Neuroscience Education Institute

HERE TO STAY: ADHD IN OLDER ADULTS

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Learning Objectives

- Review research specific to ADHD in adults over age 50
- Identify limitations of current diagnostic criteria as applied to older ADHD adults
- Understand differential diagnoses and concurrent psychiatric/medical comorbidities
- Assess tentative proposals of treatment options in this population

ADHD in Older Adults

Why is ADHD in Older Adults an Issue?

"They lived with it their whole lives.
Why bother treating it now?"

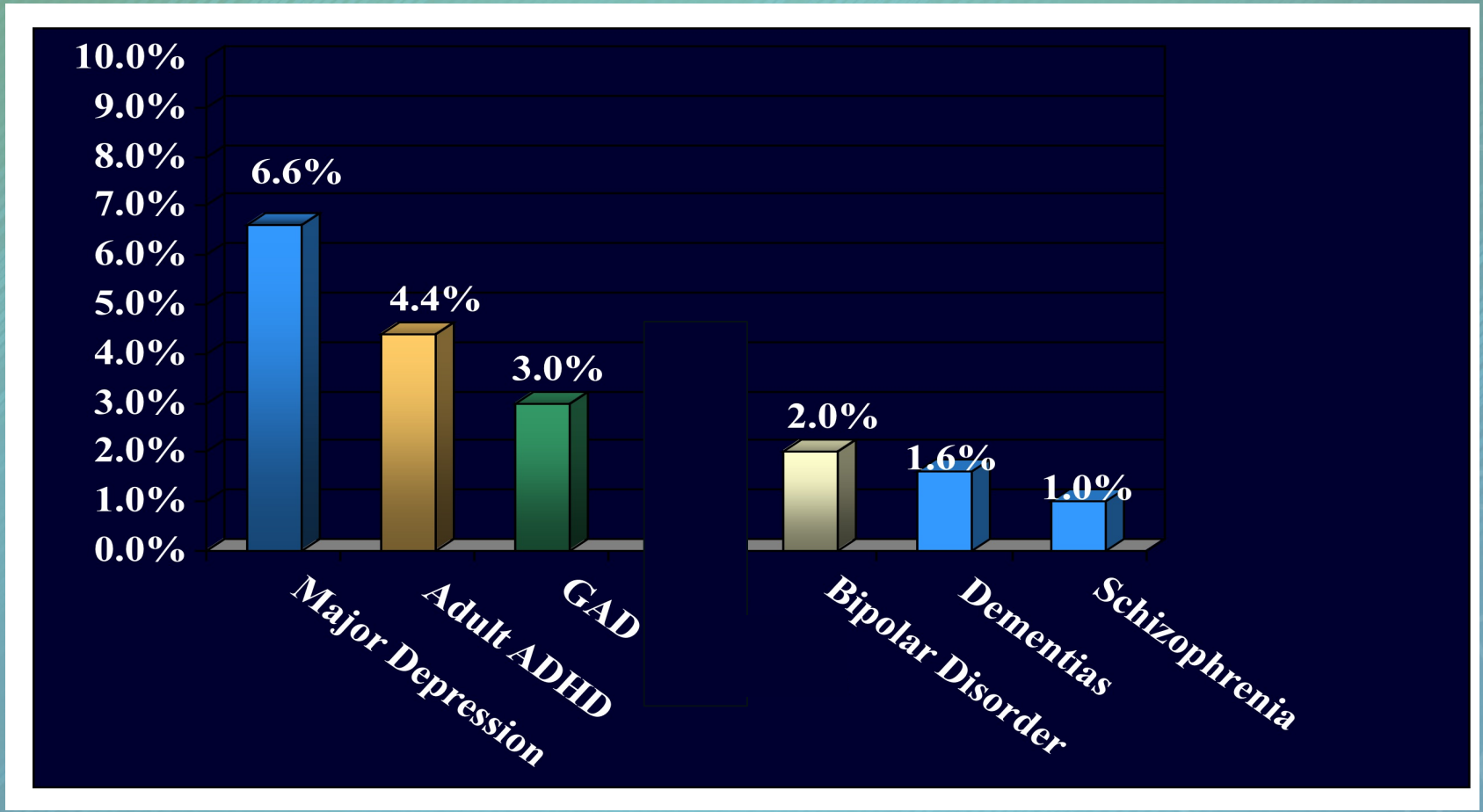
"Why is ADHD in older adults of concern?"

- ADHD continues into adulthood
  - Long-term follow-up of children
  - Genetic studies
- Limited data in adults age >50
- Adults age >65 excluded from ADHD clinical trials
  - Except lisdexamfetamine age limited to 55
- People with ADHD in this age group typically not diagnosed in childhood because of less awareness, DSM emphasized hyperactivity
- Burden with the increasing aging population

Brod M, et al. Qual Life Res. 2012;21(5):795–9.

Prevalence

Prevalence Rates of Psychiatric Disorders in U.S. Adults



Kessler RC et al. JAMA. 2003 Jan 18;278(23):3095-105; Kessler RC et al. Am J Psychiatry. 2006 Apr;63(4):415-24; Merikangas KR et al. Arch Gen Psychiatry. 2007 May;64(5):543-52; Michielsen M et al. Br J Psychiatry 2012;201:298-305.

