Treatment of ADHD and Substance Use Disorders

Margaret M. Chaplin, MD

Presented at ASAM State of the Art Course 2022

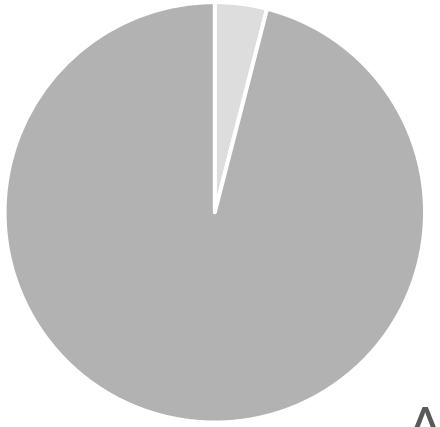
Disclosure Information

Margaret Chaplin, MD, FAPA, FASAM

- No Disclosures

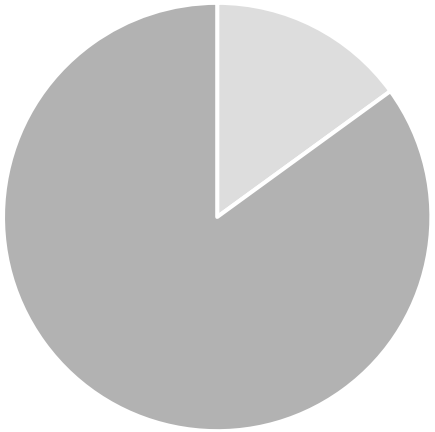
The Scope of the Problem[1-5]

All Adults- 4% ADHD[1]



Adults With SUD_ 21% ADHD[1]

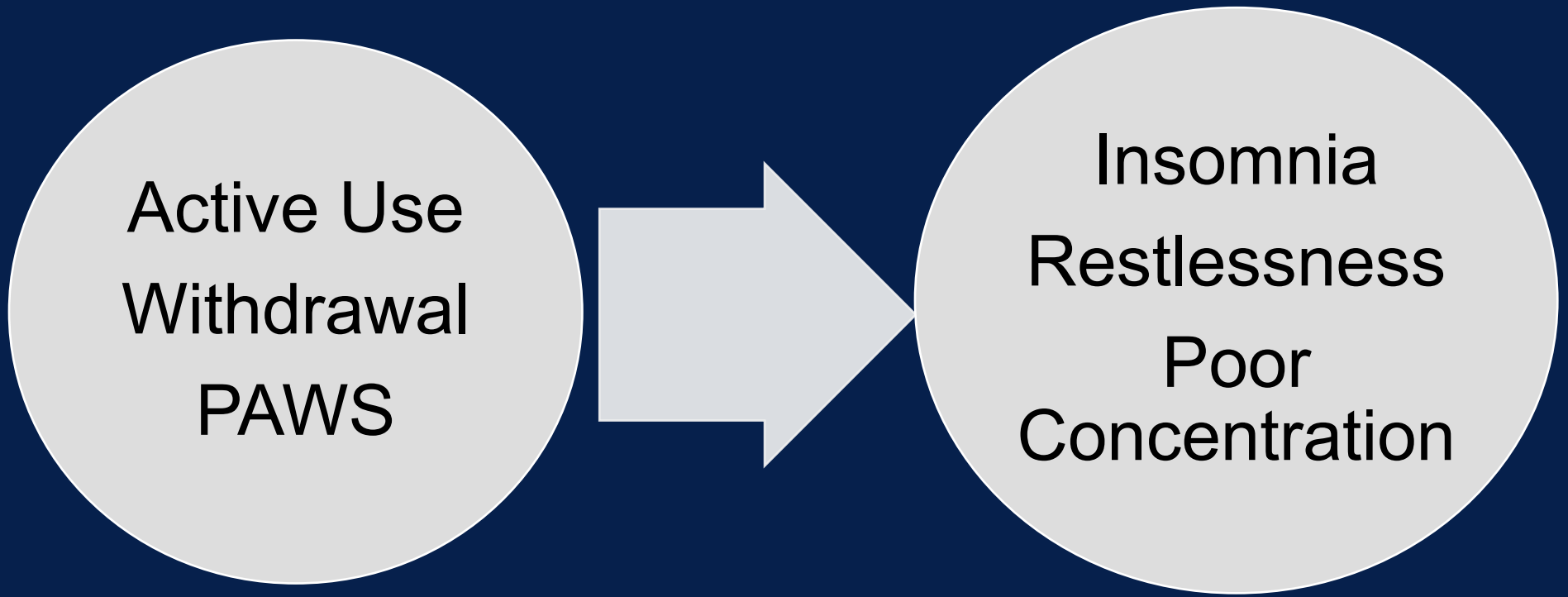
All Adult ADHD -15% SUD[5]



