcia D, et al. *Brain Sci*. 2022;12(11):1466.

Key Learning Points



- **Drug–drug interactions are a major clinical concern** in geriatric depression management, particularly with SSRIs/SNRIs and CYP inhibitors, requiring vigilant monitoring.
- Augmentation strategies (e.g., aripiprazole) **may outperform switching in treatment-resistant late-life depression**, but careful monitoring for falls and side effects is required.
- Evidence supports the use of **multimodal antidepressants such as vortioxetine** for improving depressive symptoms, cognitive performance, and health-related QoL specifically among older **patients with MDD and early dementia**.

Incorporating Measurement Based Care!

References

Geriatric Depression Scale

- 15 items – yes/no

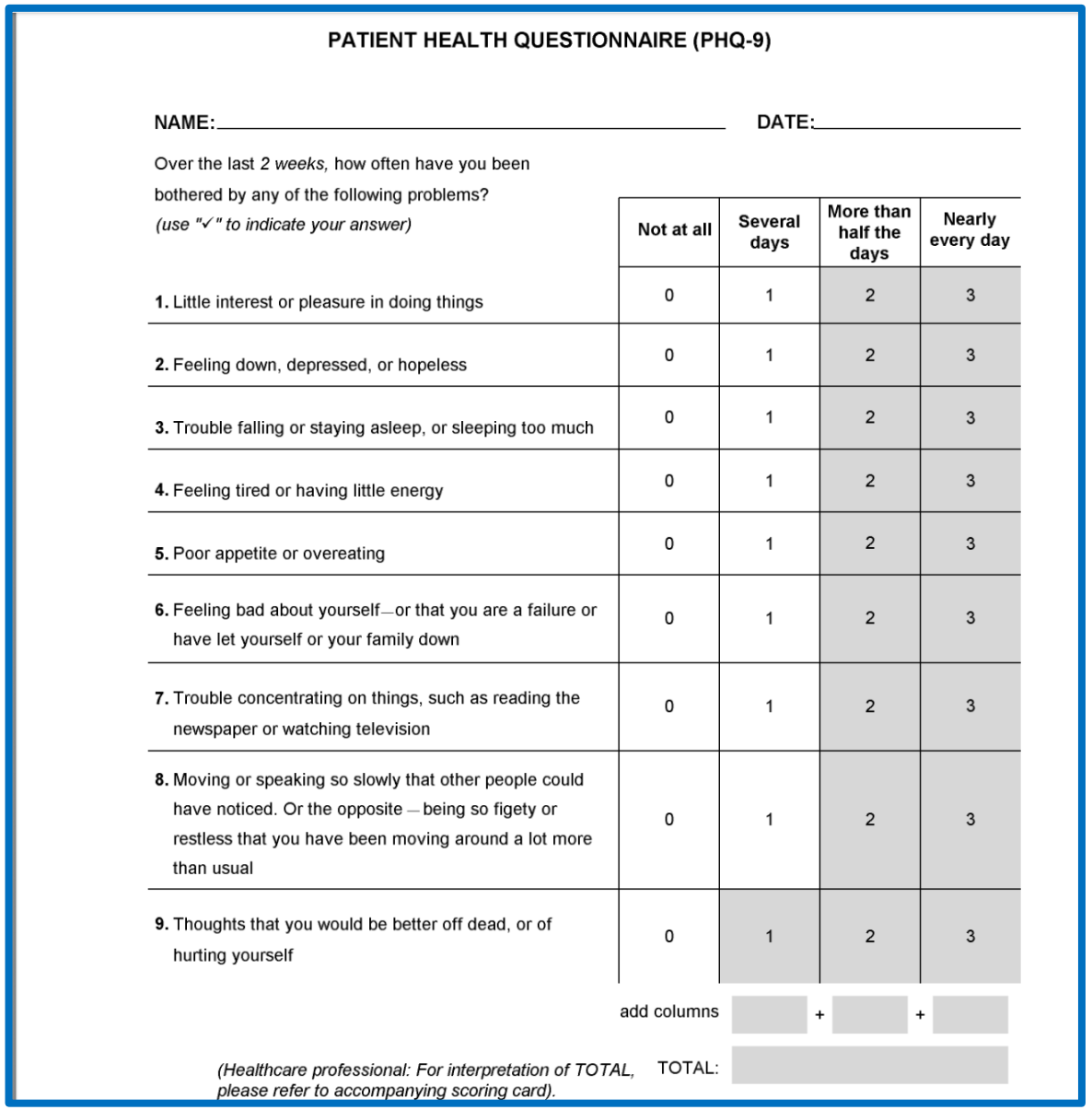
		Yes	No
1	Are you basically satisfied with your life?	**0**	**1**
2	Have you dropped many of your activities and interests?	**1**	**0**
3	Do you feel that your life is empty?	**1**	**0**
4	Do you often get bored?	**1**	**0**
5	Are you in good spirits most of the time?	**0**	**1**
6	Are you afraid that something bad is going to happen to you?	**1**	**0**
7	Do you feel happy most of the time?	**0**	**1**
8	Do you often feel helpless?	**1**	**0**
9	Do you prefer to stay at home, rather than going out and doing new things?	**1**	**0**
10	Do you feel you have more problems with memory than most people?	**1**	**0**
11	Do you think it is wonderful to be alive?	**0**	**1**
12	Do you feel pretty worthless the way you are now?	**1**	**0**
13	Do you feel full of energy?	**0**	**1**
14	Do you feel that your situation is hopeless?	**1**	**0**
15	Do you think that most people are better off than you are?	**1**	**0**