Adult ADHD Prevalence
Longitudinal Aging Study Amsterdam (LASA)

- First epidemiological study on ADHD in older persons
  - 1494 participants screened with ADHD questionnaire
  - 231 respondents administered structured diagnostic interview
  - 6 out of 9 ADHD symptoms must be present in childhood for ADHD diagnosis (relying solely on respondents' recollection of childhood symptoms)
  - Other psychiatric diagnoses not included
- **Prevalence of syndromatic ADHD in adults: 2.8%**
- **Prevalence of symptomatic ADHD in adults: 4.2%**
- Men and women reported similar levels of symptoms
- Prevalence rates of inattentive and hyperactive-impulsive subtypes were the same

Michielsen M et al. Br J Psychiatry 2012;201:298-305.

Identification and Assessment of Late-Life ADHD in US Memory Clinics

- **ONLY 1 of 5 clinics reported screening regularly for ADHD** (62 of 165 patients responded to survey)
- 1/2 reported seeing ADHD patients
  - 60% reported contact with previously diagnosed ADHD patients
- **ADHD symptomatology may not have been considered as pre-morbid baseline cognitive functioning**

Fischer BL et al. J Att Dis 2012;16(4):333-338.

Prevalence of ADHD in Older Adults: Large Meta-analysis

20 relevant studies with 32 datasets
total sample size of 20,999,871 individuals
(41,420 individuals with ADHD)

	Prevalence Estimate	95 % CI
Research Diagnosis	2.18%	1.51–3.16
Clinical diagnosis	0.23%	0.12–0.43
Treatment rates	0.09%	0.06–0.15

There is a considerable number of older adults with elevated levels of ADHD symptoms as determined via validated scales
Prevalence of treated ADHD is less than half of the pre-valence of clinically diagnosed ADHD

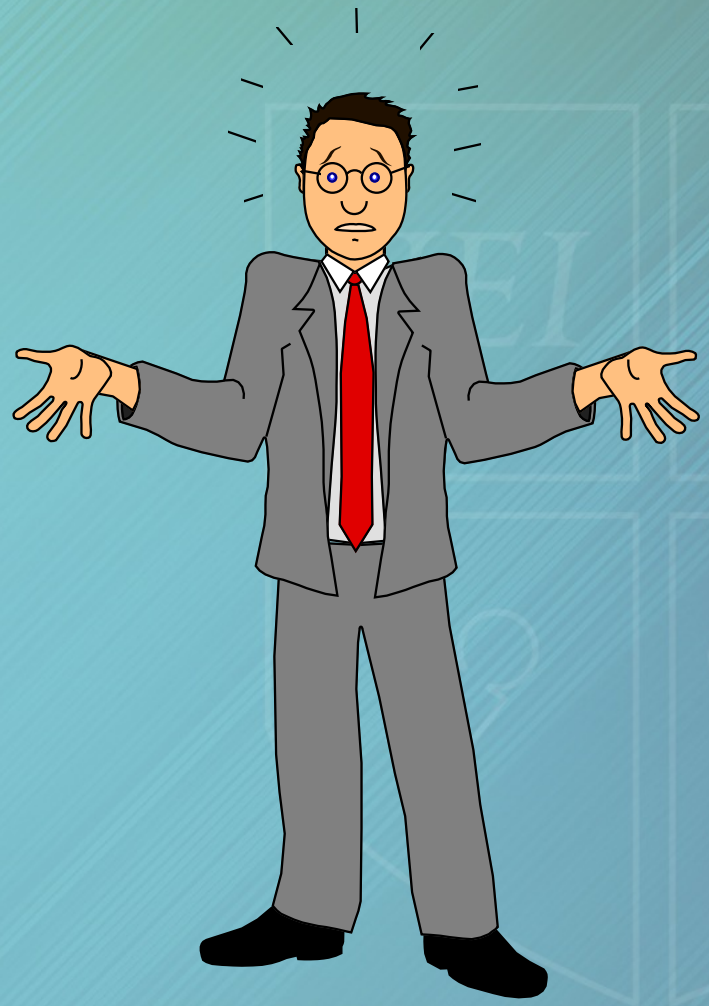
Dobrosavljevic M et al. Neuroscience and Biobehavioral Reviews. 2020.118:282-289.

Childhood Diagnosis vs Adult Diagnosis

- Most older adults with ADHD were not diagnosed as children, in part because ADHD was poorly recognized decades ago.
- 75% of adults aged were not diagnosed as children (ages 18 - 44 years with ADHD in the National Comorbidity Study-Replication (NCS-R).
- In a US phone interview of 24 adults aged 60-77 years, none were diagnosed as children and the mean age at diagnosis was 57 years

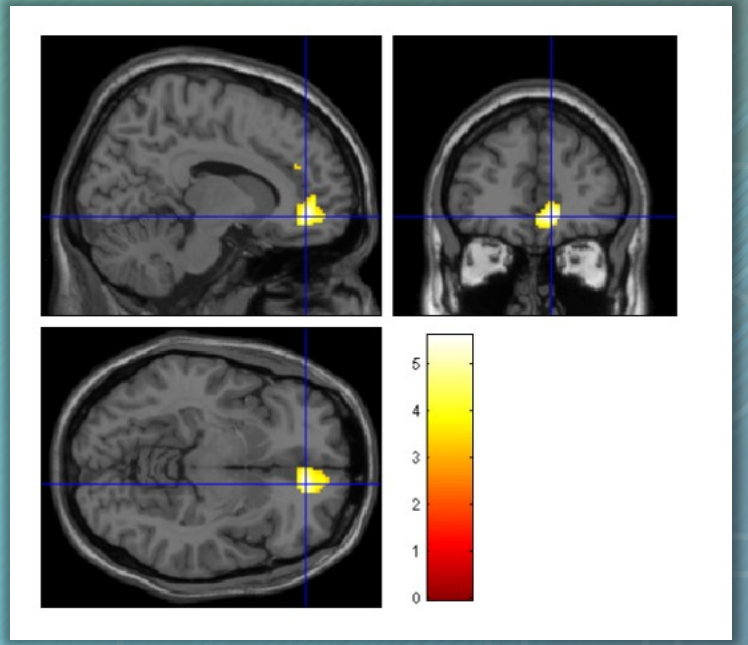
Kessler RC, et al. Am J Psychiatry. 2006;163(4):716-23
Brod M, et al. Qual Life Res. 2012;21(5):795-9