Treatment Seeking Adults With SUD_ 12-14% ADHD[2,3,4]

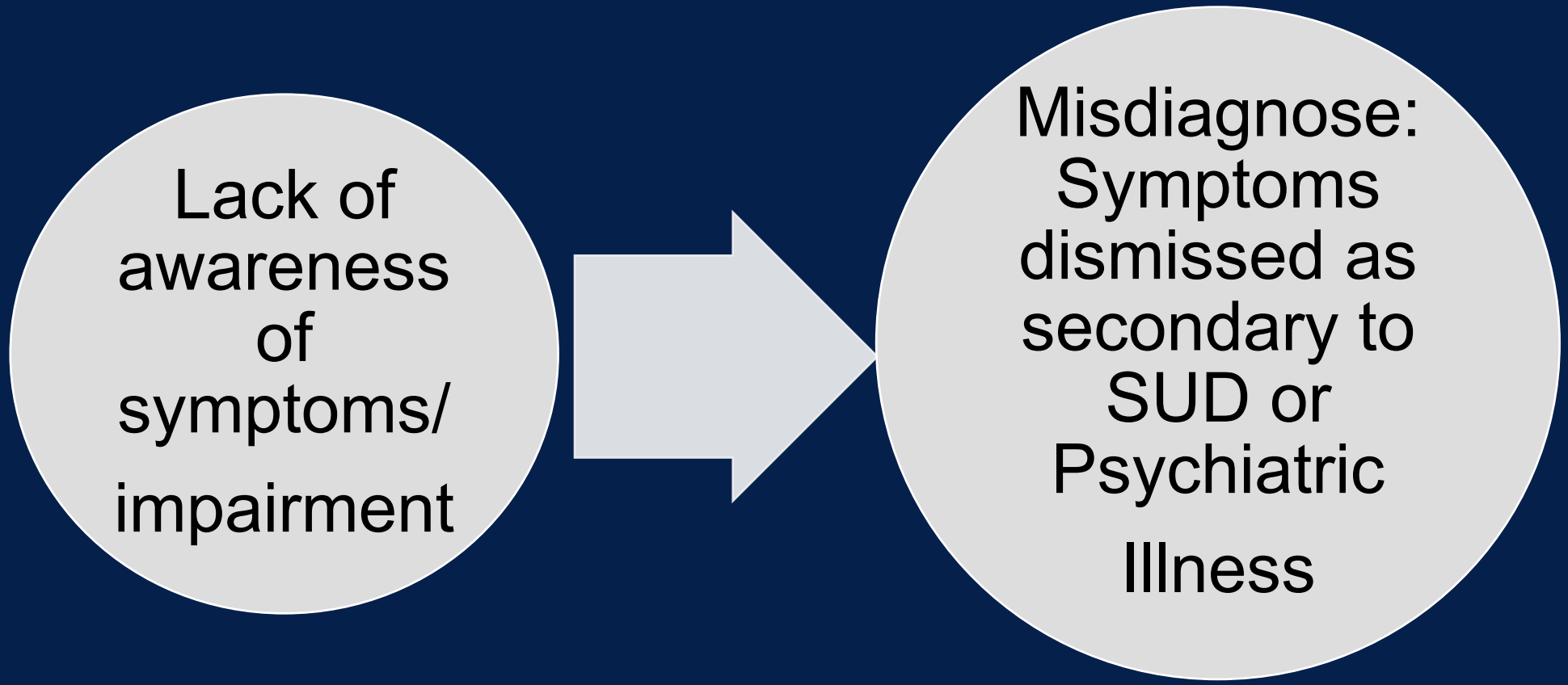
Dual Diagnosis SUD and ADHD

- Diagnosis is challenging due to overlapping symptoms[6]
- Potential to over diagnose;



Dual Diagnosis SUD and ADHD

- Diagnosis is challenging due to overlapping symptoms[6]
- Potential to under diagnose;



Diagnosis of Adult ADHD[7]

- DSM 5 Criteria- persistent pattern of inattention and/or hyperactivity (>6 months) that interferes with function:

5 Symptoms of Inattention

5 Symptoms of Hyperactivity

Symptoms Present before age 12

Impairment in 2 Domains

Reduces Quality of Social or Vocational Life

Not due to any other Mental Disorder

Nine Inattentive Symptoms[7]

- Forgetful
- Misplaces Things
- Makes Careless Errors
- Doesn't Listen
- Easily Distracted
- Doesn't stay on task
- Trouble Completing Tasks
- Trouble Organizing
- Avoids Tasks Requiring Mental Effort

Nine Hyperactive Symptoms[7]

Fidgets

Can't Remain Seated

Runs About

Can't relax

Always "on the go"

Can't tolerate lines

Blurts out answers

Talks Excessively

Interrupts or Intrudes on Others

Making a Diagnosis of Adult ADHD

Rating Scales are Reasonable Starting Point[8]

Rating Scale NOT Sufficient to Make Diagnosis

Making a Diagnosis of Adult ADHD

- The ASRS v1.1[8] : 5 Point Likert Scale
- All 18 DSM based questions- First six questions most dia

Difficulty Organizing

Forgetful
(Difficulty Remembering Appointments)

Difficulty Completing Tasks

Fidgets

Avoids Mental Effort

"On the Go"
Feeling Driven by a Motor

https://add.org/wp-content/uploads/2015/03/adhd-questionnaire-ASRS111.pdf

Making a Diagnosis of Adult ADHD

- ASRS-5[8]: 5 Point Likert Scale
  - Machine Learning Based:
    - 6 Questions only - improved Sensitivity, Specificity, and PPV.

Difficulty Listening

Difficulty Staying Seated

Difficulty Relaxing

Put things off

Depend on Others to Organize Life

Finish Other People's Sentences

- *https://www.hcp.med.harvard.edu/ncs/ftpdir/adhd/ASRS-5_English.pdf*

ASRS-5[8]

This Adult ADHD Self-Report Screening Scale for DSM-5 (ASRS-5) is intended for people aged 18 years or older.

Adult ADHD Self-Report Screening Scale
for DSM-5 (ASRS-5)

from Composite International Diagnostic Interview for DSM-5 (CIDI-5.0)

Date

Check the box that best describes how you have felt and conducted yourself over the past 6 months. Please give the completed questionnaire to your healthcare professional during your next appointment to discuss the results.

	Never	Rarely	Sometimes	Often	Very Often
1. How often do you have difficulty concentrating on what people are saying to you even when they are speaking to you directly?					
2. How often do you leave your seat in meetings or other situations in which you are expected to remain seated?					
3. How often do you have difficulty unwinding and relaxing when you have time to yourself?					
4. When you're in a conversation, how often do you find yourself finishing the sentences of the people you are talking to before they can finish them themselves?					
5. How often do you put things off until the last minute?					
6. How often do you depend on others to keep your life in order and attend to details?					

Diagnostic Interview - Follow-Up to Screen

1. At least 5 symptoms of inattention and/or hyperactivity present for more than 6 months

2. Several Symptoms present before age 12 (elementary school)

Unclear value of Adult self-reports [4,9]