Scoring:
0-4 normal
5-8 mild
9-11 moderate
12-15 severe

92% Sensitivity
89% Specificity

Yesavage JA et al. *J Psychiatr Res*. 1983;17(1):37-49.

PHQ 9



PATIENT HEALTH QUESTIONNAIRE (PHQ-9)

NAME:_____ DATE:_____

Over the last *2 weeks*, how often have you been bothered by any of the following problems?
(use "✓" to indicate your answer)

	Not at all	Several days	More than half the days	Nearly every day
1. Little interest or pleasure in doing things	0	1	2	3
2. Feeling down, depressed, or hopeless	0	1	2	3
3. Trouble falling or staying asleep, or sleeping too much	0	1	2	3
4. Feeling tired or having little energy	0	1	2	3
5. Poor appetite or overeating	0	1	2	3
6. Feeling bad about yourself—or that you are a failure or have let yourself or your family down	0	1	2	3
7. Trouble concentrating on things, such as reading the newspaper or watching television	0	1	2	3
8. Moving or speaking so slowly that other people could have noticed. Or the opposite — being so figety or restless that you have been moving around a lot more than usual	0	1	2	3
9. Thoughts that you would be better off dead, or of hurting yourself	0	1	2	3
add columns		+	+	
TOTAL:				

(Healthcare professional: For interpretation of TOTAL, please refer to accompanying scoring card).