Diagnostic Issues



Gray Matter Volume in Older Adults With ADHD

- Findings revealed a smaller total gray matter volume in males with ADHD
- Smaller gray matter volume in:
  - right medial frontal orbital area extending toward the medial frontal superior, the frontal superior, the subgenual anterior cingulate cortex (ACC)



Correlations between:

-inattentiveness and ACC (bilaterally) and left cerebellum

-hyperactivity/impulsivity and the left frontal inferior orbital

-depression and caudate (bilaterally) and the right inferior parietal lobule

Klein M et al. J Atten Disord. 2021;25(6):829-838.

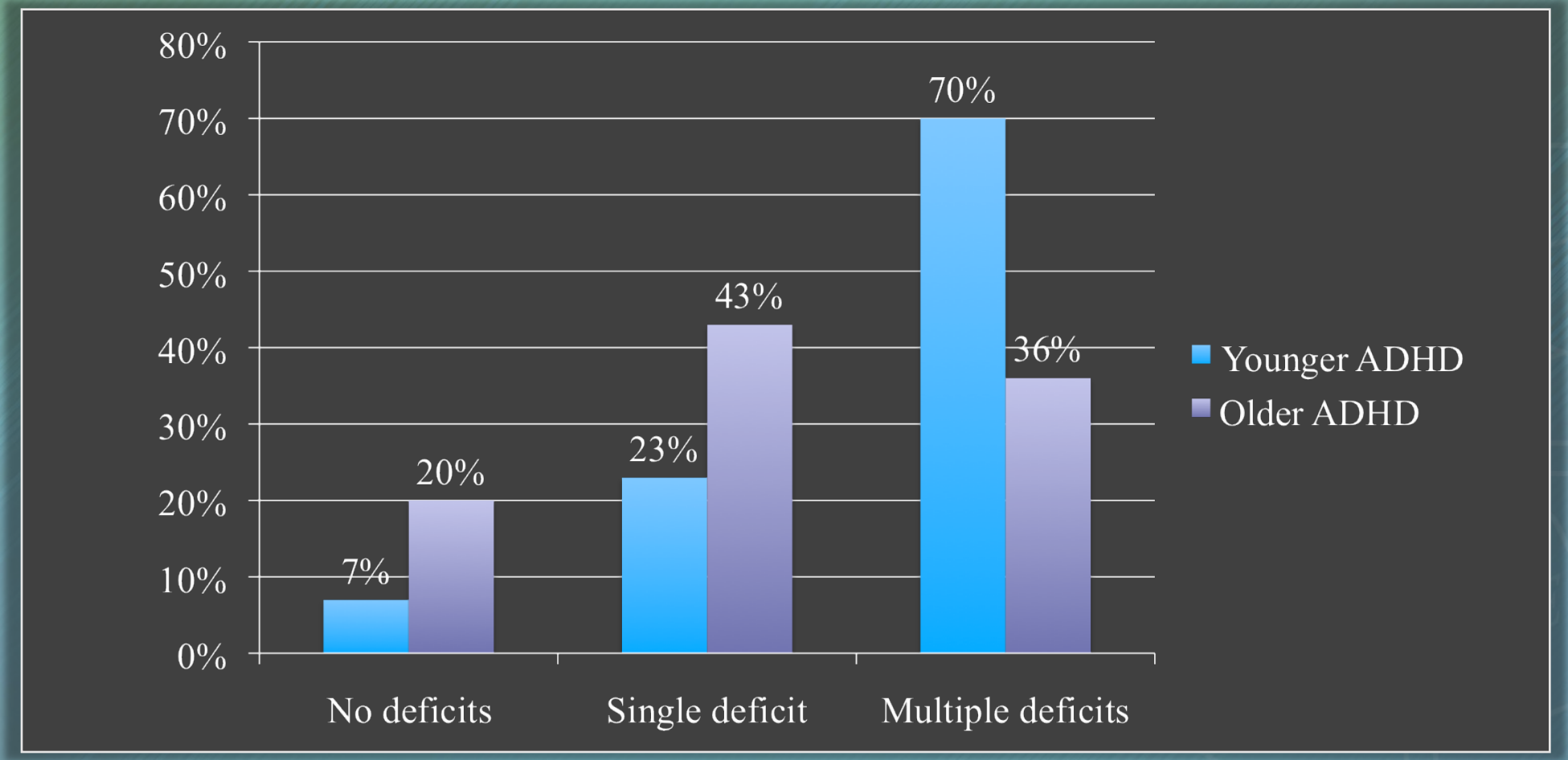
Neuropsychological Studies in Older Adults with ADHD

Neuropsychological Studies: Age Comparison

- The Swedish study included 158 participants in three groups:
  - Older adults (60-75 years of age) diagnosed with ADHD (*n* = 44)
  - Younger adults (18-45 years of age) with ADHD (*n = 56)*
  - Healthy controls of the same age (*n* = 58)
- Outpatient psychiatric clinics in Stockholm
- Among older adults with ADHD, 22/44 patients were on stimulant medication

Thorell, L.B. et al. European Psychiatry. 2017 (45):90-96.