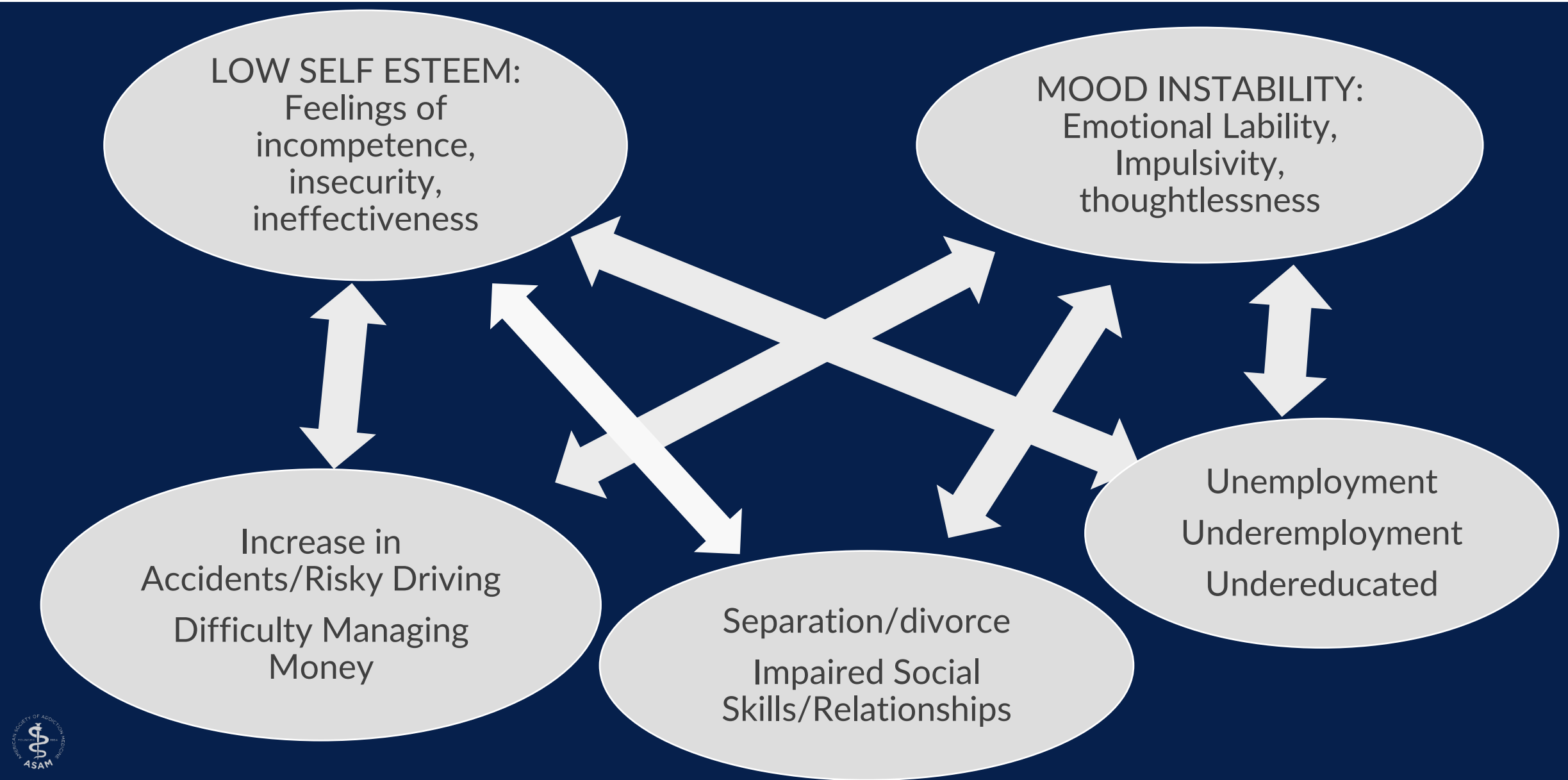
Late Onset Adult ADHD Controversial [7,10]

Diagnostic Interview - Look for IMPACT

3. Impairment in at least 2 settings:
Work, Home Life, Social Life, or School

4. Interferes with Function or Reduced Quality of Social, Academic, or Occupational Function

Diagnostic Interview- Areas of Impairment[4,11,12]



Diagnostic Interview - Excluding Other Causes

Overlapping Symptoms

- Substance Use
- Psychiatric Illness

Family History Can Help

Heritability[3] 80%

- 4-5-fold increase in First Degree Relatives[3]

Diagnostic Interview- Excluding Other Causes

Substance Use
11-13% Co-Occurring[3,4]

Acute Intoxication/Early Withdrawal[4]:
Motor restlessness, Inattention, Impulsivity

Post Acute Withdrawal[12]:
Disturbed Sleep, Mood Lability, Poor Concentration

Intoxication/Early Withdrawal[13]

Vergaga-Moragues screened 166 patients with CUD for ADHD

Cocaine Use Disorder
14.5% ADHD

Executive Dysfunction measured by 9 item scale
Distinguished ADHD from non-ADHD P< .001

Nine Symptoms that Distinguish ADHD from CUD[13]

- Impulsive Decisions
- Difficulty Disengaging
- Easily distracted
- Doesn't follow directions
- Doesn't do things in order
- Drives too fast
- Loses Track of Goals
- Doesn't follow through
- Trouble planning

Early Withdrawal[4]

Huntley (2012) screened 226 patients presenting for detoxification at admission and a week later.