Scoring:
0-5 normal
5-9 mild
10-14 moderate 15-19 mod severe
> 19 severe

Sensitivity
Specificity

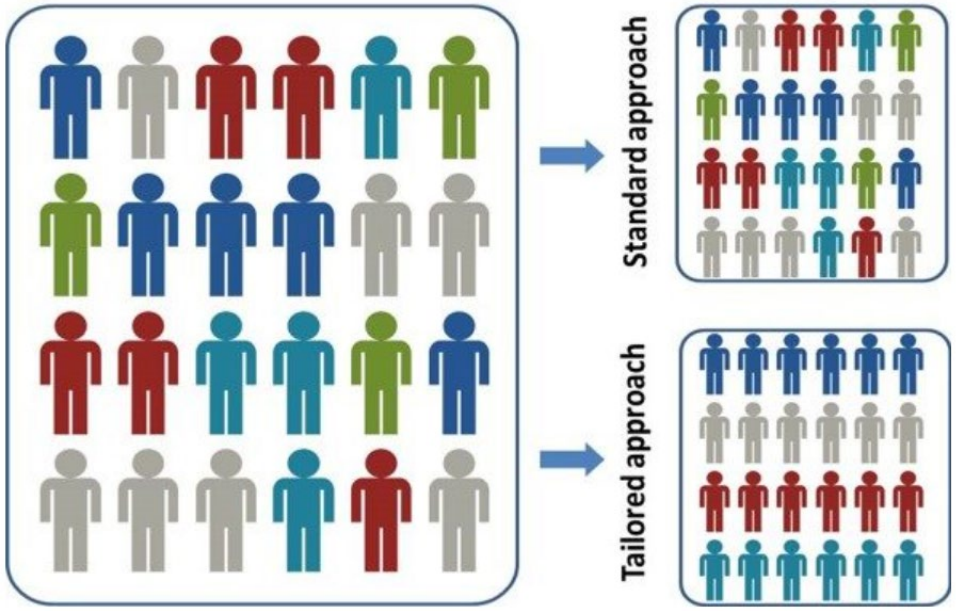
PHQ9 vs GDS?

PHQ9 with similar sensitivity and specificity

PHQ-9 Cutpoint	Sensitivity (%, 95% CI)	Specificity (%, 95% CI)	+ Likelihood Ratio	- Likelihood Ratio	15-item GDS Cutpoint	Sensitivity (%, 95% CI)	Specificity (%, 95% CI)	+ Likelihood Ratio	- Likelihood Ratio
≥8	88 (56-98)	75 (71-77)	3.6	0.16	≥5	100 (73-100)	15 (11-15)	1.2	0.00
≥9	88 (56-98)	80 (76-82)	4.4	0.16	≥6	100 (70-100)	58 (54-59)	2.4	0.00
≥10	63 (33-86)	82 (78-85)	3.5	0.46	≥7	75 (43-93)	77 (72-79)	3.2	0.33
≥11	63 (33-85)	84 (80-87)	3.8	0.45	≥8	25 (7-54)	87 (84-91)	1.9	0.86
≥12	63 (33-85)	84 (80-87)	3.8	0.45	≥9	13 (2-37)	93 (92-97)	1.9	0.94

Phelan E, et al. *BMC Fam Pract*. 2010;11:63.

What's Coming?



Precision medicine to increase remission and avoid falls

Targeting aging pathways to achieve neurorestoration and prevention

Caregiver Action Network Resources

Helping Medical Professionals Provide Better Care for Patients

- This resources helps medical professionals understand the vital role family caregivers play in patient care-how they monitor symptoms, mange medications, facilitate follow-ups, and advocate for their loved ones-to enable more informed, and personalized treatment. It also offers downloadable tools (visit checklists, symptom reporting guides, caregiver tips, etc.) that clinicians care share with caregivers to improve communication, adherence, and outcomes.

Caregiver Help Desk: Support for Family Caregivers

- The Help Desk provides free, confidential support to family caregivers via phone, email, or chat (Mon-Fri, 8:00 AM – 7:00 PM EST), staffed by experts who guide caregivers through challenges and decision points along their caregiving journey.

Practical Takeaways

- Geriatric depression treatment is often highly complex because of patients' advanced age, multimorbidity, and polypharmacy
- Beware of drug-drug interactions
  - Bupropion augmentation associated with increased falls
  - Dopamine agonists associated with increase impulse control disorders
- Clinical trial data suggests that vortioxetine > duloxetine > sertraline > other SSRIs or TCAs for improvement of processing speed in the elderly
- An antidepressant algorithm based on recent clinical trial evidence, current symptomatology and comorbid health conditions is improved with measurement-based care

Q&A