Neuropsychological Studies: Age Comparison



Thorell, L.B. et al. European Psychiatry. 2017 (45):90-96.

Childhood Diagnosis vs Adult Diagnosis

- **U.S. study**: Alzheimer's Disease Center longitudinal research program found that of 310 respondents between the ages of 62 and 91 years
  - 4.4% of respondents had childhood ADHD, as indicated by the WURS
- Neuropsychological tests did not differentiate WURS-positive from WURS-negative individuals
- This is consistent with findings that cognitive tests do not reliably distinguish ADHD cases in younger adults

Ivanchak N, et al. J Aging Res. 2011;2011:729801; Seidman LJ, et al. Clin Psychol Rev. 2006;26(4):466-85

Relationship of Quality of Life: EF Lab Tests and Self-Rated Measures

- N=158 in three groups
  - Older adults (60-75 yo) n=42
  - Younger adults (18-45 yo) n=56
  - Healthy controls (60-75 yo) n=58
- Clinically referred population
- Older adults with ADHD differed significantly from controls (same age) on all aspects of QoL, with moderate effect sizes

Thorell L et al. Nordic J of Psychiatry. 2019 Oct;73(7):409-416.

Relationship of Quality of Life: EF Lab Tests and Self-Rated Measures

Table 3. Correlations between quality of Life and executive functioning (EF) among older adults with ADHD.

	Quality of Life			
	Life outlook	Life productivity	Psychological health	Relationships
EF laboratory test				
Working memory	.10	.02	.25	.23
Inhibition	.13	.03	.02	.10
Switching	−.17	−.06	−.19	−.09
EF Self-ratings				
ADEXI Working memory	−.42**	−.50***	−.28	−.58***
ADEXI Inhibition	−.08	−.13	−.26	−.32*
ADHD symptom levels				
Hyperactivity/impulsivity	−.12	−.07	−.44**	−.39*
Inattention	−.28	−.53***	−.34*	−.49***

*$p < .05$.
**$p < .01$.
***$p < .001$.

Thorell L et al. Nordic J of Psychiatry. 2019 Oct;73(7):409-416.

Neuropsychological Studies: Inconsistent Deficits

- Neuropsychological tests alone will not make an accurate diagnosis of ADHD
- Neuropsychological tests are not a criteria for the diagnosis of ADHD
- **Symptom and executive ratings correlated better with function and quality of life than neuropsychological tests**

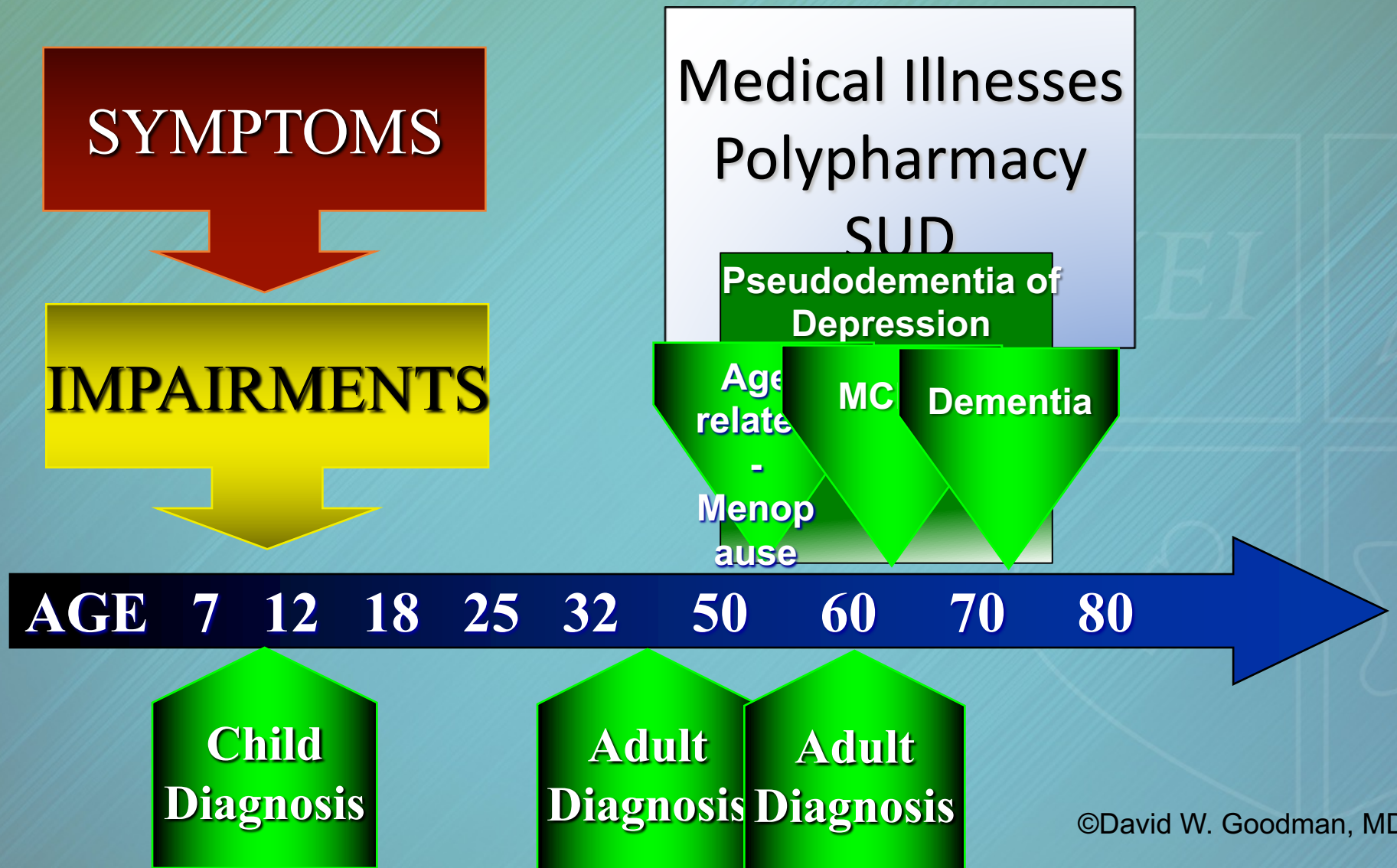
How should ADHD symptoms be identified in older adults?