Childhood symptoms were reported in 38%

Self Report Screen Positive at admission= 33%

Self report positive after one week= 20%

SUD and/or ADHD[13,14]

FOCUS ON LONGITUDINAL HX

	Memory	Mood	Restlessness	Sleep	Thought Process	Role Impairment
ADHD: Persistent	Thoughtless Careless Misplacing	Irritable Labile Short Lived	Fidgets	Initial Insomnia	Mind Wandering	Lifelong begins in childhood Doesn't improve
SUD: Largely Resolve with Sobriety	Irresponsible	Irritable Defensive	Tremors Disturbances in Vital Signs	Broken Sleep	Mild disorganization	Progresses with Disease Severity

Diagnostic Interview - Excluding Other Causes

Mood Disorders

22% Co-occurring [3]

- Mania-mood change, sleep disturbance, racing thoughts
- Depression- mood change, sleep disturbance, ruminating thoughts

ADHD and/or Mood Disorder

	Memory	Mood	Restlessness	Sleep	Thought Process	Role Impairment
ADHD Persistent Child Onset	Thoughtless Careless Misplacing	Labile Short Lived	Fidgets	Initial insomnia	Mind Wanderin g	Lifelong, begins in childhood
Mania Episodic Adolescent Onset	Impulsive	Elevated	Goal Directed On a mission	Lack of need for sleep	Tangential May be Psychotic	Good premorbid Recovers between episodes
Depression Episodic Adolescent Onset	Impaired Cognition/ Motivation	Depressed	Slowed Decreased Appetite	Excessive sleep, early morning wakening	Ruminatin g May be Psychotic	Good Premorbid Recovers between

Diagnostic Interview - Excluding Other Causes

Anxiety Disorders
34% Co-Occurring[3]

PTSD- Sleep Disturbance, Irritability, Distracted

GAD, Social Phobia- inattentive, restless

ADHD and/or Anxiety

	Memory	Mood	Restlessness	Sleep	Thought Process	Role Impairment
ADHD Persistent	Thoughtless Careless Misplacing	Labile Short Lived	Fidgets	Initial insomnia	Mind Wanderin g	Lifelong, begins in childhood
GAD Social Phobia	Worries About Forgetting	Distressed	Hand wringing Pacing	Initial Insomnia	Can't Stop Worrying	Improves when distracted by task completion
PTSD	Intrusive Flashbacks	Labile Intense Reactive	Situational	Often Intact Interrupted by nightmares	intact	Secondary to Sx

Diagnostic Interview - Excluding Other Causes

Behavioral Disorders
15% Co-Occurring[3]

- Borderline PD- Mood Lability
- Antisocial PD/Malingering-feigned symptoms

Diagnosis – Secondary Gain[14]

Screens can be Manipulated

Sprinkle Questions through Interview

Obtain Collateral Information

ADHD and/or Behavioral Disorders

	Memory	Mood	Restlessness	Sleep	Thought Process	Role Impairment
ADHD Persistent	Thoughtless Careless Misplacing	Labile Short Lived	Fidgets	Initial insomnia	Mind Wanderin g	Lifelong, begins in childhood
ASPD Malingering 2^0 Gain	Inconsistent History Fabrication	Labile- Charming Angry	Only when asked, observed	Intact	Evasive	Externalizes, not distressed
Borderline PD	Distorted	Labile Intense Reactive	Situational	Often Intact	Distorted Fanciful	Chaotic Manipulative Social>Work

Diagnosis Summary

- There is risk of both over diagnosis and under diagnosis
- Symptom Screen Alone is **NOT** diagnostic
- Clinical Interview:
  - Longstanding pattern of executive dysfunction
  - Symptoms beginning in childhood
  - Persisting through periods of sobriety and in the absence of other mental health issues
- Collateral input whenever possible

Pharmacological Treatments For ADHD/SUD

Carpentier and Levin (2018)[15]
Review of 15 RCT Medication Trials

Evidence for the use of Pharmacology is Sparse and Inconsistent [15]

Two studies favor Robust Doses of Stimulants[16,17]
One Study favors Atomoxetine for AUD[18]
None Measure Function

Pharmacologic Treatments: High Dose Stimulants

- Kostenius (2014) A-ADHD/SUD[16]
  - Placebo v OROS* methylphenidate up to 180mg - 54 men, 24 weeks
  - RESULTS:
    - Decrease in ADHD Sx
    - Decrease in drug + urines
    - Increase in treatment retention

**** OROS=osmotic controlled release oral delivery is a form of extended release.

Pharmacologic Treatments: High Dose Stimulants

- Kostenius (2014) A-ADHD/Amphetamine Use Disorder[16]
  - LIMITATIONS:
    - Low Numbers/Atypical Sample
      - 54 Men recruited while incarcerated (sober to start), followed Outpatient
    - Functional Improvement not Measured