- A substudy of LASA used ADHD screener in younger adults compared to 1494 adults age 60-94 years, then identified if ADHD was present using a structured interview in 231 of these adults
- Reasonable sensitivity (0.80) and specificity (0.77)
- Test-retest validity was moderate at 0.56
- The low test-retest validity suggests it could be important in developing a screener specifically for older adults

Semeijn EJ, et al. J Am Geriatr Soc. 2013;61(6):882-7; Barkley RA, et al. Guilford Press: 2010

Differential Diagnoses

Onset of Symptoms vs. Time of Diagnosis



Prevalence of MCI by Age

Mild Cognitive Impairment Criteria

-Memory complaint, preferably corroborated by an informant

-Objective memory impairment

-Normal general cognitive function

-Intact activities of daily living

-Not demented

Age (years)	Prevalence
60-64	6.7%
65-69	8.4%
70-74	10.1%
75-79	14.8%
80-84	25.2%

Petersen RC. J Intern Med 2004;256:183.

Differential Diagnosis of ADHD Symptoms in Older Adults

- Psychiatric conditions
- Mild cognitive impairment (MCI)
- Peri- Menopausal cognitive changes
- Dementia
  - Alzheimer's, Fronto-temporal, Lewy Bodies, Vascular
- Parkinson's disease or other parkinson-plus syndromes
- Toxic/metabolic/inflammatory/tumor (paraneoplastic syndrome)
- Infections (ie UTI)
- Other encephalopathy (generic, developmental, perinatal, trauma, or head injury)
- Increasing polypharmacy
- Sleep disturbances/apnea

Goodman DW. Drugs Aging. 2016 Jan;33(1):27-36; Ivanchak N et al. Curr Psychiatry Rep. 2012;14(5):52-560

Older Adult ADHD and Comorbidities

Comorbidity ADHD Adults Aged ≥50 years

- A **Dutch** study, with average sample age 71 years (range 60-94 years) found that participants with ADHD had more depressive and anxiety symptoms that participants without ADHD.
- Compared to older adults without ADHD, older adults with ADHD had significantly lower self-esteem and sense of mastery, and higher levels of neuroticism and social inadequacy
- Self-esteem and sense of mastery partly explained the association between ADHD and depressive symptoms.

Brod M, et al. Qual Life Res. 2012;21(5):795-799; Michielsen M, et al. J Affect Disord. 2012;148(203):220-227; Lensing MB, et al. J Atten Disord. 2015;19(5):405-413; Michielsen M, et al. Am J Geriatr Psychiatry. 2014;22(12):1623-1632

Comorbidity ADHD Adults Aged ≥50 years

- **Norway study**: Adults aged ≥50 years with (mean age: 55.7 years)
  - 46.7% of the participants reported psychiatric comorbidity
  - depression 36.7%, anxiety 26.5%, and bipolar disorder 24.5%
  - The sample was recruited from the national ADHD organization, and not necessarily representative for adults aged ≥50 years with ADHD
- **U.S. study**: 27 patients recruited from psychiatrists in private practice,
  - 63% of the participants reported having other mental health conditions
  - depression 54%, anxiety 42%, and bipolar disorder 8%

Psychopharmacological Treatment of ADHD in Adults Aged 50+

- 76.5% reported ongoing medication for co-existing medical illnesses
  - Antihypertensives, analgesics, antidepressants, anxiolytics, anticonvulsants, antipsychotics

Lensing MB et al. J Att Dis 2015;19(5):380-9.

Treatment Options

Growing Awareness

- A number of recent studies from different countries using national registers and prescription databases have shown that a growing number of patients aged ≥ 50 years are assessed and treated for ADHD worldwide.

Kristiansen CB, et al: Atten Defic Hyperact Disord. 2015;7(2):151-156;
McCarthy S. et al: BMC Pediatr. 2012;12:78

Segment Older Patients for Treatment Approach

- Diagnosed and treated as children but drop out of treatment and now return
- Diagnosed and treated for many years without interruption
- Misdiagnosed and treated for anxiety/depression and missed the ADHD diagnosis
- Newly diagnosed at older age

ADHD Treatment in Older Adults

- Israel study: 11 older adults (mean age 62)
- All patients were treated with methylphenidate (MPH) and followed for at least 2 months (8 patients tried MPH immediate release in daily doses between 20 and 35 mg, 2 patients MHP long acting agents 60-80 mg, and 1patient tried osmotic-release oral system MPH 72-108mg).
- At follow-up, only two patients had stopped using the medication
- 8 patients showed significant improvement on the test of variables of attention (TOVA).
- No adverse events were reported, and only mild physical side effects occurred that are typical of stimulant treatment.