Pharmacologic Treatments: High Dose Stimulants

- Levin (2015) A-ADHD/Cocaine UD[17]
- ER Mixed amphetamine salts 60mg or 80mg v placebo
- 126 Adults, 14 Weeks. All groups got CBT as well.
- RESULTS:
  - Decrease in ADHD Sx
  - Decrease in Cocaine Use (self report + urine)
  - Increase in Cocaine Abstinence
  - Optimal Dose for ADHD was 60mg and for SUD was 80mg

Pharmacologic Treatments: High Dose Stimulants

- Levin (2015) A-ADHD/Cocaine UD[17]
  - LIMITATIONS:
    - Short Time (14 weeks)
    - Functional Improvement not Measured
    - Only looked at Cocaine UD/ADHD

Pharmacologic Treatments: Atomoxetine

- Wilens (2008)[18] ADHD/AUD
  - Atomoxetine 25-100mg (n=32) or Placebo (n=48)
  - 147 patients enrolled/ 80 completed , 12-week trial
  - 88% Caucasian, 85% Male
  - RESULTS:
    - Reduced ADHD Symptoms
    - Reduced Heavy Drinking Days
    - No Change in time to return to heavy drinking

Pharmacologic Treatments: Atomoxetine

- Wilens (2008)[18] ADHD/AUD
  - LIMITATIONS:
    - Short time (12 weeks)
    - small numbers; large drop out
    - Alcohol Use assessed by Self Report
    - All AUD, mostly Caucasian, Mostly Male, sober to start
    - Functional Improvement not Measured

Other Pharmacological Treatments

- No RCT of Lisdexamfetamine.
- No evidence for off-label use of Buproprion, Guanfacine or Clonidine
  - One study of Bupropion - no benefit
  - No RCT for Guanfacine or Clonidine

Medication: Safety

Medications generally well tolerated[3,14,21]

Minimally elevated risk of stroke, MI, sudden cardiac death or ventricular arrhythymia[3]

Risk of Cardiac Events presumed higher if Illicit Stimulants mixed with Prescribed Stimulants[21]

No Evidence that Stimulants can cause/worsen SUD[14]

Stimulant v Non-Stimulant[21]

Drug Class	Side Effects	Abuse Potential	Onset of Action
Stimulants: Methylphenidate Amphetamines Lisdexamfetamine	Restlessness, Insomnia, Anorexia, Increase BP/HR	Moderate to High	Day 1
SNRI: Atomoxetine	Dry Mouth, N/V, Abdominal Pain Headache, Somnolence, Increase BP/HR	None	Week 1 - Week 4

Non-Pharmacological Treatments

- van Emmerick-van Oortmerssen (2019)[19]
  - CBT/integrated (n=48) v CBT/SUD only (n=59)
  - Both groups had 15 weekly sessions
  - At completion, integrated group had decreased ADHD sx
  - Two months after completion persistent improvement, though no longer significant.

Final Thoughts on Treatment

- There is preliminary evidence to support pharmacological treatments[15-18] (Stimulants, ATM) and CBT[19]
  - Psychopharmacology for A-ADHD less effective in the presence of SUD. [2,14]
  - More severe ADHD may have better response to medication[15]
  - ER formulations and High Doses of Stimulants may be most effective[16,17]
- No Head-to-Head studies of Stimulants v Nonstimulant v CBT

Misuse of Prescription Stimulants[22]

Dramatic Rise In Stimulant Prescriptions

55% of Prescriptions for Adults

NSDUH 2015-16:

6.6% of US used prescription stimulants

1.9% Misused

0.2% Use Disorder

Misuse and Use Disorder associated with Substance Use and Suicidal Ideation

Use was intermittent and for cognitive enhancement

Parallels with Opioid Crisis

Rapid Rise in Prescribing[22,23]

Illicit Stimulants obtained from Friends and Doctors[22]

Expansion of Target Population

"Non-addictive" Formulation[21]

Higher Acceptable Doses[14-17]

Increase in Stimulant OD Related Deaths

23% increase in 2021[24]

Mitigating Risk Of Abuse/Misuse

Proper Diagnosis[11,25]

Avoid Immediate Release Stimulants[21,25]

Identify Target Symptoms[11,25]

Monitor for Functional Improvement

Educate[23,25]

Abuse Potential

Consequences of Diversion

Drug Interactions

Safe Storage

Mitigating Risk

See Patient Frequently and Prescribe Small Amounts Per Prescription[25]

Check State Prescription Monitoring Systems[23,25]

Monitor for Compliance and Illicit Drug Use[25]

Drug Testing

Pill Counts

Final Takeaways

- Concurrent Adult ADHD and SUD is common clinical problem[1-5]
- Accurate Diagnosis is Time Consuming but Essential[1-5,11, 14]
- Data on optimal treatment is limited[15]
  - Some Evidence for Medication:
    - High Dose ER Methylphenidate for SUD with abstinence[16]
    - High Dose ER Mixed Salt Amphetamine for ADHD/CUD[17]
    - Atomoxetine for ADHD/AUD[18]
  - CBT directed at both SUD and ADHD may be effective[19]

- Safe Prescribing requires careful diagnosis and ongoing monitoring[24]

References

1. Van Emmerik-van Oortmerssen, K, Van de Glind, G, Van den Brink, W. (2012) Prevalence of attention-deficit hyperactivity disorder in substance use disorder patients: A meta-analysis and meta-regression analysis. Drug Alcohol Depend 122: 11–19
2. Van Emmerik-van Oortmerssen, K., van de Glind, G., Koeter, M.W.J., Allsop, S., Auriacombe, M., Barta, C., Bu, E.T.H., Burren, Y., Carpentier, P.-J., Carruthers, S., Casas, M., Demetrovics, Z., Dom, G., Faraone, S.V., Fatseas, M., Franck, J., Johnson, B., Kapitány-Fövény, M., Kaye, S., Konstenius, M., Levin, F.R., Moggi, F., Møller, M., Ramos-Quiroga, J.A., Schillinger, A., Skutle, A., Verspreet, S., , van den Brink, W. and Schoevers, R.A. (2014), Comorbidity in SUD patients with ADHD. Addiction, 109: 262-272.
3. Kooij, J., Bijlenga, D., Salerno, L., Jaeschke, R., Bitter, I., Balázs, J., Thome, J., Dom, G., Kasper, S., Nunes Filipe, C., Stes, S., Mohr, P., Leppämäki, S., Casas, M., Bobes, J., Mccarthy, J. M., Richarte, V., Kjems Philipsen, A., Pehlivanidis, A., Niemela, A., … Asherson, P. (2019). Updated European Consensus Statement on diagnosis and treatment of adult ADHD. European psychiatry : the journal of the Association of European Psychiatrists, 56, 14–34.
4. Huntley Z., Maltezos S., Williams C., Morinan A., Hammon A., Ball D. et al. Rates of undiagnosed attention deficit hyperactivity disorder in London drug and alcohol detoxification units. BMC Psychiatry 2012; 12: 223
5. Kessler RC, Adler L, Barkley R, et al. The prevalence and correlates of adult ADHD in the United States: results from the National Comorbidity Survey Replication. Am J Psychiatry. 2006;163(4):716-723
6. M.H. Sibley, L.A. Rohde, J.M. Swanson, et al. Late-onset ADHD reconsidered with comprehensive repeated assessments between ages 10 and 25. Am J Psychiatry, 175 (2) (2018), pp. 140-149.
7. American Psychiatric Association: Diagnostic and Statistical Manual of Mental Disorders, 5th edition. Arlington, VA., American Psychiatric Association, 2013.
8. Ustun, B., Adler, L.A., Rudin, C., Faraone, S.V., Spencer, T.J., Berglund, P., Gruber, M.J., Kessler, R.C. (2017). The World Health Organization Adult Attention-Deficit/Hyperactivity Disorder Self-Report Screening Scale for DSM-5. JAMA Psychiatry, 74(5), 520-526.
9. 9. Murphy P, Schachar R: Use of self-ratings in the assessment of symptoms of attention deficit hyperactivity disorder in adults. Am J Psychiatry 2000; 157:1156–1159.
10. 10. Terrie E. Moffitt RH, Asherson P, Belsky D, . Corcoran D, Hammerle M, Harrington H, Hogan S, Meier M, Polanczyk V, Poulton R, Ramrakha S, Sugden K, Williams B, Rohde L, Caspi A. Is Adult ADHD a Childhood-Onset Neurodevelopmental Disorder? Evidence From a Four-Decade Longitudinal Cohort Study American Journal of Psychiatry 2015 172:10, 967-977.

References

11. Gascon A., Gamache, D., St-Laurent, D., & Stipanicic, A. (2022). Do we over-diagnose ADHD in North America? A critical review and clinical recommendations. Journal of Clinical Psychology, 1– 18

12. Melemis SM. Relapse Prevention and the Five Rules of Recovery. Yale J Biol Med. 2015 Sep 3;88(3):325-32

13. Vergara-Moragues E, González-Saiz F, Lozano Rojas O, Bilbao Acedos I, Fernández Calderón F, Betanzos Espinosa P, Verdejo García A, Pérez García M: Diagnosing Adult Attention Deficit/Hyperactivity Disorder in Patients with Cocaine Dependence: Discriminant Validity of Barkley Executive Dysfunction Symptoms. Eur Addict Res 2011;17:279-284.