Manor I, et al. Clin Neuropharmacol. 2011;34(4):148-54

Psychopharmacological Treatment of ADHD in Adults Aged 50+

- Survey administered to adults (≥50 years) with ADHD
  - 149 participants
  - Mean age: 55.8 years
  - Mean age at time of ADHD diagnosis: 50.3 years
- ADHD medication use
  - 63.8% reported current ADHD medication use
  - 24.2% reported stopping ADHD medication
  - 23.0% reported no ADHD medication
- 35% of participants reported non-pharmacological treatment for ADHD

Lensing MB et al. J Att Dis 2015;19(5):380-9.

Psychopharmacological Treatment of ADHD in Adults Aged 50+

- Of those currently treated with ADHD medication
  - 82% methylphenidate preparations
    - Mean dose 54.1 mg (range ?-135 mg)
  - 10.5% on amphetamine
    - Mean dose 29.5 mg (range 4-50 mg)
  - 5.3% on nonstimulant medication

- Prescriber of ADHD medication
  - Family doctor: 58.9%
  - Psychiatrist: 35.8%
  - Unknown/insufficient info: 5.3%

Lensing MB et al. J Att Dis 2015;19(5):380-9.

Psychopharmacological Treatment of ADHD in Adults Aged 50+

- Currently medicated individuals reported:
  - Better attention vs non-medicated individuals
  - Better ability to manage daily demands vs individuals who had stopped ADHD medications
- Increase in use of extended-release methylphenidate formulations predicts longer treatment duration in adults with ADHD
- Timing of treatment onset may be important
  - Individuals diagnosed with ADHD later in life do not respond as strongly to ADHD medications

Lensing MB et al. J Att Dis 2015;19(5):380-9.

CBT vs Supportive Therapy in Older Adults with ADHD

- N=88 ADHD adults in clinical trial
  - 26 ADHD adults age 50+
- 12 week double blind CBT (focus on EF) vs Support group
- AISRS by clinician
- Self ratings and/or collateral on measures of attention, EF, and comorbidity

Solanto M et al. Attention Deficit and Hyperactivity Disorders Journal. 2018. Sep;10(3):223-235.

CBT vs Supportive Therapy in Older Adults with ADHD

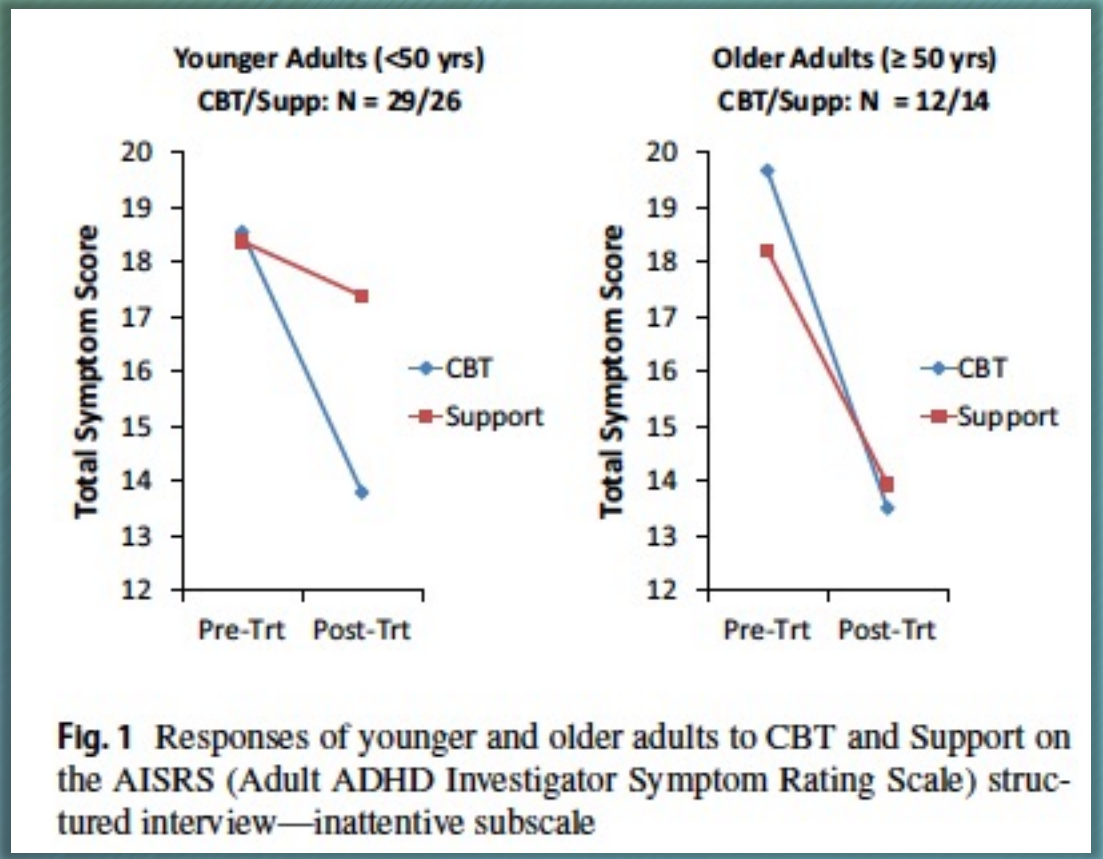


Fig. 1 Responses of younger and older adults to CBT and Support on the AISRS (Adult ADHD Investigator Symptom Rating Scale) structured interview—inattentive subscale

AISRS-IN effect size:
Younger group 0.93
Older group 0.34

"In summary, the older group derived as much benefit from CBT as did the younger group on all the dependent variables. In addition, the older group derived more benefit from the Support than did the younger group on AISRS-IN, AISRS-TMOP, and BRIEF-A."