14. Crunelle CL, van den Brink W, Moggi F, Konstenius M, Franck J, Levin FR, van de Glind G, Demetrovics Z, Coetzee C, Luderer M, Schellekens A; ICASA consensus group, Matthys F. International Consensus Statement on Screening, Diagnosis and Treatment of Substance Use Disorder Patients with Comorbid Attention Deficit/Hyperactivity Disorder. Eur Addict Res. 2018;24(1):43-51.

15. Carpentier P Levin FR, Pharmacological Treatment of ADHD in Addicted Patients: What Does the Literature Tell Us? Harv Rev Psychiatry. 2017 Mar-Apr; 25(2): 50–64

16. Konstenius M, Jayaram-Lindstrom N, Guterstam J, Beck O, Philips B, Franck J. Methylphenidate for attention deficit hyper-activity disorder and drug relapse in criminal offenders with substance dependence: a 24-week randomized placebo-controlled trial. Addiction. 2014;109:440–9

17. Levin FR, Mariani JJ, Specker S, et al. Extended-release mixed amphetamine salts vs placebo for comorbid adult attention-deficit/hyperactivity disorder and cocaine use disorder: a randomized clinical trial. JAMA Psychiatry. 2015;72:593–602

18. Wilens TE, Adler LA, Weiss MD, et al. Atomoxetine treatment of adults with ADHD and comorbid alcohol use disorders. Drug Alcohol Depend. 2008;96:145–54Cunill, R., Castells, X., Tobias, A., & Capellà, D. (2015). Pharmacological treatment of attention deficit hyperactivity disorder with co-morbid drug dependence. Journal of Psychopharmacology (Oxford), 29(1), 15-23.

19. Van Emmerik-van Oortmerssen, Katelijne ; Vedel, Ellen ; Kramer, Floor J ; Blankers, Matthijs ; Dekker, Jack J.M ; van den Brink, Wim ; Schoevers, Robert A Ireland: Elsevier B.V Integrated cognitive behavioral therapy for ADHD in adult substance use disorder patients: Results of a randomized clinical trialDrug and alcohol dependence, 2019, Vol.197, p.28-36.

References

20. F.R. Levin, S.M. Evans, D.J. Brooks, A.S. Kalbag, F. Garawi, E.V. Nunes Treatment of methadone-maintained patients with adult ADHD: double-blind comparison of methylphenidate, bupropion and placebo Drug Alcohol Depend., 81 (2006), pp. 137

21. Bolea-Alamañac, B., Nutt, D. J., Adamou, M., Asherson, P., Bazire, S., Coghill, D., Heal, D., Müller, U., Nash, J., Santosh, P., Sayal, K., Sonuga-Barke, E., Young, S. J., & British Association for Psychopharmacology (2014). Evidence-based guidelines for the pharmacological management of attention deficit hyperactivity disorder: update on recommendations from the British Association for Psychopharmacology. Journal of psychopharmacology (Oxford, England), 28(3), 179–203.

22. Compton WM, Han B, Blanco C, et al: Prevalence and correlates of prescription stimulant use, misuse, use disorders, and motivations for misuse among adults in the United States. Am J Psychiatry 2018; 175: 741–5;

23. Arria AM, DuPont RL. Prescription Stimulant Use and Misuse: Implications for Responsible Prescribing Practices. Am J Psychiatry. 2018 Aug 1; 175(8):707-708

24. U.S. Overdose Deaths In 2021 Increased Half as Much as in 2020 – But Are Still Up 15%. https://www.cdc.gov/nchs/pressroom/nchs_press_releases/2022/202205.htm accessed 8/24/22.

25. Modesto-Lowe, V., Chaplin, M., Sinha, S., & Woodard, K. (2015). Universal precautions to reduce stimulant misuse in treating adult ADHD. Cleveland Clinic journal of medicine, 82(8), 506–512.

26. van de Glind, G et al, Validity of the Adult ADHD Self-Report Scale (ASRS) as a screener for adult ADHD in treatment seeking substance use disorder patients, Drug and Alcohol Dependence,Volume 132, Issue 3, 2013, Pages 587-596