Solanto M et al. Attention Deficit and Hyperactivity Disorders Journal. 2018. Sep;10(3):223-235.

Medication

Older ADHD Adults Excluded from ADHD Studies

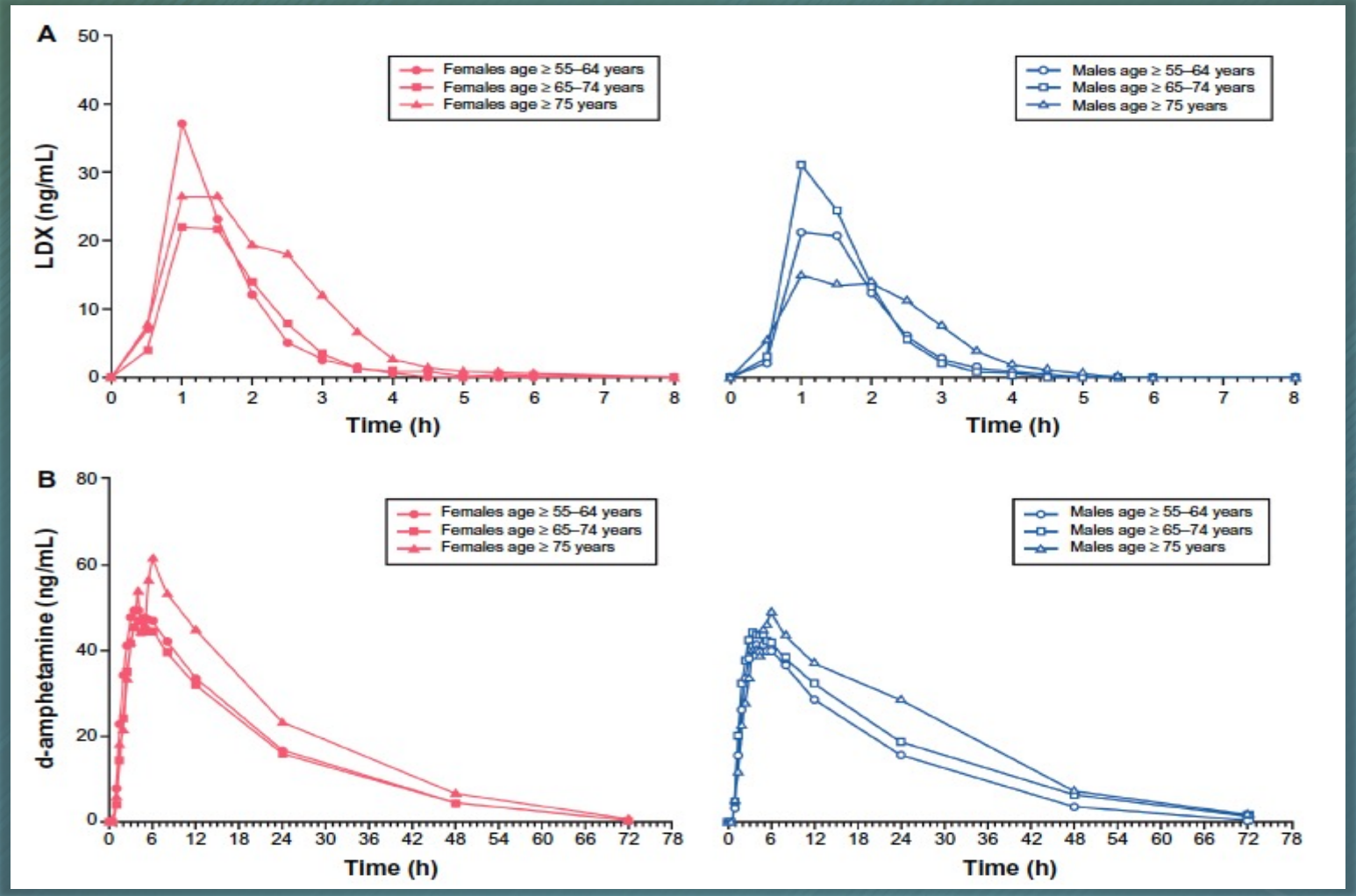
- It is common to exclude individuals over the age of 65 years from clinical trials of ADHD pharmacotherapy
- Reasons:
  - Diagnostic uncertainty (patient recall and absence of informants)
  - Possibility of more adverse events with medication
  - Safety concerns (concurrent medical illnesses)
  - Potential drug interactions due to poly-pharmacy
  - Difficult to find candidates given exclusion criteria

Drug Approval Ages

- The maximum FDA-approved age for use of these medications varies from 55 to 65 years.
  - Lisdexamfetamine max age 55
  - Mixed amphetamine sales XR/OROS MPH max age 65
- Lack of a systematic study leaves it unclear how effective stimulants help, or how well they are tolerated in older people with ADHD.
- Older adults are underrepresented in pharmacokinetic and pharmacodynamics studies.

LDX in Older Adults

(50 mg single po dose; n=47; age 55-64)



LDX: Lisdexamfetamine

Ermer J et al. Neuropsychiatric Disease and Treatment. 2013;9:219-229.

LDX: BP/P in Older Adults
50 mg single po dose

Table 3 Range of mean changes from time-matched baseline[a] in vital signs over 12 hours postdose

Mean change from time-matched baseline	55–64 years		65–74 years		≥ 75 years	
	Placebo n = 15	LDX n = 17	Placebo n = 16	LDX n = 16	Placebo n = 14	LDX n = 14
Systolic blood pressure (mmHg)	–6.7 to 5.0	–3.9 to 18.5	–5.1 to 10.3	–2.1 to 14.5	–12.1 to 8.5	–5.9 to 16.0
Diastolic blood pressure (mmHg)	–2.1 to 3.8	–2.5 to 8.3	–3.0 to 5.9	–0.8 to 9.4	–3.6 to 4.5	–0.6 to 9.5
Pulse (beats per minute)	–3.5 to 3.6	–5.0 to 14.7	–4.7 to 2.3	–4.3 to 9.5	–3.1 to 3.0	–3.0 to 14.7

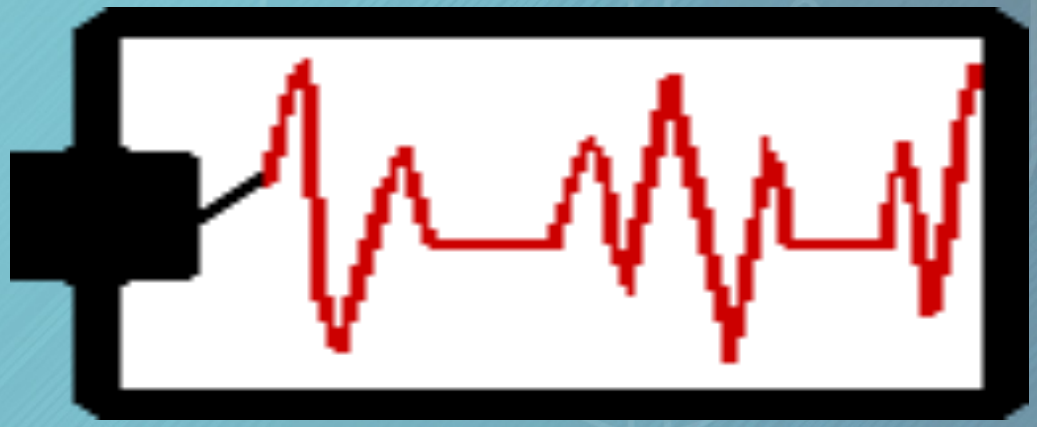
LDX: Lisdexamfetamine

Lisdexamphetamine in Older Adults with ADHD

- In older adults, pharmacokinetic parameters were generally similar to those seen previously in younger adults aged 18–55 years (LDX and d-amphetamine, including Cmax, Tmax, and AUC0–inf)

- d-Amphetamine exposure was modestly higher in participants aged 75 years than in those aged 55–64 years and 65–74 years

Safety Concerns



Medical Illness Considerations

- Hypertension
- Hypo- or Hyperthyroidism
- Diabetes Mellitus (med effect on appetite/food intake)
- Cardiac: Post MI, post-stent placement, arrhythmias, electrical/structural abnormalities
- Substance Use: caffeine, nicotine, alcohol, illicit drugs
- Closed angle glaucoma
- Benign prostatic hypertrophy
- Migraines
- Postural Orthostatic Tachycardia (POTS)

Medical Monitoring While on ADHD Medication

- Monitor conditions that might be exacerbated by increased sympathetic tone, including hypertension, arrhythmia, urologic/sexual function, narrow angle glaucoma, and compromised peripheral circulation (e.g. Raynaud's vasculopathy)

- Common stimulants such as caffeine, pseudoephedrine, or OTC appetite suppressants may compound the sympathetic effects of ADHD agents

Side Effects With Stimulant Medication

- Insomnia
- GI upset
- Decreased appetite
- Weight loss
- Headaches
- Dry mouth
- Constipation
- Hand tremors
- Jittery

- No RCT has assessed AEs in older ADHD adults on psychostimulants
- Side effect ramifications in older adults may be very clinically significant
- Some research has shown side-effects may be more likely in stimulant naïve patients

Goodman DW et al. (2005), CNS Spectr 10(Suppl 20):26-34; Weisler RH et al. (2006), CNS Spectr 11(8):625-639; Adler L et al. (2005), Presented at the 158th Meeting of the American Psychiatric Association, May 21-25

What Did You Learn?

Summary

- Screening for ADHD is an important assessment for cognitive complaints, especially in older adults
- Cognitive complaints in older patients should not be easily discounted as age-related decline
- Medical etiologies of cognitive complaints usually have their onset in adulthood, not childhood, as with ADHD
- Impairments persist in older adults with ADHD
- ADHD treatments can effectively improve cognition and daily function in older adults
- **It's never to late for treatment!**

Posttest Question 1

Which of the following statements is true?

1. ADHD symptoms slowly diminish with age
2. Neuropsychological testing is not important to distinguishing ADHD from MCI/early dementia
3. Older adults with ADHD were likely diagnosed earlier in life
4. Older adults with ADHD are likely to stop stimulant medication

Posttest Question 2

According to a large meta-analysis, the prevalence of ADHD in older adults by research criteria is 2.2% but the prevalence by clinical diagnosis is…

1. 3.2%
2. 1.5%
3. 0.93%
4. 0.23%

Posttest Question 3

Which of the following is true?

1. There are 2 stimulant medications approved for older adult ADHD age >65
2. ADHD is accessed in 52% of memory clinics in the U.S.
3. There is a specific screener for ADHD in older adults
4. Stimulant medications appear to offer similar benefits in older adults as in young adults